# RECOMMENDATIONS FOR **HIV MEDICINE** AND **SEXUAL HEALTH CARE** IN **PACIFIC SMALL ISLAND COUNTRIES** AND **TERRITORIES**

Oceania Society for Sexual Health and HIV Medicine

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# About **OSSHHM**

The **Oceania Society for Sexual Health and HIV Medicine (OSSHHM)** is the peak professional body working in the areas of HIV, STIs and sexual health care in the Pacific. OSSHHM strives to foster education and ongoing professional development for Health Care Workers (HCWs) in the areas of STIs, HIV and sexual health care. This work also includes developing resources and treatment recommendations specifically for Pacific based HCWs. OSSHHM is governed by a board of directors with an Executive Officer tasked with ensuring the implementation of the organization's strategic plan. The OSSHHM office is based and registered in Fiji. OSSHHM currently has 150 members registered from 16 Pacific Island countries and territories

Benefits of membership

Trusted advice from peers and highly skilled members through:

- Networking opportunities
- Support from a well informed and connected Secretariat

Access to training, resources and updates through

- Quarterly newsletters
- Free hard copies of all OSSHHM resources
- Opportunities to attend international conferences and meetings
- Access to in-country training at no cost
- Regular email updates/alerts on treatment and care matters through OSSHHMnet (OSSHHM's e-mailing list)
- Free or heavily discounted training opportunities

Influencing and driving policy and standards in the STI, HIV and sexual health areas through:

- Participation on reference groups, committees and working groups at regional level
- Contribution to the development of regional guidelines for STIs and HIV

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Oceania Society for Sexual Health and HIV Medicine

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# Preface

The OSSHHM recommendations were first released as an electronic resource for HIV care givers in the Pacific in 2007. It was recognized that a number of health workers did not have regular or reliable access to the Internet and/or computers, consequently the second edition was printed as hard copies and distributed to OSSHHM members throughout the Pacific. The OSSHHM recommendations provide HIV treatment and care advice for health workers who are serving in the Pacific. Additionally, the recommendations also include a comprehensive approach to STI treatment and control measures that are specific to the Pacific context.

The third edition of the OSSHHM Sexually Transmitted Infections recommendations has been written to act as a comprehensive reference document for HIV and STI within the Pacific context. The initial plan was to rewrite the 3rd edition in a 'prescriptive' style; however, following much thought the review team and OSSHHM board felt that a reference source was essential to guide the development of various other documents. OSSHHM bases the technical content of these recommendations on the latest updates from the World Health Organisation and other reliable sources of information, all which have been referenced where appropriate.

The 3rd edition of the OSSHHM recommendations includes for the first time an exclusive section on HIV virology, opportunistic infections, dental HIV and specific issues relating to Paediatric HIV. Part two of the recommendations focuses on STIs. It includes chapters that focus on STI syndromic management, aetiological management of specific STIs, a summary of the public health approach to STI control and a section on managing STIs in adolescents and children. OSSHHM recognizes that approaches to STI control and management may vary from country to country as such the reader may base their decision on a case by case basis and on the availability of resources and support in their various settings.

The OSSHHM recommendations are intended to provide a guide to countries managing STIs and HIV. Countries are free to use the recommendations in a manner that is appropriate for their settings. There are plans to further develop specific chapters of interest for health workers. Finally, OSSHHM expects to use the recommendations to guide the development of specific resources to guide treatment and care based on the needs of health workers.

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# Abbreviations

| | |
|---|---|
| AFB | Acid Fast Bacillus |
| AIDS | Acquired immunodeficiency syndrome |
| ART | Antiretroviral treatment |
| AZT | Zidovudine (ZDV) |
| CCR5 | Chemokine receptor 5 |
| CD4 | Cluster of differentiation 4 |
| CMV | Cytomegalovirus |
| CNS | Central nervous system |
| CoC | Continuum of care |
| CoCC | Continuum of care coordinating committee |
| CXCR4 | Chemokine receptor 4 |
| EFV | Efavirenz |
| FHI | Family health international |
| FNU | Fiji national university |
| FTC | Emtricitabine |
| GIPA | Greater involvement of people living with HIV/AIDS |
| HBV | Hepatitis B virus |
| HIV | Human immunodeficiency virus |
| HSV | Herpes simplex virus |
| IDU | Injecting drug use |
| IMCI | Integrated management of childhood illness |
| INH | Isoniazid |
| IRIS | Immune reconstitution inflammatory syndrome |
| MDR-TB | Multidrug resistant tuberculosis |
| mRNA | Messenger ribonucleic acid |
| NK Cells | Natural killer cells |
| NNRTI | Non-nucleoside reverse transcriptase inhibitor |
| NRTI | Nucleoside reverse transcriptase inhibitor |
| NVP | Nevirapine |
| OI | Opportunistic infection |
| OSSHHM | Oceania society for sexual health and hiv medicine |
| PI | Protease inhibitors |
| PITC | Provider initiated testing and counselling |
| PJP | Pneumocystis jiroveci pneumonia |
| PLHIV | People living with human immunodeficiency virus |
| RNA | Ribonucleic acid |
| SPC | Secretariat of the pacific community |
| STI | Sexually transmitted infection |
| TB | Tuberculosis |
| TDF | Tenofovir |
| TLC | Total lymphocyte count |
| UNAIDS | Joint united nations program on hiv/aids |
| VCCT | Voluntary confidential counselling and testing |
| VL | Viral load |
| WHO | World health organization |
| XDR-TB | Extensively drug-resistant tuberculosis |
| 3TC | Lamivudine |

# Part 1:

# HIV Medicine; the Pacific context.

SECTION 1

# Epidemiology, Basic Virology and Pathogenesis of HIV

## Chapter 1: Epidemiology of HIV in the Pacific Island Countries and Territories

There have been significant gains globally with regards to the global HIV epidemic. The UNAIDS (2011a) is now reporting a reduction in the number of new HIV cases being reported globally. This general reduction in HIV cases globally is likely due to early diagnosis and the greater availability of antiretroviral drugs. (UNAIDS, 2011a) There are also fewer AIDS-related deaths being reported. In 2010 there were 2.7 million new HIV infections reported globally, down from 21% which was reported at the height of the epidemic in 2007. (UNAIDS, 2011a) The changes in the overall epidemic is likely due to the changes in behavior among young people and members of other key affected populations including sex workers(SW), men who have sex with men(MSM) and injecting drug users(IDU).

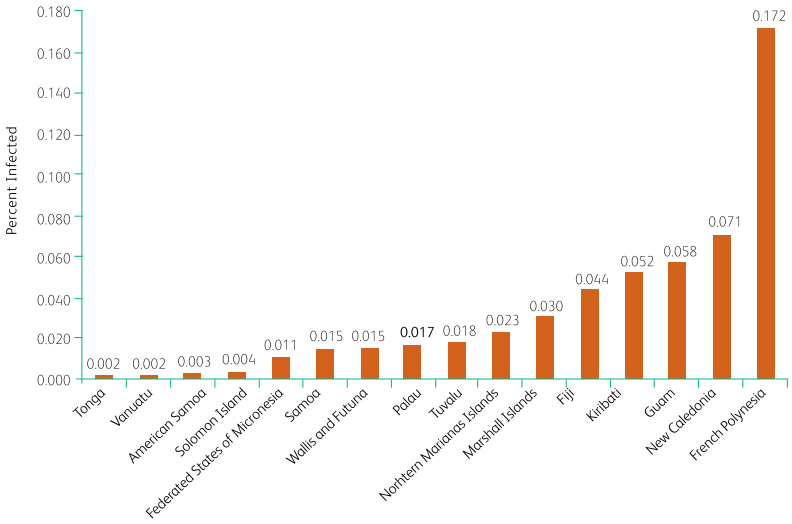
UNAIDS (2011a) reported that at the end of 2010, an estimated 34 million (31.6-35.2 million) people were living with HIV globally, an increase of 17% from 2001, indication of the success of Anti-Retroviral Therapy (ART) programmes in-country resulting in fewer AIDS-related deaths. In 2010 Sub-Saharan Africa, where 70% of the global HIV cases are reported 16% fewer HIV cases compared to the rates of 2001 being 1.9 million new HIV cases. (UNAIDS, 2011b) Southeast-Asia reported 270,000 new HIV cases in 2010 a reduction of 40% compared to 1996. Steady case reports of new HIV infections were reported by UNAIDS (2011b) for the Northern American and Western/Central Europe regions as of 2010. The regions of the Middle East, Northern Africa, Eastern Europe and Central Asia on the other hand according to the UNAIDS (2011b) report showed increasing HIV epidemics in 2010 compared to previous years.

Globally HIV transmission continues to occur following unprotected heterosexual sexual intercourse, although in some regions unprotected sex between men who have sex with men (MSM) continues to drive both HIV and STI epidemics as a sub-population group. As the global data improves it is becoming increasingly evident of the rates of HIV transmission following intravenous drug use. Globally parent to child transmission of HIV is on a steady decline however new borns continue to be born with HIV infections. These births are alarming particularly in this day of improved access to treat, care and support programmes. (UNAIDS, 2011b)

### HIV Epidemiology for the Pacific region

The Pacific remains a region which continues to report low HIV prevalence which was reported by the Secretariat of the Pacific Community (SPC) in a recently released epidemic update for the region. Since 1984 the Pacific has reported 1,609 cases of HIV with the vast majority being from Fiji, Guam, French Polynesia and New Caledonia. Excluding PNG, it reports that the Pacific continues to have a very low prevalence rate with 5 of the 21 countries continuing to report no people living with HIV (Cook Islands, Pitcairn islands, Nauru, Niue and Tokelau). The SPC (2012) update reported that for 15-49 year olds in the remaining 16 countries report prevalence's ranging from a low of 0.002% to a high of 0.172% (noted in graph 1 below)

Graph 1.1: Estimated prevalence (%) among those 15-49 by PICT



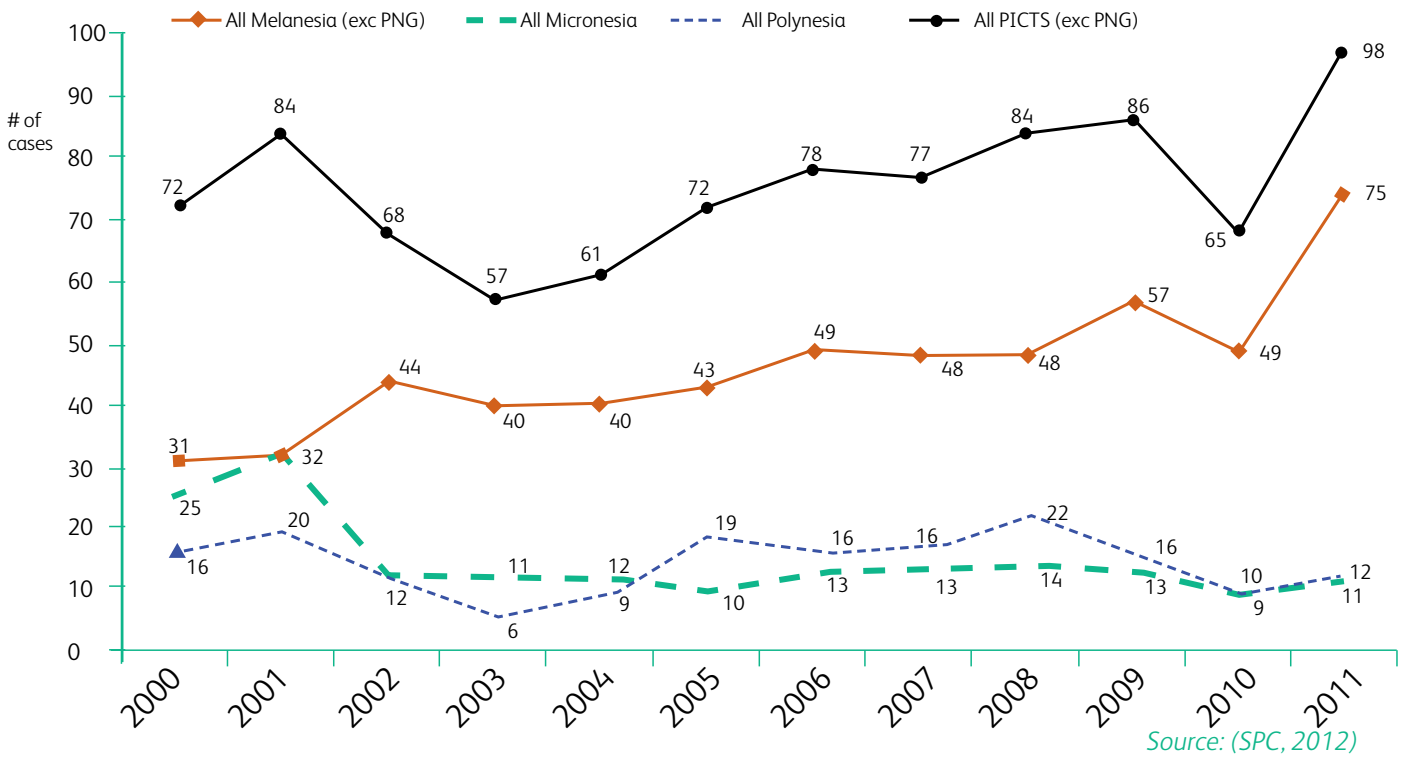

*Source: (SPC, 2012)*

Sub-regionally it has been noted that Melanesia has over the years reported an upward trend in the diagnosis of HIV infections as noted in graph 1.2. Reporting on average, 44 new cases yearly from 2001-2010. With the exception of 2011 during which the sub-region reported 75 new cases. Fiji reported a greater number of HIV infections compared to previous years. For the subregions of Micronesia (7 countries) and Polynesia (10 countries) there has been on average 13 to 15 new HIV cases per year respectively. Apart from the high rates of HIV diagnosed very early on in the epidemic, in both these sub-regions, there has been a levelling out of the HIV epidemics in both sub-regions.

The primary mode of transmission of HIV in the Pacific remains unprotected sexual intercourse with over half of all HIV transmissions attributed to unprotected sexual intercourse. A quarter or 27% of those infected with HIV acquired their HIV infections through unprotected sexual intercourse with men who have sex with men. Intravenous drug use accounted for 5% of all modes of HIV transmission reported in the Pacific. (SPC, 2012)

Overall, the Pacific reports low prevalence of HIV infection compared to other regions globally. There is however increasing evidence of poor sexual behaviour including poor or inconsistent condom use, multiple sexual partners, highly mobile populations, overlapping of sexual networks and high rates of STIs. These situations are known to drive HIV epidemics and it is imperative that the Pacific countries address these issues.

Graph 1.2: Incident of HIV cases in 12 PICTs




*Source: (SPC, 2012)*

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Secretariat of the Pacific Community (SPC), 2012, Epidemiological update: Pacific Island Countries and Territories, SPC, Noumea.

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Joint United Nations Program on HIV/AIDS (UNAIDS), 2011b, Global HIV/AIDS response epidemic update and health sector progress towards Universal Access: 2011 Progress Report.

# Chapter 2: Basic Virology and Natural History

The Human immunodeficiency virus was first isolated in 1983 by researchers Luc Montagnier and Francoise Barre-Sinoussi at the Institute Pasteur in Paris. In 1984, HIV was fully characterized in Washington at National Cancer Institute Researcher by Robert Gallo and Jay Levi in San Francisco. (Hoy et al, 2006)

This chapter provides a brief description on the human immunodeficiency virus that causes the acquired immunodeficiency syndrome, its life cycle, its effect to the immune system and the pathogenesis of HIV infection.

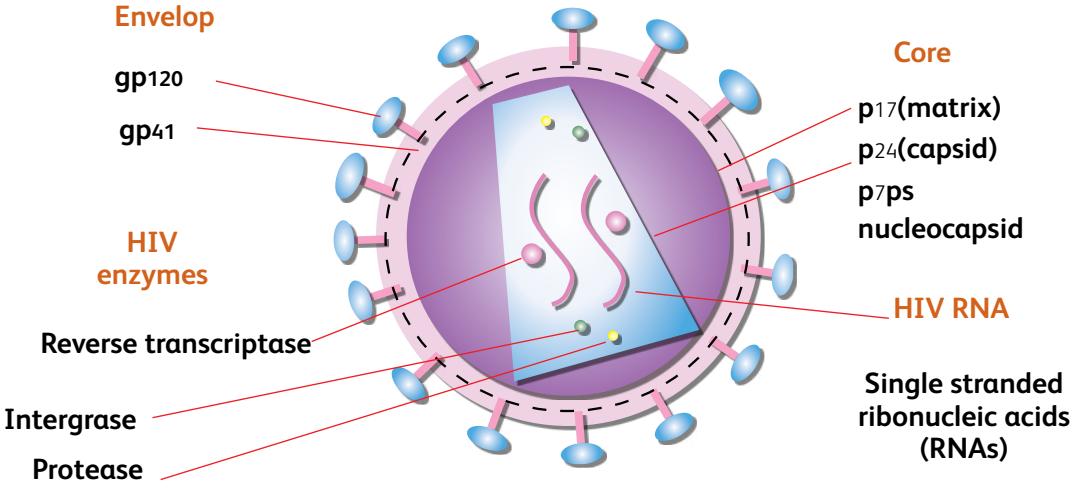
OSSHHM recommends that every clinician should have this basic knowledge on HIV virology in order to fully understand the full spectrum of the disease including the principles behind antiretroviral treatment.

## 2.1 HIV structure and organization

The human immunodeficiency virus (HIV) is a single stranded RNA virus belonging to the genus Lentivirus, in the family Retroviridae. (Maclure et al, 1989) The mature HIV virions have spherical morphology of 100 – 120 nm in diameter and consist of a lipid bilayer membrane that surrounds the viral envelope. (Sierra et al, 2005) Projecting from the viral envelope are around 72 little spikes, which are formed from the proteins gp120, the outer envelope protein and gp41, the transmembrane protein that anchors the glycoprotein complex to the surface of the virion. Just below the viral envelope is a layer called the matrix, which is made from the protein p17. (Hoy et al, 2006)

The capsid (the viral core) is made from the protein p24. Inside the core are three enzymes required for HIV replication called reverse transcriptase, integrase and protease. The HIV's genetic material which consists of two identical strands of RNA is also held within the capsid.

Figure 2.1 The HIV Structure




*Source:( http://www.avert.org/hiv-virus.htm)*

## 2.2 HIV Lifecycle

HIV can only replicate (make new copies of itself) inside human cells. The steps in HIV replication are as follows:

### 1. HIV Fusion (binding, attachment) and entry

The process of infecting the host cell typically begins when HIV particle bumps into a cell that carries on its surface a special protein called CD4 and binds to a CD4 receptor and one of two co-receptor proteins – CCR5 (CC chemokine receptor 5) or CXCR4 ( CXC chemokine receptor 4) on the surface of a CD4+ T- lymphocyte.

The spikes (gp120) on the surface of HIV stick to the CD4 receptor and the co-receptor, causing a conformational change in gp41allowing the viral envelope to fuse with the cell membrane. This facilitates entry of HIV into the cytoplasm of the cell. The contents of the HIV particle are then released into the cell, leaving the envelope behind (step 3 in Figure 2.2).

### 2. Revere transcription.

Upon entry into the new host cell, this HIV RNA genome (where genetic information of HIV is contained) is reverse transcribed into single-stranded DNA that is then further transcribed to double-stranded DNA for integration into the host-cell genome. These steps are performed by the viral enzyme reverse transcriptase.

### 3. Integration.

The newly formed double-stranded HIV genome enters the host cell's nucleus and is randomly integrated into the host cell genome by the enzyme viral integrase to form the provirus. The provirus may remain inactive for several years, producing few or no new copies of HIV.

### 4. Transcription.

When the host cell receives a signal to become active, the provirus uses a host enzyme called RNA polymerase to create copies of the HIV genomic material, as well as shorter strands of RNA called messenger RNA (mRNA). The mRNA is used as a blueprint to make long chains of HIV proteins.

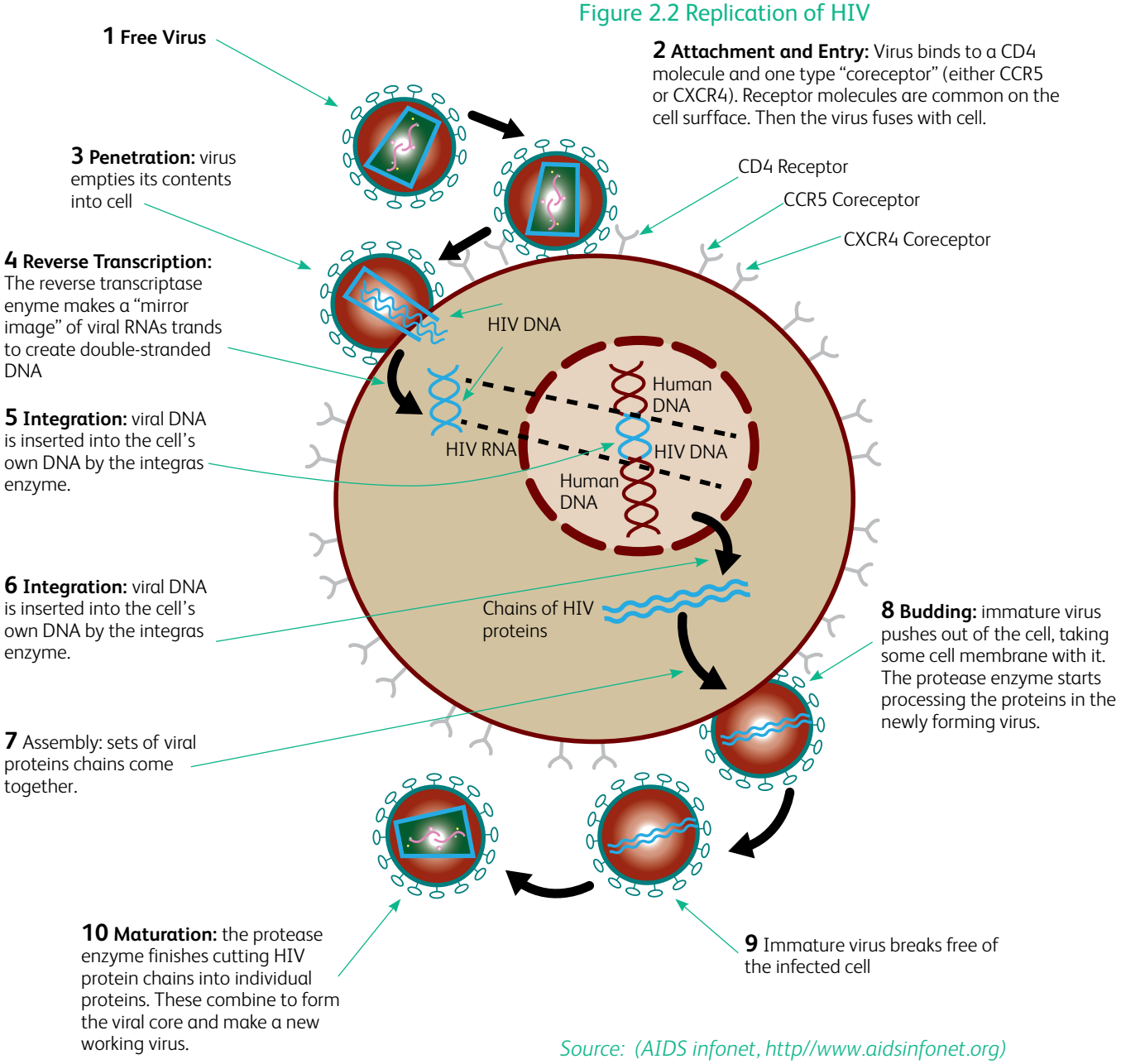
### 5. Assembly:

The assembly of HIV's RNA and proteins into virions is orchestrated by an HIV enzyme called protease which cuts the long chains of HIV proteins into smaller individual proteins. As the smaller HIV proteins come together with copies of HIV's RNA genetic material, a new virus particle is assembled.

