



GUIDELINES

FOR

HIV CARE AND TREATMENT

IN

PAPUA NEW GUINEA

May 2012

FOREWORD

Close to three decades have passed since the HIV epidemic was first recognized in Papua New Guinea. During this period, the country has responded in several ways, including formulating and implementing a series of strategic plans. Many of the initial interventions were geared towards preventing further spread of HIV.

Despite the earlier efforts, the epidemic has grown and established itself into a generalized epidemic in both rural and urban communities. The epidemic has been more severe in certain vulnerable groups including sex workers, women, children, youth and migrant populations. As a result of this, more than 46,000 people are currently estimated to be living with HIV in the country. This calls for a broadening of our approach to the epidemic through the strengthening and expansion of the care and treatment component of our response.

The National scale up plan, which includes prevention, care and treatment, is a culmination of different initiatives including the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). The National program will result in the need to train more healthcare workers as well as the need to develop tools to guide the safe and effective implementation of care and treatment.

The National Guidelines for HIV Care and Treatment in PNG are one of the many tools that have been developed to provide healthcare worker with guidance on various aspects of care and treatment. In this the third edition of the Guidelines, there is much wider coverage of such areas as; Adult and Paediatric HIV management including adherence issues; PPTCT; Treatment of opportunistic infections; PPTCT, and infant feeding options. The guidelines can also serve as reading and reference material for a wide range of healthcare professionals.

HIV is a rapidly changing and growing field and therefore frequent revision of the material contained within these Guidelines will be required. I look forward to receiving feedback from the users of the document to assist in this continual process.

Mr. Pascoe Kase
Secretary for Health

Acknowledgement

These guidelines were prepared by the Papua New Guinea National Department of Health (NDoH). The guidelines are based on best international evidence in practice in resource limited settings and are designed to ensure that HIV Care and Treatment in Papua New Guinea is implemented in a way that will benefit both individuals and the country overall. In particular, the use of antiretroviral medications needs to be regulated to ensure that the public benefit is not eroded by the development of viral resistance.

This document would not have been possible without the contribution and commitment of the many national healthcare workers who are at the forefront of this epidemic. In particular, acknowledgement is given to all HIV Medical Doctors, all Physicians, Paediatricians and Obstetrics and Gynecology, Sexual Health societies and NDOH HIV Care and Treatment team. The National Department of Health also appreciates and acknowledges the valuable support given by various partners including WHO, the Clinton Health Access Initiative (CHAI), UNICEF and the Oil Search Health Foundation.

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ABBREVIATIONS and Acronyms

3TC	Lamivudine
ABC	Abacavir
AFB	Acid fast Bacilli
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral
BBA	Born Before Arrival
BSL	Baseline sugar level
CD4	Cluster Differentiation 4 cells
CMV	Cytomegalovirus
CNS	Central Nervous System
CSF	Cerebral Spinal Fluid
CT	Computerized Tomography
CXR	Chest X-ray
d4T	Stavudine
DBS	Dry Blood Spot
ddI	Didanosine
ECG	Electrocardiogram
EFV	Efavirenz
ESR	Erythrocyte Sedimentation Rate
FBC	Full Blood Count
FTC	Emtricitabine
HAART	Highly active antiretroviral therapy
HBsAg	Hepatitis B Surface Antigen
HIV	Human immunodeficiency virus
HSV	Herpes Simplex Virus
INH	Isoniazid
LFT	Liver Function Test
LP	Lumbar Puncture
LPV	Lopinavir
MAC	Mycobacterium Avium Complex
MTCT	Mother to child transmission of HIV
NAC	National AIDS Council
NDoh	National Department of Health
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside analogue reverse transcriptase inhibitor
NtRTI	Nucleotide analogue reverse transcriptase inhibitor
NVP	Nevirapine
OHL	Oral Hairy Leukoplakia
OI	Opportunistic infection
ORS	Oral Rehydration Therapy
PCP	P neumo C ystis Jirovecii P neumonia (previously known as Pneumocystis Carinii Pneumonia)
PEP	Post Exposure Prophylaxis
PGL	Persistent Generalized Lymphadenopathy
PI	Protease inhibitor

PMTCT	Prevention of Mother To Child Transmission of HIV
PNG	Papua New Guinea
PPE	Pruritic Purpura Eruption
r	Ritonavir boosted
RTV	Ritonavir
ROM	Rupture of Membrane
sAg	Surface antigen
SQV	Saquinavir
TB	Tuberculosis
TDF	Tenofovir
TLC	Total lymphocyte count
UNICEF	United Nations Children's Fund
UPNG	University of Papua New Guinea
VCT	Voluntary counseling and testing
WHO	World Health Organization
ZDV	Zidovudine (also known as AZT)
VZV	Varicella Zoster Virus
VL	Viral Load

CHAPTER ONE

THE USE OF ANTIRETROVIRAL DRUGS IN ADULTS AND ADOLESCENTS

1.1. PURPOSE

The following guidelines have been prepared to guide healthcare workers in their choice of antiretroviral treatment for HIV infected individuals. The guidelines should be read in conjunction with the WHO document

"Antiretroviral therapy for HIV infection in adults and adolescents: Recommendations for a public health approach 2010 revision" "Antiretroviral Therapy for HIV Infection in Adults and Adolescents in Resource-Limited Settings: Toward Universal Access" which is available at the web address <http://www.who.int>. This document also provides guidance on using antiretroviral drugs for treating pregnant women and preventing HIV infections in infants, feeding HIV exposed children as well as treatment of HIV infected children. It is envisaged that public, private, and NGO sectors will use these guidelines to assist them in their planning for the use of ART within the country.

Knowledge about efficacy of various antiretroviral combinations and their adverse effects is rapidly evolving, as is the price structure for individual drugs and drug combinations. These guidelines will therefore be subject to regular review by a panel of experts nominated by the National Department of Health. The guidelines will be disseminated to healthcare workers and other partners involved in the HIV/AIDS National Response.

1.2. WHO CAN PRESCRIBE ART DRUGS

Initiation of antiretroviral therapy (ART) is a complex undertaking, and requires a complete understanding of the rationale, pharmacology and adverse effects of medication. In addition the healthcare worker needs to be knowledgeable about the treatment of coexisting conditions and the treatment of HIV in special patient groups. The prescribers will be required to be:

1. Certified by NDOH and recognized to prescribe ART in PNG
2. Trained in HIV/AIDS care and treatment
3. Have access to sustainable drug supply and to health facilities to monitor therapy
4. Participate in the continuous medical education in the use of ARVs and monitoring of patients on HIV treatment

For this reason the prescribing of antiretroviral medication will be restricted to registered medical practitioners (i.e. Medical Doctors, Nurses, Health Extension Officers (HEOs) trained in IMAI and demonstrated clinical competence through a training program approved by the National Department of Health (NDoH). A list of accredited medical practitioners will

be distributed from time to time by the NDoH to pharmacies dispensing Antiretroviral (ARV) drugs. Delegation by these practitioners to appropriately trained Nurses or HEOs and Community Health Workers (CHWs) who have support and mentoring will occur to enable timely access to treatment throughout PNG. Recognition of courses attended elsewhere will be at the discretion of the Secretary (or delegate) of the NDoH. Applications for recognition must be made in writing to the Secretary.

1.3. WHO CAN INITIATE, MONITOR AND SUPPLY TREATMENT

Uncomplicated patients can have ART initiated by HEOs and Nursing Officers who have completed training and demonstrated clinical competence through a training program approved by the National Department of Health (NDoH). This initiation of ART treatment can ONLY occur after consultation with, and authorization (verbal or written) by an accredited medical practitioner. These healthcare workers may also monitor patients on ART and re-supply ART to patients they are monitoring.

1.4. WHEN TO START TREATMENT

1. The patient has written confirmation of HIV positive status.
2. They are medically eligible (Refer to table 1 below)

A patient is medically eligible for ART if they have one of the following:

- WHO stage IV of HIV disease (clinical AIDS), regardless of the CD4 Count
- Advanced WHO stage III disease (Characterized by HIV wasting, chronic diarrhoea, prolonged fever, atypical pulmonary tuberculosis, recurrent invasive bacterial infections, or recurrent/persistent mucosal candidiasis), regardless of the CD4/TLC;
- WHO stages I, II of HIV disease with CD4 below 350 or Stage II with TLC equal or below 1200/mm³

WHO Clinical Staging	CD4 Available	CD4 not Available
I	Treat if <350	No treatment
II	Treat if <350	Treat if TLC <1200
III	Treat irrespective of CD4 but consider CD4 values for better management and decision making in some situations (eg. TB)	Treat irrespective of TLC
IV	Treat irrespective of CD4 count	Treat irrespective of TLC count

* WHO clinical staging is attached as appendix 1

3. The patient has a treatment supporter
4. Any opportunistic infection has been or is being treated/stabilized
5. The patient has been prepared and is ready for ART therapy
6. There is a reliable drug supply
7. Favorable social criteria should be considered.
8. Baselines tests must be done

1.5. BASELINE TESTS

The absolute minimum laboratory tests before initiating antiretroviral therapy are:

- A confirmed HIV antibody positive test (in persons over 18 months of age)
- Haemoglobin
- CD4 (if available) or total lymphocyte count (TLC)

Additional basic testing, where available, can include:

- Liver functions test, especially serum alanine (ALT) or aspartate aminotransferase (AST)
- Renal Function tests – Creatinine clearance and electrolytes tests
- A full blood count of white blood cell count and differential cell count (to identify anaemia or a decline in neutrophils and the possibility of the occurrence of neutropenia during ART)
- Hepatitis B surface antigen (HBsAg)
- Serum glucose
- Pregnancy tests for women
- Pap Smear (if available)
- Syphilis serology
- Sputum for AFB and/or CXR

As an example some routine tests to be performed during the course of the treatment:

Table 1: Schedule of Routine Laboratory Monitoring of ART

Laboratory test	Three months	Six months	Nine months	Every six months thereafter if stable
CD4 or TLC		✓		✓
Viral Load		✓		✓
Hb for AZT	✓	✓	✓	✓
LFT for NVP	✓	✓	✓	✓
RFT for TDF	✓	✓	✓	✓

- HIV positive patients who are not on ART should have the same baseline testing as described above and then monitored in accordance with the following chart.
- Lab monitoring is not a pre-requisite to the initiation of ART
- CD4 is a useful marker for initiating ART and in the absence of VL it can assist with treatment failure decisions
- VL is not essential as a baseline, but it's used for monitoring treatment failure decisions. A persistent VL of >5000 copies/ml confirms treatment failure
- Symptom directed lab monitoring for safety and toxicity is recommended for those on ART
- If resources permit, use VL in a targeted or routine approaches
- Other testing may be added according to the patients' clinical condition.

Table 2: Schedule of Essential Laboratory Monitoring of HIV Positive Patients NOT on ART

Laboratory test	Six months
Hb	✓
CD4 or TLC (if available)	✓

1.6. WHAT DRUGS TO USE

What to start:

First line therapy

First-line therapy should consist of a non-nucleoside reverse transcriptase inhibitor (NNRTI) + two NRTIs, one of which should be AZT or Tenofovir (TDF). Start one of the following regimens in ART-naïve individuals eligible for treatment:

1. Tenofovir (TDF) + Lamivudine (3TC) + Efavirenz (EFV)
2. Zidovudine (AZT) + Lamivudine (3TC) + Nevirapine (NVP)
3. Zidovudine (AZT) + Lamivudine (3TC) + Efavirenz (EFV)
4. Tenofovir (TDF) + Lamivudine (3TC) + Nevirapine (NVP)

TDF+3TC+EFV is the preferred option for most adults; adolescents and infected pregnant women. Use EFV when there is HIV/TB co-infection or liver toxicity. Use TDF when anaemia is present.

ART for HIV/HBV co-infection

- Start ART in all HIV/HBV co infected individuals who require treatment for their HBV infection, regardless of CD4 cell count or WHO clinical stage.

Use TDF and 3TC + NVP/EFV antiretroviral regimens.

(Note: if providing TDF+3TC+EFV, 3TC can be given at 300mg once daily to align with daily TDF & EFV regimen)

ART for HIV/TB co-infection

- Start ART in all HIV/TB co-infected individuals regardless of CD4 count or WHO clinical stage.
- Start TB treatment first, followed by ART as soon as possible afterwards (and within the first 8 weeks).
- Use AZT + 3TC + EFV *or* TDF + 3TC + EFV

If a NNRTI regimen is used, EFV is the preferred drug, as its potential for aggravating the hepatotoxicity of TB treatment appears smaller than that of NVP.

If a PI based regimen needs to be administered concurrently with Rifampicin LPV 400mg/RTV 400mg twice daily or SQV 400mg/RTV 400mg twice daily can be considered.

Patients need close clinical and laboratory monitoring for hepatotoxicity when boosted PIs are administered concurrently with Rifampicin.

DRUG SUBSTITUTION

1.7. For Drug Toxicity

Substitution of single agents can be made if drug toxicity occurs and can be ascribed to a component of the triple therapy given as first line.

ALL clients on Stavudine should be changed to Tenofovir.

Table 3: Drug toxicity and Substitution

If toxicity...	Due to ...	Then switch to ...
d4T/3TC/NVP	d4T – neurological or → pancreatitis → d4T – lipodystrophy → NVP – hepatotoxicity → NVP – Steven Johnson → Syndrome	AZT or TDF AZT or TDF EFZ (except in early pregnancy)
AZT/3TC/NVP	AZT – Bone Marrow Suppression → NVP – see above	TDF
d4T/3TC/EFV	EFV – Unremitting CNS toxicity → d4T – see above	NVP
TDF/3TC/NVP	TDF - Renal Failure →	AZT

1.8. Treatment Failure

Failure of a drug regimen is usually on the basis of viral resistance, and can only be confirmed by documentation of a rising viral load. In the absence of this measurement, a lack of clinical response (such as persistent diarrhoea, weight loss, appearance of a previous or new OI) after 6 months of treatment in a patient adherent to medication is likely to be due to viral resistance. If the treatment failure is due to non-adherence, consideration

should be given to dis-continuation of therapy until adherence can be improved.

WHO recommends that the entire regimen be changed if treatment failure occurs. The new second line regimen has to involve drugs that retain activity against the patient's virus strain and should ideally include a minimum of three active drugs, one of these drawn from a new class, in order to increase the likelihood of treatment success and minimize the risk of cross-resistance. The Protease Inhibitor (PI) class is thus reserved for second line treatments, preferably supported by two new NRTIs.

Table 4: Clinical and Immunological indications of Treatment Failure

Viral Load Criteria for Treatment Failure
<ul style="list-style-type: none"> ▪ Where available, use viral load (VL) to confirm treatment failure ▪ Where routinely available, use VL every 6 months to detect viral replication ▪ A persistent VL of >5000 copies/ml confirms treatment failure
CD4 Cell Criteria for Treatment Failure
<ul style="list-style-type: none"> ▪ Fall of CD4 cell count to pre-therapy baseline or below without other concomitant infection to explain transient CD4 cell decrease¹; or ▪ >50% fall from on therapy CD4 peak level without other concomitant infection to explain transient CD4 cell decrease¹; or ▪ persistent CD4 levels below 100cells/mm¹
Clinical Failure
<ul style="list-style-type: none"> ▪ New or recurrent WHO stage 3 and 4 condition. The new or recurrent condition must be distinguished from immune reconstitution syndrome^{2 3 4}.
<p>¹. If patient is asymptomatic and treatment failure is being defined by CD4 cell criteria alone, a confirmatory CD4 cell count should be performed. One off CD4 counts are difficult to interpret and longitudinal measurements are more meaningful.</p> <p>². Recurrence of tuberculosis may not represent HIV disease progression as re-infection may occur. Clinical evaluation necessary.</p> <p>³. Immune reconstitution syndrome is characterized by the appearance of signs and symptoms of an opportunistic disease a few weeks to a few months after the start of potent antiretroviral therapy in the setting of advanced immuno-deficiency.</p> <p>⁴. Certain WHO clinical stage 3 conditions (eg. pulmonary TB, severe bacterial infections) may be an indication of treatment failure and thus require consideration of second-line therapy.</p>

Drugs for Second line treatment

- Use a boosted protease inhibitor (PI/r) plus two nucleoside analogues (NRTIs).
- LPV/r (Kaletra) is the preferred boosted PI for second-line ART.
- Simplification of second NRTI options is recommended

If d4T or AZT has been used in first-line use, then use

1. TDF+3TC + LPV/r

If TDF has been used in first-line use

1. AZT+3TC+ LPV/r *or*
2. ABC+3TC+ LPV/r
3. TDF + ABC + LPV/r

The second line for HIV/HBV Co-infection

1. AZT + TDF+3TC +LPV/r

Third-line regimens

1. The Government has not provided recommendations for third line ARV drug regimen given the costs and capacity to monitor patients. However, as the treatment programme evolves NDOH could consider this.
2. Patients failing a second-line regimen with no new ARV options should continue with a tolerated regimen.

1.9. PREVENTION OF OPPORTUNISTIC INFECTIONS

1. Cotrimoxazole Prophylaxis:- Cotrimoxazole 960mg once daily (two single strength tablets or one double strength tablet daily) should be given to all patients meeting the following clinical criteria

- WHO Clinical Stage II, III and IV whose CD4 <350

Stop Cotrimoxazole prophylaxis in patients who have had a sustained clinical response (CD4>350 for >12 months).

2. Isoniazid Prophylaxis: - INH –300mg daily for 6 months, after exclusion of active TB. Vitamin B6 or Pyridoxine 25mg daily should also be co-administered. TB preventive therapy is safe and effective in HIV positive individuals and can reduce the risk of TB by 33-67% for up to 4 years.

1.11. ADHERENCE

For patients on antiretroviral therapy (ART), medication adherence is critically important to treatment success. Patients for whom there is concern about adherence should not be commenced on ART. Near-perfect pill taking is required to achieve viral suppression and to avoid the emergence of viral resistance. When patients skip doses and do not take their ART medications regularly, viral resistance develops and the patient does not improve or condition may even deteriorate while on treatment. Missing doses is a common problem, and all patients need help to take 100 percent of their medicines as prescribed. The risks of non-adherence are so clear and so large that adherence assessment and support are integral parts of HIV care programs worldwide. Missing as little as 3 doses per month can trigger drug resistance. Antiretroviral therapy should not be prescribed in the absence of adherence support, including a treatment supporter. Ongoing counseling about the importance of adherence, the role of a treatment supporter in assisting with adherence, and the measurement of adherence are an essential component of HIV Care and Treatment.

1.12. DATA COLLECTION

It is very important that ART use is monitored within PNG to define how improvements can be made in the management of the HIV/AIDS conditions. It will be a requirement for healthcare workers to maintain a database of patients on treatment and forward specified data to NACS/NDOH when and as required. For more detailed guidelines and procedures on ART (or HIV treatment) data collection, please refer to the Standard Operating Procedures (SOPs) for HIV Routine Data Reporting (NDOH, 2008). The SOPs includes the following components:

- How to fill out ART Monthly Data Collection Sheet (Form SURV2)
- How, where, and when to report Form SURV2
- How to store, manage and secure the SURV2 data and forms
- How to request Form SURV2, ARVs, and other supplies

Training of HCW at clinics will be important to be able to collect, enter quality data in ART site data bases

The staff at clinic should be able to conduct clinic monthly analysis of ART data in their specific clinics to improve the quality of services delivered

They should be able to conduct patients' retention rates analysis in their clinics to inform their quality of their programmes

1.13. DRUGS INTERACTIONS

All antiretroviral medications have the potential to interfere with other medications. Particular drug interactions that more commonly will be encountered in PNG are listed in the following table.

Table 5: Drug Interactions

Drug	ART Agent	Interaction	Suggested Action
Alpha blockers, beta blockers and calcium channel blockers	All PI's and Efavirenz	Hypotension and syncope due to decreased drug clearance, at times potentially life threatening.	Monitor closely and adjust dose if signs of toxicity
Amitriptyline	RTV	Over sedation	Reduce dose
Anti-psychotic drugs	RTV	Increased potential for side effects due to decreased drug clearance.	Monitor closely and adjust dose if indicated, particularly with Haloperidol.
Benzodiazepines especially Midazolam	All PI's	Over sedation and risk of respiratory depression	Avoid the use of these drugs unless clinically indicated ie. Status epilepticus.
Cimetidine	RTV	Increased potential for side effects due to decreased drug clearance.	Monitor closely and adjust dose if indicated.
Ergometrine	All PI's and EFV	Ergotism due to decreased clearance of ergot alkaloids	Use syntocin, and/or Misoprostol as clinically indicated.
Ketonconazole	NVP, SQV, RTV and EFV	Potential for toxicity due to decreased drug clearance.	Ketoconazole should not be used with NVP due to risk of hepatotoxicity. Max. dose of 200mg/day if used with PI's. Fluconazole is recommended with PI's.

Nonsteroidal anti-inflammatory drugs	RTV	Increased potential for side effects due to decreased drug clearance.	Avoid the use of these drugs unless clinically indicated and no alternative available.
Oral Contraceptives (OCP)	EFV, NVP, LPV, and RTV	Failure of OCP due to increased clearance	Alternate or additional form of contraception
Oral hypoglycaemics	All PI's	Risk of hypoglycaemia due to decreased drug clearance	Close monitoring of BSL
Pethidine	RTV	Increased potential for side effects due to decreased drug clearance especially seizures	Avoid the use of this drug unless clinically indicated and no alternative available.
Phenytoin and Carbamazepine	LPV, RTV, EFV and possibly other ART agents	Two-way interaction- LPV, EFV and Phenytoin have increased clearance. RTV may reduce Carbamazepine clearance.	Monitor clinically for toxicity or reduced levels. Monitor serum anticonvulsant drug levels if able.
Prednisone and Dexamethasone	RTV and SQV	Increased potential for side effects due to decreased drug clearance.	Monitor closely and adjust dose if indicated.
Rifampicin	PI	Increased PI levels due to decreased drug clearance	Avoid combining Rifampicin and PI's. EFV preferred drug for co-administration.
Thyroid Replacement Therapy	PI	Increased potential for side effects due to decreased drug clearance.	Monitor closely and adjust dose if indicated.
Warfarin	RTV	Unpredictable levels	Monitor closely

CHAPTER TWO

PREVENTION OF PARENT TO CHILD TRANSMISSION OF HIV (PPTCT)

2.1. Four Prongs for Comprehensive PREVENTION OF PARENT TO CHILD TRANSMISSION

The best way to avoid mother to child transmission of HIV is to prevent women of reproductive age from becoming HIV-infected. However, for those women who are pregnant and are already infected, there is sufficient evidence that there are effective ARV regimes that can significantly reduce transmission of HIV from the mother to her child during pregnancy, childbirth and breastfeeding from approximately 35% to 2-4%. In order to achieve this reduction in mother to child transmission, the PNG Government has decided to treat all pregnant women with ART, regardless of CD4 count or WHO clinical stage.

PPTCT entails more than just ART. A comprehensive approach to the prevention of HIV infection in infants should consist of:

- ❖ Primary prevention of HIV infection among women and men of reproductive age;
- ❖ Prevention of unintended pregnancies among women living with HIV;
- ❖ Prevention of transmission from mothers living with HIV to their infants; and
- ❖ Care, treatment and support for mothers living with HIV, their children and their families.

2.2. When to Start ART for HIV infected pregnant women

Start ART in all pregnant women regardless of CD4 count or WHO clinical stage. They should continue taking ART throughout the breastfeeding period and for the rest of their lives.

2.3. What ARV drugs to use for HIV infected pregnant women who need ART for their own health

HIV-infected pregnant women should start ART as soon as feasible regardless of gestational age and continue throughout pregnancy, delivery, breastfeeding and thereafter.

Start one of the following regimens in ART-naïve pregnant women eligible for treatment:

Preferred regimen:

1. TDF + 3TC + EFV
2. TDF + 3TC + NVP

Alternative regimen

3. AZT + 3TC + NVP
4. AZT + 3TC + EFV

What ARV prophylaxis should be given to infants born of HIV infected mothers

All infants should receive daily NVP or AZT from birth up to six weeks regardless of infant feeding method

Infant Dose:

AZT 15mg twice daily if birth weight greater 2.5kg

AZT 10mg twice daily if birth weight between 2.0-2.5kg

For NVP dosing, see appendix 8 (Pediatric ARV Dosing Schedules)

2.5. GUIDELINES ON HIV & INFANT FEEDING

Background:

Infant feeding practices recommended to mothers known to be HIV infected should support the greatest likelihood of HIV free survival of their infants. In order to achieve this infant feeding recommendations for prevention of HIV transmission through breast feeding needs to be balanced with meeting the nutritional requirements and protection of infants from non- HIV morbidity and mortality. For many reasons including limited availability of appropriate replacement feeds and low access to safe and clean water, non-breast fed infants in Papua New Guinea, have a far high risk of morbidity and mortality compared to breast fed infants.

Birth	Infant feeding counselling (reinforce with each visit) Dispensing 6 weeks of neonatal ARV
2 – 10 weeks	Fortnightly -begin Cotrimoxazole at 6 weeks -DNA PCR at 6 weeks (DBS) -routine immunizations
12 weeks to 1 yr	Monthly (repeat HIV testing 6 weeks after cessation of all breast-feeding)
1 -2 yrs	Every 1-2 months
18 months	Confirmatory HIV Antibody test for all
Child is sick	Any time

Table 6: Infant Feeding

Ensuring mothers receive the care they need

Provide lifelong antiretroviral therapy to HIV infected postpartum mothers to reduce HIV transmission through breastfeeding.

Which breastfeeding practices and for how long

In PNG the government recommends that all mothers known to be HIV-infected should exclusively breastfeed their infants for the first six months, introducing appropriate complementary foods thereafter, and continue breastfeeding as long as the mother wants and is able to do so. This is the same recommendation for HIV negative mothers and those who do not know their HIV status.

Breastfeeding should only stop when a nutritionally adequate and safe diet without breast milk can be provided.

All health facilities should counsel and support mothers known to be HIV infected to breast feed and receive ARV drugs while breastfeeding.

Health facilities should inform all mothers the above recommendation for feeding infants born to HIV positive mothers but should also inform them of other alternative methods mothers may wish to adopt.

A decision to use alternative methods of infant feeding (i.e. other than breastfeeding) should be made on an individual basis and depending on availability of individual and family resources to provide affordable, feasible, acceptable, sustainable and safe infant feeds.

Skilled counseling should be provided to HIV infected mothers to support them to feed their infants and to adhere to ARV prophylaxis or ARV treatment.

Mothers known to be HIV infected who decide to stop breast feeding at any time should stop gradually within one month. Stopping breast feeding abruptly is not advisable.

What to feed infants when mothers stop breastfeeding

When mothers known to be HIV infected decide to stop breastfeeding at anytime, infants should be provided with safe and adequate replacement feeds to enable normal growth and development.

Alternatives to breastfeeding for infants less than six months of age include:

- Commercial infant formula milk so long as home conditions are fulfilled
- Expressed, heat-treated breast milk

For children over six months old:

- Commercial infant formula milk so long as home conditions are fulfilled,
- Animal milk (boiled for infants under 12 months) as part of a diet providing adequate micronutrient intake. Meals, including milk-only feeds, other foods and combination of milk feeds and other foods, should be provided four or five times per day. All children need complementary foods from six months old.

Conditions needed to safely formula feed

Only give commercial infant formula milk as a replacement feed to their infants, when specific conditions are met: (*referred to as AFASS – affordable, feasible, acceptable, sustainable and safe*),

- a. safe water and sanitation are assured at the household level and in the community, and,
- b. the mother, or other caregiver reliably can provide sufficient infant formula milk to support normal growth and development of the infant, and
- c. the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhea and malnutrition, and,
- d. the mother or caregiver can, in the first six months, exclusively give infant formula milk, and,
- e. the family is supportive of this practice, and,
- f. the mother or caregiver can access health care that offers comprehensive child health services.

Heat-treated, expressed breast milk

Consider expressing and heat-treating breast milk as an interim feeding strategy:

- In special circumstances such as when the infant is born with low birth weight or is otherwise ill in the neonatal period and unable to breastfeed or
- When the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis or
- To assist mothers to stop breastfeeding or

When the infant is HIV-infected

Mothers are strongly encouraged to exclusively breastfeed for the first six months of life and continue breastfeeding as per the recommendations for the general population, which is up to two years or beyond.

CHAPTER THREE

THE USE OF ANTIRETROVIRAL DRUGS IN CHILDREN

3.1. BACKGROUND OF ART IN CHILDREN

The underlying principles of ART in children are similar to those of adults. However there are specific physiological, clinical, practical and social issues to consider when treating HIV-infected children with ART.

The following are some of these specific issues.

- a. Data on efficacy of ART agents in adults can be extrapolated to children but issues on pharmacokinetics, formulation and ease of administration require special consideration. Young children metabolize drugs differently from adults and there is a particular need for data on pharmacokinetics in children under 3 years.
- b. There are laboratory limitations to diagnosing HIV infection in children under 18 months old in resource limited settings. Detection of HIV DNA by PCR is the gold standard diagnostic test however it lacks sensitivity in the first weeks of life (as does plasma RNA and P24) and is not usually available in resource poor settings. Test sensitivity is close to 100% at 6 weeks of age.
- c. The natural history of the infection is different from adults. The disease progression in infants is more rapid and aggressive. Children are also more susceptible to neurologic complications and some WHO staging conditions are different. (see Appendix 4)
- d. Predictive values of surrogate markers to start and switch therapy is different from adults.