### 6. Budding:

The newly assembled virus pushes out from the host cell during the process called budding where the new virus steals part of the cell's outer envelope. This envelope, which acts as a covering, is studded with protein/sugar combinations called HIV glycoproteins. These HIV glycoproteins are necessary for the virus to bind to CD4 and co- receptors. The new copies of HIV can now move on to infect other cells.

Figure 2.2 Replication of HIV




*Source: (AIDS infonet, http//www.aidsinfonet.org)*

## 2.3 HIV and the Immune System

The Human Immune System

The white blood cells (leukocytes) are the cells of the immune system and originate from the bone marrow. These white blood cells are divided into four main types:

- Lymphocytes
- Phagocytes
- Granulocytes
- Dendritic cells

### Lymphocytes

Lymphocytes originate from the bone marrow but migrate to parts of the lymphatic system such as the lymph nodes, spleen and thymus where they mature. There are three main classes of lymphocytes: T-cells, B-cells and NK cells (natural killer).

### T-cells (T- lymphocytes)

T cells are responsible for cell- mediated immunity. Unlike antibodies produced by B cells, T cells require other cells to activate (mediate) their response. They work not so much by "directly" attacking invaders but by attacking cells that have been infected by the virus and cancer. (Barron, 2011)

There are two primary types of T-cells: CD4+ T cells (T cell that carries cluster of differentiation 4 proteins on its surface) and CD8+ T cells (carrying an 8 protein). CD4+ T cells are known as helper T-cells because they don't attack invaders themselves, but rather identify foreign invaders and activate B-cells, other T-cells, natural killer (NK) cells and macrophages to attack the invader.

CD8+ T cells on the other hand are known as cytotoxic T-cells (NK – natural killer cells). They are activated and transformed by CD4+ T cells into NK cells. Once activated and transformed by the CD4+ T cell, the CD8+T cell undergoes further growth and differentiation when stimulated by interleukin-2 released by the same CD4+ T cell that locked onto it and activated it. This exponentially increases the number of NK cells (Immune System - in more detail, 2012).

### B -cells (B- lymphocytes)

B – cells produce antibodies and are responsible for humoral (antibody – mediated immunity). They are produced from the bone marrow, but unlike the T cells that are processed in the lymphoid tissue; they are directly released into the bloodstream.

### Phagocytes

Phagocytes are large white blood cells that eat and digest invading pathogens, primarily through protease enzyme activity. There are several kinds of phagocytes: macrophages, neutrophils and monocytes.

### Granulocytes

Granulocytes include neutrophils (which function like phagocytes, but have the granular texture of granulocytes), eosinophils, basophils, and mast cells. They destroy invaders by releasing granules filled with potent chemicals such as histamines and prostaglandins.

### Dendritic Cells

Dendritic cells have long threadlike tentacles that are used to wrap up antigens and expended lymphocytes and carry them to the lymph nodes for removal from the body. Their primary function is to identify antigens, process them, and present them to the T-cells and B-cells to initiate the immune response.

### Invasion of Immune System by HIV

The HIV proteins named gp 120, "recognizes" a protein on helper T-cells named CD4+, and physically associates with it. The CD4+ protein is a normal part of a helper T-cell's membrane. Thus, CD4 is a specific receptor for HIV. This virus however, can also infect other cells which include macrophages and certain other kinds of cells which can engulf substances through a process known as phagocytosis. As a consequence of the interaction with CD4 on helper T-cells, HIV specifically infects the very cells necessary to activate both B-cell and cytotoxic T-cell immune responses. Without helper T-cells, the body cannot make antibodies properly, nor can infected cells containing HIV (an intracellular pathogen) be properly eliminated. Consequently, the virus can: multiply, kill the helper T-cell in which it lives, infect adjacent helper T-cells, repeat the cycle, and on and on, until eventually there is a substantial loss of helper T-cells.

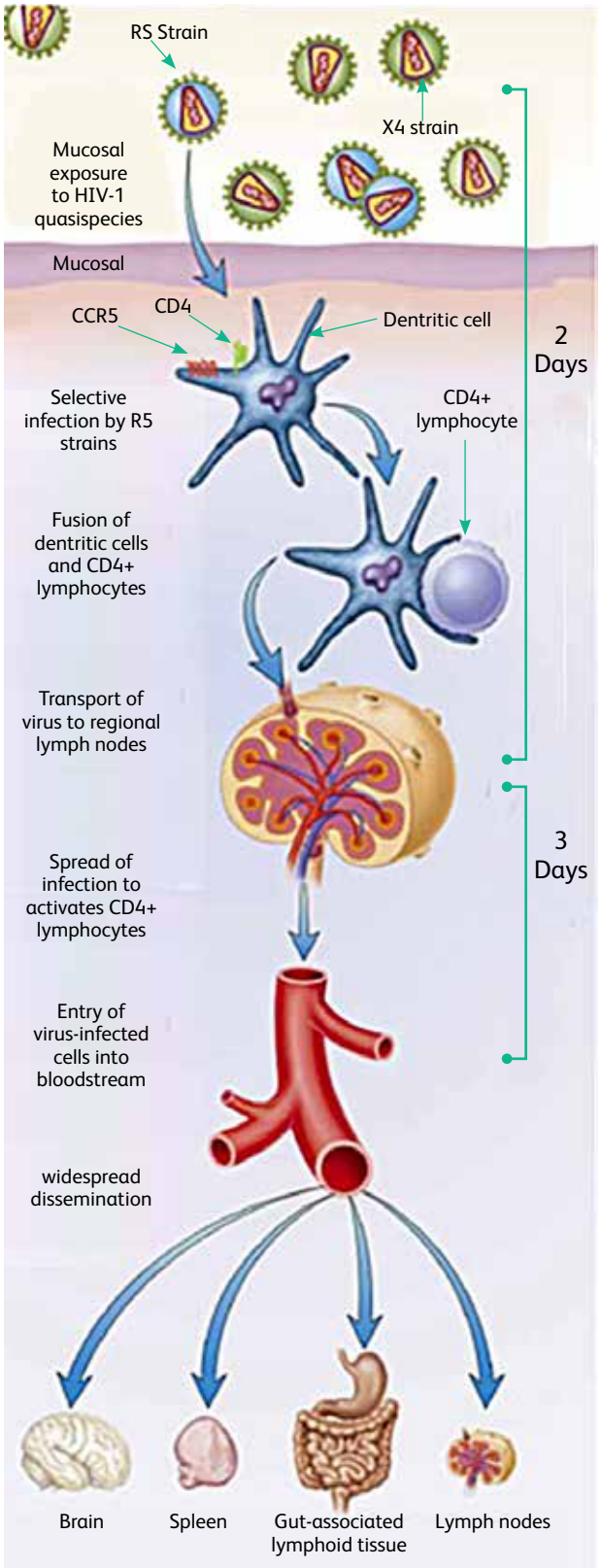
Cells able to be infected by HIV are CD4+ T cells which are killed leading to low CD4 count in patients' blood; monocytes and macrophages unlike CD4 lymphocytes, however, appear to be relatively resistant to the cytopathic effects of HIV infection and may therefore constitute a persistent reservoir of infection (Epstein AG, 2011); and dendritic cells.

## 2.4 HIV Pathogenesis

HIV enters the bloodstream via mucous membranes lining the vagina, rectum and through sexual intercourse or directly into the blood stream during blood transfusion of infected blood and intravenous drug use.

Macrophages and dendritic cells on the surface of mucous membranes bind the virus and shuttle it into the lymph nodes, which contain high concentrations of helper T cells (CD4+ T cells), establishing infection.

Figure 2.3 Pathway of HIV




*Source: Path of HIV (Kahn JO &Walker BD, 1998)*

The viral-envelope protein binds to the CD4 molecule on dendritic cells. Entry into the cells requires the presence of CCR5, a surface chemokine receptor. Dendritic cells, which express the viral coreceptors CD4 and CCR5, are selectively infected by R5 (macrophage-tropic) strains.

Within two days of mucosal exposure, virus can be detected in lymph nodes. Within another three days, it can be cultured from plasma.

The following are the sequence of events after HIV infection:

- Cytotoxic lymphocyte production follows the rise of HIV in the blood.
- HIV specific CD4+ T cells may be especially susceptible to attack and destruction by HIV. HIV binds to CD-SIGN, a glycoprotein expressed on dendritic cells. Migration of HIV bearing activated dendritic cells to helper T cell areas of lymph nodes may specifically infect helper T cells specific for HIV peptides
- Reductions in HIV specific helper T cell numbers may lead to decreased activation and survival of cytotoxic CD8 T cells
- Reduced CD4 T cells may also result in an incomplete activation of CD8 T cells that can remove HIV infected cells, resulting in a decreased ability to destroy virally infected cells
- The rapid loss of memory helper T cells, and the inability to replace these cells leads to increasing immunodeficiency
- The rate of CD4 cell loss is variable and depends on viral and host factors. On average, infected persons lose 40 to 80 CD4 cells/mm3/year. (Mellors et al, 1997)
- High mutation rates of HIV also allow the virus to escape adaptive immune responses

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# SECTION 2 HIV counseling and testing in the Pacific

HIV-related stigma and discrimination are not unique to the Pacific but their effect is particularly strong in the region. It is not uncommon to hear reports of banishment from villages and violence against people who are known, or just believed, to be HIV positive. In addition breaches of confidentiality in health care services have been well reported region-wide. This issue is heightened by the small, close-knit and interrelated nature of many communities.

The Pacific, with the exception of Papua New Guinea, has a low HIV prevalence however the occurrence of sexual risk behavior and practices has resulted in the high rates of specific sexually transmitted infections (STIs) in many countries in the region. If more people in the Pacific region who are concerned about having HIV infection or are vulnerable to it are to access HIV testing, they need more than the availability of testing services. Testing for HIV (and STIs) should be offered by applying the '3 C's' principles which are: confidentiality; counseling; and informed consent. (UNAIDS/WHO, 2004)

Research shows that good counselling helps people to decide to be tested. (OSSHHM, 2008) People requesting or being offered testing for HIV should be taken through the HIV testing process by a health care worker with counseling skills. The input of someone with these skills will ensure that the patient or client can provide appropriate informed, if they decide to be tested. It will also minimise the potential for harm from misunderstanding, discrimination and stigma.

The contents of this chapter is based on the publications of international organisations, including Family Health International, the United Nations Joint Program on AIDS (UNAIDS) and WHO, and on the operational guidelines of national AIDS organizations. They reflect international best practice in relation to HIV test counseling and that they are applied with the Pacific's unique geographic, cultural, economic and epidemiological factors taken into consideration in the context of HIV testing and counseling.

This section of the recommendations is but a summary of the requirements of good counseling and testing for HIV. OSSHHM recommends that readers refer to the HIV/STI counseling and testing policy guidance (FNU, 2012) and for front line health workers (providing counseling to women in the antenatal setting) refer to the OSSHHM VCCT counseling flip chart available also on the OSSHHM website at: www.osshhm.org. Furthermore OSSHHM recommends that Essential Standards for HIV Testing and Counselling Services in the Pacific Island Countries and Territories developed by the Albion Street Centre for SPC be read in line with these recommendations.

## Chapter 3: HIV counseling

### 3.1 Basic HIV counseling principles

#### What is HIV test counseling?

There are several models for HIV test counseling. For the purposes of these recommendations, OSSHHM uses the following definition:

> "HIV test counseling is a confidential process that enables a person(s) to assess their relative risk of acquiring or transmitting HIV. The process also helps people to decide whether to be tested for HIV antibodies, manages their stress responses and provides support when they receive the test results and afterwards." (OSSHHM, 2008)

#### HIV test counseling serves two main purposes:

1. It helps prevent further transmission of HIV (and other STIs). Knowing their HIV status may encourage people who are infected to avoid transmitting the virus to others and can motivate people who are uninfected to remain so. HIV test counselling can prompt people to start to use or increase their use of condoms. It can also help to reduce sexually transmitted infections and increase the use of safer injecting practices amongst injecting drug users.
2. It determines who requires treatment and care. A person must know that they have HIV before they can access HIV care services. These services include general clinical care and antiretroviral therapy, as well as interventions to prevent mother-to-child transmission of HIV.

#### Approaches to HIV test counseling

There are currently two approaches to how HIV testing is being offered to persons presenting to health facilities. The first being Voluntary Confidential Counselling and Testing (VCCT) and Provider Initiated Testing and Counselling (PITC).

VCCT involves an individual voluntarily asking a health worker for a HIV test following which they are provided with pre-test counseling, followed by signed informed

consent. Each person regardless of the outcome of the HIV testing will receive post-test counseling, dependent on the outcomes of the HIV testing.

PITC involves a health care provider routinely offering HIV testing and counseling with the right to 'opt out' to specific population subgroups such as antenatal attendees, STI and Tuberculosis (TB) patients and key population groups (these may vary from population to population) who are accessing health services.

Regardless of the approach that is used all persons must receive full pre- and post-test counseling for HIV. All persons are free to 'opt out' with either approach and they need to be assured that the decline of a HIV test will not affect the patients access to services NOT dependent on knowledge of HIV status.

## Who should conduct HIV test counseling?

OSSHHM recommends that all health workers who provide counseling for HIV testing are trained in basic counseling skills. It is further recognized that while each country may recognize various training models for HIV test counseling, it is important that they abide by the 'Essential Standards for HIV Testing and Counselling Services in the PICTs'. It is also recognized that:

> "…responsibilities and processes for testing and counselling can differ across the Pacific, and even between testing sites, according to human resources available. In some circumstances only doctors are able to request HIV/STI testing and provide results; in others nurse practitioners are able to fulfil this duty. In some places HIV/STI pre and post-test counselling is the responsibility of the requesting health worker, whereas in others specifically trained nurses or counsellors undertake this role, either alone or in conjunction with the health worker requesting the test..." (FNU, 2012)

These standards and processes in-country and at individual testing and treatment sites need to be well documented and that systems are in place to support the delivery of counselling and testing for HIV including other STIs.

## What are the indications for HIV testing?

Testing for HIV was not intended to be considered a routine test for individuals. There are however a number of indications for which a HIV tests may be requested for or offered.

These are summarised in text box 3.1 below.

**Text box 3.1: HIV testing indications**

- unprotected sexual intercourse;
- sharing of injecting equipment;
- being the sexual partner of an HIV positive person;
- being from a country with a high HIV prevalence and with indication of HIV exposure;
- after occupational exposure to HIV;
- pregnancy;
- requesting an HIV test in the absence of clear risk factors;
- diagnosis of a sexually transmissible infection;
- diagnosis of TB; and
- being the sexual partner of anyone with any of the above mentioned indicators.

*(Source: FNU, 2012)*

## Characteristics of HIV test counselling

It is vital that HIV testing and counseling respect basic human rights. International public health organisations recommend that providers:

- ensure an ethical counseling and testing process where the purpose of both the counseling and the test, and their benefits are explained to the person considering testing;
- guarantee the confidentiality of all medical information;
- make certain that testing and any associated counseling is voluntary and provides the person with the right to refuse; and
- address the implications of a positive test result, including its impact on the person's life and the need for access to sustainable treatment and care.

HIV test counseling needs to be client-centered. This means that it must be aimed at achieving effective risk reduction for the client based on their specific needs, strengths and abilities. Counselling for behaviour change needs to be tailored to the person's unique situation and their capacity to deal with stress and trauma.

HIV testing should not be mandatory. Testing without informed consent and confidentiality is a violation of fundamental human rights. In addition, there is no evidence that mandatory testing achieves public health goals.

## Confidentiality

Testing information must only be reported to the person who was tested unless the person clearly says that they want to share information such as a test result with family, a partner or a close friend. Confidentiality is defined as keeping 'private' any information relating to someone. Maintaining a person's privacy by restricting access to personal and confidential information, especially with respect to HIV test results and counseling records, demonstrates sensitivity and respect for their basic rights.

## Breaches of confidentiality

Even if breaches of confidentiality are unintentional, the effect can be serious and immediate for the person in terms of stigma and discrimination. Outside of very limited circumstances,[1] a deliberate breach of confidentiality is unethical and should lead to disciplinary action of the health care worker concerned. Breaches of confidentiality may deter others from accessing counseling and testing if the community comes to believe that a service cannot keep sensitive information private. Text box 3.2 describes a number of examples of how confidentiality may be reached.

**Text box 3.2: Examples of breaches of confidentiality**

- A health centre uses protective gear such as gloves only with people who are HIV positive. Health care staff should adopt the same standard precautions with all patients, irrespective of their HIV status.
- Telephone conversations, written counseling records or medical files are not held privately under lock and key.
- A health care worker tells others, 'Guess who came to the clinic for a test today.' This is breaching the person's right to privacy.
- A health care worker who meets a patient in the community greets and starts talking to them. Workers should wait for the patient to recognise and approach them rather than initiating contact.

*Source: (OSSHHM, 2008)*

## General principles

- Regardless of who initiates the process for counseling and testing, HIV testing should be voluntary.
- The person should have sufficient information, understanding and freedom of choice to be able to give informed consent to testing.
- Health care workers offering the HIV test counseling must ensure that the person understands that there is a real choice as to whether to test or not.
- Appropriate information, counseling and, where required, referral must be provided when the test result is available.
- People considering HIV testing should be encouraged to consider attending and being tested together with their regular sexual partner where appropriate.
- People receiving HIV test results should be encouraged to share the results with people who are close to them and who might be expected to be trustworthy and to provide emotional support.
- People whose test results are positive should receive counseling and referral to care, support and treatment. They should also be encouraged to disclose their results voluntarily to previous and current sexual partners who may themselves benefit from testing.
- People whose test results are negative should receive counseling to assist them to remain uninfected with HIV.
- In low prevalence environments (such as Pacific small island countries and territories), people whose test results are reactive but not yet confirmed should receive intensive counseling and support to enable them to manage in the difficult period when their HIV status is unclear.

[1]. Ethical or legal breaches of confidentiality: Under very limited circumstances, a health care worker or counsellor may be compelled either ethically or legally to breach the confidentiality of a person being counselled. Wherever possible, this breach of confidentiality must be made with the knowledge of that person and only when all other options have been considered or tried. The health care worker or counsellor has a duty to prepare the counselled person for such a breach. Generally confidentiality may only be breached by the counsellor when the person being counselled presents a danger either to themselves or another person(s). For example, a danger to another person might exist if a person communicates in counselling that they cannot disclose their HIV status to a specific sexual partner and that they will not use condoms to protect their partner. In this situation, ideally another health care worker would disclose the necessary information to the person's partner. Another example is when a counsellor or health care worker has strong reason to believe, or the person being counselled indicates, that the counselled person has a clear plan to harm or kill themselves or others.

In other very rare circumstances, a court may compel a counsellor or health care worker to provide the medical and counselling records or other details of a person who is being counselled, or who has previously been counselled. Public health and criminal law regarding HIV varies throughout the Pacific Island region, and so the legal limits to confidentiality may differ among countries and territories.

- HIV test results and counseling records should be treated confidentially. Only those health care workers with a direct role in the management of patients should have access to this information.

## Requirements for HIV test counseling

In order to be effective and avoid the potential for harm, a number of essential elements need to be in place wherever HIV test counseling is offered.

### Personnel

Health care workers need training in counseling skills. Increasingly, HIV test counseling is performed by medical, nursing, midwifery or laboratory staff. This approach helps to improve access to testing and facilitates referral for prevention, treatment, care, counseling and support. All health care workers providing HIV test counseling need knowledge of, and skills in:

- providing general information about HIV and how it is transmitted;
- providing pre-test and post-test counseling;
- addressing difficult issues (such as managing suicidal tendencies, explaining the meaning of reactive but as yet unconfirmed results, fears about death and dying, safe disclosure of results to partners);
- HIV prevention and behaviour change; and
- referral mechanisms.

Delivering high-quality HIV test counseling also requires proper personnel management. Such management includes skillfully and regularly supervising staff, and identifying needs for further capacity development.

### Infrastructure

The minimal physical requirements for HIV test counseling include a consulting space that ensures privacy (that is, where others cannot see or hear the person providing the counseling or the person being counselled).

### Quality assurance

Mechanisms should be established to ensure that ethical and technical standards are upheld for both counseling and testing services.

### Linkages and referrals

Referral system or linkages should be established among HIV test counseling sites, health facilities and community organisations to enable delivery of comprehensive prevention, care, treatment and support services. The existence of these referral system or linkages will also help ensure that everyone who is HIV tested (irrespective of the test result) has access to ongoing services, such as psycho- social support and legal assistance.

## 3.2 Essentials of Pre-test counseling

Pre-test counseling helps a person decide whether they want to have an HIV test and, if they decide to be tested, to prepare them for the result. The person providing the counseling needs to balance between providing information to the counselled person and jointly assessing risk with them and responding to their emotional needs. This session explains the implications of knowing that you are or are not infected with HIV.

### Pre-test counseling aims to:

- ensure that any decision to take the test is fully informed and voluntary;
- prepare the person for any type of result, whether negative, confirmed positive, or reactive but unconfirmed;
- provide risk reduction information and advice on strategies, irrespective of whether testing proceeds; and
- provide options for the prevention of mother-to-child transmission of HIV where this is relevant.

### Pre-test counseling checklist:

1. Establish rapport by extending a warm welcome to the person considering testing
2. Provide emotional support and explain about confidentiality (and its limits)
3. Explore the person's reasons for seeking a test and their understanding about HIV and its transmission
4. Correct any misconceptions
5. Determine the person's marital or relationship status and their social supports
6. Assist the person to assess their personal risk of HIV infection and to make a risk reduction plan, including safer sex practices. Provide condoms and ensure that the person knows how to use them, using a practical demonstration on a 'penis substitute', such as a banana, where required. This information should be provided to both males and females considering testing.
7. Explore what the person knows about the test and provide information about the testing procedure
8. Explain clearly what is meant by 'HIV positive', 'HIV negative' and 'indeterminate' results– and the implications of each

9. Where confirmatory testing is not available on-island, explain that a reactive initial HIV test may represent a true or false positive (see 'HIV screening tests' in chapter 4) and emphasise that only after confirmatory testing will a clear result be known
10. Explain what is meant by the 'window period'.
11. Explain when the results will be ready and how these will be delivered during a post-test counseling session to allow the results to be discussed. Never agree to deliver results over the phone
12. Remind the person that the results are confidential and explain how their confidentiality is protected
13. If relevant, inform the person of the cost of the test
14. Allow the person to think through the issues, ask questions and get clarification.
15. Discuss with the person how they imagine they might react and how they might cope depending on the result. Discuss how others they know might react (partner, wife, husband, family, village community)
16. Explore risk of depression, suicide, homicide, and other violent or adverse outcomes.
17. Assist the person to come to their own decision about taking the test, restating that the process is entirely voluntary
18. If the person decides to take the test, obtain signed written consent where required by law, or clearly document that you have obtained informed verbal consent
19. If the person decides not to take the test, help to summarise their risk reduction plan, and tell them that they are welcome to come back to discuss anything further or to be tested at a later time
20. Provide information about referral services appropriate for the person's needs identified during the session (such as contraception, treatment for other STIs, help with responding to domestic violence, support for drug users and support for people who report having been raped)
21. Recommend that the person, if possible, plan for some 'quiet time' immediately after their post-test results appointment – such as taking the rest of the day off work or getting someone else to look after the children
22. Discuss follow-up arrangement for further post-test counseling

## 3.3 Essentials of post-test counseling

### Post-test counseling

The form of the post-test counseling session depends on what the test result is. The foundation of good post-test counseling is laid during the pre-test session. If the pre-test counseling is done well, the counsellor will already have a good relationship with the person who has been tested. People attending for HIV test results are likely to be anxious, and those receiving a positive HIV antibody result will usually be distressed. It is therefore desirable that the counsellor who provided pre-test counseling also provides post-test counseling.

Post-test counseling aims are to:

- communicate the test result promptly and clearly;
- assist the person to understand and cope with the HIV test results;
- provide the person with any further information they require;
- help the person make immediate and short-term plans;
- help the person decide what to do about disclosing their test results to partner(s) and others;
- help the person to reduce their future risk of acquiring HIV or take action to prevent infection of others;
- help the person to access the immediate and ongoing medical, emotional and social care and support they need; and
- establish links the client with organisations serving people living with HIV, if the person wants this.

### Post-test counseling checklist for when a result is HIV negative

1. Cross-check all results with the person's file and blood samples
2. Discuss the meaning of the result – including the need to repeat the test if the person may have been exposed to HIV in the 3 months before testing
3. Discuss a personal risk reduction plan (as in text box 3.3) and information to prevent future infection. This discussion should cover safe sex practices and should build the person's skills in using condoms and in negotiating their use
4. Discuss follow-up plan options and resources for support, and check for other referral needs (see text box 3.3)
5. Address issues of 'HIV-phobia', hypochondriasis or anxiety disorder and arrange for referral if these are significant

### Text Box 3.3: Preventing future risk-taking for people who test HIV negative

A primary aim of HIV test counseling is to assist people who are HIV negative to remain this way. However, some recent international studies suggest that testing negative for HIV may potentially foster a personal sense of invincibility and cause some people to increase rather than decrease their sexual risk-taking.

It is not uncommon for people who have had a 'near miss' or 'lucky escape' following risk-taking to misunderstand this outcome in a personal way. They begin to believe that they are 'special', are in some way 'blessed' or 'protected against' or even 'immune to' HIV infection.

It is therefore vital that in a post-test counseling session where the result is HIV negative, health care workers routinely discuss this phenomenon and explore the way that the person interprets the meaning of their own result. It may be useful to ask the HIV negative person to describe in their own words what they now understand about their future risk for HIV (or other STIs) and to discuss the behaviours required to remain HIV negative.

Depending on the result of this assessment, it may be helpful to refer or invite the person to return for further personalised primary prevention counseling.

*Source: (OSSHHM, 2008)*

## Post-test counseling checklist for when a result is not clear

1. Discuss the meaning of the result and explain the procedure that will be required to clarify the person's true HIV status
2. Help the person to cope with and adjust to the intervening period of uncertainty and anxiety
3. Provide the person with any information they require
4. Encourage the person to adopt safer sex practices or to abstain from sex until their HIV status is clarified
5. Reassure the person that their records and results are confidential
6. Post-test counseling checklist for when a result is confirmed to be positive
7. Cross-check all results with the person's file
8. Be calm and be aware of non-verbal forms of communication when calling the person to the counseling room

## Post-test counseling checklist for when a result is confirmed to be positive

1. Cross-check all results with the person's file
2. Be calm and be aware of non-verbal forms of communication when calling the person to the counseling room
3. Briefly prepare the person for the result
4. Be prompt and direct in providing the result (see text box 3.4)
5. After providing the result, give the person the paper copy of the result to view/hold if possible
6. Deal with the immediate emotional reactions and provide warm, emotional support.
7. Provide reassurance about the person's immediate safety
8. Discuss health, reproductive and treatment issues or schedule another session to discuss these issues
9. If the person does not have an AIDS-defining illness, remind the person of the difference between HIV and AIDS. Also inform them that people with HIV can remain healthy for a long time
10. Discuss the personal, family and social implications of the result. Help the person to identify the main concerns at this stage (such as anxiety, depression, and disclosure of test result to their main partner or family, and implications of their disclosure, such as the potential for discrimination, rejection or violence)
11. Make a short plan for follow-up counseling and medical referral
12. Reiterate the person's right to privacy and confidentiality with respect to medical information
13. Help the person to strengthen their emotional resources

**Text Box 3.4: Important things to do when delivering a positive HIV result**

- Invite the person to sit down and deliver the news of the result in a quiet, emotionally supportive and private environment
- Give a clear explanation of the result promptly: An HIV positive test result means that you have HIV infection
- Allow the person time to absorb the result
- Provide silence
- Check what the person understands by the result
- Gently enquire about the meaning of the result for the person: I'm wondering what you are thinking or feeling right now
- Respond to any emotional reactions, such as anger, crying, silence

Don't

- Blame the person for the result
- Make judgmental statements about their prior actions or negative comments about their reaction to the results

*Source: (OSSHHM, 2008)*

## Some common emotional responses to HIV-positive test results

- Crying. If the person starts to cry, it is important to let them do so. Give the person 'room' to cry, offer tissues and give them 'permission' to express their emotions by saying something like, 'It is normal to cry in these circumstances'. After some time, comment on the process by saying something like, 'This must be very difficult for you, would you like to talk about it?' or 'Would you like to tell me what thoughts are making you cry?'
- Anger. The person might start swearing or have outbursts of anger. If this occurs, do not panic but stay calm and give the person 'room' to express their feelings. Acknowledge that the feelings they are experiencing are normal and encourage the person to talk about what is making them angry.
- No response. This may be due to shock, denial, or a sense of doom or helplessness.
- Check that the person has 'heard' and understands the result. Be alert for suicidal or homicidal thoughts.
- Denial. This may be verbal or non-verbal. It is important to acknowledge that it can be difficult to accept information like a positive HIV result. Allow the person to talk about what they are thinking and feeling.

## Safety considerations for the person providing the test counseling

Any stage of HIV test counseling can be stressful and the process may provoke strong emotions for the person being counselled, including anxiety, guilt or shame, panic, a sense of hopelessness or doom, or anger. Also, for some people, the stress of HIV testing may worsen an underlying mental illness. In all of these circumstances the reaction to test counseling and the behaviour of the person testing may become 'out of character' and difficult to predict.

Many health care workers will be focused on providing a quiet, private and comfortable environment for the person undertaking the test counseling process. However, at all stages of testing it is good practice for the health care worker to have considered their safety as well.

## The following are some simple tactics for increasing counselor safety:

1. Plan the layout of the counseling room carefully. Always place the 'counselor's chair' closest to the door or exit, while at the same time not 'cornering' or blocking easy exit for the person being counselled
2. Avoid allowing the person being counselled to stand or sit between the counsellor and the door during a session. At the start of the session, always guide them to their seat and invite them to sit there
3. Avoid providing test results or undertaking other counseling when there is no one else in the building
4. Have a service emergency plan in place to deal with violent or distraught people. Practice the emergency plan with colleagues
5. Establish a relationship with local mental health services (where they exist) and the local police. Ensure that they understand that a rapid response may be required

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# Chapter 4: HIV testing in the Pacific

Being diagnosed with HIV infection is a very significant life event. Accordingly, it is important to take great care that the diagnosis is made reliably. Prior to 2010, technical and geographical constraints in many Pacific Island countries made it difficult to obtain definitive confirmation of the diagnosis of HIV infection quickly. Screening tests for HIV are antibody tests, which are designed to detect the presence of antibodies for HIV. Samples which were found to be reactive were sent off shore for confirmation at high level laboratories. This testing strategy led to serious delays in testing response times, was expensive and caused great confusion among health workers in the Pacific.

The regional technical agencies (WHO, CDC, SPC, OSSHHM, UNAIDS, UNFPA, UNICEF, PPTC, PIHOA and Life foundation) formed a HIV task force with the aim of establishing in-country confirmatory testing for HIV. The National Reference Laboratory (NRL) in Melbourne, Australia was tasked with a laboratory based validation of a rapid test based algorithm for HIV, using specimens from the Pacific. The testing algorithm was recommended and communicated to the various Ministries of Health with a number of countries now implementing the testing algorithm. This chapter focuses on the basics of HIV testing as they relate to the tests that are in use in the Pacific. OSSHHM recommends that the reader refer to the national level laboratory for advice on the testing strategy used in-country.

## 4.1 Basic principles of HIV testing

### HIV antibody tests

Initial testing for HIV infection usually uses techniques that identify the presence of antibodies to HIV proteins in the blood (or occasionally other body fluids) of people being tested.

All pathological tests have to balance sensitivity (the ability to correctly identify a condition when it is present) against specificity (the ability to indicate that a condition is present only when it actually is, and not in a range of other circumstances that may cause a test to be reactive). Because of this balance, there are five possible outcomes when any screening test for HIV antibodies is undertaken:

1. True positive – the test is reactive (it indicates that HIV antibody is present) and the person from whom the specimen was taken is actually infected with HIV
2. False positive – the test is reactive but the person from whom the specimen was taken is not actually infected with HIV
3. Inconclusive – the test is unable to decide whether HIV antibody is present or not
4. True negative – the test is non-reactive (it indicates that HIV antibody is not present) and the person from whom the specimen was taken is not actually infected with HIV
5. False negative – the test is non-reactive but the person from whom the specimen was taken is actually infected with HIV

Failing to identify that a person has HIV could have serious consequences. For this reason most pathological tests for HIV antibody are 'calibrated' so that they have a high sensitivity. This means that, provided that the test is properly conducted, that the test kit has not expired and that it has been correctly stored (and provided that the person being tested is not in the 'window period'); false negative results are very rare for HIV tests.

Following the validation studies, conducted by NRL, the HIV task force now recommends three antibody tests for the purposes of HIV testing and confirmation. Therefore, HIV confirmation can now be done in-country. In many countries these testing algorithms have replaced previous HIV testing strategies, while other countries have included the three tests (and the testing algorithm) into existing testing strategies. Again it is important that the reader consult with the national level laboratory for clarification.

### New HIV antibody tests recommended for the Pacific

The following three antibody tests are now available for a number of countries who use it exclusively to test and confirm HIV infection.

1. Determine HIV 1/2 (Inverness);
2. Uni-Gold (Trinity Biotech); and
3. Insti HIV 1/2 (Biolytical ).

Details of the testing algorithm will be discussed further in the next sub-chapter.

### 'Window period'

As has already been discussed, most HIV antibody tests are 'calibrated' to maximise sensitivity (at the cost of reduced specificity). For this reason, it is very rare for samples from a person with established HIV infection to test falsely negative, provided that the test has been conducted according to manufacturer's instructions, that the test kit has not expired and that it has been stored under appropriate conditions.

The exception to this general statement is where people have only recently been infected with HIV. In this situation, the person's body may not have developed detectable levels of antibody by the time the sample is taken.

If, for example, a person's blood sample is drawn and tested for HIV antibodies two weeks after an unprotected sexual exposure at which they became infected with the virus, the sample would be likely to be non-reactive even though at the time the person is actually infected with HIV. This result is obtained because the new HIV infection is still becoming established in the person's body and the immune system is in the process of developing an antibody response to it.

On average, HIV antibody tests become reactive about three to four weeks after the occasion when a person has been newly infected with HIV. Sometimes, for a range of reasons, this 'window period' is rather longer.

For practical purposes, a non-reactive HIV antibody test done on a sample taken 12 weeks or more after the last occasion on which the person might have been exposed to HIV can be regarded as definitive evidence that the person has not been infected.

If a test has been done for whatever reason on a sample drawn during this 'window period' and found to be non-reactive, it is important to repeat the test more than 12 weeks after the last exposure. If it is negative at this stage, the patient can be counseled that they have not acquired HIV from the exposure incidents concerned.

### HIV antigen testing

HIV tests in the Pacific are in general HIV antibody tests which are only able to make a diagnosis of HIV after the 'window period' in the majority of cases this period is often after 12 weeks from the time of infection. HIV antigen testing, while not widely available in the Pacific, is able to detect the presence of HIV antigens in as little as six weeks after infection (as is the case with DNA PCR for example). Antigen testing is important component of HIV testing for paediatrics which will be discussed in greater detail later on. In some testing modalities it has been possible to couple HIV antigen and antibody tests together. There are a number of available antigentic tests both simple and enhanced. The discussion of those tests however is beyond the scope of these recommendations.

## 4.2 HIV testing algorithm currently recommended

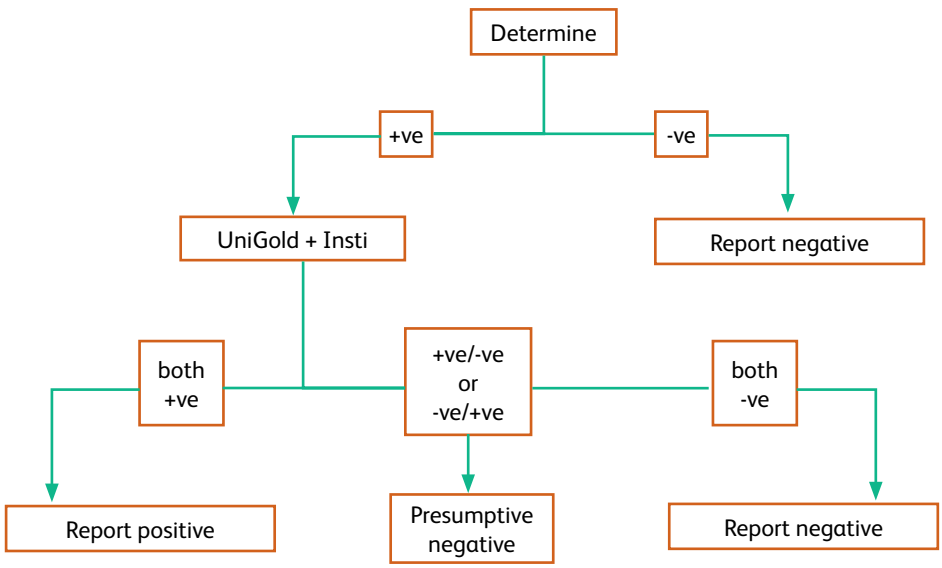
The current HIV testing algorithm that is being implemented in most Pacific Island countries call for the use of three rapid HIV tests used in sequence. These have been validated using blood samples from the Pacific. They are:

1. Determine HIV 1/2 (Inverness);
2. Uni-Gold (Trinity Biotech); and
3. Insti HIV 1/2 (Biolytical).

The validation of the testing algorithm has revealed a sensitivity of 99.24%; specificity 100%; positive predictive value of 100% and negative predictive value of 99.82%. This makes the current algorithm highly reliable particularly in our low prevalence settings of the Pacific. There must be no substitution of tests and the sequence in which the tests are conducted cannot change. In this stage, there are strict quality control measures in place with all positive, presumptive negative and 5-10% of negative tests sent to NRL for further validation. There also internal and external quality control measures in place within and between laboratories.

The sequence and response to results of each level of the testing sequence is noted in the flow chart below.

Figure 4.1: HIV testing algorithm for the Pacific




*Adapted from (SPC, 2012)*

The recommendations for responding to the outcomes of the tests are noted in the table below.

Table 4.1: HIV testing algorithm result interpretation

| Test results | | | Report | Comment |
|---|---|---|---|---|
| Determine | Unigold | Insti | | |
| - | TNR* | TNR | Anti-HIV Negative | HIV antibody not detected |
| + | - | - | Anti-HIV Negative | HIV antibody not present, false positive screen. Refer to NRL for quality assurance |
| + | + | - | Presumptive Anti-HIV negative | Most likely HIV negative. There is a small possibility that these may indicate early HIV infection. Refer to NRL for quality assurance and confirmatory testing. It is strongly recommended that another sample be drawn in 4-6 weeks for testing to confirm these results. |
| + | - | + | | |
| + | + | + | Anti-HIV Positive | Reactivity in HIV tests indicative of HIV infection. Refer to NRL for quality assurance purposes. Should the NRL result differ a second sample should be drawn as soon as possible for further testing at NRL. |

*TNR=Testing Not Required*

Using the current algorithm persons receiving HIV testing can be given their HIV results within at least a week of blood collection, although, technically this algorithm can be completed within 30 minutes of blood collection. It is however not practical in the current clinic/laboratory set up.

## 4.3 Paediatric HIV testing

Without intervention vertical HIV transmission can be as high as 40% however effective prevention of parent to child transmission of HIV programmes are able to reduce this significantly. This will be discussed in a later part of these recommendations. Once a child is born to a mother who is known to be HIV positive the correct and timely diagnosis of the serostatus of the child is essential to:

1. Provide life saving treatment; and
2. To evaluate the effectiveness of the PPTCT programme.

The current testing abilities in most Pacific countries only allow for antibody testing which is problematic for paediatrics as maternal antibodies in the infant remain present for up to 18 months. Infants receiving antibody testing under 18 months of age are likely to return a HIV positive test even if they are actually HIV negative (false positive). Seeing that HIV testing is essential for treatment and monitoring purposes and it's essential to guide your response. Currently there are virological assays available to make a diagnosis of HIV in those infants that are less than 18 months of age.

### When to test for HIV in Paediatrics?

Currently in the Pacific, prior to 18 months of age, it is recommended that babies undergo direct virological tests (also known as virological assays). The WHO (2010) recommends that all new born infants are tested for HIV from 4-6 weeks or earlier thereafter.

After 18 months of age it is recommended that antibody tests be used for the purposes of diagnosis and these should follow the individual country's HIV testing strategy.

For children who are breast feeding and whose HIV status remains unknown the WHO recommends that these infants receive antigentic testing 6 weeks after the complete cessation of breast feeding.

### What tests to use?

DNA-PCR is thought of as being the 'gold standard' for HIV antigenic testing. PCR testing uses amplification of specific sequences of viral genetic material which is then amplified into millions or billions of copies allowing for their detection. (WHO, 2004) There is currently a testing programme being used in the Pacific where infants under 18 months are provided with this PCR testing following a heel prick. In practice blood is placed on blotting paper which is then dried and sent to Australia to undergo HIV antigentic testing. This is known commonly as 'dried blood spot' (DBS). Dried blood spots allow for the 'true' diagnosis of an infant's HIV status to accommodate for early treatment and care. The only caution with the antigenic testing is to take into consideration the possibility of testing in the 'window period' (especially if transmission had taken place after birth) in which case the results returned may be a false negative. The 'window period' for a DNA-PCR test is 6 weeks.

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# SECTION 3 HIV treatment, care and support in the Pacific context

To support clinicians to make sense of the complexity involved in antiretroviral therapy and provide the best advice to their patients, a number of expert bodies have produced guidelines for antiretroviral therapy. (Examples of guidelines come from WHO, the British HIV Association, the European AIDS Clinical Society, the French Ministère de la Santé et des Solidarités and the United States Department of Health and Human Services.) High-level technical analysis of the available evidence is undertaken in the development of these guidelines. In addition, they are updated frequently to take account of the evolving body of science in this area.

Most of the information in this section was adapted from the WHO 2010 guidelines, Antiretroviral therapy for hiv infection in adults and adolescents recommendations for a public health approach.

These guidelines are focused on 'resource-limited settings' and advocate a 'public health approach' to care provision. With this orientation, in place of individualised therapy that takes account of the circumstances of each person starting treatment, there are prescribed, standardised approaches that enable clinicians with limited experience to treat large numbers of people.

Certainly, most Pacific small island countries and territories are 'resource-limited' but none has the very large numbers of people with HIV needing treatment for which this approach to HIV care was developed.

Utilising the approach developed in Australia, key elements of the 2010 WHO guidelines are distilled in this document along with commentary that takes account of other published guidelines and the experience of OSSHHM members. From this approach, these recommendations relevant for Pacific small island countries and territories have been produced.