The CD4 count and percentage are less sensitive in identifying infants at risk for disease progression compared to older children and adults.

Plasma HIV-1 RNA (VL) levels are very high in infected infants (several million copies/ml) and persist at high levels for much longer (years rather than months) than in infected adults following primary infection. In developed countries there is no agreed cut-off for starting ART in children.

- e. CD4 cell counts are higher and more variable in young children than in adults. They decline with age and reach adult values at 5-8 years. CD4 cell percentage is less variable although it also decreases with age. It is therefore preferable to use the CD4 cell percentage instead of the absolute cell count for decision-making on ART for infected children under 5 years.
- f. Younger children have difficulties swallowing tablets and may require different formulations compared to adults.

- g. This may also lead to adherence issues hence adherence counselors working with children should receive training specific for this population.
- h. The absolute lymphocyte count is also higher and more variable in children than in adults. Age related thresholds have been developed to be used where CD4 counts are not available. These are less accurate and are not useful markers for longitudinal follow up.

As a general principle, the ART regimen that the parents or guardians are, or will be taking, should also be taken into consideration when deciding on the most appropriate regimen for the child. In determining the initial choice of ART the availability of a suitable formulation and the simplicity of the dosage schedule are also important and should be taken into consideration.

Establishing a diagnosis of HIV infection in infants and children:

HIV virological testing be used to diagnose HIV infection in infants and children less than 18 months of age

It is strongly recommended that all HIV-exposed infants have HIV virological testing at six weeks of age or at the earliest opportunity thereafter. The country will use HIV PCR testing laboratory method on Dry Blood Spots (DBS) specimens taken from the children.

In infants with an initial positive PCR test result, it is strongly recommended that ART be started without delay and, at the same time, a second specimen be collected to confirm the initial positive PRC test result. Do not delay ART. In infected infants immediate initiation of ART saves lives and commencement of ART should not be delayed while waiting for the results of the confirmatory test.

Testing laboratories should return the test results from PCR testing in infants to the clinic and child/mother/career as soon as possible, but at the very latest within four weeks of specimen collection. Positive test results should be fast-tracked to the mother – baby pair as soon as possible to enable prompt initiation of ART.

All infants with unknown or uncertain HIV exposure being seen in health-care facilities at the first postnatal visit (usually 6 weeks), or other child health visit, have their HIV exposure status ascertained.

It is strongly recommended that infants with signs or symptoms suggestive of HIV infection undergo HIV serological testing and, if positive (reactive), PCR testing should be done.

In breastfeeding infants or children, it is strongly recommended that breastfeeding is not discontinued in order to perform any kind of diagnostic HIV test.

Children aged 18 months or older, with suspected HIV infection or HIV exposure, have HIV serological testing performed according to the standard diagnostic HIV serological testing algorithm used in adults.

In sick infants in whom HIV infection is being considered as an underlying cause of symptoms and signs, and PCR testing is not available, HIV serological testing and use of the clinical algorithm for presumptive clinical diagnosis of HIV infection is strongly recommended.

3.2. CRITERIA TO INITIATE ART IN CHILDREN

Initiating antiretroviral therapy in itself is a complex undertaking. To prescribe ART to the children of PNG whose compliance with routine drug regimens is in general, already a challenge will be a major task. Therefore in order to gain the benefits of being on ART and to minimize the risk of poor adherence and subsequent viral resistance, the use of both clinical and "social" selection criteria are recommended.

Box 1: Summary of WHO recommendations for initiation of ART in infants and children.

1. Initiate ART for all HIV-infected children less than 24 months of age irrespective of CD4 or WHO clinical stage.
2. Initiate ART for all HIV-infected children between 24 and 59 months of age with CD4 count less than 750 cells/mm³ or %CD4 less than 25%, whichever is lower, irrespective of WHO clinical stage.
3. Initiate ART for all HIV-infected children more than 5 years of age with a CD4 count less than 350 cells/mm³ (as in adults), irrespective of WHO clinical stage.
4. Initiate ART for all HIV-infected children with WHO clinical stages 3 and 4, irrespective of CD4 count.
5. Initiate ART for any child less than 18 months of age who has been given a presumptive clinical diagnosis of HIV infection.

BOX 2: Infants under 18 months of age

For infants and children aged under 18 months definitive diagnosis can be made at 6 weeks of age or at the earliest opportunity using HIV DNA PCR.* However if there are symptoms suggestive of HIV infection a presumptive clinical diagnosis of severe HIV infection may be necessary in order to permit decision-making on the need for the initiation of potentially life-saving ART whilst arranging for a definitive diagnosis.

A presumptive diagnosis of HIV disease should be made if :

- a) The infant is confirmed as being HIV antibody positive
And
- b) Diagnosis of any AIDS indicator condition can be made**
Or

The infant is symptomatic with 2 or more of the following:

- oral thrush
- severe pneumonia
- severe sepsis

Other factors that support the diagnosis of severe HIV disease in an HIV-sero positive infant include:

- Advanced disease or recent AIDS-related death of the mother
- CD4% <20***

Confirmation of the diagnosis of HIV infection should be sought, either by DNA PCR as soon as possible or HIV antibody at 18 months of age

*DNA PCR methods using dried blood spots (DBS) are being implemented through a separate training program in Papua New Guinea, but may not be available at all sites.

**AIDS indicator conditions include some but not all HIV paediatric clinical stage IV conditions, such as PCP, cryptococcal meningitis, HIV wasting, Kaposi sarcoma, extra pulmonary TB

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

ARV treatment in Children

All Children Less than 3 years of Age should be given the following regimen:

1. Zidovudine (AZT) + Lamivudine (3TC) + Nevirapine (NVP)
Preferred regimen all ARV Naïve children with no prior Exposure to NVP)
2. Lopinavir/ Ritonovir (LPV/r) + Lamivudine (3TC) + Zidovudine (AZT)
Preferred Regimen for children exposed to NVP or EFV for example through PPTCT
3. Stavudine (D4T)/Lamivudine (3TC)/ Nevirapine (NVP)
(for children < 3yrs of age with TB)

Those children with TB and are less than 3 years can continue with NVP.

ZDV/3TC plus ABC may be used if concomitant anti-tuberculosis therapy is being received but caution should be exercised as the regimen has shown lower virological potency in adult studies and therefore its use should be restricted to special circumstances and in consultation with experts only.

Children aged 3 - 12 years of age should be started on AZT + 3TC + EFV if exposed to or with TB

All children above the age of 12 years should be given the following regimes as first line:

What to start

First-line therapy should consist of a non-nucleoside reverse transcriptase inhibitor (NNRTI) + two NRTIs, one of which should be AZT or Tenofovir (TDF). Start one of the following regimens in ART-naïve individuals eligible for treatment:

1. AZT + 3TC + NVP
2. TDF + 3TC + NVP
3. TDF + 3TC + EFV (preferred if adolescent has Hepatitis B co-infection)
4. AZT + 3TC + EFV

Table 7: Immunological Criteria for Initiation of ART in children

Age	HIV status (determined by appropriate method)	TLC	CD4 count	CD4%
Infants <24 months	Positive	Treat all	Treat all	Treat all
24 - 59 months	Positive	<3000 cells/mm ³	<750 cells/mm ³	<25%
5 years or older months	Positive	<2500/mm ³	<350 cells/mm ³	N/A

Table 8: Recommendation for Initiating ART in HIV infected infants and children according to WHO Clinical Staging and immunological markers:

Age	Clinical staging	Immunological
<24 months	TREAT ALL	
>24 months	Stage 4	Treat All
	Stage 3	Treat All
	Stage 2	Treat if CD4 below adjusted threshold
	Stage 1	Don't treat if CD not available but refer to lab for CD4 testing

REMEMBER

- ART is recommended in all HIV infected infants under 24 months of age irrespective of clinical or immunological stage.
- Associated clinical conditions (OIs) need to be treated before ART initiation.

3.3. Social Criteria for Initiation of ART in children

- Children considered for treatment should live within 2 hours walking distance from the ART distributing health facility.
- In the situation in which the child's parents were detected in the antenatal period, they should have had adequate (ideally >3 visits) counseling in the antenatal period followed by more than three sessions of follow-up counseling after birth. Information given should include details of ART.

- iii. Children born to parents detected to be HIV positive in the antenatal period must have had regular monthly follow-up after birth.
- iv. Parents (not on ART) of children whose diagnosis is made during an illness should also have a minimum of three counseling sessions before a decision of ART is made.
- v. Parents are required to nominate a treatment support person who should also attend their counseling sessions. This is to ensure continuation of treatment in the event that the parents become ill.
- vi. The family should be referred to a community-based organization within the area in which they live. The organization must be credible and acceptable to the family and be able to provide continued support outside of the hospital.

Social Criteria is a guide to consider for better treatment outcome. Each case should be assessed on individual bases. It should not be used to stop initiation of treatment

3.4. BASELINE TESTS IN CHILDREN

- Full blood count (**HB, TLC, WBC and Differential**)
- CD4 if available
- Electrolytes, Urea, Creatinine, Hepatic transaminases and Blood Glucose
- Sputum for AFB and/or CXR

In general children metabolize NNRTI and PI drugs faster than adults and require weight for kilogram higher doses than adults to achieve appropriate drug levels. ABC causes a potentially fatal hypersensitivity reaction in 5% of patients. This usually occurs in the first six weeks of treatment. Treatment should not be restarted if hypersensitivity has occurred.

NVP can be used for children of all ages while EFV should only be used in children over 3 years because of the lack of pharmacokinetic data for children under 3 years. NVP should be given as once per day for the first 14 days to reduce toxicity. Children using FDC should take the triple FDC (containing NVP, d4T and 3TC) in the morning and the dual FDC (containing d4T and 3TC ONLY) in the evening for the first 14 days.

ZDV is associated with anemia due to bone marrow toxicity in 5-10% of patients. If hemoglobin prior to initiation is less than 8g/dl (without a correctable cause) combination with d4T should be used.

TDF is not recommended for children under 12 due to concerns about bone mineralization and renal toxicity and a lack of dosing information or appropriate formulations for children.

Children who have had previous exposure to ART through PPTCT and/or breastfeeding should be considered eligible for the standard first line regimen using the same dose and criteria until other preferred regimens are more widely available.

3.5. SWITCHING FOR SIDE EFFECTS AND TOXICITIES

Substitution of single agents can be made if drug toxicity occurs and can be ascribed to a component of the triple therapy given as first line. Children switching a drug for toxicity purposes should be assessed for evidence of treatment failure at the same time, which would require a more comprehensive change in regimen.

Table 9: Drug substitution for toxicity

If toxicity...	Due to ...	Then switch to ...
d4T/3TC/NVP	d4T – neurological or pancreatitis → d4T – lipodystrophy or lactic acidosis → NVP – hepatotoxicity → NVP – Steven Johnson Syndrome →	ZDV or Tenofovir (not recommended for children <3years) ABC, ZDV EFZ (except in children <3yrs) alternatively ABC or PI
ZDV/3TC/NVP	ZDV – Bone Marrow Suppression → NVP – see above	d4T or ABC
d4T/3TC/EFV	EFV – CNS toxicity → d4T – see above	NVP.
NVP or d4T/3TC/ABC	Hypersensitivity to ABC	NVP or EFV

3.6. SWITCHING FOR TREATMENT FAILURE

WHO recommends that the entire regimen be changed if treatment failure occurs. The new second line regimen has to involve drugs that retain activity against the patient's virus strain and should ideally include a minimum of three active drugs, one of them drawn from a new class, in order to increase the likelihood of treatment success and minimize the risk of cross-resistance.

The Protease Inhibitor (PI) class is thus reserved for second line treatments, preferably supported by two new NRTIs. Definitive diagnosis of failure of a drug regimen is the same as in adults.

Clinical failure: A lack of growth response to treatment or a decline in growth among those who show initial response to therapy (in the absence of another identifiable cause such as malnutrition or tuberculosis); a loss of neuro-developmental milestones or the development of encephalopathy and the recurrence of infections, such as oral candidiasis that is refractory to treatment.

Immunological Failure: Continued decline of the CD4 cell count/CD4 % despite assured drug adherence. The definition of immunologic failure can follow 3 types: 1) by a drop in CD4 to values below their age-related CD4 threshold for initiation of treatment after an initial recovery, 2) a return to pre-treatment baseline levels following initial recovery, and 3) a 50% decline from peak values after initial recovery.

These values must be confirmed on repeated measurement. Decisions regarding change in regimen should not be made based on a single laboratory value. Correlation with clinical symptoms is advised.

Virological failure: Develops as a consequence of viral resistance and can only be confirmed by documentation of a rising viral load. In the absence of this measurement the important clinical signs of antiretroviral drug failure in an adherent patient include a lack of clinical response (such as persistent diarrhea, weight loss, appearance or a previous or new OI).

If treatment failure is due to non-adherence, considerations should be given to discontinuation of therapy.

Table 10: Drug substitution for Treatment Failure

First-line regimen	Second-line regimen
AZT or d4T + 3TC + NVP or EFV	ABC +3TC + LPV/r
AZT or d4T/3TC/ABC	ddl + EFV + LPV/r or ddl +NVP + LPV/r

3.7. MONITORING AND WHEN TO CHANGE

The important clinical signs of response to therapy include improvement in growth for those failing to thrive, improvement in neurological symptoms, development in those with delayed developmental milestones and decrease in the frequency of opportunistic infections.

Clinical monitoring should include weight and height growth, developmental milestones and neurological symptoms. Children with evidence of developmental delay should be referred to a paediatrician for more detailed evaluation. In the absence of CD4 cell assays charted height and weight growth may be the most important indicator of response to therapy. Monitoring height and weight for height can also provide additional information.

NB: It is recommended that all children on ART have their WEIGHT and (if possible) HEIGHT measured on each visit to the clinic.

3.8. PREVENTION OF OPPORTUNISTIC INFECTIONS

Cotrimoxazole Prophylaxis

Cotrimoxazole prophylaxis should be given to all babies with the following conditions;

- All HIV exposed infants from 6 weeks to 18 months of age (until confirmed negative) to prevent PCP and other bacterial infections when born to an HIV infected mother (irrespective of whether the woman received ART prophylaxis during pregnancy).
- All HIV positive infants from 6 weeks to 5 years regardless of clinical stage or CD4 percentage. Reassess after 5 years of age.
- A CD4 cell percentage of <15% in children older than 5 years.
- Symptomatic HIV disease or Clinical stage II, III or IV.