## Chapter 5: HIV treatment

### 5.1 Initial assessment of a newly diagnosed HIV person

Initial assessment of a person newly diagnosed with HIV should include:

- Detailed medical history
- Physical examination
- Laboratory investigations
- WHO clinical stage of HIV infection
- Functional status
- Family status
- TB status
- Social implications of HIV infection
- Psychological impact of the diagnosis

## Table 5.1 Checklist on initial assessment of a newly diagnosed person with HIV

| | |
|---|---|
| Detailed medical history | • Chief complaints<br>• History of present illness<br>• Past medical history including history of STI infection<br>• Immunization or vaccination history<br>• Family history especially TB infection<br>• Social history which includes smoking, alcohol drinking, drug abuse, etc.<br>• Sexual history – sexual preference, condom use, number of sexual partners<br>• Obstetrics & gynaecological history for women including last menstrual period, family planning use, pap smear, pregnancies and outcomes, HIV infected infant or children<br>• HIV or hepatitis B risk: MSM, bisexual men, sex worker or client of sex worker, blood transfusion, tattooing, sexual assault, unsafe medical procedure, etc.<br>• Current medications if any<br>• History of allergy |
| Physical examination | • Weight, height, BMI (body mass index)<br>• Vital signs: temperature, pulse, respiratory rate, heart rate<br>• Skin<br>• Head, eyes, ears, nose, neck and mouth including ophthalmoscopy and visual acuity<br>• Lymph nodes<br>• Chest and lungs<br>• Heart<br>• Abdomen<br>• Extremities<br>• Genitalia including speculum examination for women<br>• Neurological examination: cranial nerves, reflexes, motor function, etc<br>• Mental status examination<br>Note: Look for signs of jaundice and opportunistic infections |
| Laboratory investigations | • HIV test confirmation<br>• Full blood count and differential count<br>• CD4 count, if available<br>• Viral load , if available<br>• VDRL/RPR test for syphilis<br>• HBsAg<br>• Liver function tests, if required<br>• Renal function tests, if required<br>• Serum glucose and lipids<br>• Pregnancy test for females<br>• Chest X-ray<br>• Urinalysis<br>• Faecalysis and stool culture, if required |

| | |
|---|---|
| WHO Clinical stage of infection | See appendix A for details. |
| Functional status | • Work - Able to work, go to school, do household chores<br>• Amb - Ambulatory but not able to work<br>• Bed - Bedridden |
| Family status | • Pregnancy<br>• Family planning<br>• Sexual activity<br>• Breastfeeding<br>• Child's HIV status |
| Tuberculosis status | • Coughing for > 2 weeks, persistent fever, unexplained weight loss, severe under nutrition, suspicious nodes, night sweats<br>• Sputum examination for acid fast bacilli (AFB) – 3 consecutive tests<br>• Review of chest X-ray<br>• Isoniazid (INH) prophylaxis<br>• Ongoing TB treatment<br>• Tuberculin (Mantoux) testing |
| Social implications of HIV infection | • Level of understanding of HIV infection and its consequences.<br>• Stigma and discrimination<br>• Domestic violence<br>• Job loss, family/social networks, cultural and religious contexts |
| Psychological impact of HIV diagnosis | • Disclosure of HIV status<br>• Suicide risk, depression<br>• Coping mechanisms to stress |
| *Adapted from: (ASHM, 2006)* | |

## 5.2 Principles of antiretroviral therapy

### The Goals of Antiretroviral Therapy are:

- Suppression of HIV replication.
- Reduction in plasma viral load to below undetectable level for a maximum duration.
- Restoration and/or preservation of immunological function by improving, maintaining and preventing the on-going decline of CD4 cells.
- Reduction of HIV-related morbidity, mortality and improvement of quality of life.
- Reduction in HIV transmission, including mother to child transmission. (WHO, 2006)

### Criteria for effective and sustainable Antiretroviral Therapy

Effective provision of combination antiretroviral therapy is an essential component of HIV care. Almost all people living with HIV will need to start on these medications during the course of their infection in order to avoid becoming ill and dying from opportunistic infections.

**Text Box 5.1: The nine criteria for effective and sustainable antiretroviral therapy:**

1. There is a clear commitment to provide antiretroviral therapy in the country or territory from national or territorial decision-makers.
2. A clearly assigned central unit, with an identified leader, responsible for oversight of medical care for people receiving antiretroviral therapy in the country or territory.
3. People living with HIV have been involved in development of care services.
4. An ongoing supply of antiretroviral therapy has been secured and at least six months' supply for the number of people to be treated is available in the country or territory.
5. A technically sound antiretroviral therapy protocol has been developed and is available. (Adoption of these OSSHHM recommendations would fulfill this criterion.)
6. A local partnership exists between public health services, clinical services and community organizations to ensure continuum of care and support for people living with HIV, including support for adherence to treatment.
7. A core multidisciplinary HIUV care team has been identified at each treatment site and has received appropriate training.
8. Diagnostic services are available to perform HIV antibody tests and essential routine tests to monitor for drug toxicity.
9. An adequate patient record system exists to ensure that the progress of people living with HIV being cared for by the core team can be effectively monitored.

*Source: (OSSHHM, 2008)*

Once someone with HIV starts on antiretroviral therapy, current evidence indicates that they will need to take it continuously and very accurately for the rest of their lives.

In 2004 WHO convened a meeting of HIV coordinators from a number of Pacific Island countries. The participants agreed to nine criteria for effective and sustainable antiretroviral therapy provision. OSSHHM endorses these criteria (see text box 5.1 above)[2] and believes that all Pacific Island countries and territories in which there are people living with HIV should strive to achieve them as soon as possible.

[2] OSSHHM has slightly modified the original wording of the criteria to take account of subsequent developments in HIV care. It endorses the criteria as they appear in this document.

Many people with HIV need access to treatment urgently if they are to survive. It is important that the nine criteria for effective and sustainable antiretroviral therapy (see text box 5.1) should not form a barrier to commencing treatment for people with HIV whose lives depend on it. Rather, they should be seen as 'aspirational'criteria that needs to be achieved in parallel with initiating treatment programmes.

OSSHHM recommends that a country or territory that decides to initiate antiretroviral therapy develops and implements a timed, costed and funded plan, as a matter of urgency, to achieve the criteria within a short timeframe from the commencement of treatment.

## 5.3 Basic principles on Antiretroviral Therapy:

The WHO (2006) has summarized the following principles of antiretroviral therapy in the clinical settings:

A continuous high level of replication of HIV takes place from the early stages of infection. At least $10^{10}$ particles are produced and destroyed each day. Despite this high level of viral replication; most patients remain well for many years without any antiretroviral therapy.

Ongoing HIV replication leads to progressive immune system damage resulting in susceptibility to opportunistic infections (OI), malignancies, neurological diseases, wasting and, ultimately, death.

Plasma HIV RNA (Viral load) levels indicate the magnitude of HIV replication and the associated rate of CD4+ T cell destruction, whereas CD4+ T cell counts indicate the extent of HIV induced immune damage.

Measured concentration of viral load is predictive of the subsequent risk of disease progression and death. Regular measurements of CD4+T cell and plasma HIV RNA levels (if possible to perform) are necessary to determine the risk of disease progression in HIV infected patients and to determine when to initiate or modify ART regimens.

Rates of disease progression differ among HIV infected persons. Treatment decisions should be individualized by CD4+ T cell counts and by plasma HIV RNA levels (where it is possible to perform).

Combination antiretroviral therapy to suppress HIV replication to below the levels of detection of sensitive plasma HIV RNA assays limits the potential for selection of antiretroviral resistant HIV variants and delay disease progression. Therefore, maximum achievable suppression of HIV should be a goal of therapy.

The most effective means to establish durable suppression of HIV replication is the simultaneous initiation of a combination of effective anti-HIV drugs with which the patient has not been previously treated

and that are not cross-resistant with ARV drugs with which the patient has been previously treated.

Antiretroviral drugs used in combination therapy regimens should be used according to optimum schedules and dosages. ARV drugs are limited in number and mechanism of action, and cross resistance between specific drugs has been documented. Change in ART increases future therapeutic constraints.

Women should receive optimal antiretroviral therapy regardless of pregnancy status.

The same principles of ART apply to HIV infected children, adolescents and adults, although the treatment of HIV infected children involves special considerations.

HIV infected persons, even those whose viral loads are below detectable limit should be considered infectious. Therefore, they should be counseled to avoid sexual and drug use behaviours that are associated with either transmission or acquisition of HIV and other infectious pathogens.

## Initiating a person on antiretroviral therapy

Evidence is now emerging to suggest that HIV causes significant and probably irreparable damage to the immune systems of people who acquire it within weeks of first infection. At a clinical level, however, these effects are subtle, meaning that many people in the first few years of their HIV infection remain well and have few symptoms.

Within a few months of infection, a near-equilibrium is usually achieved where immune cells are replaced almost as quickly as they are damaged and virus is destroyed by the body almost as quickly as it replicates.

## The CD4 T-cell count

Measurement of the number or proportion of lymphocytes in the person's blood that carry the 'CD4' marker (known as the 'CD4 count' or simply 'T cell count') has proven to be a useful measure of the degree of immune damage that has occurred. It is also a powerful predictor of whether the person will develop a severe complication in the succeeding few months.

## Use of CD4 count for initial assessment

Where it is available, this test provides an excellent tool to guide advice on when it is appropriate to commence antiretroviral therapy. CD4 counting is already used in many Pacific island countries and territories and the advent of low-cost technologies means that it will soon be available in all treatment centres in the region.

Experience in other parts of the world has shown that while CD4 counting is very useful in informing decisions about when to recommend antiretroviral therapy, it is not essential. OSSHHM recommends CD4 count testing is undertaken when a person is first assessed. Where CD4 count testing is not available, lives can be saved by initiating antiretroviral therapy on the basis of clinical staging alone.

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*"OSSHHM recommends CD4 count testing is undertaken when a person is first assessed. Where CD4 count testing is not available, lives can be saved by initiating antiretroviral therapy on the basis of clinical staging alone."*

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The WHO 2010 guidelines advocate that antiretroviral therapy should be recommended in relation to CD4 lymphocyte count according to the scheme in Table 5.2 below. In the context of the Pacific Islands, where fewer people are in need of antiretroviral therapy, OSSHHM recommends a slightly less conservative approach to the recommendation of antiretroviral therapy based on CD4 count.

## Use of CD4 Count for Monitoring Therapeutic Response

OSSHHM recommends that CD4 results be recorded on patient monitoring card so that the approximate slope of their decline becomes apparent.

An adequate CD4 response for most patients on therapy is defined as an increase in CD4 count in the range of 50–150 cells/mm$^3$ per year, generally with an accelerated response in the first 3 months. Subsequent increases in patients with good virologic control show an average increase of approximately 50–100 cells/mm$^3$ per year for the subsequent years until a steady state level is reached. Patients who initiate therapy with a low CD4 count or at an older age may have a blunted increase in their count despite virologic suppression.

## Frequency of CD4 Count Monitoring

In general, CD4 counts should be monitored every 3 months. The goals of CD4 count monitoring are:

- to determine when to start ART in untreated patients;
- to assess immunologic response to ART; and
- to assess the need for initiation or discontinuation of prophylaxis for opportunistic infections. (DHHS, 2012)

## Clinical Staging

The WHO guidelines include a detailed, recently revised clinical staging system to which readers are referred (see Appendix A for the summary.) Even when CD4 counting is available, the classification system is useful.

Table 5.2 Recommendations for initiating ART in adults and adolescents in accordance with clinical stages and the availability of immunological markers

| Target Population | Clinical Condition | Recommendation |
|---|---|---|
| Asymptomatic individuals (including pregnant women) | WHO clinical stage 1 | Treat if CD4 count is ≤ 350 cells/mm$^3$ |
| Symptomatic individuals (including pregnant women) | WHO clinical stage 2 | |
| | WHO Clinical stage 3 or 4 | Treat irrespective of CD4 cell count |
| TB and Hepatitis B co-infections | Active TB disease<br>Chronic active Hepatitis B | |

*Adapted from :( WHO, 2010)*

OSSHHM recommends undertaking WHO clinical staging when people with HIV are first assessed and after significant new clinical events.

OSSHHM advocates more simply that, where CD4 testing is not yet available, all people with confirmed HIV who is in WHO clinical stage 3 & 4 should be recommended to start on combination antiretroviral therapy as soon as they are emotionally and socially 'ready' to begin.

### Viral Load

Plasma HIV RNA (viral load) should be measured in all patients at baseline and on a regular basis thereafter, especially in patients who are on treatment, because viral load is the most important indicator of response to antiretroviral therapy.

### Importance of Viral Load testing:

- Viral load testing serves as a surrogate marker for treatment response and can be useful in predicting clinical progression. The minimal change in viral load considered to be statistically significant (2 standard deviations) is a threefold, or a 0.5 log10 copies/mL change. For most individuals who are adherent to their antiretroviral (ARV) regimens and who do not harbor resistance mutations to the prescribed drugs, viral suppression is generally achieved in 12–24 weeks, even though it may take longer in some patients.
- Confirm potency of new regimen in patients who have viral suppression but therapy was modified due to drug toxicity or regimen simplification.

### Frequency of Viral Load testing

Plasma viral load should be measured before initiation of therapy and preferably within 2–4 weeks, and not more than 8 weeks, after treatment initiation or after treatment modification.

## 5.4 Criteria in starting antiretroviral therapy

OSSHHM recommends the criteria listed in Table 5.2 as adapted from WHO guidelines 2010 for initiating ART in adults and adolescents in accordance with clinical stages and the availability of immunological markers.

### What to start: which medications are recommended for first-line therapy?

'based on available evidence, clinical experience and programmatic feasibility for the wider introduction of ART in resource-limited settings'.

The regimen chosen at the initiation of antiretroviral therapy represents the patient's best chance of achieving prolonged suppression of HIV replication. It should be selected carefully given that it is intended that the patient will continue to take this combination for the rest of their life.

An ideal initial antiretroviral regimen would have the following characteristics: simple, effective, low pill burden, minimal side effects, long term and affordable.

The WHO 2010 guidelines recommend that starting regimens should include two nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs) and a non-nucleoside reverse transcriptase inhibitor (NNRTI) 'based on available evidence, clinical experience and programmatic feasibility for the wider introduction of ART in resource-limited settings'.

Regimens based on combination of two NRTIs plus one NNRTI are efficacious, are generally less expensive than other regimens, have generic formulations, are often available as fixed dose combinations and do not require a cold chain. In addition, they preserve a potent new class (protease inhibitors) for second-line treatments.

Table 5.3 First-line ART regimens in adults and adolescents

| Target Population | Preferred Option | | | Comments |
|---|---|---|---|---|
| | Either | plus either | plus either | |
| Adults and adolescents | Zidovudine (AZT) 300mg twice daily or Tenofovir (TDF) 300mg once daily | Lamivudine (3TC) 150mg twice daily or Emtricitabine (FTC) | Efavirenz (EFV) 600mg at night or Nevirapine (NVP) 200 mg once daily for 14 days, followed by 200 mg twice daily | • Select the preferred regimens applicable to the majority of PLHIV.<br>• Use fixed-dose combinations.<br>• To be taken with food. |
| Pregnant women | Zidovudine | Lamivudine | Nevirapine or Efavirenz | • Do not initiate Efavirenz during the first trimester.<br>• In HIV women with prior exposure to PMTCT regimens, see ART recommendations in Table 10.4 |
| HIV/TB co-infection | Zidovudine or Tenofovir | Lamivudine or Emtricitabine | Efavirenz | • Initiate ART as soon as possible (within the first 8 weeks) after starting TB treatment.<br>• NVP or triple NRTIs are acceptable options if EFV cannot be used. |
| HIV/HBV co-infection | Tenofovir | Lamivudine or Emtricitabine | Nevirapine or Efavirenz | • Consider HBsAg screening before starting ART, especially when Tenofovir is not the preferred first-line NRTI.<br>• Use of two ARVs with anti-HBV activity required. |

*Adapted from: (WHO, 2010)*

## 5.5 How to start antiretroviral therapy

OSSHHM recommends the following steps in starting antiretroviral therapy.

| Steps | What to do |
|---|---|
| 1 | Do clinical staging and CD4 testing and/or viral load testing if available. Test for TB, hepatitis B, haemoglobin and liver function. |
| 2 | Assess patient eligibility for **ART** using the criteria in **Table 5.2** |
| 3 | Discuss and decide in ART committee or HIV core team patient's eligibility for **ART.** |
| 4 | Discuss adherence to ART including drug side effects, dosing schedules, emotional and social readiness. |
| 5 | Recruit ART support person. |
| 6 | When the patient decides to have ART, ask the patient to give a written consent. |
| 7 | Start patient on ART. OSSHHM recommends to start patient on the following first line regimen:<br><br>**Zidovudine** 200mg twice daily **+ Lamivudine** 150mg twice daily **+ Efavirenz** 600mg with dinner |

## 5.6 Monitoring people taking Antiretroviral Therapy

Monitoring people taking ART can be classified into three categories:

1. Clinical monitoring - clinical assessment, weight, signs and symptoms of opportunistic infection, WHO staging;
2. Immunological monitoring – CD4 count testing; and
3. Virological monitoring – Viral load testing.

### Follow-up of people on ART

When a person starts on antiretroviral therapy, it is very important to give them information about who to contact if they need help urgently in the first few days of treatment.

### OSSHHMM recommends the following schedules in following up people on ART:

1. Following day after starting ART by telephone or have a core teavm member visit them (with their consent):
    - Ensure that all has gone well with the first doses.
    - Provide reassurance about side effects if necessary.
2. One week and two weeks from starting therapy in the clinic:
    - Enquire about any side effects that the person has experienced.
    - Enquire about adherence to therapy.
    - Take blood for haemoglobin testing.
3. One month from starting ART, in addition to above:
    - Repeat haemoglobin
    - Viral load.

*Note: It can be expected that by one month the viral load should have been reduced at least a 'one-log reduction', e.g. from 100,000 to less than 10,000 copies per millilitre; or from 30,000 to less than 3,000 copies per millilitre).*

*If reduction in viral load as above is not seen, it is important to enquire about adherence to therapy or whether the treatment has been interrupted for some reason.*

4. Every one to three months:

The frequency of clinical review after the first month is at the discretion of the care team. Many Pacific Island care teams review their patients monthly to ensure that they remain in close contact. Once the pattern of treatment adherence is established, review the patient every three months:

- Clinical assessment: weight, general well being, new signs and symptoms suggestive of opportunistic infections; e.g. screening for TB, WHO clinical stage.
- Functional activity
- Side effects
- Adherence
- CD4 count every 3 months, if available
- Targeted Viral Load testing, if available
- Haemoglobin every 3 months for the first year if on Zidovudine.
- Creatinine clearance if on Tenofovir.
- Liver function tests if on Nevirapine.
- Ensure women of reproductive age have access to contraception.

Where it is available, the Viral Load should be measured every three months. By three months from the time of starting antiretroviral therapy, it is expected that the viral load should be below 400 copies of virus per millilitre and by six months it should be below the limit of detection of the test (which may be as low as 50 copies per millilitre). If these targets are not achieved, make further gentle enquiries about adherence and seek advice from a more experienced colleague through the OSSHHM network.

CD4 counting is also valuable during immune recovery. If it is available, it should be performed every three months until the count has been over 500 cells per microlitre for two consecutive tests. Thereafter it need only be performed once a year provided the viral load remains below the limit of detection.

## 5.7 Immune Inflammatory Reconstitution Syndrome (IRIS)

The immune reconstitution inflammatory syndrome (IRIS) is the paradoxical deterioration in clinical status after ART initiation despite improved immune function due to inflammatory response against infectious antigen, which may or may not have been diagnosed at initiation of ART.

Typically, IRIS occurs in patients with low initial CD4 count (usually <50) and rapid decline in viral load. It is usually seen within two to twelve weeks of the initiation of ART, although it may present later. The incidence of IRIS is estimated to be 10% among all patients initiating ART and up to 25% among patients initiating ART with a CD4 cell count below 50 cells/mm$^3$. (French et al, 2000)

Risk factors predicting the likelihood of IRIS include initiating ART close to the time of diagnosis of an opportunistic infection, being antiretroviral-naive at the time of diagnosis of an opportunistic infection, initiating ART when the CD4 count is below 50 cells/mm$^3$, and having a more rapid initial decrease in the HIV-1 RNA level in response to ART than in patients with higher CD4 counts.

IRIS has been reported in association with a large number of HIV-related infections and inflammatory conditions. The most frequently occurring IRIS events are associated with mycobacterial disease (tuberculosis or Mycobacterium avium complex infection) and cryptococcal disease. Together, mycobacterial and cryptococcal disease account for approximately 60% of all cases of IRIS in developed country settings.

IRIS may be mild and resolve without treatment, e.g. it may involve a transient flare of hepatic enzymes in a patient with HIV/hepatitis B coinfection, or it may be severe and life-threatening, as in patients with cryptococcal meningitis or tuberculosis. The development of a new or recurrent OI soon after ART initiation does not indicate treatment failure and is not an indication to stop or switch ART. If possible, ART should be continued and the OI or inflammatory condition should be treated. If this is impossible, ART should be temporarily interrupted, the OI or inflammatory condition should be treated, and the same ART regimen should be restarted.

The management of IRIS includes treatment of the causative pathogen in order to decrease the antigenic load, continuation of ART, and the use of corticosteroids. The dose and duration of corticosteroid treatment is unclear. Prednisolone (or prednisone) at 0.5 mg/kg/day for five to ten days is suggested in moderate to severe cases of IRIS. (WHO, 2006)

## 5.8 Drug Substitution for Toxicity.

Where a person on the recommended first-line regimen experiences severe, persistent clinical toxicity, it may be necessary to substitute one of the drugs in the regimen with an alternative (see Table 5.4). OSSHHM recommends seeking advice from more experienced practitioners, whenever practicable, through the OSSHHM network before making such a substitution.

More information on drug substitution for toxicity is available in the WHO 2010 guidelines. Decisions in these scenarios can be difficult and it is recommended that they be undertaken in full partnership with the patient and with advice from more experienced colleagues through the OSSHHM network.Table 5.5 shows common side effects of antiretroviral therapy.

Table 5.4 Possible substitutes for drugs causing severe, persistent clinical toxicity

| Common Toxicity | Drug causing it | Alternative substitute | Comments |
|---|---|---|---|
| Persistent anaemia (<6.5 g/dl | Zidovudine | Tenofovir<br>or<br>Abacavir<br>Stavudine (30mg twice daily) | Both of these alternate drugs are quite expensive and it is preferred to reserve them for a second-line regimen.<br>Long term use of Stavudine is associated with high incidence of lipodystrophy. To avoid this outcome, it is sometimes recommended to substitute to Stavudine for a defined period (usually 12 months) and then substitute back to Zidovudine (when the bone marrow may have recovered) with close monitoring of the haemoglobin. |
| CNS symptoms, e.g. hallucinations or frank psychosis | Efavirenz | Nevirapine | Nevirapine should only be used if the patient's CD4 count is low (below 400 for males or below 250 for females) and should be used with caution for higher or unknown CD4 counts. |

Table 5.5 Common side effects of antiretroviral therapy

| Drug | Adverse Events | Comments |
|---|---|---|
| **Nucleoside Reverse Transcriptase Inhibitors (NRTIs):** | | |
| Abacavir | • Hypersensitivity syndrome (fever, myalgia, malaise, nausea, vomiting, symptoms suggestive of upper respiratory tract infection, anorexia); symptoms progressively worsen with each subsequent dose; rash occurs in about half of cases.<br>• Rash<br>• Headache, nausea, vomiting, diarrhoea | • Hypersensitivity reaction usually occurs in the first six weeks of treatment.<br>• Hypersensitivity reaction may be more severe with once-daily abacavir dosing.<br>• Risk of hypersensitivity is related to certain genetic factors, particularly HLA B*5701; consider screening for this before prescribing abacavir.<br>• Counsel patients on signs of hypersensitivity syndrome.<br>• In case of hypersensitivity syndrome, abacavir must be discontinued permanently. |
| Emtricitabine | • Headache, nausea, insomnia<br>• Hyperpigmentation of palms and soles (occurs most frequently in dark skinned people) | • Active against hepatitis B virus (not approved by the US Food and Drug Administration (FDA) for treatment of hepatitis B).<br>• In patients with HIV and hepatitis B co-infection, hepatitis may flare on discontinuation of emtricitabine.<br>• Adjust dosage for renal insufficiency or failure. |
| Lamivudine | • Headache, dry mouth | • Adverse effects are infrequent.<br>• Active against hepatitis B virus. In patients with HIV and hepatitis B co-infection, hepatitis may flare on discontinuation of lamivudine.<br>• Adjust dosage for renal insufficiency or failure. |
| Stavudine | • Peripheral neuropathy<br>• Pancreatitis<br>• Dyslipidaemia<br>• Diarrhoea | • Of the NRTIs, stavudine appears to convey the greatest risk of lipodystrophy and other mitochondrial toxicity.<br>• Risk of lactic acidosis and hepatic steatosis increases when combined with didanosine; this combination should be avoided when possible, especially during pregnancy.<br>• Risk of peripheral neuropathy increases when combined with didanosine.<br>• Consider dosage adjustment for peripheral neuropathy.<br>• Adjust dosage for renal insufficiency or failure. |
| Tenofovir | • Flatulence, nausea, diarrhoea, abdominal discomfort<br>• Asthenia<br>• Acute renal insufficiency, Fanconi syndrome<br>• Chronic renal insufficiency | • Active against hepatitis B but not FDA approved for treatment of hepatitis B. In patients with HIV and hepatitis B co-infection, hepatitis may flare on discontinuation of tenofovir.<br>• Gastrointestinal symptoms may be worse in lactose-intolerant patients; tenofovir is formulated with lactose.<br>• There are case reports of renal insufficiency; association between tenofovir and renal insufficiency is not clear.<br>• Adjust dosage for renal insufficiency or failure. |

| | | |
|---|---|---|
| Zidovudine | • Anaemia, neutropenia<br>• Fatigue, malaise, headache<br>• Nausea, vomiting<br>• Myalgia, myopathy<br>• Hyperpigmentation of skin and nails. | • Twice-daily dosing is preferred over thrice-daily dosing.<br>• Fatigue, nausea, headache and myalgia usually resolve two to four weeks after initiation.<br>• Adjust dosage for renal insufficiency or failure. |
| Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs): | | |
| Efavirenz | • Elevations in liver function tests<br>• Abnormal dreams, drowsiness, dizziness, confusion<br>• Hyperlipidemia | • Central nervous system symptoms are common; severity usually decreases within two to four weeks.<br>• It is teratogenic in animal studies; contraindicated during pregnancy and for use by women who may become pregnant. |
| Nevirapine | • Elevations in liver function tests, hepatitis, liver failure<br>• Rash | • Initial dose of 200 mg per day for first 14 days, then 200 mg twice daily, decreases frequency of rash.<br>• Most rash develops within first six weeks of therapy; rash is most common in women.<br>• Hepatotoxicity may be life threatening. It is more common at higher CD4 cell counts, in women and in patients with hepatitis B or C.<br>• Nevirapine should not be initiated for women with CD4 counts of >250 cells/PL or men with CD4 counts of >400 cells/uL, unless the benefit clearly outweighs the risk.<br>• Monitor liver function tests closely for the first 16 weeks of treatment. |
| Protease Inhibitors (PIs): | | |
| Lopinavir/ ritonavir | • Diarrhoea, nausea, vomiting<br>• Dyslipidaemia<br>• Elevations in liver function tests<br>• Taste perversion | • Available in tablets or oral solution. Tablets do not require refrigeration.<br>• Oral solution contains 42 per cent alcohol.<br>• Avoid combining oral solution with metronidazole or disulfiram. Alcohol in the oral solution may cause disulfiram-like reaction. |
| Ritonavir | • Nausea, vomiting, diarrhoea, abdominal pain<br>• Elevations in liver function tests<br>• Fatigue<br>• Circumoral or peripheral numbness<br>• Taste perversion<br>• Hyperuricaemia | • Capsules are stable at room temperature for up to 30 days.<br>• Avoid combining oral solution with<br>• metronidazole or disulfiram. Alcohol in the oral solution may cause disulfiram-like reaction.<br>• It has significant interactions with many other medications. |

### Principles in the management of ARV drug toxicity

The WHO 2006 guidelines recommend the following principles in managing antiretroviral drug toxicity:

- Determine the seriousness of the toxicity
- Evaluate concurrent medications and establish whether the toxicity is attributable to an ARV drug or drugs, or to a non-ARV medication taken at the same time
- Consider other disease processes (e.g. viral hepatitis in an individual on ARV drugs who develops jaundice) because not all problems that arise during treatment are caused by ARV drugs
- Manage the adverse event according to severity. The classification shown below was adapted from the WHO 2006 guidelines
- Stress the maintenance of adherence despite toxicity for mild and moderate reactions
- If there is a need to discontinue ART because of life-threatening toxicity, all ARV drugs should be stopped until the patient is stabilized
- A change in drug regimen from the initial first-line regimen may be required if a patient develops severe adverse toxicities or if treatment failure occurs

| Grade | Classification | Recommended management |
|---|---|---|
| 4 | Severe life-threatening reactions | Immediately discontinue all ARV drugs, manage the medical event (i.e. symptomatic and supportive therapy) and re-introduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized. |
| 3 | Severe reactions | Substitute the offending drug without stopping ART. |
| 2 | Moderate reactions | Consider continuation of ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single-drug substitutions. |
| 1 | Mild reactions | Bothersome but do not require changes in therapy. |

## 5.9 Antiretroviral therapy failure and second-line regimens

The best chance to achieve durable and effective antiretroviral therapy is when treatment is first initiated. For this reason, the importance of careful assessment and preparation of the patient cannot be overemphasized.

The WHO 2006 guidelines provide detailed advice on how to identify antiretroviral therapy failure by clinical, immunological and virological means, as well as on how to manage this outcome.

It is expected that relatively few people will be treated for HIV in the small island countries and territories of the Pacific in the foreseeable future, and fewer still will experience antiretroviral therapy failure. For this reason, OSSHHM recommends undertaking individualized assessment, with advice from more experienced clinicians, whenever antiretroviral therapy failure is suspected in patients in the region. This assessment will involve the use of viral load tests conducted at reference laboratories, as well as careful and sensitive assessment of the patient's prior adherence and the factors that have influenced it.

Similarly, OSSHHM recommends that where second-line regimens are required for people experiencing definite antiretroviral failure, these should be individualized on the basis of expert advice and, where possible, genotypic resistance testing conducted in a reference laboratory.

In general terms, second-line regimens are likely to include a ritonavir-booster protease inhibitor (most often lopinavir), with two carefully-selected nucleoside drugs.

Table 5.6 Criteria for Switching ART

| Failure | Definition | Comments |
|---|---|---|
| Clinical Failure | New or recurrent WHO stage 4 condition | • Condition must be differentiated from immune reconstitution inflammatory syndrome.<br>• Certain WHO clinical stage 3 conditions (e.g. pulmonary TB, severe bacterial infections), may be an indication of treatment failure. |
| Immunological Failure | • Fall of CD4 count to Baseline (or below) or<br>• 50 % fall from on-treatment peak value or<br>• Persistent CD4 levels below 100 cells/mm3 | • Without concomitant infection to cause transient CD4 cell decrease |
| Virological Failure | Plasma viral load above 5000 copies/ml | • The optimal viral load threshold for defining virological failure has not been determined.<br>• Values of >5 000 copies/ml are associated with clinical progression and a decline in the CD4 cell count. |

*Adapted from: (WHO, 2010)*

Table 5.7 Second-line Regimen

| Target Population | | Preferred Option | Comments |
|---|---|---|---|
| Adults and adolescents (including pregnant women) | If Zidovudine or Stavudine used in first-line therapy | Tenofovir (TDF) + Lamivudine (3TC) or Emtricitabine (FTC) + ritonavir boosted (Atanavir) ATV/r or ritonavir boosted Lopinavir (LPVr) | • NRTI sequencing based on availability of FDCs and potential for retained antiviral activity, considering early and late switch scenarios.<br>• ATV/r and LPVr are comparable and available as heat-stable DCs or co-package formulations. |
| | If Tenofovir used in first-line therapy | Zidovudine (AZT) + Lamivudine(3TC) + Ritonavir boosted Atanavir (ATV/r) or ritonavir boosted Lopinavir (LPVr) | |
| TB/HIV co-infection | If Rifabutin available | Same regimens as recommended above for adults and adolescents | • No difference in efficacy between rifabutin and rifampicin<br>• Rifabutin has significantly less drug interaction with bPIs, permitting standard bPI dosing |

| | | | |
|---|---|---|---|
| TB/HIV co-infection | If Rifabutin not available | Same NRTI backbones as recommended for adults and adolescents plus LPVr or SQV/r with super boosted dosing of RTV (LPV/r 400 mg/400 mg twice daily or LPV/r 800 mg/200 mg twice daily or SQV/r 400 mg/400 mg twice daily) | • Rifampicin significantly reduces the levels of bPIs, limiting the effective options.<br>• Use of extra doses of ritonavir with elected bPIs (LPV and SQV) can overcome this effect but with increased rates of toxicity |
| Hepatitis B co-infection | | Zidovudine (AZT) + Tenofovir (TDF) + Lamivudine (3TC) or Emtricitabine (FTC) + ritonavir boosted Atanavir (ATV/r) or ritonavir boosted Lopinavir (LPVr) | • In case of ART failure, TDF + 3TC or FTC should be maintained for anti-HBV activity and the second-line regimen should include other drugs with anti-HIV activity. |

## 5.10 Role of HIV core teams in treatment and care

The concept of a 'core multidisciplinary HIV care team' introduced in the nine criteria (as discussed in text box 5.1) has been further developed from the experience of several Pacific Island countries and territories in setting up and operating core teams. This team needs to be able to provide comprehensive care for people living with HIV that takes account of the biological, psychological and social aspects of their health and provides ongoing support and follow-up to help them adhere accurately to antiretroviral treatment over the long term.

OSSHHM recommends the following membership for an effective core team at any Pacific Island HIV treatment and care site:

1. An identified team leader – the primary HIV care doctor for the site;
2. A nurse coordinator for the team (often the 'HIV coordinator' of the country or territory, but the person needs to be able to be closely involved in the care of people living with HIV);
3. At least one additional doctor (a physician, primary health care, sexual health or public health doctor who can fill in for the primary doctor when the latter is off-island)[3]
4. An obstetrician;
5. A midwife;
6. A paediatrician;
7. A counsellor (if a qualified counsellor exists or is available – if not, the nurse coordinator takes on this role);
8. A pharmacist (who will take responsibility for antiretroviral stock management and, for countries accessing medications through the Regional Procurement Mechanism, communication with the regional pharmacist, as well as supporting patient adherence. At some smaller island sites, the nurse coordinator takes on this role also if no pharmacist is available);
9. A laboratory officer (who can take responsibility for referral of confirmation and monitoring specimens to overseas laboratories and after further support perform low-cost CD4 counting in the country or territory);
10. A person living with HIV.

### Note:

It is recognised that in countries and territories with smaller case loads, membership of the core HIV care team will not be the only, or even the primary, job of many of the team members. In these circumstances, the team would generally operate as a 'virtual team', whose members such as the obstetrician and paediatrician have received training and undertake to stay up to date with HIV care knowledge so that they can be called upon when required.

[3] In settings where different doctors have responsibility for the outpatient and inpatient care of people living with HIV, it is essential that both an inpatient doctor and a public health or outpatient doctor are included in the core team.

Some larger centres may nominate other health care workers to participate in the core team and provide skilled services to people living with HIV. These health care workers may include a dentist, a surgeon, a psychiatrist, a physiotherapist and/or a nutritionist.

## Process and content for initial training of core teams

OSSHHM believes that one or more clinicians with extensive practical experience in HIV care should facilitate initial training of core HIV care teams. Further, such training should be undertaken in the Pacific Island country or territory where the team is to operate.

It is only through visiting the treatment site that training facilitators can gain an appreciation of the particular issues that will bear on effective HIV care in that setting. In-country training also allows all team members to participate and starts to build cooperation and cohesiveness within the team. Additionally, the approach allows the facilitator to work with the team to identify and develop plans to overcome structural barriers that might impede the scale-up of HIV care services at the site.

A further advantage of in-country training is that it begins the development of an ongoing collegial relationship between members of the team and the training facilitator, who should provide ongoing remote mentorship for team members after the training. Finally, in-country training minimises the negative impact on service delivery that results from taking essential personnel out of their countries and territories for regional or international training events.

The HIV and STI Section in the Public Health Programme, SPC developed and refined basic content for the initial training of core HIV care teams on Pacific Islands. OSSHHM has assessed and endorses this content. (See Appendix c for details of the training content.)

## Mentorship and support of core teams

The comprehensive care of people living with HIV is technically demanding. Moreover, the outcomes of care have been shown to be related to the level of experience of the health care workers providing it.

Many Pacific Island countries and territories are early in the development of their response to HIV and especially of treatment and care systems for people who are living with the virus.

Accordingly, as the newly formed care teams begin to care for people with HIV following the initial training, it is essential to provide them with intensive remote mentorship by experienced HIV clinicians.

OSSHHM recommends that, where possible, ongoing mentorship should be provided by the same experienced HIV clinician who has facilitated the initial in-country training sessions. In this way, an ongoing collegial relationship between the mentor and members of the core team can develop.

Health care workers in core HIV care teams should be encouraged to become active members of OSSHHM as a further source of collegial support and continuing education. As OSSHHM members they can also engage with issues and developments in relation to HIV medicine and sexual health care that are bearing on the Pacific region so that they can be effective advocates for the welfare of patients and clients in their country or territory and in their region.

As the network of OSSHHM members gains experience, knowledge and skill in HIV care, it is intended that members of the society will increasingly be able to provide support and mentorship for each other. Eventually, over a number of years, this growing capacity should remove the need for expert mentors from outside of the region. Since the recommendation of the formation of HIV core teams, for the care of HIV positive persons, it has been noted by OSSHHM that the concept has not taken a strong hold in the Pacific region. In particular, the mentorship aspect of the concept, consequently OSSHHM has written it into its organizational strategic plan. Countries will have greater support in the establishment and sustaining of HIV care teams.

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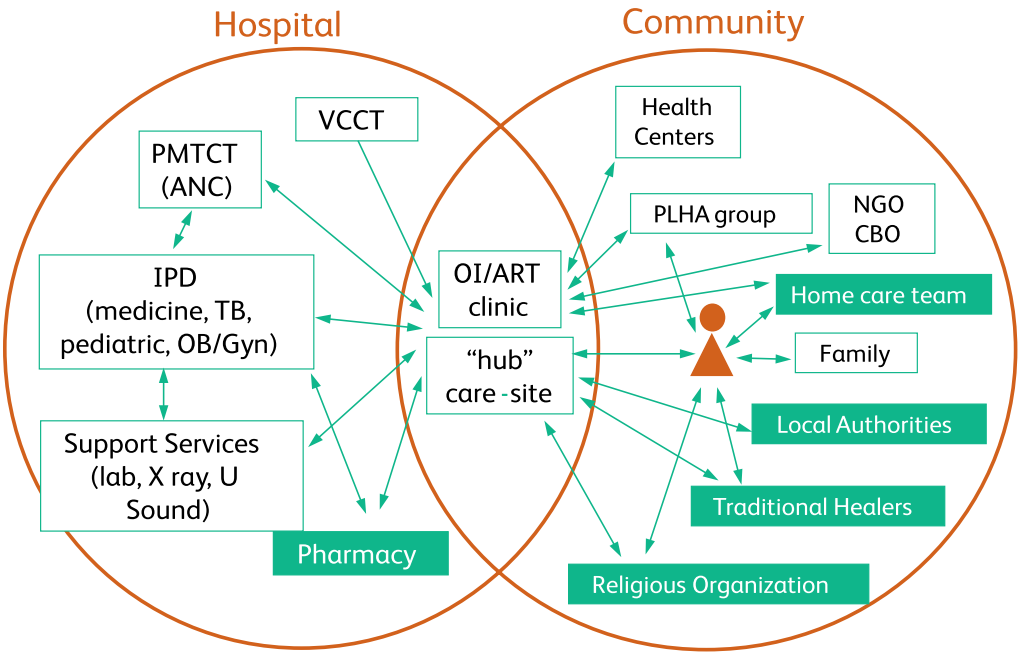
# Chapter 6: HIV support

In the early days of HIV treatment and care much focus was given to the management of HIV as a terminal illness with emphasis on hospice or home based care. Much has changed since then with HIV being managed like any other chronic illness requiring more than just treatment and care. But rather an approach to care which is supportive of the holistic requirements for those not only infected but also affected by HIV. This chapter hopes to provide but an overview of the Continuum of Care (CoC) framework.

OSSHHM recommends that HIV treatment is provided within CoC framework in recognition of the multifaceted challenges that HIV brings. OSSHHM will further develop this concept directly with countries to support the roll-out of the CoC frameworks in countries keen to establish this initiative. OSSHHM recognizes that there are serious gaps currently in place with regards to providing specific services for other key affected populations. This chapter focuses on the needs of People Living with HIV (PLHIV) through the CoC-framework development. However to address the needs of other key affected populations OSSHHM is exploring opportunities for meeting the needs of specific population groups that is also inclusive of PLHIV. This is likely to take the form of a lessons learnt and implementers' guidance document following the pilot of an initiative in the Fiji Islands.

The CoC framework removes the 'silo' approach to HIV care common in many other disease responses. It is needs based and client focused with a strong emphasis on the rights-based approach. Unlike other areas of medicine the HIV response calls for the meaningful involvement of people living with and affected by HIV (PLHIV). This is commonly referred to as the greater involvement of people living with and affected by HIV (GIPA) principles. OSSHHM believes strongly in partnerships and meaningful involvement of the various stakeholders involved in the HIV response both regionally and locally especially with regards to the establishment and sustaining CoC frameworks.




## 6.1 Continuum of Care frameworks

Continuum of Care is a network that links, coordinates and consolidates treatment and support services for PLHIV which are provided at home, communities and health facilities. (FHI, 2007) CoC addresses HIV as a chronic disease; developing systems to provide quality holistic services for PLHIV. It helps to:

- Improve the quality of life for PLHIV;
- Support better adherence to anti-retroviral therapy;
- Increases acceptance of PLHIV; and
- Reduces the costs of service delivery.

The CoC framework is about linking diverse services across the various delivery sites. OSSHHM recognizes that there are marked or subtle differences between each country in the region and the same can be recognized within countries from one clinic site to another. As such, the CoC framework must be locally designed with the majority input and ongoing support coming from the countries concerned.

Figure 6.1: Continuum of care framework example

The CoC brings together the five major components of the response to HIV:

1. Care
2. Treatment
3. Support
4. Testing and counseling
5. Prevention

Each of these components are closely linked and cannot exist in isolation. There may be significant variations in the extent to which these components are delivered in the different countries and territories in the Pacific. Figure 6.1 graphically depicts how a CoC framework may exist in a particular setting. In this scenario a HIV care site (e.g. HUB centre) acts as the central coordinating body which creates links for all the services that may be required for a PLHIV. The following summarises what each component should strive to address.

## 1. Care

PLHIV prior to the commencement of antiretroviral therapy need to maintain good health both physical and psycho-socioeconomic. Once on ART emphasis should be on continued general health support and with the support of ensuring adherence and keeping complications to a minimum. This may include but not limited to:

- Prophylaxis with cotrimoxazole
- Treatment for opportunistic infections
- Prevention, early detection and treatment of tuberculosis
- Nutritional therapy
- Palliative care
- Immunizations for children living with HIV

Care is not limited to the care that is received within the health setting but can come from other clinical services provided by NGO-clinics, faith based organisations and others. It is important however that all services are known of and good referral networks are in place to ensure support to PLHIV and their families. The same must exist within the Ministry of Health, where there are good referral networks and collaboration with other health departments such as with the national TB programme or outpatients for example.

## 2. Treatment

Anti-retroviral therapy is the single most effective intervention for prolonging the quality of life for PLHIV. Anti-retroviral therapies are also an important contributor for the prevention of ongoing transmission of HIV infections. Treatment is also prevention. Anti-retroviral therapy have now become widely available in the Pacific with support given to health workers from the regional level.

## 3. Support

PLHIV may have medical and non-medical needs that need to be addressed, as they are necessary for the support of Anti-Retroviral therapy adherence and simply for the improvement of the quality of life of PLHIV. Support services for PLHIV may include but are not limited to:

- Psychosocial support
- Income generation activities
- Assistance finding employment
- Housing services and provision
- Child care
- Legal support
- Planning for the future

## 4. Testing and counselling

Regardless of the counselling and testing strategy used, be it VCCT or PICT, the ultimate goal is to prevent new infections, to link PLHIV towards treatment programmes and to the CoC framework. In the majority of situations counselling and testing are the gateways to PLHIV accessing treatment, care and support programmes. Failure to get these programmes right in the first instance may result in PLHIV not receiving the services they need and quality of life may be compromised. Counselling and testing may exist as standalone services or integrated (as they do in most settings) into existing services such as in national TB programmes, ante (pre)-natal services or as part of the general outpatients.

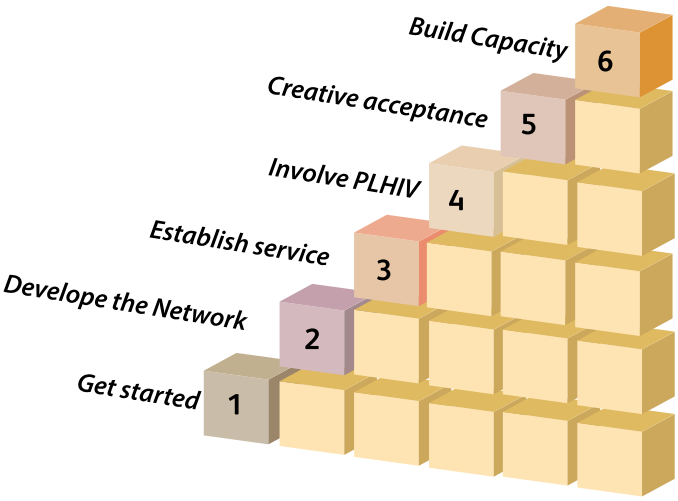
## 5. Prevention

The CoC-frameworks provides an opportunity to reach out (through the various networks) to key affected population groups including PLHIV (positive prevention). Prevention programmes should ideally focus on lowering high risk activities and how they relate to HIV and STI prevention. This should be both primary and secondary prevention measures and furthermore tertiary prevention in the case of advanced HIV infections.