Table 11: Dosage of cotrimoxazole in children

	Age	Dosage
1	Less than 6 months	100mg SMX/20 mg TMP (2.5 mls of syrup)
2	6 months to 5 years	200 mg SMX/40 mg TMP (5 mls of syrup or half single strength adult tablet)
3	6 – 14 years	400mg SMX/80mg TMP (10 mls of syrup of one single strength adult tablet)
4	>14 years	800mg SMX/160mg TMP (2 adult single strength tablets)

INH prophylaxis (5-10mg/kg orally once daily for 6 months) should be given to children whose mothers have TB, together with multivitamins.

It is important that all children whether HIV infected or not should receive immunizations according to the normal schedule

**Table 12: Simplified, weight- based dosing for Isoniazid:
10 mg/Kg/day**

Weight Range (Kg)	Number of 100mg tablets of INH to be administered per dose	Dose given (mg)
< 5	½ tablet	50
5.1 -9. 9	1 tablet	100
10 – 13.9	1 1/2	150
14 – 19.9	2 tablets	200
20 – 24.9	2 ½ tablets	250
> 25	3 tablets or one adult tablet	300

3.9. CHILDREN WITH TUBERCULOSIS AND HIV COINFECTION

It is recommended that any child with active TB disease should begin TB treatment immediately, and start ART as soon as tolerated after 2 weeks of starting TB therapy, irrespective of the CD4 count and clinical stage.

The preferred first-line ARV regimen for children more than 3 years of age with tuberculosis (TB), the preferred regimen is EFV + 2 NRTIs.

The preferred first-line ARV regimen for infants and children less than 3 years of age with TB, the preferred regimens are NVP + 2 NRTIs or a triple nucleoside regimen.

The preferred first-line ARV regimen for infants and children less than 2 years of age who have been exposed to NVP and are taking a rifampicin-containing regimen for TB is a triple NRTI regimen.

HIV-infected infants and children who develop TB while receiving ART treatment should be started immediately upon the diagnosis of TB and ART should continue.

3.10. OTHER TYPES OF EXPOSURE TO HIV IN CHILDREN

In cases of significant or potential exposure of a child to HIV either through percutaneous injury or mucosal (sexual) exposure, consideration may be given to the use of antiretroviral drugs for the prevention of infection. Whether to give prophylaxis and which drugs to use depends on the nature and risk of the exposure.

In any case, even following significant non-occupational exposures the risk of transmission with no intervention may be estimated at approximately 0.5 -1%.

This risk needs to be balanced against the potential risk of toxicity from the medications and the associated inconvenience and side effects. The benefits of non-occupational post exposure prophylaxis (nPEP) diminish with time.

Children suffering sexual and percutaneous exposures to a person of unknown HIV status that occur less than 72 hours prior to evaluation may be offered a 2 drug prophylaxis combination of either AZT/3TC or d4T/3TC (for doses see appendix 2) beginning as soon as possible and continuing for 28 days.

Children exposed to a person known or likely to have HIV infection may be offered an expanded regimen that includes the above drugs with the addition of either Efavirenz or a protease inhibitor if available. Because of reported severe reactions to Nevirapine when used for this indication, it is not recommended to use this drug for prophylaxis.

Children evaluated more than 72 hours after the exposure occurred are generally not offered prophylaxis but still require care and follow-up. If possible the source case should be tested and if HIV negative, nPEP may be stopped.

Baseline evaluations following exposure should include a rapid HIV antibody test. This helps to avoid treating patients already infected with HIV using sub-optimal regimens. Since individuals with HIV are often co-infected with other pathogens, such as syphilis, gonorrhea and hepatitis B, baseline evaluation and treatment should include these pathogens. A pregnancy test, as well as prevention of unintended pregnancy should be offered to older children. Prior to giving a female of reproductive potential Efavirenz a pregnancy test should be performed since Efavirenz is associated with birth defects.

Other baseline laboratory tests should include a full blood count, liver enzymes, and a Creatinine. After 2 weeks or if the child experiences symptoms a full blood count and liver enzymes may be repeated to monitor for toxicity.

Finally, HIV testing should be repeated at 1 month, 3 months, and 6 months following the exposure, with additional STI and hepatitis virus testing as clinically indicated. Negative results at 6 months effectively exclude infection and routine follow-up may continue. Children who are victims of sexual assault must have appropriate evaluation and referral for psychological support.

Table 13: Antibiotic Drug Regimen for Sexual Assault

Weight	Azithromycin	Amoxicillin	Augmentin	Probenecid
<10 kg	250 mg (1/2 tab)	1 G (4x250mg)	½ tab	½ tab
>10 kg	500 mg (1 tab)	1 ½ G (6x250)	1 tab	1 tab

CHAPTER FOUR

PROTECTIVE MEASURES AGAINST HIV TRANSMISSION IN HEALTH CARE SETTINGS AND POST EXPOSURE PROPHYLAXIS

4.1. INTRODUCTION

HIV and other blood borne diseases such as Hepatitis B may be transmitted in health care settings from a patient to a health care worker, patient to patient or from health care worker to patient. HIV is likely to be present in body fluids from infected person. The occupational risk of becoming HIV infected from patients in health care settings although minimal is mostly associated with needle stick injuries from a patient infected with HIV. Patient to patient transmission usually results from contaminated equipment, which has been incorrectly or inadequately disinfected. Infection control practices should therefore be in accordance with the PNG Infection Prevention Policy Guidelines for Health Facilities¹.

Most patient care settings should not pose any significant risk of HIV transmission. At the same time, minimal infection control measures such as washing hands with soap and water can prevent transmission during care. Nevertheless, all healthcare workers must adopt appropriate infection risk assessment and apply accident prevention procedures. The context and environment in which health care is provided must offer safety to the health care provider.

Prevention of the transmission of HIV through applying Standard Precautions (previously known as Universal Precautions) is very important. Standard Precautions are simple standards of infection control practices to be used in the care of all patients, at all times, to reduce the risk of transmission of infections.² These include:

Hands should be washed with soap and water;

- Before and after contact with each patient
- Before and after each procedure
- Before wearing and after removal of gloves
- When hands are visibly soiled
- Before preparing, handling, serving or eating food and before feeding a patient
- Before leaving the area of work

Adequate supply of disposable towels (paper towels) is encouraged in order to avoid reusable towels. (If disposable towels are not available, reusable towels should only be used once then washed and dried in the sun.)

¹ NDoH (2008) *Infection Prevention Policy Guidelines for Health Facilities*, 2nd Ed. Port Moresby.

² WHO (2004) *Practical Guidelines for Infection Control in Health Care Facilities*, Geneva

4.2. USE OF PROTECTIVE BARRIERS

Gloves should be worn in all procedures involving contact with blood or other body fluids. Gloves must be discarded after each patient (Hazardous waste management Guidelines). Gloves are not required for routine care activities in which contact is limited to a patient's intact skin.

Clean non-sterile gloves will be worn:

- For invasive examination and non-surgical procedures;
- Contact with blood, body fluids, secretions, excretions, mucous membranes, draining wounds, or non-intact skin; and
- For handling items visibly soiled with blood, body fluids or, secretions.

Protective clothing such as waterproof gowns, aprons, eye protection and or masks should be worn where there is likelihood of exposure to large amounts of blood or body fluids such as in theatre, labour room or in the laboratory.

4.3. CAREFUL HANDLING AND DISPOSAL OF SHARP INSTRUMENTS

- All sharps should be handled extremely carefully to avoid needle stick or other sharp injuries.
- Needles should not be recapped, bent, broken or removed from syringes. If they must be removed from syringes, then use forceps.
- Remove vacutainers with forceps.
- Holders must be used for all blades.

All needles and other sharp instruments should be deposited in puncture resistant sharps containers that must be placed near the working place. The containers (safety boxes) should be clearly labelled, easily accessible and incinerated when three quarters full.

4.4. SAFE DISPOSAL OF WASTE CONTAMINATED WITH BODY FLUIDS

Soiled waste that is contaminated with blood, body fluids, laboratory specimen or other tissues, should be placed in leak proof containers with special labels and incinerated, or buried in a 7 feet deep pit at least 30 feet away from any water source or in a pit latrine. Liquid waste such as blood or body fluids should be poured down a drain connected to a septic tank or an adequately treated sewer or pit latrine

4.5. DISINFECTION OF CONTAMINATED EQUIPMENT

All material including linen used repeatedly must be properly disinfected and or sterilized. Disinfections should be by immersing in 1.0% hypochlorite solutions, using bleach powered or liquid bleach as described in the PNG Infection Prevention Policy Guidelines. Thorough cleaning with soap and hot water removes a high proportion of micro-organisms. All equipment should

be dismantled before cleaning. Gloves must be worn during cleaning of equipment and if splashing with body fluids is likely, additional protective clothing such as water proof aprons, gowns, boots, protective eye wear or masks should be worn. The method of decontamination can be decided based on the following table.

Table 14: Criteria for selecting decontamination method

Level of risk	Items	Decontamination method
High risk	Instruments which penetrate the skin/body	Single use of disposables and sterilization of re-usable equipment
Moderate risk	Instruments which come in contact with non-intact skin or mucous membrane	Sterilization, boiling or chemical disinfection
Low risk	Equipment which comes in contact with intact skin	Thorough washing with soap and water

4.6. PROPER HANDLING OF SOILED LINEN

Soiled linen should be handled with care, they should be collected in bags and not rinsed or sorted out at the patient care area. If possible linen with large amounts of blood should be transported in leak proof containers, and if not available they should be folded with the soiled parts inside, and handled carefully with gloves. Soiled linen should be soaked in 0.5% bleach solutions as per PNG Infection Prevention Policy Guidelines for not less than thirty (30) minutes, then washed separately in hot soapy water and then air dried in direct sun light.

4.7. STERILIZATION AND DISINFECTION

The Human Immunodeficiency Virus does not survive well outside the human body. Nevertheless, it is mandatory that healthcare workers and other care providers caring for HIV infected persons take precautions in order to prevent accidental spread of the virus.

All forms of sterilization will destroy HIV. Recommended methods of sterilization include steam under pressure e.g. autoclave or pressure cooker, or dry heat such as oven. Disinfection will usually inactivate HIV. Recommended disinfectants are Bleach (corresponding to a 1.0% sodium hypochlorite solution) and 1% Lysol. Commonly methods used are boiling and chemical disinfection with hypochlorite solution. If there is a need for boiling equipment, then the equipment must be cleaned and then boiled for at least 20 minutes at sea level and longer at higher altitudes.

4.8. SPILLAGE MANAGEMENT

Detergents and hot water are adequate for routine cleaning of floors, beds and toilets. In case of spillage of blood or body fluids, the area should be cleaned with chlorine based disinfectant which is left for 20 minutes and followed by thorough cleaning with soap and hot water. Alternatively, pour hypochlorite solution 0.5% on the site and leave it for 20 minutes. Then clean with a mop or disposable rag. Then pour hypochlorite solution again and clean. All healthcare workers and other care givers must be made conversant with Standard Precautions

4.9. POST EXPOSURE PROPHYLAXIS (PEP)

The most common mode of exposure to occupationally acquired HIV is in health care and first aid settings where health care providers are at increased risk of HIV infection through exposure to infectious body fluids through accidents or when safety precautions are not followed. However the other most common method of exposure is through sexual assault.

Occupational exposure

Exposure prevention remains the primary strategy for reducing occupational HIV transmission. In the event that an occupational exposure occurs, the following should be done.

Treatment of an Exposure Site

Wounds and skin sites that have been in contact with blood or body fluids should be washed with soap and water; mucous membranes should be flushed with tap water. Little evidence exists that using antiseptics for wound care or expressing fluid by squeezing the wound further reduces the risk of blood borne pathogen transmission; however, the use of antiseptics is not contraindicated. The application of disinfectant agents (e.g. bleach) or the injection of antiseptics or disinfectants into the wound is not recommended.

Exposure Report

If an occupational exposure occurs, the circumstances and post exposure management should be recorded in the exposed person's confidential form for easy follow up and care. The exposure should also be documented in accordance with any institutional requirements and the appropriate authorities notified.

Evaluation of the Exposed Health Care Worker (EHCW)

Healthcare workers exposed to HIV should ideally be evaluated as soon as possible after their exposure in order to allow early initiation of PEP. At the latest, this must occur within 24-72 hours of the exposure. The exposed healthcare worker should be counseled and tested for HIV before PEP is given (i.e., to establish infection status at the time of exposure). In case of refusal to test, PEP should not be started.

For purposes of considering HIV PEP, the evaluation also should include the following information that might influence drug selection:

- Medications that the exposed person might be taking
- Any current or underlying medical conditions or circumstances (i.e., pregnancy, breast feeding, or renal or hepatic disease).

Hepatitis B vaccination should also be considered.

4.10. PEP DRUG REGIMENS

For most HIV exposures, a combination of ZDV and 3TC should be used. For exposures that pose a substantially increased risk for transmission (e.g. hollow needle, fresh blood and advanced HIV illness in source patient):

Zidovudine 300 mg orally 12 hourly

Plus

Lamivudine 150 mg orally 12 hourly

Plus

Efavirenz 600 mg once daily

NOTE

Nevirapine should not be used for post exposure prophylaxis

TDF may be used in place of Zidovudine for patients with anaemia. Ensure negative pregnancy test and adequate contraception for women being administered Efavirenz.

Lopinavir/ritonavir (Lop/r) may be considered after consultation with a HIV trained physician.

Dual drug therapy should only be considered in the absence of other alternatives if the risk is high.

4.11. TIMING OF POST EXPOSURE PROPHYLAXIS (PEP)

PEP should be initiated within 12 hours but up to 72 hours maximum

4.12. DURATION OF POST EXPOSURE PROPHYLAXIS (PEP)

The optimal duration of PEP is 28 days. This is based on evidence from occupational and animal studies where AZT, administered for 4 weeks if tolerated, appeared protective.

4.13. FOLLOW-UP OF HEALTH CARE WORKER EXPOSED TO HIV

Healthcare workers with occupational exposure should be tested at baseline, 4 weeks, 12 weeks and 6 months post exposure to HIV.

4.14. MONITORING AND MANAGEMENT OF PEP TOXICITY

If PEP is used, Health care provider should be monitored for drug toxicity. The scope of testing should be based on medical conditions in the exposed person and the toxicity of drugs included in the PEP regimen. Minimally, laboratory monitoring for toxicity should include a complete blood count and renal and hepatic function tests.