## 6.2 Building blocks for Continuum of Care frameworks in the Pacific

In the following section OSSHHM summarizes the building blocks for the development of a CoC-framework. This has come from the documented experiences from South East (SE)-Asia. It is important to note that this may not apply to your individual settings however it does highlight the process that worked well in a number of settings in SE-Asia. OSSHHM in no way suggest that strict adherence to these steps is necessary but they could guide a way in moving the CoC initiative forward into the future. These are only summary points and OSSHHM encourages you to visit a CoC progamme in action or read about the experiences of others.

**Figure 6.1:** Building blocks for a CoC




*Source: (FHI, 2007)*

### Getting started:

1. Identifying a recognized leader to be the head of the CoC
2. Holding meetings with stakeholders to discuss why a CoC is needed
3. Taking stakeholders on study tours to see a CoC in action
4. Inviting people who have developed CoCs in other areas to meet with stakeholders

### Develop the network-creating a co-ordination and referral system

In this building block the emphasis is on creating and supporting the referral networks. In summary these activities may be to:

1. Oversee the system: role of CoC coordinators (it may not be feasible for many Pacific countries to have CoC-coordinators, thus OSSHHM would recommend having a chairperson who is active and able to keep the CoC alive);
2. Build a partnership: creating and sustaining a CoC Coordination Committee;
3. Connect the dots: linking PLHIV to the services they need; and
4. Knock down fences: identifying and removing barriers to care.

### Establish services- improving existing services and integrating new ones

The outcome of this building block will be best achieved following a needs assessment aimed at identifying the personnel and organisational strengths, weaknesses and identifying ways forward to improve the overall response to treatment and care needs for PLHIV. The recommendations are to:

1. Develop a hub of care - comprehensive care sites;
2. Improve existing services;
3. Develop and link community and home-based care services; and
4. Enhance the role of NGOs, CBOs and FBOs in providing care.

### PLHIV – partners in leading, planning and service provision

The GIPA[4] principles are at the center of any HIV response. The following building block focuses on ensuring the meaningful involvement of PLHIV in the response.

1. Provide vision – PLHIV shaping the CoC;
2. Caregivers and clients – PLHIV providing and receiving services;
3. United we stand – PLHIV groups at the core of the CoC; and
4. Ensure accountability – PLHIV monitoring CoC services.

[4] GIPA-Greater involvement of people living with HIV is a principle of care which aims to ensure that the rights and responsibilities of people living with HIV are maintained. PLHIV are involved in all decision making processes that involve them from laws through to treatment and careprogrammes.

GIPA ensures that PLHIV are involved in the whole HIV response. (UNAIDS, 2007)

### Create acceptance – enabling PLHIV and their families to use the CoC

Many services both in the health area and beyond continue to have issues with regards to stigma and discrimination. Without addressing these issues services will not be accessed by PLHIV and others. Three main activities may assist in addressing any issues to improve the accessibility of services to PLHIV and others.

1. Develop client-friendly services
2. Involve families
3. Mobilize the community

### Build capacity – developing human resources and tools to support the CoC

The response to the needs of PLHIV (and others) will not be adequately delivered if the capacity of the service providers and service cites are of high quality. Two main strategies may assist address these issues:

1. Build capacity through training, mentoring and supportive supervision; and
2. Develop procedures and tools to support the CoC.

## 6.3 Role of the Continuum of Care coordinating committee

The CoC-coordinating committee (CoC-CC) is a group of people who support the CoC coordinating activities and maximizing PLHIV access to services. It identifies the needs of PLHIV and identifies the need for new services or improvement in existing services. It is also responsible for mobilizing the necessary resources required to support the work of the CoC-network of organizations and individuals.

The CoC-CC is generally led by Government and includes, as part of the membership, PLHIV organizations, NGOs, CBOs, FBOs and others.

### Functions of the CoC-CC:

- Improve referrals across all services (including a referral directory, forms and procedures);
- Conduct yearly (or as required) planning meetings for HIV needs;
- Ensuring that services do not overlap
- Identify training gaps and needs; and
- Conduct social mobilization activities to reduce stigma and discrimination.

Depending on the country in question there may be more than one CoC-CC inclusive of a national committee. For example in Fiji there are three HIV treatments clinic cites in the three main centres, there may be one CoC-CCs in each of the three centres. In addition there may be a national committee that exists to support national policy development and providing overarching support to the three CoC-CCs. It is important that all committees have clear terms of reference to guide their existence.

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SECTION 4

# Common Clinical manifestations

## Chapter 7: Opportunistic infections

People with advanced HIV infection are vulnerable to infections and malignancies that are called **'opportunistic infections'** because they take advantage of the opportunity offered by a weakened immune system.

A partial list of the most common HIV-related opportunistic infections and diseases includes:

- Bacterial diseases such as tuberculosis, bacterial pneumonia and septicaemia
- Protozoal diseases such as toxoplasmosis, microsporidiosis,
- Fungal diseases such as Pneumocystis jiroveci (PJP), candidiasis, cryptococcosis and penicilliosis.
- Viral diseases such as those caused by cytomegalovirus, herpes simplex and herpes zoster virus
- HIV associated malignancies such as Kaposi's sarcoma, lymphoma and squamous cell carcinoma.

Different conditions typically occur at different stages of HIV infection. In early HIV disease people can develop tuberculosis, malaria, bacterial pneumonia, herpes zoster, staphylococcal skin infections and septicaemia. These are diseases that people with normal immune systems can also get, but with HIV they occur at a much higher rate. It also takes longer for a person with HIV to recover than it takes for someone with a healthy immune system.

When the immune system is very weak due to advanced HIV disease or AIDS, opportunistic infections such as PJP, toxoplasmosis and cryptococcosis develop. Some infections can spread to a number of different organs, which is known as 'disseminated' or 'systemic' disease. Many of the opportunistic infections that occur at this late stage can be fatal.

### Why is there still a need to prevent and treat opportunistic infections?

Antiretroviral Therapy can reduce the amount of HIV in someone's body and restore their immune system. The introduction of ART has dramatically reduced the incidence of opportunistic infections among HIV-positive people who have received the drugs. Yet the prevention and treatment of opportunistic infections remains essential.

Around the world, millions of people living with HIV in resource-poor communities have no access to antiretroviral drugs. And even where the drugs are available, they do not entirely remove the need for preventing and treating opportunistic infections. Usually it is advisable for people with acute opportunistic infections to begin HIV treatment right away, especially if the infection is difficult to treat. However in certain cases it may be better to delay beginning HIV treatment and instead only to administer treatment for the opportunistic infection, especially if there are concerns about drug interactions or overlapping drug toxicities.

Those who have already started taking antiretrovirals may require other drugs in certain circumstances. In particular, some opportunistic infections may be unmasked shortly after starting HIV treatment as the immune system starts to recover, and these may require specific treatment. Measures to prevent and treat opportunistic infections become essential if antiretrovirals stop working because of poor adherence, drug resistance or other factors.

Providing prevention and treatment of opportunistic infections not only helps HIV-positive people to live longer, healthier lives, but can also help prevent TB and other transmissible opportunistic infections from spreading to others.

### Prevention of HIV-related opportunistic infections

HIV-positive people can reduce their exposure to some of the germs that threaten their health. They should be especially careful around uncooked meat, domestic animals, human excrement and lake or river water. However there is no practical way to reduce exposure to the germs that cause candidiasis, bacterial pneumonia and other diseases because they are generally common in the environment.

### Co-trimoxazole Prophylaxis:

Several HIV-related infections (including tuberculosis, bacterial pneumonia, malaria, septicaemia and pneumocystis jirovecii can be prevented using drugs. This is known as prophylaxis. One particular drug called co-trimoxazole is effective at preventing a number of opportunistic infections and has shown to significantly reduce mortality among HIV-positive individuals initiating antiretroviral therapy.

The World Health Organisation (WHO, 2010) recommends that, in resource-limited settings, the following groups of people should begin taking co-trimoxazole:

- HIV-exposed infants and children, starting at 4-6 weeks after birth, or at first contact with health care, and continued until HIV infection is excluded
- HIV-positive children less than 1 year old
- HIV-positive children aged 1-4 years who have mild, advanced or severe symptoms of HIV disease, or a CD4 count below 25 %
- HIV-positive adults and adolescents who have mild, advanced or severe symptoms of HIV disease, or a CD4 count below 350 cells per ml
- HIV-positive people with a history of treated PJP.

According to WHO guidelines, treatment of HIV-positive children should continue until at least five years.

Drug prophylaxis is usually recommended for those who have started ART and have a very weak immune system or considered vulnerable. Cotrimaxole proplylaxis may be stopped once immune status is stronger or >350 cells/ul.

For people who have already contracted an opportunistic infection and undergone successful treatment, secondary prophylaxis may be advisable to prevent recurrence. This applies to diseases such as tuberculosis, salmonella, cryptococcosis and PJP.

Opportunistic infections such as toxoplasmosis, and cytomegalovirus infection can be diagnosed and treated in places with advanced infrastructure. In the Pacific region, treating these infections may be difficult for some PICTs. Therefore, clinical assessment and treatment is usually the option.

## 7.1 Respiratory infections

### Bacterial pneumonia

Pneumonia can be caused by various bacteria. Symptoms among HIV-positive people are much the same as in those without HIV infection, and include chills, rigours, chest pain and pus in the sputum. The vaccine PPV can protect people against some of the more common pneumonia.

Because other forms of respiratory infection, including PJP, are common among HIV-infected people, doctors must be certain of diagnosis before administering antibiotics. This may require a chest radiograph, blood cultures, a white blood cell count and tests to eliminate other infections. Treatment is usually aimed at the most commonly identified disease-causing bacteria.

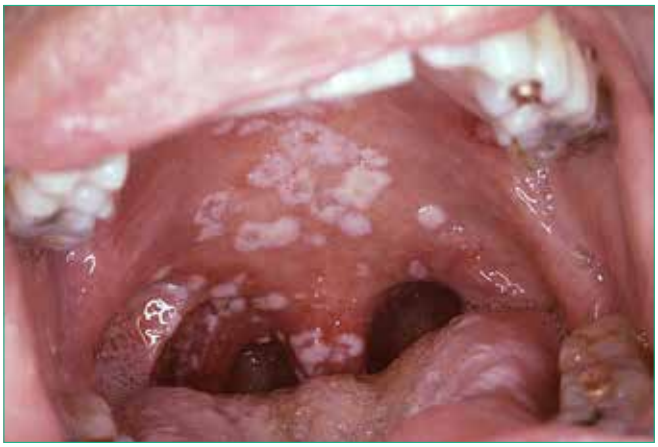
### Candidiasis

There are two main types of candidiasis: localised disease (of the mouth and throat or of the vagina) and systemic disease (of the oesophagus, and disseminated disease). HIV-positive women commonly acquire the mouth and throat variant commonly known as Oral Thrush. Candida in HIV-positive patients indicates a decline in immunodeficiency and, when ART is absent, is a sign of the onset of AIDS related illness depending on site of infection. However, the vaginal variant is a common occurrence among HIV-negative women.

The symptoms of candidiasis of the vagina include itching and possibly a thick vaginal discharge. Candidiasis of the mouth and throat can cause oral pain and make swallowing difficult. The main symptom is creamy white legions in the mouth that can be scraped away. Oesophageal candidiasis is a more serious condition which can cause pain in the chest that increases with swallowing. Disseminated candidiasis causes fever and symptoms in the organs affected by the disease e.g blindness if it affects the eyes and can be life threatening.

Localised disease may be treated at first with relatively inexpensive drugs such as nystatin, miconazole or clotrimazole. Systemic candidiasis requires treatment with systemic antifungal agents such as fluconazole 200mg once daily for 7-14 days, ketoconazole 200mg once daily for 14 days, itraconazole 200mg daily for 15 days or amphotericin allow 1 lozenge to dissolve slowly in the mouth 4 times daily for 10-15 days.

Figure 7.1 Oral Thrush



*Source: (CDC Website)*

### Pneumocystis Jiroveci Pneumonia (PJP)

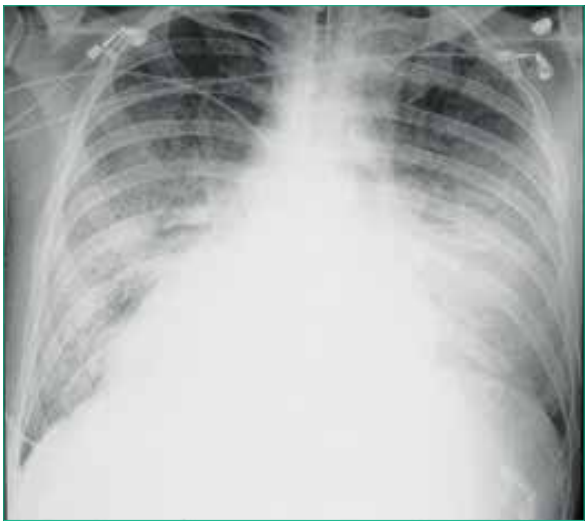
PJP is caused by a fungus, which was formerly called pneumocystis carinii (PCP) but has now been renamed pneumocystis jirovecii. PJP is a frequent HIV associated opportunistic infection which occurred in 70%-80% of patients with AIDS prior to the widespread use of primary PCP prophylaxis and ART, leading to a significant decline of cases of PJP. The symptoms are

mainly pneumonia along with fever and respiratory symptoms such as dry cough, chest pain and dyspnoea (difficulty in breathing). Definitive diagnosis requires microscopy of bodily tissues or fluids.

Severe cases of PJP are initially treated with Cotrimaxole or clindamycin 450mg-600mg orally every 6 hours for approximately 21 days, AIDS patients should receive lifelong therapy, the drug of choice for that is Cotrimaxole Adult and Child over 4 weeks 120mg/kg in2-4 divided doses for 14 days. Oral primaquine 30mg is effective with Clindamycin. Mild cases can be treated with Cotrimaxole throughout. With both of these regimens, toxicity (notably allergic-type reactions) often requires changes in therapy.

Prevention of PJP is strongly recommended for HIV-infected persons with very weak immune systems wherever PJP is a significant health, and also after their first episode of PCP. The preferred drug is usually cotrimaxole. For those who are hypersensitive to co-trimoxazole please refer to appendix E for a cotrimoxazole desensitisation protocol.

Figure 7.2 Radiological Image of PJP



*Source: (JAAFP website)*

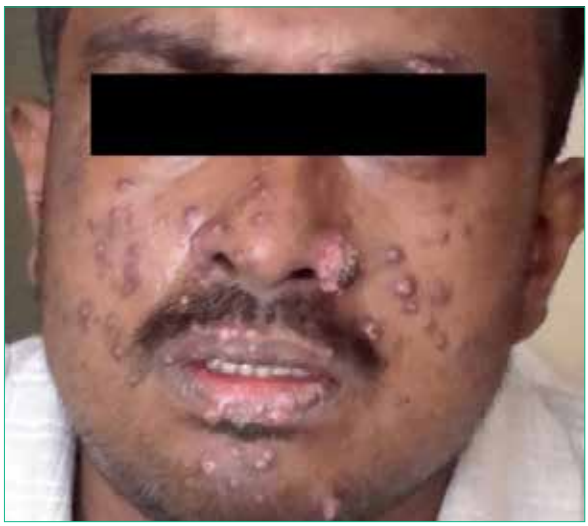
## Histoplasmosis:

Histoplasmosis is a fungal infection that primarily affects the lungs but may also affect other organs. Infection occurs through inhalation of fungus spores.

Symptoms can include fever, fatigue, weight loss and difficulty in breathing.

Disseminated histoplasmosis infection may be diagnosed using an antigen test, and can be fatal if left untreated.

Figure7.3 Histoplasmosis



*Source: (Indian Journal of Sexually Transmitted Disease and AIDS, 2010)*

## Treatment:

**Adults:** Itraconazole 200 mg PO TDS for the first 3 days followed by 200 mg BID for 8 weeks

**Children**: Itraconazole 100 mg PO, daily for children older than 3 years.

## Penicilliosis:

Penicilliosis is an infection caused by ***Penicillium marneffei***, a dimorphic fungus endemic to Southeast Asia and the southern part of China. Infection is thought to occur by the respiratory route. In the years of increased HIV globally this has been seen to be the 3rd most common OI

## Clinical Features:

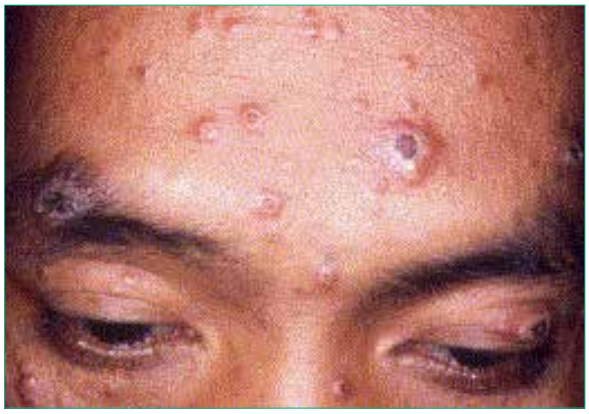
Usually reported to be in the late stage of HIV CD4 count <100. Signs of :

- Fever
- Weight Loss occur in almost 95 % of patients
- Cough and pulmonary symptoms occur
- Concomittant oral Candidiasis may occur in 50 % patients

## Treatment:

Adults: Itraconazole 200 mg PO TID for the first 3 days followed by 200 mg BID for 8 weeks. Children: Itraconazole 100 mg PO daily for children older than 3 years

Figure 7.4 Penicilliosis



*Source: (Journal of the American Academy of Dermatology, 2005)*

## 7.2 Gastro-intestinal manifestations

### Cryptosporidiosis and isosporiasis:

Cryptosporidiosis and isosporiasis are both caused by protozoan parasites. These diseases are easily spread by contaminated food and water or by direct contact with an infected person or animal. They cause diarrhoea, nausea, vomiting and stomach cramps. In people with healthy immune systems, these symptoms do not last more than about 14 days. However, if the immune system is damaged then they can continue for a long time. Diarrhoea can interfere with the absorption of nutrients and lead to serious weight loss.

To confirm diagnosis of either disease, the stool is normally checked for parasites and their eggs. There is no cure for cryptosporidiosis, but optimizing ARV therapy. There is no effective therapy for this infection, although Paromomycin (500-750mg qid) may be partially effective for some HIV-infected patients. Supportive treatment is used, including fluid, electrolyte replacement and antidiarrheal agents. (Source: Internal Medicine 1998)

For **isosporiasis** Cotrimaxole is often the preferred treatment, effective treatment is Cotrimaxole 960mg four times daily for 10 days, and then twice daily for 3 weeks, or Sulfadiazine, 4g, and Pyrimethamine, 35-75mg in four divided doses daily, plus Leukovorium calcium, 10-25mg daily, for 3-7 weeks. It may deem necessary to indefinitely continue with Cotimaxole three times weekly or Fansidar once weekly.

### Microspridiosis

Microspridiosis is an opportunistic intestinal infection that causes diarrhea and wasting in immunocompromised individuals. It results from different species of microsporidia, a group of microbial fungi.

In HIV infected individuals, microsporidiosis generally occurs when CD4+ T cell counts fall <100 cells/ul.

### How is microsporidiosis diagnosed?

There are several tests available to diagnose microsporidia infection. Microscopic examination of stained samples of body fluids, primarily fecal samples, allows for rapid diagnosis. Urine samples can be used to detect spores when the kidney and/or bladder are involved. In a resource limited country, such as the pacific, clinical diagnosis is made and treated presumptively.

Treatment: achieved with medications and supportive care. Depending on the site of infection and the microsporidia species involved, different medications are utilized.

### Albendazole and Fumagillin-400mg twice daily for at least 28 days for adults.

For patients with diarrhea, IV fluid administration and electrolyte repletion may be necessary. Dietary and nutritional regimens may also assist with chronic diarrhea. Finally, improvement of immune system function with antiretroviral therapy in HIV-infected individuals may also lead to improvement of symptoms.

### How is microsporidiosis prevented?

For patients with immune-system deficiency, frequent hand washing and limiting exposure to animals suspected of being infected with microsporidia is recommended

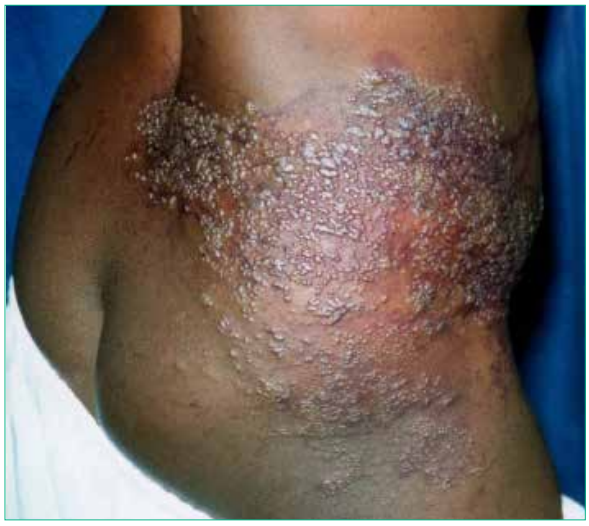
## 7.3 Dermatological testing

### Herpes simplex and Herpes zoster:

The usual symptoms of herpes simplex virus infection (HSV, which causes sores around the mouth and genitals) and herpes zoster virus infection (or varicella zoster virus (VZV), which causes chickenpox (varicella) and shingles (zoster)) are not life-threatening but can be extremely painful. Both viruses are also capable of causing retinitis and, less often, encephalitis (which can be life-threatening). Herpes Zoster is transmitted usually through the respiratory route, whereas Herpes Simplex Virus is transmitted through contact with secretions from an infected area.

Both herpes simplex and herpes zoster are usually diagnosed by simple examination of the affected area, and may be treated with drugs such as Acyclovir 800mg orally four or five times per day for 7 days, Famciclovir 250mg 3 times a day for 7 days and Valacyclovir 1g three times daily for 7 days (BNF 2003).

Figure7.5 Herpes Zoster infection in a patient affected by HIV



*Source: (Internal Medicine Website)*

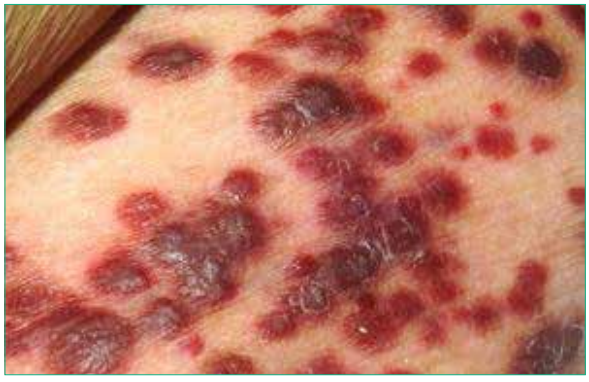
## 7.4 Common cancers

### Kaposi's sarcoma:

HIV-associated Kaposi's sarcoma causes dark blue lesions, which can occur in a variety of locations including the skin, mucous membranes, gastrointestinal tract, lungs or lymph nodes. The lesions usually appear early in the course of HIV infection.

Treatment depends on the lesions' symptoms and location. For local lesions, injection therapy with vinblastine has been used with some success. Radiotherapy can also be used, especially in hard-to reach sites such as the inner mouth, eyes, face and soles of the feet. For severe widespread disease, systemic chemotherapy is the preferred treatment. Though in resource limited countries it is difficult to diagnose and treat a patient with Kaposi' Sarcoma.

Figure 7.6 Kaposi's sarcoma on the skin of an AIDS patient



*Source: (Avert Media Gallery)*

### Non-Hodgkins Lymphoma:

Incidence is 50 to 200 times higher in HIV-infected patients. Most cases are B-cell, aggressive, high-grade histologic subtype lymphomas. At diagnosis, extranodal sites are usually involved; they include bone marrow, GI tract, and other sites that are unusual in non–HIV-associated non-Hodgkin lymphoma, such as the CNS and body cavities eg, pleural, pericardial, peritoneal.

Common presentations include rapidly enlarging lymph nodes or extranodal masses or systemic symptoms (eg, weight loss, night sweats, and fever).

Diagnosis is by biopsy with histopathologic and immunochemical analysis of tumor cells. Abnormal circulating lymphocytes or unexpected cytopenias suggest involvement of the bone marrow, mandating bone marrow biopsy. Tumor staging may require CSF examination and CT or MRI of the chest, abdomen, and other areas where tumors are suspected.

Combined Chemotherapy, combined with antiretrovirals, prophylactic antibiotics and antifungals, and hematologic growth factors.

## 7.5 Neurological conditions

### Cryptococcosis

Cryptococcosis is caused by a fungus that primarily infects the brain. It most often appears as meningitis and occasionally as pulmonary or disseminated disease. Untreated cryptococcal meningitis is fatal.

Cryptococcosis is relatively easy to diagnose. However, its treatment (either amphotericin B with or without flucytosine or in mild cases with oral fluconazole) and secondary chemoprophylaxis are often impossible in developing countries because of high cost and limited availability of drugs required.

It is recommended that ARV Therapy should be administered to those diagnosed with cryptococcal disease. In the case of cryptococcal meningitis there are risks of initiating ART as there is evidence that IRIS may develop. HIV progression versus the onset of IRIS is risks that must be weighed when treating HIV and cryptococcosis meningitis.

**Treatment:** Therapy usually begins with IV Amphotericin B (with or without flucytosine) and continues with oral Fluconazole 400mg daily during active infection. After infection is controlled, suppressive therapy with oral Fluconazole 200mg daily is continued indefinitely.

| Table 7.1 Symptoms and Signs of HIV-1- associated Dementia (HAD) | |
|---|---|
| **Symtoms** | **Comments** |
| Poor Concentration, Forgetfulness, Slow thought process, difficulty in performing fine motor tasks , Clumsiness, Change in Personality, Progression of HAD leads to profound dementia, mutism, incontinence, and paraparesis. | Patients family or partner may notice these changes first, these changes may take place over several months, they may notice difficulty with their handwriting or using computer, and may report difficulty with driving. |
| **Signs** | **Comments** |
| Decreased facial expression, poor performance of fine finger movements, impaired tandem gait, hyperreflexia, action tremor | Patients may demonstrate one or more of these signs, and focal sensory or motor signs, or cranial nerve palsies are not a feature of HIV associated dementia. |

*Adopted from HIV Management in Australasia, a guide for clinical care, 2011*

## HIV Related Dementia:

The availability of Antiretroviral Therapy has been associated with a significant decrease in the incidence of HAD. It occurs in settings of moderate to severe immune suppression.

No single clinical, laboratory or neuroradiological finding is pathognomic of HAD, rather it is seen as a diagnosis of exclusion.

Combination antiretroviral therapy has been shown to improve the neurocognitive performance of patients with HIV associated neurocognitive impairment. Some data suggests that the optimum treatment for HAD should include at least 3 antiretrovial agents that have good central nervous system penetration.

## Toxoplasmosis

Toxoplasmosis is caused by a protozoan found in uncooked meat and cat faeces. This microbe infects the brain and can cause raised intracranial pressure, which leads to headaches and vomiting. Other symptoms include confusion, motor weakness and fever. In the absence of treatment, disease progression results in seizures, stupour and coma. Disseminated infection is less common, but can affect the eyes and cause pneumonia.

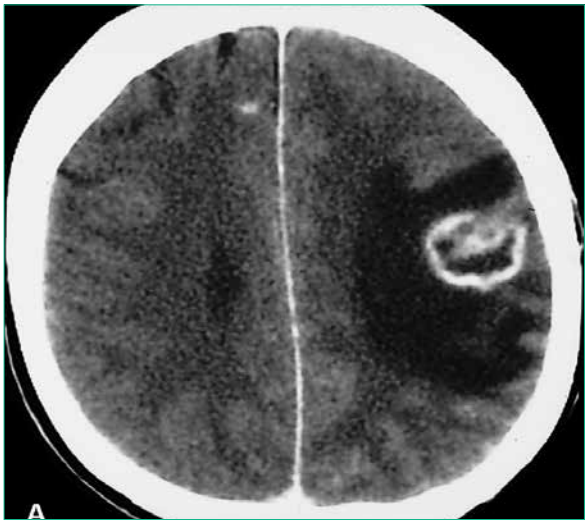
Definitive diagnosis requires radiographic testing usually an MRI or CT scan. The infection is treated with drugs such as Pyrimethamine, Sulfadiazine and Clindamycin. Leucovorin may also be used to prevent the side-effects of Pyrimethamine. Prophylaxis against toxoplasmosis is through taking Cotrimaxole. Prevention of toxoplasmosis can be done.

## Treatment:

| **Primary prophylaxis** | | **Note** |
|---|---|---|
| **First-line regimen** | **Alternative regimen** | **Duration:** |
| Pyrimethamine: 200-mg PO loading dose, then maintenance dose of 50–75 mg/d; plus Sulfadiazine: 4–6 g/d PO, divided into 4 doses; plus Leucovorin: 10–20 mg/d PO | Pyrimethamine: 200-mg loading dose PO, then 75 mg/d; plus Clindamycin: 450 mg four times daily PO. Glucocorticoids are often used to treat intracerebral edema or macular disease because of their anti-inflammatory effect. | at least 6 weeks with correlating radiographic improvement, **followed by secondary prophylaxis** |
| **Secondary prophylaxis** | | |
| **First-choice medications** | **Second-choice medications** | **Discontinuation** |
| Pyrimethamine, 25–50 mg/d; plus sulfadiazine, 2–4 g/d; plus leucovorin, 10–25 mg/d | Pyrimethamine, 25–50 mg/d; plus Clindamycin, 300–450 mg tid or qid; plus Leucovorin, 10–25 mg/d; or Atovaquone, 1500 mg PO bid, with or without Pyrimethamine and Leucovorin dosed as above | Therapy can be stopped after completion of initial therapy for Toxoplasma encephalitis if patient remains asymptomatic and has a CD4+ T lymphocyte count > 200/µL for at least 6 months after ART. Repeated MRI of the brain is recommended to determine whether discontinuing therapy is appropriate. Secondary prophylaxis should be reintroduced if the CD4+ T lymphocyte count falls below 200/µL. |

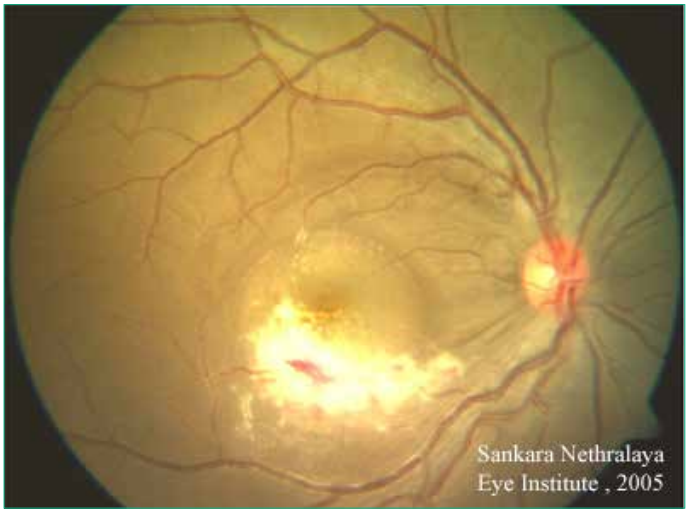
*Adapted from Harrisons Practice*

Figure 7.7 Toxoplasmosis




*SSource: (Courtesy of Dr. P. Harrison, Vancouver)*

Figure 7.8 Cytomegalovirus retinitis




*Source:( Sankara Nethralaya, Eye Institute, 2005)*

### How is Toxoplasmosis Prevented?

- Avoid ingestion of undercooked meat
- To wash hands after any contact with soil
- To avoid emptying cat litter trays, or to empty trays daily and wash hands thoroughly after every disposal.

## 7.6 Other common presentation

### Cytomegalovirus

Cytomegalovirus (CMV) is a virus that infects the whole body. Infection usually occurs in childhood yet the virus remains dormant unless the immune system is suppressed. It most commonly appears as retinitis, which causes blurred vision and can lead to blindness, and also as gastrointestinal disease. CMV can also affect other organs such as the lungs or liver, and is capable of causing fever, diarrhoea, nausea, pneumonia-like symptoms and dementia.

CMV infection may be treated with drugs such as Ganciclovir, Valganciclovir, Cidofovir and Forscarnet.

Before the roll out of ART, studies identified that up to 40 % of AIDS patient's acquired CMV. ART now reduces the chances of infection as immune systems can be supported. It is recommended to initiate ART following anti-CMV treatment in order to reduce the chance of a relapse.

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# Chapter 8: HIV Co-infections

HIV co-infections are infections affecting people living with HIV at the same time. Co-infections commonly seen in people infected with HIV include:

- Tuberculosis (TB)/HIV co-infection
- Hepatitis B virus (HBV)/HIV co-infection
- Hepatitis C virus (HCV)/HIV co-infection

Information presented in this chapter were adapted from the ASHM, avert tuberculosis, CDC and WHO guidelines and fact sheets relevant to Pacific Island Countries and Territories.

## 8.1 HIV and Tuberculosis co-infections

### The global and regional epidemic of tuberculosis and HIV co-infections

According to UNAIDS (2012), TB is the leading cause of death among people living with HIV. Almost one in four deaths among people with HIV is due to TB. In 2010 350,000 people died of HIV-associated TB. It is also the most common presenting illness among people living with HIV, including those who are taking antiretroviral treatment.

There was an estimated 1.1 million HIV positive new TB cases globally in 2010. Around 82% of patients live in sub-Saharan Africa. At least one-third of the 34 million people living with HIV worldwide are infected with TB. Persons co-infected with TB/ HIV is 21-34 times more likely to develop active TB disease than persons without HIV.

Although the prevalence of HIV infection is currently low in the PICT's, there is always an increased risk of TB in people with HIV infection. To date, relatively low numbers of TB patients co-infected with HIV have been reported in the Pacific. The data must be treated with caution, however, as the proportion of TB patients tested for HIV remains low overall and available data on HIV prevalence among TB patients are scarce and incomplete. Available data from the latest WHO reports on global TB control show that to date most people co-infected with TB and HIV have been diagnosed in Kiribati and Fiji (PNG excluded). (SPC, 2010)

People living with HIV are facing emerging threats of drug-resistant TB. Multidrug-resistant TB or MDR-TB is resistance to first-line anti-TB drugs; extensively drug-resistant TB or XDR-TB is resistance to second-line anti-TB drugs. Worldwide, there were an estimated 650,000 MDR-TB cases in 2010.

For patients, integrating HIV and TB services means a better quality of life. They spend less time going from clinic to clinic and waste less money on visits to multiple care providers. It can also mean the difference between life and death. Every day a thousand people living with HIV die of TB. These deaths aren't acceptable when TB is preventable and curable with inexpensive drugs.

There is a need to intensify the integration of HIV and TB services at every level of the health system. There is also a need to strengthen focus on preventing, diagnosing and treating TB in children living with HIV, who are particularly vulnerable to TB infection. All TB patients living with HIV must be put on antiretroviral therapy as quickly as possible. In 2011, countries committed for the first time to cut in half the number of deaths among people living with HIV by 2015.

### Tuberculosis

Tuberculosis (TB) is a disease caused by an organism called *Mycobacterium tuberculosis*. The *M. tuberculosis* bacteria can attack any part of the body, but most commonly attack the lungs.

A person can have either **active** or **latent tuberculosis**. **Active TB disease** means the bacteria are active in the body and the immune system is unable to stop them from causing illness. People with active tuberculosis in their lungs can pass the bacteria on to anyone they come into close contact with. When a person with active TB coughs, sneezes or spits, people nearby may breathe in the tuberculosis bacteria and become infected.

People can also be infected with TB bacteria that are not active in their body. If a person has latent tuberculosis, it means their body has been able to successfully fight the TB bacteria and prevent any active illness. People who have **latent tuberculosis** do not feel sick, do not have symptoms and cannot pass tuberculosis on to other people. In some people tuberculosis bacteria remain inactive for a lifetime without becoming active. But in some other people the inactive tuberculosis may become active tuberculosis if the person's immune system becomes weakened for e.g. with HIV.

### What are the symptoms of tuberculosis?

The symptoms of tuberculosis depend on where in the body the TB bacteria are growing. Tuberculosis bacteria often grow in the lungs, causing pulmonary tuberculosis. Pulmonary tuberculosis may cause a bad cough that lasts longer than three weeks, pain in the chest and coughing up of blood or sputum.

The general symptoms of TB disease include:

- Unexplained weight loss
- Loss of appetite
- Night sweats
- Fever
- Fatigue
- Chills

The symptoms of TB of the lungs include:

- Coughing for 2 weeks or longer
- Haemoptysis (coughing up blood)
- Chest pain
- Other symptoms depend on the part of the body that is affected.

Table 8.1: Difference between a person with TB disease and latent TB infection

| | TB Disease | Latent TB Infection |
|---|---|---|
| Skin and blood tests | positive | positive |
| Chest x-ray and AFB sputum smear | May have an abnormal chest x-ray, or positive sputum smear or culture | Has a normal chest x-ray and a negative sputum test |
| TB bacteria | Has active TB bacteria in his/her body | Has TB bacteria in his/her body that are alive, but inactive |
| Signs and symptoms | Patient usually feels sick and may have symptoms such as cough, fever, and weight loss | Patient does not feel sick |
| infectious | May spread TB bacteria to others | Cannot spread TB bacteria to others |
| Treatment | Needs treatment to treat TB disease | Needs treatment for latent TB infection to prevent TB disease; however, if exposed and infected by a person with multidrug-resistant TB (MDR TB) or extensively drug-resistant TB (XDR TB), preventive treatment may not be an option |

*Adopted from: (CDC TB Fact Sheets)*

## How is tuberculosis diagnosed?

Tuberculosis can be diagnosed by:

- Mantoux Test
- 3 Early Morning Sputum and Culture
- Chest X-Ray

Despite the above tests used, these may not give a clear indication of active TB infection in HIV positive people, because their immune systems are not strong enough to mount an inflammatory reaction against the bacteria. In cases of extra-pulmonary tuberculosis fluid or tissue samples may be tested.

## How is tuberculosis treated? Is there a cure for tuberculosis?

As part of the DOTS strategy, a patient with tuberculosis takes daily doses of pills during supervised treatment

Active tuberculosis disease can almost always be cured with a combination of antibiotics. A combination of anti-tuberculosis drugs provides both prevention and cure. Effective treatment quickly makes the person with tuberculosis non-contagious and therefore prevents further spread of tuberculosis. Achieving a cure for TB takes about six to eight months of daily treatment.

Several drugs are needed to treat active tuberculosis. Taking several drugs does a better job of killing all of the bacteria and is more likely to prevent them from becoming resistant to the drugs. The most common drugs are:

- Isoniazid
- Rifampin (Rifadin, Rimactane)
- Ethambutol (Myambutol)
- Pyrazinamide

## Can tuberculosis be prevented?

The BCG vaccine against TB prevention is available. It provides protection from TB, which generally only lasts for around 15 years. The BCG can also cause false-positive readings on the tuberculin skin test. If given to HIV positive adults or children with very weak immune systems, the BCG can occasionally cause disseminated BCG disease, which is often fatal.

A drug called isoniazid (INH) can be used as a preventative therapy for those who are at high risk of becoming infected with tuberculosis or for those who have inactive TB. People who have inactive tuberculosis but are not yet sick can take a course of isoniazid for several months to stop them developing active tuberculosis.

The WHO recommends that HIV positive people who have latent tuberculosis should be offered isoniazid preventive therapy as needed.

The emergence of first drug resistant TB cases in PICT poses an additional public health threat, not only to people with HIV but also to the broader community. The treatment of a MDR /XDR TB co-infected with HIV does not deter HIV management. HIV treatment remains the same, just the TB treatment changes accordingly.

MDR-TB is a serious problem and is very difficult to treat. In the first line treatment for TB, patients take the drugs isoniazid and rifampicin plus other drugs for

around six to eight months. If a person is resistant to isoniazid and rifampicin, they are said to have MDR-TB, and will need to change to a regime containing newer and often less widely-available 'second-line' drugs. Treatment with second-line drugs can take a very long time, and is usually far more expensive.

XDR-TB is even more serious. If someone has XDR-TB, it means they are not only resistant to isoniazid and rifampicin, but to three or more of the six available second-line drugs too. This can make it virtually impossible to formulate an effective treatment regime for them. Many people with XDR-TB will die before it is even realized that they have the extreme resistant strain.

HIV infection does not itself increase the chance of drug resistance occurring, both MDR-TB and XDR-TB are very serious threats to HIV positive people.

## Tuberculosis and HIV positive people

"Because tuberculosis can spread through the air, the increase in active tuberculosis among people infected with both tuberculosis and HIV results in:

- more transmission of the tuberculosis bacteria
- more people with latent tuberculosis
- more TB disease in the whole population.

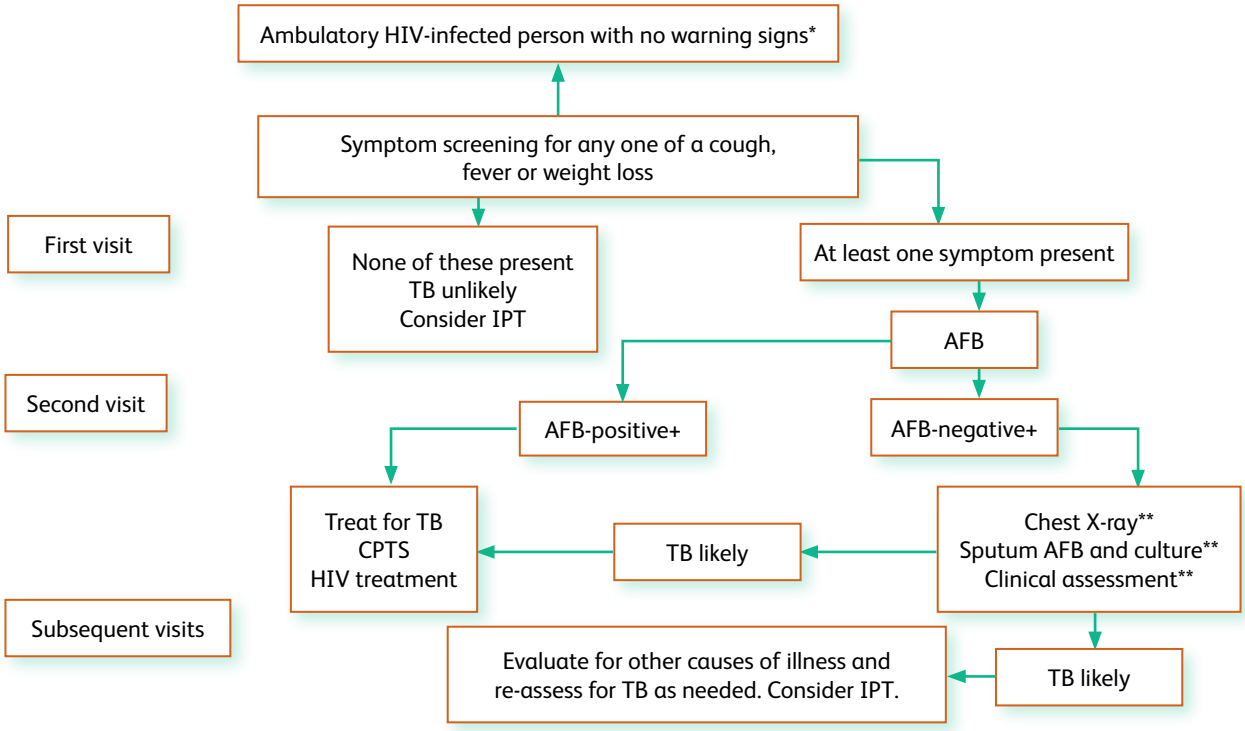
People with latent tuberculosis are increasingly becoming infected with HIV, and many more are developing active TB because HIV is weakening their immune system. People who are co-infected with both HIV and latent TB have an up to 50 times greater risk of developing active tuberculosis disease and becoming infectious compared to people not infected with HIV (Avert Tuberculosis).

"…There are several important associations between the epidemics of HIV and tuberculosis:

- Tuberculosis is harder to diagnose in HIV positive people.
- Tuberculosis progresses faster in HIV-infected people.
- Tuberculosis in HIV positive people is more likely to be fatal if undiagnosed or left untreated.
- Tuberculosis occurs earlier in the course of HIV infection than other opportunistic infections…." (Avert Tuberculosis).

TB and HIV are closely interlinked and collaboration between TB and HIV programs is crucial in supporting general health service providers who are managing patients with TB and HIV. They need support to provide the full deliverables to the co-infected.

Figure 8.1: Algorithm for TB screening for ambulatory people living with HIV




* Warning sings include any one of: respiratory rate >30/minute, fever > 39°C, pulse rate > 120/min and unable to walk unaided.
+AFB-positive is defined as at least one positive smear and AFB-negative as two or more negative as two or more negative smears
§ CPT = Co-trimoxazole preventive therapy. Administer as per national guidelines.
¶ HIV treatment includes CD4 and clinical staging, as well as referral for HIV treatment
** The investigations within the box should be done at the same time wherever possible inorder to decrease the number of visits and speed up diagnosis. If culture is not available, then the decision should be made based on chest X-ray and clinical assesment, as per national guidelines/

*Source: modified from: Improving the diagnosis and treatment of smear-negative pulmonary and extrapulmonary tuberculosis amang adults and adolescents: recommendation for HIV-prevalent and resource-constrained setting.* Geneva, World Health Organisation, 2007.