4.15. PEP FOR VICTIMS OF SEXUAL ASSAULT

Counseling

All persons presenting to a health facility after allegedly being raped should be counseled by the examining healthcare worker about the potential risks of HIV transmission post rape. Children below 12 years of age need to be managed at Hospitals.

When to start PEP

All persons presenting to a health facility within 72 hours of being allegedly raped should be offered PEP if it is available. Before starting PEP and following counseling and the obtaining of informed consent, blood must be taken for HIV status. Persons who are previously known or found to be HIV positive should be referred to an appropriate health care clinic for long-term management of their HIV infection.

Drug Regimen

The recommended treatment regimen is Triple therapy (first line regimen) daily for 4 weeks. The noted contraindications for each of these drugs must be considered as detailed in these guidelines. In addition, women should be offered:

Treatment for Syphilis, Gonorrhea and Chlamydia:

Amoxicillin 2g plus
Augmentin 2 tabs plus
Probenecid 1g plus
Azithromycin 1g
(all above orally, stat, supervised)

Emergency oral contraception:

If there is a possibility that the assault may cause pregnancy and the assault occurred in the past 72 hours, then after counseling and consent:

Give 3 Morning after pills stat and another 3 after 12 hour. (The woman should be told to expect nausea after this high dose).

NB: Make sure that she takes the actual hormone pills not the 7 Iron/Fefol pills that are on the card.

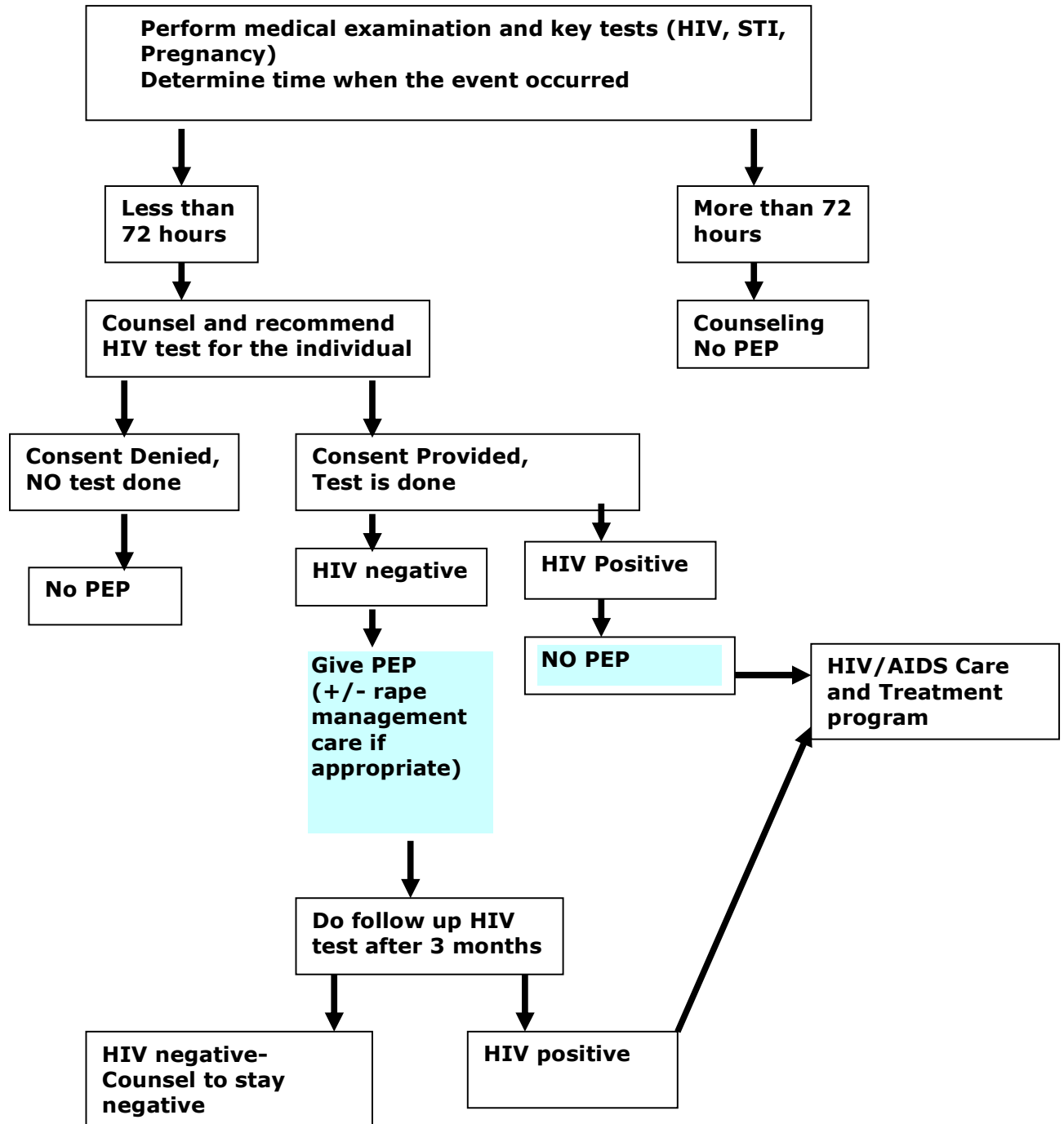
OR

20 Microlut tabs stat and another 20 tabs after 12 hours. (This dose of Microlut does not cause nausea). (This regimen is obviously more cumbersome with the larger number of pills but is mentioned in case at a health centre there is only Microlut in stock or for any reason the woman cannot take the combined pill.)

Patient monitoring

Routine testing with a full blood count and liver enzymes for patients on ZDV and 3TC is not recommended for such a short duration of therapy. Blood tests should be performed according to patient's condition. Three (3) months after the PEP period, the individual should return for a confirmatory set of HIV tests to determine that the treatment was effective. If it was not effective and they have sero-converted, they should be enrolled in a HIV Care and Treatment program and monitored appropriately as all HIV positive individuals.

Table 15: Recommended Algorithm for assessment before PEP initiation



CHAPTER FIVE

OPPORTUNISTIC INFECTIONS (OIs)

5.1. INTRODUCTION

Currently there is no cure for HIV infection. There is however prophylaxis and treatment for some opportunistic infections resulting from HIV induced immune deterioration. It should always be recognized that we only treat and cure the associated diseases and symptoms and not HIV itself. Patients don't die from HIV-infection, but succumb to the complications that the HIV induced immune deterioration cannot handle. With this approach the length and quality of life of the HIV infected patient can be substantially improved.

The purpose of the investigations recommended in these guidelines is to identify and manage treatable causes of morbidity in HIV infected individuals. Treatment is available for most of the opportunistic infections, and all efforts should be made to deal with all treatable conditions in people with HIV and AIDS. Cancer conditions in HIV positive patients should be managed as in sero-negative individuals.

In the following section, the guidelines also recommend how to identify and manage treatable causes of morbidity in HIV infected individuals. All efforts should be made to deal with all treatable conditions in people with HIV and AIDS. These conditions will be managed at various levels of care from aid posts to national level health care facilities, and as such, require all health care workers to be able to detect, treat and undertake appropriate referral for these conditions.

5.2. PROPHYLAXIS

Many opportunistic infections can be prevented by the use of Cotrimoxazole prophylaxis. The diseases include; Bacterial pneumonias, Pneumocystis Carinii Pneumonia, and Toxoplasmosis.

Prophylactic treatment using Cotrimoxazole

Indications:

- In all HIV positive adults and adolescents in stage II, III, or IV regardless of CD4.
- Asymptomatic HIV infected individuals with CD4+ counts <350 cells/ml.*

NB: Baseline Liver Function Tests (LFT) and Renal Function Tests (RFT) are recommended before long term administration of Cotrimoxazole.

* For children, see appropriate section of the guidelines.

Dose

Adults – One double strength tablet (960 mg) or two single strength tablets once a day on a daily basis.

Duration

- It is recommended that HIV positive adults remain on Cotrimoxazole prophylaxis for life. For those on ART, cotrimoxazole prophylaxis can be stopped if CD4 is >350 for 6 months or if ART commenced when CD4 >200, 6 months after ART commenced if CD4 count is increasing.
- If cessation of treatment is based on CD4 count, Cotrimoxazole prophylaxis should be recommenced if the CD4 count falls below the initiation threshold or a new or recurrent WHO clinical stage II, III or IV condition occurs.

Criteria for stopping

- Occurrence of severe side effects such as cutaneous reactions, or fixed drug reactions.
- Renal and/or hepatic insufficiency or severe haematological toxicity

Follow up

Regular follow up initially every month for the first three months, then every three months if the medication is well tolerated. It is mandatory to monitor for side effects and adherence. It is recommended that monitoring includes assessment of skin reactions, measurements of haemoglobin, and white blood counts every six months and when clinically indicated.

Preventive therapy against TB in PLHIV

The dramatic spread of the HIV epidemic throughout PNG has been accompanied by up to a fivefold increase in the number of TB cases registered.

There is thus a need for strong collaboration between HIV and AIDS and TB programs. Therefore strategies to control HIV must also include interventions to control TB. TB preventive therapy is the use of one or more anti-tuberculosis drugs given to individuals with latent infection with *M. tuberculosis* in order to prevent progression to active TB disease. Trials have shown that maximum benefits from TB preventive therapy are achieved in HIV infected patients with evidence of latent tuberculosis infection. Development of clinical Tuberculosis is reduced by about 60% and survival is also prolonged. However, some benefit is also shown in HIV positive groups in general, regardless of the tuberculin test result.

TB preventive therapy is an intervention that should be part of the package of care for people living with HIV. However it should only be offered in the following situations (prerequisites):

- Effective screening for active TB before initiating TB preventive therapy
- Capacity for follow up and monitoring of patients to encourage adherence to preventive therapy in order to address eventual side effects and exclude active TB disease

INH will be provided to eligible clients through collaboration between HIV/AIDS and TB Control Programs. It is also essential that HIV inpatients in health care facilities are isolated from those patients with active TB.

It is essential to exclude active tuberculosis in every patient prior to starting preventive therapy. This is critical in order to avoid drug resistance when drugs are given to patients with TB disease who require the full regimen.

Symptoms and signs to be noted

Patients for TB preventive therapy should be specifically asked about signs and symptoms of tuberculosis:

- Cough > 2 weeks
- Fever > 2 weeks
- Night sweats
- Weight loss of > 1.5 kg in the past 4 weeks. Weight should be measured at each clinic visit to allow documented evidence of weight loss. A weight loss of >1.5 kg should be considered a positive screen indicator.
- Pleuritic chest pains and haemoptysis
- Other symptoms suggesting extra pulmonary TB

Investigations to be done

All patients with 1 or more signs and symptoms must be investigated further for TB and are not immediately eligible for TB preventive therapy. Sputum specimens must be collected for AFB. Chest x-ray is also recommended in the screening for TB Preventive therapy, and has an important role in those who are TB suspects with negative sputum smears as per the national TB guidelines.

Eligibility for TB Preventive Therapy

All HIV positive people who have no signs and symptoms suggestive of active TB are eligible for TB preventive therapy. For patients with history of TB treatment:

- Patients who had active tuberculosis in the past 2 years should not be considered for preventive therapy.
- Patients who were treated for tuberculosis more than 2 years earlier may be considered because they may have already been re-infected with TB.

Patients who receive TB preventive therapy and who are required to start antiretroviral therapy can complete their TB preventive therapy even if the ART is started as there is no interaction between isoniazid and the current ART regimen used. Whenever INH is used, pyridoxine (B6), 25mg daily is recommended to be given concurrently with the INH

Recommended Regimen

The standard regimen for TB preventive therapy is Isoniazid (INH) daily 5 mg/kg/day (maximum 300 mg per day) and Vitamin B6 (Pyridoxine) 25mg daily. The recommended duration is 6 months.

5.3. CLINICAL FEATURES

COUGH AND DYSPNOEA

Persistent cough and or dyspnoea can usually be attributed to one of the following:

- Bacterial pneumonia
- Viral pneumonia
- Pulmonary TB
- PCP
- Cardiac failure
- Allergic bronchitis
- Chronic bronchitis
- Bronchial asthma

It may not be possible to determine the underlying cause of cough and dyspnoea on clinical history and physical examination alone and hence laboratory tests may be of critical value.

Investigations:

- Full Blood Count
- Sputum for AFB x 3
- Sputum for pyogenic culture and sensitivity
- Chest x-ray
- FBC
- ECG (where available)

SKIN RASHES, SORES AND GENERALIZED PRURITIS.

Causes include:

- Generalized pruritic papular eruption (PPE)
- External parasites e.g. scabies
- Generalized fungal skin infections
- Herpes zoster
- Herpes simplex
- Kaposi sarcoma
- Generalized bacterial skin infection e.g., Impetigo
- Drug reaction

Investigations

- Exclude scabies, bacterial and fungal infections for which treatment are available
- Skin scraping for fungal element
- Pus swab for culture and sensitivity

Management

- Treat the underlying cause

ALTERED MENTAL STATUS AND PERSISTENT SEVERE HEADACHE

Amongst the numerous causes of altered mental status and severe headache are:

- Malaria
- Typhoid
- Severe dehydration
- Hypoglycemia
- Bacterial and/or fungal meningitis
- Toxoplasma encephalitis
- HIV-dementia
- Depression
- Psychotic conditions

NB: In altered consciousness, cerebral malaria must always be excluded since this is a common and curable infection.

Investigations

- Blood slide for malarial parasites
- Lumbar puncture for CSF examination including Indian ink stain for Cryptococcal meningitis
- Blood cultures and sensitivity studies.
- CT Scan (where available)

WEIGHT LOSS

Weight loss in persons with HIV disease including AIDS may be due to:

- Reduced food intake
- Difficulty/painful swallowing
- Diminished gastrointestinal uptake (malabsorption, diarrhoea),
- TB (a frequent cause of rapid weight loss)
- Intestinal worms
- Other debilitating diseases e.g. cancer
- Intractable vomiting

Treatment of weight loss

- Treat underlying cause
- High calorie and protein food intake

5.4. CLINICAL STAGE I – DISEASE STATES AND TREATMENT

PERSISTENT GENERALIZED LYMPHADENOPATHY (PGL)

Lymphadenopathy may be due to a number of causes including those listed below:

- HIV itself. (It is however not a bad prognostic sign.)
- Mycobacterium tuberculosis infection.
- Kaposi's Sarcoma, or lymphomas.
- Other causes e.g. pyogenic bacterial infection

Investigations

- Aspirate the node with a 21G needle and stain the aspirate for acid-fast bacilli (AFB).
- Lymph node biopsy for histological diagnosis.
- Chest X-ray
- FBC and ESR

5.5. CLINICAL STAGE II – DISEASE STATES AND TREATMENT

IMPETIGO

A highly contagious bacterial infection, impetigo often starts when a small cut or scratch becomes infected. This type of bacterial infection is usually more common in children but can affect HIV positive adults. The nose is most often the source of the infection.

The symptoms of impetigo are honey-colored, crusty sores that often appear on the face between the upper lip and nose. The rash consists of red spots or blisters that rupture, discharge, and become encrusted. People with impetigo

should not scratch the sores because they may inadvertently spread the infection to other parts of their bodies.

This skin infection is caused by one of two bacteria; group A Streptococcus, which is the bacteria also responsible for "Strep throat," or Staphylococcus. If impetigo is caused by streptococcus it will begin with tiny blisters. These blisters will eventually erupt revealing small, wet patches of red skin. Gradually, a tan or yellowish brown crust will cover the affected area giving the appearance that it is coated with honey. If caused by staphylococcus, people will notice larger blisters that appear to contain a clear fluid. These blisters stay intact for a longer period of time compared to the smaller ones.

Treatment

Local antiseptics to clean lesions.

If infection severe:

- Amoxicillin 500 mg TDS PO for 5 days.

If no response try:

- Flucloxacillin 250mg QID PO for 10 days OR
- Erythromycin 500mg QID PO for 7 days

SEBORRHOEIC DERMATITIS

Seborrheic dermatitis is a disease that causes flaking of the skin. It usually affects the scalp. In adolescents and adults, it is commonly called "dandruff." In babies, it is known as "cradle cap." Seborrheic dermatitis can also affect the skin on other parts of the body, such as the face and chest, and the creases of the arms, legs and groin. Seborrheic dermatitis usually causes the skin to look a little greasy and scaly or flaky.

Treatment

Good general hygiene including washing with soap removes oils from affected areas and improves seborrhea. Pharmacologic treatment options for seborrheic dermatitis include antifungal preparations (selsun shampoo for the head; Clotrimazole 1% with Hydrocortisone 1% topically OR azole drugs (such as Fluconazole) for unresponsive or extensive diseases) to decrease colonization by yeast. If topically Clotrimazole not used, apply Hydrocortisone 1% cream twice daily to the affected area until inflammation clears.

For severe disease, Keratolytics such as Salicylic acid or coal tar preparations may be used to remove dense scale; then topical steroids may be applied. Other options for removing adherent scale involve applying any of a variety

of oils (peanut, olive or mineral) to soften the scale overnight, followed by use of a detergent or coal tar shampoo.

A severe, explosive onset of seborrheic dermatitis may be evident in HIV infection, regardless of age. It may appear as a butterfly rash, similar to the acute facial eruption associated with Systemic Lupus Erythematosus (SLE) . The dermatitis may be treated with topical preparations, but if severe, treatment with Fluconazole 150mg/day PO for 5-10 days, OR *Ketoconazole 200 mg/day PO for 5-10 days OR *Itraconazole 200mg/day PO for 5-7 days may be necessary

TINEA CAPITIS/CORPORIS/CRURIS/PEDIS

Use of topical treatments such as Benzoic Acid Compound Ointment (Whitfield's) or Clotrimazole 1% cream is often adequate. Where there is no response, or there is extensive spread, and/or involvement of two or more body areas, systemic azole therapy may be indicated.

Treatment

Fluconazole 100 mg/day PO for 7 days, OR *Ketoconazole 200mg/day PO for 2 - 4 weeks OR *Itraconazole 100mg/day PO for 2 – 4 weeks.

*Due to liver toxicity concerns, Ketoconazole and Itraconazole should not be given to patients taking Nevirapine (NVP)

PAPULAR PRURITIC ERUPTIONS

Hyper pigmented papules and nodules (up to 1 cm) with severe itching. Often ulcerations and scars because of scratching. Most frequently on the extensor side of arms and legs.

Treatment

- Antihistamines
(Phenergan 10 mg TDS PO if bothersome during the day otherwise just Phenergan 25mg Nocte PO)
- Mild topical steroids
(such as Hydrocortisone 1%) applied BID to QID as necessary
- Calamine lotion for comfort
- Commence ART ASAP

HERPES ZOSTER

Herpes Zoster (or Shingles as it is commonly known) is caused by a reactivation of the varicella-zoster virus (VZV). Chicken pox is the clinical manifestation of primary infection with VZV. After recovery from primary infection, VZV is not eliminated from the body but rather, the virus lies dormant in the sensory nervous system. When latent infection reactivates, the result is an episode of shingles, which is characterized by localized rash and pain along a dermatomal distribution. This can involve any dermatome, including the lower sacral dermatome. However, as lower sacral dermatomal zoster is much less common than genital herpes, so-called "recurrent zoster" is usually recurrent HSV infection.

The rash of zoster is often intensely pruritic and spreads throughout the dermatome, evolving through papular, vesicular and crusting stages. It usually lasts two to four weeks. The most troubling symptom is usually pain, which ranges from mild to severe, and from burning to lancinating (piercing knifelike pain). Paraesthesiae, or anaesthesia and allodynia (pain induced by touch, often from trivial stimuli), can accompany severe pain. The pain may be self-limited or persist beyond the rash for up to a year ("post herpetic neuralgia").

It is important to note that primary VZV infection in immuno-compromised persons may be associated with the following:

- Numerous lesions
- Disseminated disease associated with pneumonitis, hepatitis and hemorrhagic skin lesions.
- CNS manifestations including encephalitis and cerebellar ataxia
- Prolonged healing time
- Bacterial super-infection
- Herpes zoster in HIV infected individuals may be more severe, with more recurrences and may involve more than one dermatome

Treatment

Antiviral therapy is appropriate for all patients presenting with shingles within 72 hours of rash onset. On current evidence, Valaciclovir is probably the most effective agent available, based on the knowledge that it speeds pain resolution faster than Aciclovir and offers more convenient dosing than Aciclovir but either can be used.

- Valciclovir 1 gram TDS PO for 7-14 days; OR
- Aciclovir 800mg PO 5 times/day for 7 – 14 days
- With disseminated VZV or ophthalmic nerve involvement give IV/Oral Acyclovir 10 mg/kg 8hourly for 7 - 14 days
- Strong analgesics are indicated (Codeine with Paracetamol or Codeine phosphate). The pain may be refractory even to potent analgesics.

- Erythromycin or Cloxacillin 500mg 6 hourly times daily for 7 days for bacterial super-infection if present.
- Patients on NVP or LPV/r should not be provided with Cabamazapine for post-herpetic neuralgia however Amitriptyline may be used. The usual dose is 25mg orally nocte. The dose may be increased every 2 to 3 days but care should be taken to avoid excessive drowsiness. Most adults require less than 100mg daily.
- Evidence has shown that the complications of steroid therapy (prednisolone) tends to outweigh the benefits in herpes zoster and is therefore not recommended.

UPPER RESPIRATORY TRACT INFECTIONS (eg. bacterial sinusitis)

Bacterial sinusitis usually caused by Streptococcus Pneumoniae or H. Influenza. In health adults spontaneous resolution will occur in about 70% of people within about 2 weeks. HIV positive patients however should be treated with antibiotic therapy to avoid complications.

Treatment

- Amoxicillin 500 mg TDS PO for 5 – 7 days
- If no response use Amoxicillin + Clavulanate 875 + 125 mg (Augmentin) TDS PO for 7 – 14 days.
- If hypersensitive to Penicillin, use Doxycycline 100mg PO daily for 5 – 7 days.

5.6. CLINICAL STAGES III – DISEASE STATES AND TREATMENT

FEVER

Fever may be due to a variety of causes and clinical features may suggest diagnosis. If no pointing features to a diagnosis are present, as a minimum the following should be done:

- Blood slide for malaria parasites,
- Blood and urine cultures if clinically indicated.
- Chest X-ray
- Blood for culture
- Urinalysis
- Full blood Count and ESR
- Sputum for AFB if indicated

ORAL CANDIDIASIS

Patients with oral candidiasis will have white “curd like” lesions in the oral cavity. These are characteristically painful lesions and may be scrapped off with a spatula.

Treatment

For treatment any of the following may be used:

- Fluconazole 100/200mg/day PO for 5-7 days; OR
- Nystatin oral suspension (100,000 u/ML) 1 ml QID for 10 – 14 days,OR
- Miconazole Gel 2% 2.5ml PO QID for 10 – 14 days OR
- *Itraconazole 100mg/day PO for 10 – 14 days, OR
- *Ketoconazole 200mg/day PO for 10 – 14 days.

Where none of the above is available, 5mls of Gentian Violet 1% can be used BD as a mouth gargle for 5 – 7 days.

*Due to liver toxicity concerns, Ketoconazole and Itraconazole should not be given to patients taking Nevirapine (NVP)

ORAL HAIRY LEUKOPLAKIA

Oral hairy leukoplakia (OHL) is a white thickening or coating of the lining of the mouth. It looks like white vertical folds or ridges. These ridges are almost always located on the sides of the tongue, although in unusual cases they can sometimes they can be found under the tongue or on the inside of the cheek. Oral hairy leukoplakia may look like oral candidiasis (thrush). Thrush can be scraped off. The white ridges of oral hairy leukoplakia do not scape off nor is OHL painful. Oral hairy leukoplakia occurs in people who have HIV and who have moderate to severe immune system damage.

It is associated with Epstein-Barr virus (EBV) and occurs almost exclusively in patients who are immuno-compromised. Whether OHL develops after super infection with EBV or activation of a latent infection due to reduced immune surveillance is not known. OHL is more common in immuno-compromised patients who smoke.

Treatment

OHL is rarely treated. Painful super infection with *Candida* can be addressed with Nystatin and other antifungals. Patients with OHL are generally eligible for ART. Immune restoration with ART will eliminate the condition.

VAGINAL CANDIDIASIS

This is one of common illnesses presenting with itchy curd-like discharge. It can be managed with:

- Clotrimoxazole pessaries
- Nystatin Pessaries

If unresponsive or pessaries unavailable; give:

- Fluconazole 150mg PO Stat; or
- *Itraconazole 400mg PO TDS for 2 doses only (total of 800mg).

*Due to liver toxicity concerns, Ketoconazole and Itraconazole should not be given to patients taking Nevirapine (NVP)

DIARRHOEA

Diarrhoea in persons with HIV disease including AIDS can be due to a number of causes including:

- Common pathogens such as: Amoebiasis, Salmonella or Shigella
- Chronic malabsorption
- Cryptosporidiosis
- Mycobacterium Avium Complex (MAC) infection
- Isosporidiosis.
- Clostridium Difficile infection

Investigations

Examine stools for treatable causes

Treatment

- Rehydration, Oral Rehydration Therapy (ORT)
- Treat underlying cause – give antibiotic therapy* and Albendazole 400mg stat.
- Nutritional therapy
- In persistent diarrhoea among adults with no obvious treatable cause and no response to antibiotic therapy, give anti diarrhoeal drugs such as Loperamide to minimize fluid loss and commence on ART. Cease Loperamide ASAP.

***NB: Due to resistant of Shigella and Campylobacteria to Cotrimoxazole, Ciprofloxacin is the drug of choice**

PULMONARY TUBERCULOSIS

Please see national treatment guidelines for Tuberculosis

SEVERE BACTERIAL INFECTION

Bacterial pneumonia is a common cause of HIV-1-related morbidity and mortality. Incidence of approximately 100 cases per 1,000 HIV-1-infected persons per year have been reported, a rate much higher than that in the non-infected population. In a study comparing rates among cohorts with similar other risk factors for bacterial pneumonia, those with HIV-1 infection were 7.8 times more likely than HIV-sero-negative persons to develop bacterial pneumonia. For certain persons, bacterial pneumonia is a symptom of HIV-1 disease. Patients can develop serious pneumococcal infections with relatively preserved CD4+ T lymphocyte counts. The high rates of bacterial pneumonia and other pyogenic respiratory tract infections probably result from multiple factors including qualitative B-cell defects that impair the ability to produce pathogen-specific antibody, impaired neutrophil function or numbers or both.

The etiology of bacterial pneumonia among patients with HIV-1 infection shows a relative prominence of *Streptococcus Pneumoniae*, followed by *Haemophilus Influenzae*, *Pseudomonas aeruginosa*, and *Staphylococcus Aureus*. In the majority of studies, the pathogens of atypical pneumonia (*Legionella Pneumophila*, *Mycoplasma Pneumoniae*, and *Chlamydia Pneumoniae*) are rarely encountered.

On the basis of data derived from studies of pneumococcal bacteremia, infection with *S Pneumoniae* is 150–300 times more common in patients with HIV-1 infection than in age-matched HIV-uninfected populations. Recurrent pneumococcal pneumonia, either with the same or unrelated serotype, is also more common among HIV infected patients, with a rate of 8%–25% within 6 months. Reinfection with a different strain is more common than relapse.

The presentation of bacterial pneumonia in HIV positive patients will be similar to that in HIV negative patients*.

Treatment

As for HIV negative patients:

- Amoxicillin 500 mg TDS PO for 5 – 7 days if mild; **OR**
- Benzyl Penicillin 1,000,000 units QID parentally then change to oral Amoxicillin when improved; **OR**
- If no response or deteriorating, Chloramphenicol 1gram QID parentally then when improved and no fever, change Chloramphenicol 750mg TDS PO for a total period of at least 10 days.

- Adjunct treatment such as oxygen, pain relief etc. as required – see Standard Treatment Manual

***NB: Remember that in immuno-compromised patients pneumonia can be caused by fungal infection such as Aspergiullus and Cryptococcus.**

If suspected, treat patient with Amphotericin B parentally (0.7 mg/kg for Cyprotococcus and 1.0/mg/kg for Aspergillus). Alternatively Fluconazole can be used (20mg/kg daily for the first dose (PO or IV) then 10mg/kg daily for subsequent doses for at least 4 weeks).

5.7. CLINICAL STAGE IV – DISEASE STATES AND TREATMENT

NORWEGIAN SCABIES

Clinical diagnosis is made by observing typical lesions on wrists, finger web spaces, axillae, penis or thighs or on eliciting the classic pattern of pruritus (at night, after a hot shower/bath). If associated with exposure to an infected person, the index of suspicion should be high even in the context of non-specific symptoms. Immunosuppressed patients may present with Norwegian scabies. Large numbers of mites are present and the condition may not be pruritic. Extensive crusting may be seen.

Treatment

Immunosuppressed/HIV patients are generally resistant to the topical therapy of Permethrin 5% applied topically. If used, Permethrin should be applied from the neck down. Pay particular attention to the areas between the fingers and toes, under fingernails and toenails, wrists, armpits, genitals, buttocks and perianal area. It is usually helpful for a second person to assist with the application of cream to areas that are not easily accessible. Permethrin should be kept on for at least 8 hours but no more than 24 hours. Reapply to hands if washed before 8 hours. This treatment needs to be given weekly for 6 weeks. Oral antihistamines can be given for pruritus.

If there is no response to Permethrin, if no Permethrin is available or if clinically indicated, Ivermectin is given at a dose of 200ucg/kg stat with a further 200ucg/kg dose repeated one week later. If clinically indicated, a third dose can be given after a further week but this is generally not needed. Washing in warm water, drying clothes/linens in the sun and observing personal hygiene is part of treatment

HERPES SIMPLEX VIRUS (HSV) INFECTION

Clinical features:

Classical presentation of primary HSV infection includes:

- Lymph node enlargement
- Small painful vesicles
- Painful ulcers on the mucosa and skin
Pain along gluteal and upper thigh muscles (Sacral radiculomyelitis) may occur with genital/rectal HSV
- Lymph node enlargement
- Headache

Lesions usually resolve within 10-21 days after primary infection. The HSV then becomes latent in trigeminal and sacral nuclei and may reactivate. Clinical features common in those with HIV and AIDS include persistent/erosive genital/peri-rectal ulcerations. These are mainly associated with HSV-2 and more recurrent herpetic lesions.

Diagnosis

The diagnosis is usually based on clinical history and physical findings. Laboratory tests include serology, culture, immunofluorescence or immunoassay. Neither immunofluorescence nor immunoassay is available in the public health system in PNG.

Treatment

- Acyclovir 400mg PO TDS for 7 – 10 days; OR
- Valaciclovir 500mg PO TDS for 7 – 10 days.
- With severe HSV infections, give IV/Oral Acyclovir 10 mg/kg/day TDS, for 7 - 14days

CYTOMEGALOVIRUS (CMV) INFECTION

Clinical features

HCMV is a common human pathogen, infecting approximately 50% of adult populations in developed countries. CMV infections are typically sub-clinical but can become life threatening in immuno-compromised individuals. HCMV infection itself causes immunosuppression and has been linked with the progressive immunosuppression in persons infected with HIV. The most common manifestation is retinitis but colitis and pneumonitis are also frequently seen. HCMV may also present as encephalitis, hepatitis, adrenalitis, pancreatitis and/or epididymitis.

Diagnosis

The definitive diagnosis relies on clinical and laboratory findings:

- End organ disease such as retinitis with cotton wool and haemorrhage changes seen in retina, severe diarrhea and
- Microscopic finding of cytomegalic cell containing large central basophilic intranuclear inclusion (Papanicolaou or hematoxylin eosin stain).
- HCMV Antigen detection (monoclonal antibodies) of tissue, blood or bronchoalveolar lavage specimens
- Serology – seroconversion is a good marker for primary CMV infection but many individuals have past infection and are antibody positive at baseline..

Treatment

- Ganciclovir – IV infusion over 1 hour at 5mg/kg given twice a day during initial induction (2 – 3 weeks) and then 5mg/kg IV once daily for 7 days. (Decrease dose in renal impairment). Maintenance dose of 3 grams orally daily for 20 weeks.
- **It should be noted that oral Ganciclovir is not recommended for induction therapy of acute CMV disease. In acute CMV disease, IV Ganciclovir must be used for induction therapy.**

Valganciclovir is more effective and produces higher blood levels than ganciclovir but is not available in PNG.

CRYPTOCOCCUS NEOFORMANS INFECTION

A major cause of meningitis in HIV infected persons and disseminated disease. Contrary to bacterial meningitis, fever may be absent in these cases. Diagnosis depends on demonstration of positive CSF Indian Ink preparation.

Treatment

The preferred regimen is Amphotericin B 0.7mg/kg/day IV and 5 Fluorocytosine 100mg/kg/day orally for 14 days (induction phase) then:

- Fluconazole IV 400mg/day for 3 days (consolidation phase) then
- Fluconazole 400mg per day orally for 10 weeks (maintenance phase) then
- Fluconazole 200mg daily as secondary prophylaxis until CD4 >200 for 6 months or indefinitely if no CD4 count available.
- Child: 6-12mg/kg daily (every 72 hours in neonate up to 2 weeks old, every 48 hours in neonate 2-4 weeks old); maximum, 400mg daily.

OESOPHAGEAL CANDIDIASIS

Candidiasis is the most common fungal infection in HIV and AIDS. Clinical manifestations depend on the site of disease, which can include mouth, pharynx, esophagus, and vagina.

NB. Candidiasis in the esophagus, trachea, bronchi or lungs is diagnostic of WHO Clinical Stage IV.

Diagnosis

The diagnosis is mainly based on clinical findings.

Treatment

For oesophageal candidiasis patients will usually complain of painful swallowing. If the patient has oral candidiasis or has a recent history of this, a presumptive diagnosis should be made of esophageal candidiasis. The following treatment options are available:

- Fluconazole 200mg PO Stat then 100mg daily for 14 days; OR
- Itraconazole 200mg PO daily for 14 days.

If unresponsive or unable to swallow;

- Amphotericin B 0.5mg/kg IV daily for 14 days.

Once oesophageal candidiasis is treated with Fluconazole, the dose should be reduced to 100 mg daily and then continued indefinitely or until immune recovery occurs on HAART.

PNEUMOCYSTIS JIROVECCI PNEUMONIA (PCP)

Quite common in HIV infected individuals.

Clinical presentation:

- Non-productive cough, fever, chest tightness and shortness of breath that has evolved over 2-4 weeks.
- Chest signs may be minimal despite severe shortness of breath
- CXR may show diffuse and symmetrical increased interstitial markings to diffuse alveolar pattern with infiltrations characterized by asymmetry, nodularity or cavitations. Chest radiograph may appear normal in 10% of patients. Pneumothorax is sometimes seen.

Diagnosis

In our circumstances diagnosis is based on clinical presentation and exclusion of other common causes of severe dyspnoea.

Treatment of PCP

The management of PCP depends on the severity of the disease.

Severe Disease (Dyspnoea without exertion and severe hypoxia)

- Cotrimoxazole (Trimethoprim 15-20 mg/kg/day + Sulphamethoxazole 75-80 mg/kg/day) IV or oral for 21 days in 3 divided daily doses plus corticosteroids (see below).

Mild and Moderate Disease PCP is normally considered moderate if there is dyspnoea on minimal exertion)

- Cotrimoxazole 1920 mg 3 times /day for 21 days (4 tabs 8 hourly for 7 days, Then 4 Tablets 12 hourly for 7 days, then 4 Tablets daily for 7 days). With patients with moderate disease, consideration should be given to commencing initial therapy IV, particularly where treatment compliance may be an issue.
- Trimethoprim 12-15mg/kg/day + Dapsone 100mg/day for 21 days

For those allergic to Sulphur

Trimethoprim 12-15mg/kg/day + Dapsone 100mg/day for 21 days

Use of Corticosteroids in PCP ³

Research has demonstrated that there is reduced morbidity and mortality with PCP if corticosteroids are administered concomitantly with antimicrobial therapy. In moderate and severe disease, Prednisone 40mg PO BD for five days, then 40mg PO Daily for five days, then 20mg PO Daily until completion of therapy. If oral corticosteroid therapy is not possible, then hydrocortisone (100mg IV q6h) may be used until oral therapy can be commenced (Methylprednisolone at 75% of the prednisone dose can be used if parenteral therapy is indicated and there is no parenteral prednisone). The 21 day course can then be completed orally in accordance with the above schedule. Corticosteroid therapy can be complicated by CNS toxicity and other opportunistic infections.

³ John Hopkins University School of Medicine (2006) *Adult HIV/AIDS treatment*.

Prophylaxis (Primary and Secondary) therapy for PCP

Adults – One double strength tablet (160/800 mg) or two single strength tablets once a day on a daily basis.

CEREBRAL TOXOPLASMOSIS**Clinical features**

- Focal paralysis or motor weakness depending on area affected
- Neuro-psychiatric manifestation corresponding to the affected area in the brain
- Altered mental status (forgetfulness etc.)

Treatment**Acute infection**

Tabs Sulphadiazine 1 g (<60kg) or 1.5 g (>60kg) 6hourly + Tabs Pyrimethamine 200mg loading dose then 50mg /day (<60kg) or 75mg (>60kg)+ Tabs Folinic acid 10 - 20mg /day for 6 weeks. After six weeks of treatment move to prophylaxis regimen

Alternative Treatment Regimen (less effective)

Cotrimoxazole (TMP 10mg/kg and SMX 50 mg/kg daily) given 12 hourly either IV or PO. Continue for 4 – 6 weeks after the resolution of signs/symptoms then on to secondary prophylaxis.

Secondary Prophylaxis Regimen

- Tabs Sulphadiazine 500mg 6hourly + Tabs Pyrimethamine 25-50mg /day + Tabs Folinic acid 25mg /day.
- For those allergic to sulphur:
- Replace Tab Sulphadiazine with capsule Clindamycin 450mg 6 hourly.
- Discontinue maintenance therapy when CD4 count>200 cells/ml for 6 months

Alternative Secondary Prophylaxis

Use Cotrimoxazole 2 SS or 1 DS (SMX 800/TMP 160mg) twice daily.

5.8. OTHER

HUMAN PAPILLOMA VIRUS (HPV) INFECTION

Clinical features

The virus may be present for years before symptoms develop. Genital warts develop following infection with some sub-types of HPV and usually progress rapidly whenever there is a decline in immune status (such as in pregnancy or in HIV infection). The warts are soft and fleshy and are easily traumatized during sexual activity. In pregnancy or in immuno-compromised individuals the warts may develop so greatly as to completely cover the vulva and occlude the introitus and urethral meatus.

Women who have ano-genital HPV infection (ano-genital warts) have an increased risk of developing cancer of the cervix and both men and women who have anal warts have an increased risk of later developing anal cancer.

Diagnosis

The diagnosis in PNG is based on clinical history and physical findings.

Treatment

The options in PNG are limited:

- Trichloroacetic acid in 80% to 90% solution may be used to treat small moist warts. It should be applied by the clinician to each wart (being careful not to burn surrounding tissue) weekly for up to 6 weeks. This is only appropriate for small numbers of discrete warts.
- Imiquimod 5% cream is applied to warts (with the fingers) 3 times a week (alternate nights) for up to 16 weeks. This medication stimulates the production of interferon and other cytokines. It is not available in the public health system but can be obtained by prescription from some private pharmacies. Safety in pregnancy has not yet been established.
- Electrocautery is probably the only real option available in PNG to treat the large mass genital warts that are becoming increasingly seen. Female patients are usually referred to the Gynaecology Clinic and males to the Surgical Clinic for booking. Cautery will usually need to be done under general (ketamine) anaesthesia.

INTESTINAL PROTOZOA INFECTION

For intestinal protozoa, which is a common cause of diarrhoea and difficult to diagnose, the recommended treatment:

Tabs Albendazole 800mg BD for one week.

Other alternatives are Metronidazole Tabs or Thiabendazole.

APPENDIX 1

LIST OF RECOMMENDED DRUGS FOR ADULTS AND ADOLESCENTS

Drug class/drug	Dose
Nucleoside RTIs	
Zidovudine (ZDV)	300 mg twice daily
Lamivudine (3TC)	150 mg twice daily (can be given as 300mg once daily when other ARVs are dosed on a daily basis, e.g. TDF+3TC+EFV can be given as a daily dose)
Didanosine (ddI)	400 mg once daily if >60 kg (250 mg once daily if <60 kg)
Abacavir (ABC)	300 mg twice daily or 600mg once daily
Tenofovir (TDF)	300 mg once daily
Emtricitibine (FTC)	200mg once daily- oral
Non-nucleoside RTIs	
Efavirenz (EFZ)	600 mg once daily
Nevirapine (NVP)	200 mg once daily for 14 days, then 200 mg twice daily
Protease inhibitors	
Lopinavir/ritonavir (LPV/r) (Kaletra)	400/100 twice daily or 800/200 once daily*
Saquinavir/ritonavir (SQV/r)	1000 mg/100 mg twice daily

ZDV/3TC/NVP (300mg/150 mg /200 mg), combination tablets

ZDV/3TC (300 mg /150 mg), combination tablets

NVP syrup (50mg/5ml)

ABC (300 mg)

ZDV (300 mg)

DDI (EC 250 mg and EC 400 mg)

EFZ (200 mg and 600 mg)

TDF (300mg)

LPV/r (133/33; 200/50)

SQV (200 mg)

RTV (100/200 mg)

*Once daily dosing is only recommended for treatment naive adults. If Lopinavir/Ritonavir is used with Efavirenz or Nevirapine, the dose should be increased to 533/133 twice daily.

APPENDIX 2: DRUGS FORMULATIONS AND DOSES FOR CHILDREN

<u>Drug</u>	<u>Dose and method of Administration</u>	<u>Absorption and meal</u>
ZDV (Syrup 10mg/ml) (Capsule:100mg & 300mg)	Oral: 180mg- 240/m² 12 hourly	Can be administered with food
d4T (Solution 1mg/ml) Capsules: 15, 20, 30 and 40mg	1mg/kg 12 hourly (up to 30kgs) >30kgs see adult dose	Can be administered with food
ddl (powder) (solution 10mg/ml) Chewable tablets With buffers 25, 50, 100 & 150mg	90 – 120mg/m² 12 hourly	Administer on an empty stomach
3TC (Solution 10mg/ml) Capsule 100mg	4mg/kg 12 hourly	Can be administered with food
EFV Capsule 50, 100, And 200mg	15/mg/kg/day 10-14kg 200mg 15-19kg 250mg 20-24kg 300mg 25-32.5kg 350mg 32.5-40kg 400mg >40kg 600mg Not before 3 years of age	Not with high fat meal
NVP (50mg/ml) Tab 200mg	200mg/m² 12 Hourly	During first two week once a day
ABC 20mg/ml Tab. 300mg	8mg/kg/dose 12 Hourly	Use in children >3/12

APPENDIX 3. WHO HIV/AIDS CLINICAL STAGING FOR ADULTS AND ADOLESCENTS

<p>Clinical stage I</p> <ul style="list-style-type: none"> Asymptomatic Persistent generalized lymphadenopathy <p>Performance scale 1: asymptomatic, normal activity</p>
<p>Clinical stage II</p> <ul style="list-style-type: none"> Weight loss, <10% of body weight Minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis) Herpes zoster within the last five years Recurrent upper respiratory tract infections (i.e. bacterial sinusitis) <p>And/or performance scale 2: symptomatic, normal activity</p>
<p>Clinical stage III</p> <ul style="list-style-type: none"> Weight loss, >10% of body weight Unexplained chronic diarrhoea, >1 month Unexplained prolonged fever (intermittent or constant), >1 month Oral candidiasis (thrush) Oral hairy leukoplakia Pulmonary tuberculosis within the past year Severe bacterial infections (i.e. pneumonia, pyomyositis) <p>And/or performance scale 3: bedridden <50% of the day during the last month</p>
<p>Clinical stage IV</p> <ul style="list-style-type: none"> HIV wasting syndrome Norwegian Scabies > 1 month Pneumocystis carinii pneumonia Toxoplasmosis of the brain Cryptosporidiosis with diarrhoea >1 month Cryptococcosis, extrapulmonary Cytomegalovirus disease of an organ other than liver, spleen or lymph nodes Herpes simplex virus infection, mucocutaneous >1 month, or visceral any duration Progressive multifocal leukoencephalopathy Any disseminated endemic mycosis (i.e. histoplasmosis, coccidioidomycosis) Candidiasis of the oesophagus, trachea, bronchi or lungs Atypical mycobacteriosis, disseminated Non-typhoid Salmonella septicaemia Extrapulmonary tuberculosis Lymphoma Kaposi's sarcoma HIV encephalopathy, as defined by the Centers for Disease Control and Prevention^b <p>And/or performance scale 4: bedridden >50% of the day during the last month</p>

Note: both definitive and presumptive diagnoses are acceptable.

^a HIV wasting syndrome: weight loss of >10% of body weight, plus either unexplained chronic diarrhoea (>1 month) or chronic weakness and unexplained prolonged fever (>1 month).

^b HIV encephalopathy: clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection which could explain the findings.

APPENDIX 4: WHO HIV/AIDS CLINICAL STAGING FOR CHILDREN

Clinical stage I Asymptomatic Persistent generalized lymphadenopathy
Clinical stage II ⁽¹⁾ Unexplained persistent hepatosplenomegaly Papular pruritic eruptions Extensive wart virus 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 III ⁽¹⁾ Unexplained moderate malnutrition not adequately responding to standard therapy Unexplained persistent diarrhoea (14 days or more) Unexplained persistent fever (above 37.5° C, intermittent or constant, for longer than one month) Persistent oral candidiasis (after first 6 weeks of life) Oral hairy leukoplakia Acute necrotizing ulcerative gingivitis/periodontitis Lymph node TB Pulmonary TB Severe recurrent bacterial pneumonia Symptomatic lymphoid interstitial pneumonitis Chronic HIV associated lung disease including bronchiectasis Unexplained anemia (<8), neutropenia (<0.5 x 10 ⁹), or chronic thrombocytopenia (<50 x 10 ⁹)
Clinical stage IV ⁽¹⁾ Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy Norwegian Scabies > 1 month Pneumocystis pneumonia Recurrent 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 TB
Kaposi sarcoma
Oesophageal candidiasis (or Candida of trachea, bronchi or lungs)
CNS Toxoplasmosis (after the neonatal period)
HIV encephalopathy
Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age over 1 month
Extrapulmonary cryptococcosis (including meningitis)
Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
Chronic cryptosporidiosis (with diarrhea) or chronic isosporiasis
Disseminated non-tuberculous mycobacteria infection
Cerebral or B cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy
HIV associated cardiomyopathy or nephropathy

Note: both definitive and presumptive diagnoses are acceptable.

1 Unexplained refers to where the condition is not explained by other causes

APPENDIX 5: ART ADHERENCE PREPARATION, SUPPORT AND MONITORING

Assess	<p>Person's goals for today's visit</p> <p>Understanding of ART therapy</p> <p>Interest in receiving therapy</p>
Advise	<p>HIV illness, expected progression</p> <p>ART therapy</p> <ul style="list-style-type: none"> o Benefits-lifesaving drugs. Your life depends on taking them every day at the right time o Very strong medicines o The pills do not cure HIV o The pills do not prevent HIV transmission to others – you must still use condoms and practice safer sex <p>Need for complete adherence to daily treatment (more than other drugs you may be familiar with – essential to maintain drugs levels in the blood for ART therapy to work).</p> <p>Must be taken twice daily without interruption</p> <p>If you forget a dose, do not take a double dose</p> <p>Must be taken at right time, every 12 hours (adjust this if on different regimen)</p> <p>If you stop, you will become ill (not immediately – after weeks, months or years)</p> <p>Possibility of side effects and drug interactions</p> <p>Importance of disclosure of HIV+ status (partner, family etc)</p> <p>Importance of testing partner and children</p> <p>Drugs must not be shared with family or friends</p>
Agree	<p>Establish that the person is willing and motivated and agrees to treatment, before initiating ART therapy</p> <ul style="list-style-type: none"> o Has the person demonstrated ability to keep appointments, to adhere to other medications? o Has the person disclosed his or her HIV status? If not, encourage him / her to do so. Disclosure to at least one person who can be the supporter is important o Does the person want treatment and understand what treatment is? o Is the person willing to come for the required clinic follow-up?
Assist	<p>Help the person develop the resources / support / arrangements needed for adherence:</p> <ul style="list-style-type: none"> o Ability to come for required schedule of follow-up. Discuss how the person will do this o Home and work situation that permits taking medications every 12 hours without stigma o Regular supply of free or affordable medication o Supportive family or friends o ART adherence support group o Treatment supported
Arrange	<p>When the person is ready for ART therapy, discuss at the clinical team meeting then make a plan</p>

APPENDIX 6: GUIDE FOR SUPPORTING ART INITIATION

Assess	<p>Person's goals for today's visit</p> <p>Check understanding of the information given before – make sure the person understands the illness, treatment and possible side effects</p>
Advise	<p>Reinforce the information given before</p> <p>Advise on the details of first line regimen</p> <ul style="list-style-type: none"> o Explain the purpose of and how to take each pill. Provide and explain card summarizing treatment (with drawing of each pill and common side effects) <p>Make sure person understands the importance of adherence</p> <p>Advise on diet</p> <p>Explain limits on alcohol and drug use. These are important for adherence.</p> <p>Explain side effects</p> <ul style="list-style-type: none"> o Prepare person and treatment supporter to handle common side effects. Most side effects can be treated symptomatically. o Explain which side effects are likely to be transitory (related to the initiation of treatment) and their likely duration. o Explain which are more serious and require return to clinic. <p>Explain that person can still transmit HIV infection when on ART therapy.</p> <p>It is very important to still practice safer sex and other practices to prevent transmission.</p>
Agree	<p>Make sure the person agrees to the regimen and is a true partner in the treatment plan</p> <p>Make sure the person understands that his / her life depends on taking the medicine every day</p> <p>Agree on plan for support by treatment buddy and support groups.</p>
Assist	<p>Develop (then reinforce on each visit) a concrete plan for the specific ART regimen</p> <ul style="list-style-type: none"> o When to take / times for every 12 hour dosing / how to make it a habit o Explain escalating dose of nevirapine o How to remember – provide and explain written schedule, pillbox, pill chart, other aids <p>Prepare person and treatment supporter for adherence, possible common side effects, what to do if they occur, and when to seek care.</p> <p>Provide psychosocial support.</p> <p>Encourage person to join ART adherence support group.</p> <p>Arrange home visit.</p>
Arrange	<p>Next follow-up in clinic, home visit.</p> <p>Agree on best way to access help between visits.</p> <p>Make sure the person understands where / when s/he will see health worker.</p>

APPENDIX 7: GUIDE FOR MONITORING AND SUPPORTING ADHERENCE

Assess	<p>Do clinical review and respond to any problems or changes in status. To assess adherence:</p> <p>Review the medications with the person and their treatment supporter. Determine whether there is an adherence problem.</p> <p>Ask questions in a respectful and non-judgmental way:</p> <ul style="list-style-type: none"> o "Many people have trouble taking their medications, what troubles are you having?" o "Can you tell me when and how you take each pill?" o "When is it most difficult for you to take the pills?" <p>Ask about the common and locally important factors that may interfere with adherence.</p> <p>Ask about stigma related to taking the pills.</p> <p>Count pills.</p> <p>How many pills forgotten yesterday, last 3 days, last month?</p> <p>If poor adherence: Determine what the problem is:</p> <p>Side effect? Simply forgot?; Ran out of pills?; Which dose missed morning or evening? Why?; Cost?; Reminds you of HIV?; Misunderstood?; Changed work situation?; Not comfortable taking medications around others?; Stigma?; Different timing when away from home or holiday, travel, weekend?; Seldom at home and disorganised?; Problems with diet?; Another medical problem?; Screen for excess alcohol use and depression and treat, if present. Advise</p>
Advise	<p>Reinforce the information given before</p> <p>Give additional information that may help with adherence problem</p> <p>Advice on any suggested changes in the regimen.</p>
Agree	<p>Agree on any changes in Treatment Plan and solutions to adherence problems (if present).</p> <p>Discuss the agreements you have reached and check for their commitment.</p>
Assist	<p>Provide adherence support</p> <p>Reinforce interventions which match the person's needs and adherence problems, if present.</p> <p>Make sure that the person has:</p> <ul style="list-style-type: none"> o Plan to link taking medications with daily events such as meals o Any device or skills that he or she needs (e.g. how to use a diary) <p>Make sure person has the support he or she needs</p> <ul style="list-style-type: none"> o Get help from supporter, other family and friends or peers o Help person and supporter to find solutions <p>If adherence problem:</p> <ul style="list-style-type: none"> o Get help – call for advice o Link with home based care or home visits
Arrange	<p>Record adherence estimate on persons card.</p> <p>Arrange for refills</p> <p>Arrange for next follow-up visits:</p> <ul style="list-style-type: none"> o In clinic o Home visits <p>Make sure that the person and supporter understand the follow-up plan and how to contact the clinic team if there is a problem.</p>

APPENDIX 8: PAEDIATRIC ARV DOSING SCHEDULE

Drug		Strength of child tab (mg)	Number of tablets by weight band (twice daily)							Strength of adult tab (mg)	Number of tablets by weight band (twice daily)	
			3-3.9 kg	4-4.9 kg	5-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg		25-29.9 kg	30-34.9 kg
AZT		60	1*	1*	1	1.5	2	2.5	3	300	1	1
AZT/3TC		60/30	1*	1*	1	1.5	2	2.5	3	300/150	1	1
AZT/3TC/NVP		60/30/50	1*	1*	1	1.5	2	2.5	3	300/150/200	1	1
ABC		60	0.5	0.75	1	1.5	2	2.5	3	300	1	1
ABC/3TC		60/30	0.5	0.75	1	1.5	2	2.5	3	300/150	1	1
ABC/AZT/3TC		60/60/30	0.5	0.75	1	1.5	2	2.5	3	300/300/150	1	1
3TC		30	1	1	1	1.5	2	2.5	3	150	1	1
d4T		6	1	1	1	1.5	2	2.5	3	30	1	1
d4T/3TC		6/30	1	1	1	1.5	2	2.5	3	30/150	1	1
d4T/3TC/NVP		6/30/50	1	1	1	1.5	2	2.5	3	30/150/200	1	1
NVP		50	1	1	1	1.5	2	2.5	3	200	1	1

* Except in the infant less than 6 months of age where 3-3.9 kg 0.5/0.5 and 4-4.9 kg 1/0.5 is recommended.

Drug	Strength of child tab (mg)	Number of tablets by weight band (once daily)							Strength of adult tab (mg)	Number of tablets by weight band	
		3-3.9 kg	4-4.9 kg	5-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg		25-29.9 kg	30-34.9 kg
EFV	100	n/r	n/r	n/r	n/r	2	2.5-3	3.5	600	1	1
FTC	35	0.5	0.5	1	1.5	1.5-2	2.5-3	3.5	200	1	1
EFV/FTC	100/35	n/r	n/r	n/r	n/r	1.5-2	2.5-3	3.5	600/200	1	1

Drug	Strength of child tab (mg)	Number of tablets by weight band (twice daily)*							Strength of adult tab (mg)	Number of tablets by weight band	
		3-3.9 kg	4-4.9 kg	5-6.9 kg	7-11.9 kg	12-16.9 kg	17-19.9 kg	20-24.9 kg		25-29.9 kg	30-34.9 kg
Lop/Rit	100/25	n/r	n/r	1	1.5	2	2.5	3	200/50	1.5	2

*Note different weight bands

Drug	Strength of child tab (mg)	Number of tablets by weight band (twice daily)							Strength of adult tab (mg)	Number of tablets by weight band	
		3-3.9 kg	4-4.9 kg	5-5.9 kg	6-8.9 kg	9-13.9 kg	14-19.9 kg	20-24.9 kg		25-29.9 kg	30-34.9 kg
Rit	25	0.5	0.5	0.75	1	1.5	2	2.5	100	0.75	1

*Note different weight bands

Annex 9: Clinical Staging events to guide decision-making on switching

NEW OR RECURRENT EVENT ON ART ¹	RECOMMENDATIONS	ADDITIONAL MANAGEMENT OPTIONS
Asymptomatic (T1)	Do not switch regimen	<ul style="list-style-type: none"> Maintain scheduled follow-up visit including CD4 monitoring (if available) Continue to offer adherence support.
Stage 2 Event (T2)	Do not switch regimen ²	<ul style="list-style-type: none"> Treat and manage staging event. Assess and offer adherence support. Check if on treatment for at least six months. Assess continuation or reintroduction of OI prophylaxis. Schedule earlier visit for clinical review and consider CD4 (if available).³
Stage 3 Event (T3)	Consider switching regimen ^{2 4}	<ul style="list-style-type: none"> Treat and manage staging event and monitor response. Assess and offer adherence support. Check if on treatment for at least six months. Check CD4 count (if available).^{3 4} Assess continuation or reintroduction of OI prophylaxis. Institute more frequent follow-up.
Stage 4 Event (T4)	Switch regimen ^{2 5}	<ul style="list-style-type: none"> Treat and manage staging event and monitor response. Check if on treatment for at least six months. Assess continuation or reintroduction of OI prophylaxis. Check CD4 cell count (if available).³ Assess and offer adherence support.

1. Refers to clinical stages while on ART for at least six months (termed T1, T2, T3 and T4)

2. Differentiation of OIs from immune reconstitution syndrome is necessary.

3. Treat and manage the staging event before measuring the CD4 cell count.

4. Certain WHO clinical stage 3 conditions (eg. pulmonary TB, severe bacterial infections) may be indicators of treatment failure and thus require consideration of second line therapy. Response to appropriate antimicrobial therapy should be used to evaluate the need to switch therapy.

5. Some WHO clinical stage 4 conditions (lymph node TB, uncomplicated TB pleural disease, oesophageal candidiasis, recurrent bacterial pneumonia) may not be indicators of treatment failure and thus do not require consideration of second line therapy. Response to appropriate antimicrobial therapy should be used to evaluate the need to switch therapy.