**Table 8.2 WHO Recommendations for HIV/TB co-infection**

1. Start ARV therapy in all HIV-infected individuals with active TB, irrespective of the CD4 cell count.
2. Start TB treatment first, followed by ARV therapy as soon as possible afterwards (and within the first eight weeks).
3. Use Efavirenz (EFV) as the preferred NNRTI in patients starting ARV therapy while on TB treatment.

*Source: (WHO Recommendations, 2010)*

### Tuberculosis treatment and HIV

ARV therapy decreases the risk of death among people with HIV/TB co-infection.

There has been noted an improved morbidity and mortality of Patients who are co-infected, and a reduction of TB recurrence and improved management of TB for co-infected HIV/TB patients.

### The recommended First Line Therapy for ARV therapy is maintained (WHO, 2010):

EFV is recommended because of less interaction with Rifampicin compared to NVP, for patients who aren't able to tolerate EFV, the option there would be; AZT+3TC+ABC or AZT+3TC+TDF. For patients who have been initiated on ARV therapy prior to TB treatment, NVP should be switched to EFV.

ART in individuals undergoing treatment for TB is challenging because of the overlapping drug toxicities of ART and TB drugs, pill burden, adherence issues and the IRIS. Health Care Workers should seek expert advice when faced with this.

Prevention and treatment of TB in people living with HIV is an urgent priority for both HIV/AIDS and TB programmes. The 3 I's:

- Isoniazid preventive treatment (IPT)
- Intensified case finding (ICF) for active TB
- TB Infection Control (IC)

The above mentioned 3 I's are the key public health strategies to decrease the impact of TB on people living with HIV. TB preventive therapy with INH is safe and effective in people living with HIV, reducing the risk of TB by 33–62%.Screening and diagnosing TB in people living with HIV can be challenging but TB is curable in people living with HIV and TB infection control is essential to keep vulnerable patients, health care workers and their community safe from getting TB. (WHO, 2010)

## 8.2 HIV and common viral hepatitis

The three major blood-borne viruses, HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV), are members of different virus families but have one thing in common: their major mode of transmission is via blood or bodily fluids. They are also different in their epidemiological profile, modes of transmission and natural histories and spread. All three viruses lead to chronic infection in many infected individuals.

HBV is also transmitted through mucous membrane contact, including unprotected sexual contact, blood to blood contact, mother to child transmission, and **intrafamilial transmission**. An effective vaccine against HBV is available, the age of the infection is crucial in determining the natural history of HBV. For patients who develop chronic Hepatitis B, treatment is effective in a substantial minority of patients, otherwise chronic hepatitis B may progress to chirrosis and hepatocellular carcinoma.

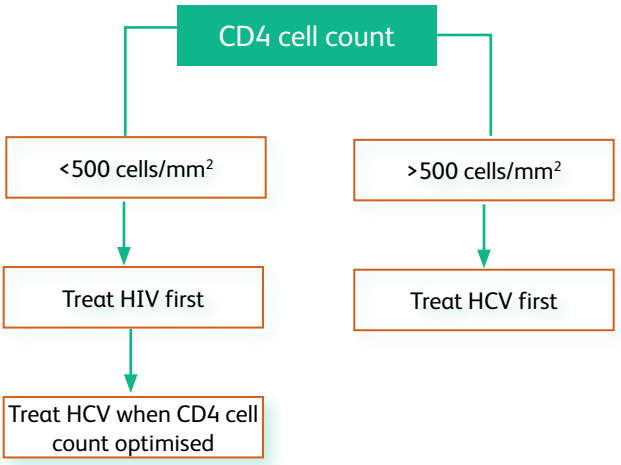
HCV is transmitted predominantly via parenteral means. In the pacific HCV is not commonly seen, maybe we have not done much testing in the pacific for it to be a known problem. A minority of people clear HCV from the body but the majority develop a chronic infection, though some chronically infected individuals will develop symptoms such as fatigue and nausea. A small proportion will progress to develop liver failure or hepatocellular carcinoma.

In the PICT's Injectable Drug Use (IDU) is not commonly seen, and IDU's are the most common parenteral means of spread of the above mentioned viruses.

It is important for all patients with HIV to be tested for both Hepatitis B and C. Important to note that adverse effects of both HCV antiviral therapy and ARV therapy are increased in people with HIV-HCV co-infection. Though appropriate management of it has seen to increase life expectancy, treatment for HCV is not seen in the resource limited countries, as it is not seen to be a major problem, but it should not be ignored.

**If CD4 count is >500 cells/mm3 treat HCV first, but if <500cells/mm3 treat for HIV first.**

## Figure 8.2: Recommended Sequence of Therapy in HIV/HCV co-infection




*Adopted from: (ASHM, 2010)*

## WHO (2010) treatment recommendations for HV/HBV co-intection:

Start ARV therapy in all HIV/HBV co-infected individuals who require treatment for the HBV infection (chronic active hepatitis), irrespective of the CD4 cell count or the WHO clinical stage.

Start TDF and 3TC (or FTC) containing antiretroviral regimens in all HIV/HBV co-infected individuals needing treatment.

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SECTION 5

# Special Topics

## Chapter 9: HIV in Children

Based on the UNAIDS report published in 2012, about 330 000 [280 000–380 000] children were newly infected with HIV in 2011. The number of newly infected children in 2011 declined by half when compared to 2003, and 24% lower than 2009. The significantly decline of number of newly infected children with HIV is dependent on the commitment and the progress made by the countries. (UNAIDS, 2012)

The probability of transmission from mother to child is higher if the mother gets infected with HIV during pregnancy or breast feeding. (Walz et al, 2011)

After having established a diagnosis for the patient, comes about the next steps of initiating therapy or prophylaxis.

The recommendations mentioned here are in line with the WHO recommendations 2010, thus these guidelines can be used along with the **WHO Guideline: Antiretroviral Therapy for HIV infection in Infants and Children: Towards Universal Access, Recommendations for a public health approach.**

### Key issues that need to be looked at when talking about starting therapy for a particular patient:

- When to Start Therapy?
- What to Start?
- What Clinical and laboratory monitoring to do?
- What to expect in the first six months of therapy?
- ARV drug toxicity and substitution
- First line regimen failure, when to switch regimens
- Second line therapy
- ART in adolescents
- Adherence to ART

The initiation of ART not only dependent on CD4 count but also takes into consideration clinical staging. Prior to ARV initiation it is paramount for caregivers to understand the prognosis of HIV and the implications of ARV therapy for the child, its side effects, toxicities and non-adherence consequences. Access to adequate and appropriate nutrition and support for families is essential. Informing older children and family of their diagnosis of HIV improves adherence. The process of informing family and children would best be carried with the help of health care workers.

### 9.1 When to start Antiretroviral Therapy in Infants and Children:

Infants: Initiate ART for all HIV-infected infants diagnosed in the first year of life, irrespective of CD4 count or WHO clinical staging.

Children:

1. It is important to initiate ART for all HIV-infected children between 12-24 months of age irrespective of CD4 count or WHO clinical staging.
2. Initiate ART for all HIV-infected children between 24 and 59 months of age with CD4 count ≤750 cells/mm3 or %CD4+ ≤25, whichever is lower, irrespective of WHO clinical stage.
3. Initiate ART for all HIV-infected children more than 5 years of age with CD4 count ≤350 cells/mm3n (as in adults), irrespective of WHO clinical stage.
4. Initiate ART for all HIV-infected children with WHO clinical stages 3&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.

Clinical staging is useful to identify when to start ART. However, clinical staging is not as useful in infants and children less than two years of age.

Asymptomatic or mildly symptomatic HIV-infected children should be considered for ART when immunological values fall near the described threshold values. A drop below threshold values should be avoided. Treatment with a potent and efficient ARV regimen improves clinical status and effectively reverses the clinical stage.

Being mindful that in many times Clinical and Immunological staging doesn't go hand in hand. Thus, having a CD4 count is a better predictor for a patient's health at any given point though. For countries who do not have a CD4 counter, clinical staging is helpful.

The predictive value of total lymphocyte count (TLC) for mortality is not reliable, especially for infants, and it is therefore not recommended to use TLC to guide decisions on starting ARV therapy.

Viral Load testing is not pre-requisite for initiating anyone on ART, to determine adherence or recognizing treatment failure in resource limited settings.

In resource limited settings where virological testing is not available, WHO has made a criteria for presumptive diagnosis for children < 18 months of age. Any presenting acute illness should be treated first before initiating ARV therapy.

In infants where a presumptive diagnosis has been made, a testing appropriate to age should be made soon as, and treatment adjusted accordingly. Criteria for presumptive diagnosis of severe HIV disease in infants and children <18months of age where viral testing is not available is stated in table 9.1.

**Note: T**he above conditions are as per the IMCI condition definition.

**Table 9.1 Diagnostic criteria in infants and children <18months**

| **A Presumptive Diagnosis of Severe HIV disease should be made if:** | |
|---|---|
| 1. The Child is confirmed as being HIV antibody-positive<br>AND<br>Having any signs stated in 2a or 2b | 2a. The infant is symptomatic with two or more of the following:<br>• oral thrush<br>• severe pneumonia<br>• severe sepsis<br>OR<br>2b. A diagnosis of any AIDS-indicator conditions can be made. |
| Other findings that support the diagnosis of severe HIV disease in an HIV-Seropositive infant include:<br>• recent HIV-related maternal death or advanced HIV disease<br>• Child's %CD4 + <20% | |
| **Confirm the diagnosis of HIV infection as soon as possible** | |

*Source: (Adapted from WHO, 2010)*

## 9.2 What to Start:

The use of three ARV medications is the current standard treatment for HIV infection, in order to achieve the best possible suppression of viral replication and to arrest the progression of HIV disease.

| **Standard Regimen for first line ART** |
|---|
| **2 NRTI's + 1 NNRTI** |

*The above combination is efficacious and generally less expensive.*

Dosing in children is usually dependent on weight or body surface area. As these change with growth, drug doses must be adjusted in order to avoid the risk of under dosing.

| Table 9.2 Choice of First line Regimen | |
|---|---|
| **The choice of the ART and its doses** | **Comments** |
| **CHOICES OF NRTI** | |
| LAMIVUDINE **(3TC)**<br>**<30days=2mg/kg/bd**<br>**>30days=4mg/kg/bd** | Potent NRTI with an excellent record of efficacy safety and tolerability in HIV infected children, and is a core component of the dual NRTI backbone of triple therapy. It is usually given twice daily in children. |
| EMTRICITABINE (FTC) | Newer NRTI. It can be given once daily. FTC is structurally related to 3TC and shares its resistance profile. Where available, it can be used in children more than three months of age as an alternative to 3TC. |
| ZIDOVUDINE **(AZT)**<br>**180-240mg/m2 b/d** | Generally well tolerated in children but has been associated with metabolic complications. Initial drug-related side-effects are more frequent with AZT and the drug can cause severe anaemia and neutropenia; regular full blood count is advised. Particularly important in areas where malaria is endemic or where malnutrition is common and anemia is highly prevalent in young children. Large volumes of AZT liquid formulation are often poorly tolerated. In the event of intolerance, ABC or TDF can be substituted for AZT, except in cases of suspected lactic acidosis, where ABC is preferred. |
| ABACAVIR **(ABC)**<br>**8mg/kg twice daily** | Alternative NRTI in first-line therapy. Data from clinical trials indicate a similar safety profile in children to that in adults, with very little haematological toxicity. Therefore, NRTI combinations containing ABC provide a good<br>NRTI backbone for use with NNRTIs or as part of a triple nucleoside regimen. In infants and children suspected of having a hypersensitivity reaction, ABC should be stopped and never restarted. Children starting ABC and/or their caregivers should be advised about the risk of hypersensitivity |
| TENOFOVIR (TDF)<br>**300mg/day for >12yrs** | Due to the potential effects on bone mineralization)the use of TDF in younger children is not yet recommended |
| DIDANOSINE (ddl)<br>• **50mg/m2 b/d <3months**<br>• **>3months<13yrs**<br>**90-120mg/m2** | An adenosine nucleoside analogue NRTI. Its use is usually reserved for second line regimens |
| **CHOICES OF NNRTI'S** | |
| EFAVIRENZ **(EFV)**<br>**15mg/kg/day** | Currently not recommended for use in children less than three years of age because there is no established dosing. Should be avoided in adolescents as EFV is teratogenic for foetus in first trimester. EFV is preferred as the NNRTI of choice in children more than three years of age with TB/HIV co-infection |
| NIVERAPINE (NVP)<br>**160-200mg/m2, maximum dose of 200mg per day** | Should be given only in combination with other ARVs, except when used for prophylaxis to reduce the risk of perinatal HIV transmission. NVP has a higher incidence of rash than other ARVs. NVP-related rash may be severe and life-threatening, including Stevens – Johnson syndrome and NVP is associated with a rare but potentially life-threatening risk of hepatotoxicity where NVP should be permanently discontinued and not restarted. This makes the drug less suitable for treating children who are on other hepatotoxic medications, or drugs that can cause rash. NVP is currently the only NNRTI that can be used in infants. |
| **Choice of Protease Inhibitors(PI)** | |
| Ritonavir/Lopinavir<br>**230-350mg/m2 twice daily** | Usually are not used in first-line therapy. However, for infants and children <24 months who have been exposed to NVP or other NNRTIs, either directly or via maternal treatment before labour, during delivery or when breastfeeding, the PI LPV/r is now recommended as part of the first-line regimen |

| Table 9.3 ART for infant | | |
|---|---|---|
| **INFANTS AND CHILDREN < 24 MONTHS** | | **ART USED** |
| - No prior exposure to maternal or infant NNRTIs<br>- Whose exposure is unknown | Standard NVP containing triple therapy | **NIVERAPINE(NVP)**<br>**+**<br>**LAMIVUDINE(3TC)**<br>**+**<br>**ZIDOVUDINE(AZT)** |
| - history of exposure to NVP or other NNRTIs used for maternal treatment in PPTCT | Protease Inhibitor (PI's) is preferred<br>drug of choice | **LOPINAVIR/**<br>**RITONVIR (LPv/R)**<br>**+**<br>**3TC**<br>**+**<br>**AZT** |
| **CHILDREN > 24 MONTHS** | | |
| **RECOMMENDED FIRST LINE REGIMEN FOR**<br>**HIV INFECTED CHILDREN ≥24 MONTHS: 1 NNRTI+ 2 NRTI** | | |
| Children 24 months-3 years | | **NVP + 2NNRTI** |
| Children > 3 years | | **NVP or EFV**<br>**+2 NRTI** |

| Table 9.4 Preferred First Line Regimen for specific situations: | |
|---|---|
| **Situation** | **Preferred First Line Regimen** |
| Child or Adolescent with severe Anemia | **NVP+ 2 NRTI (Avoid AZT and DO NOT USE TDF)** |
| Child < 3 yrs with TB treatment | **NVP + 2 NRTIs**<br>**or**<br>**3NRTI's:**<br>**AZT+ABC+3TC** |
| Child > 3yrs or adolescent with TB treatment | **EFV+ 2NRTIs**<br>**or**<br>**2NRTI's**<br>**AZT+3TC+ABC** |
| Adolescent with Hepatitis B | **TDF+FTC or 3TC+ NNRTI**<br>***( preferable not to start Female adolescents on EFV)*** |

## 9.3 Clinical and laboratory monitoring:

Clinical and laboratory assessments should be performed at baseline at point of entry into HIV treatment and care. WHO recommends that clinical parameters be used in conjunction with laboratory assessment, where available, for monitoring of children with HIV who are on ART. However, the inability to perform laboratory monitoring, notably for CD4 or viral load, should not prevent children from receiving ART.

**Table 9.5 BASELINE CLINICAL ASSESSMENT FOR CHILDREN**

Following confirmation of HIV status, baseline clinical assessment needs to be made:

- Weight, height, and head circumference and other measures of growth
- Clinical staging of HIV disease
- Developmental status
- Screening of malaria, TB disease, and exposure to TB
- Identification of concomitant medical conditions, e.g Hepatitis B or C infection, TB or other co-infections or OI's, pregnancy in adolescents.
- Nutritional status
- For those eligible for ARV therapy, assessment of child's and caregivers preparedness for therapy.

**Table 9.6 BASELINE LABORATORY ASSESSMENT FOR CHILDREN**

- Confirmation of HIV infection using virological or antibody testing
- Measurement of CD4 cell count where available
- Haemoglobin Measurement where AZT-containing first line regimens are being used
- White blood cells if available
- Pregnancy test, if indicated from history, for sexually active adolescent girls
- Hepatitis B, C, where available
- Viral Load (VL) where available.

*Note: Routine monitoring for children who aren't eligible for ART should continue having regular, 3-6 month reviews with the baseline clinical and laboratory assessment as mentioned above .If child is eligible for therapy it can be initiated at the appropriate time and where CD4 count not available, clinical assessment is an indicator for initiating therapy.*

## Routine Monitoring of Child on ART:

Once an infant or child is on therapy, the frequency of clinical monitoring will depend on their response to ART. The routine monitoring for infant and children stated in table 9.7. Adherence to the treatment and monitoring schedule should be emphasis to all cases.

**Table 9.7 ROUTINE MONITORING FOR INFANT AND CHILDREN**

| | |
|---|---|
| INFANTS | At 2, 4, 8, weeks and then every 4 weeks for the first year |
| CHILDREN >24 MONTHS | At 2,4,8, 12 weeks and then every 2-3 months once the child has stabilized on therapy |

**Table 9.8 Key signs of an infants and child's response to ARV therapy includes:**

| | |
|---|---|
| 1 | Improvement in growth in infants and children who have been failing to grow |
| 2 | Improvement in neurological symptoms and development in children with encephalopathy or those who have demonstrated delay in the achievement of development milestones. |
| 3 | Decreased frequency of infections (bacterial infections, oral thrush, or other opportunistic infections.) |
| 4 | Being aware of drug toxicities |

Laboratory assessments are desirable at the age of 6 months after initiation of ART, and every 6 months thereafter. Otherwise more frequent of 3 months can be done depending on clinicians assessment and accessibility of laboratory infrastructure.

CD4 cell will rise with the initiation of therapy. It usually rises over the course of the first year of treatment, reach a plateau and then continue to rise further over the second year. In some children, severe immune-suppression may persist, the lower the CD4 levels at the start of the ART, the slower the recovery, thus do not hesitate to make both clinical and laboratory assessment at the same time on your choice of regimen. If patients CD4 count does not increase within the year, it's not an indicator to change regimen. A good indicator to include here is Viral Load, if you have an access to viral load testing, when VL has reduced significantly or undetectable and CD4 count maintaining, your therapy is still working, though VL is not an indicator for Substitution.

## Antiretroviral Therapy Toxicity:

Frist line drug toxicities fall into two categories, early toxicity, usually presenting in the first few weeks to months of therapy, and late toxicity.

**Table 9.9 GUIDING PRINCIPLES FOR THE MANAGEMENT OF ARV DRUG TOXICITY**

1. Determine the seriousness of the toxicity
2. Evaluate concurrent medications and establish whether the toxicity may be attributable to an ARV drug or drugs or to non ARV medications taken at the same time.
3. Consider other disease processes (e.g. viral hepatitis in a child on ARV drugs who develops jaundice). Not all problems that arise during treatment are caused by ARV drugs.
4. Manage the adverse reaction according to its severity (Appendix D)
5. In general:
   a. Severe life-threatening reactions: Immediately discontinue all ARV drugs, manage the medical event (i.e. provide symptomatic and supportive therapy) and reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized
   b. Severe reactions: Substitute the offending drug without stopping ART
   c. Moderate reactions: Consider continuation of ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single-drug substitution.
   d. Mild reactions: Reassure child and caregiver that while the reaction may be bother some, it does not require a change in therapy;
   e. Provide counseling and support to mitigate adverse reactions.
6. Stress the maintenance of adherence despite toxicity for mild and moderate reactions.

*(Refer to Appendix D for more details)*

## Principles of Substitution:

1. Drug substitutions should be limited to situations where toxicity is severe or life-threatening.
2. If toxicity is related to an identifiable drug in a regimen, the offending drug can generally be replaced with another drug from the same class that does not have the same adverse effect.

**Immune reconstitution inflammatory syndrome (IRIS)** is a spectrum of clinical signs and symptoms thought to be associated with immune recovery brought about by a response to antiretroviral treatment. While most HIV-infected children experience rapid benefit from ART, some undergo clinical deterioration.

IRIS in infants and children is not known off much, but the onset of IRIS in children most often occurs within the first weeks to months following the initiation of ART and is seen most often in children who initiate ART with very low CD4 count.

The most common OI associated with IRIS in children is TB though other OI's may also be seen.

Most cases of paradoxical IRIS resolve spontaneously, or can be managed with non-steroidal anti- inflammatory drugs, although some episodes of IRIS can be severe and even lead to death.

The same ART regimen should be restarted once IRIS has improved.

## Reference:

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# Chapter 10: Preventing HIV transmission from mother to child

In 2006 WHO published the guidelines Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants in resource-limited settings – Towards Universal Access. (WHO, 2006)

These guidelines build on earlier United Nations agency policy that recommends a four- pillared approach to the prevention of HIV infection in infants:

1. primary prevention of HIV infection in adults, especially women of childbearing potential;
2. prevention of unintended pregnancy in women living with HIV;
3. prevention of HIV transmission from mothers living with HIV to their infants; and
4. development of effective systems for the care, treatment and support of mothers living with HIV, their children and families. (WHO, 2003)

A regional consultation on the prevention of mother-to-child transmission in the Pacific was conducted by the United Nations Children's Fund (UNICEF) in Suva in April 2007. It identified a fifth area of focus (which could also be considered a particularly important aspect of the first pillar):

5. prevention of HIV infection in women who are already pregnant.

The promotion and ready availability of counseling and HIV testing (with fully informed consent) for women who are pregnant is an important overarching strategy because, without it, pillars 3 and 4 cannot be implemented. The counseling associated with antenatal testing also provides an opportunity to address pillar 5, especially if regular male partners of antenatal women (where they have them) are invited to undergo HIV testing at the same time.

In 2010, WHO has released the revised update the recommendation on ***Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants***. The new guidelines provide the basis for more effective PMTCT interventions in resource-limited settings, and will virtually eliminate the number of new paediatric HIV infections. (WHO, 2010) The revised recommendation is based on two key approaches:

1. Provide life-long ART for HIV infected women in need of treatment for their own health, which is safe and also effective in reducing MTCT.
2. Provide ARV prophylaxis to prevent MTCT during pregnancy, delivery and breast feeding among HIV infected women who not need ART for their own treatment

OSSHHM endorses this enhanced comprehensive approach to prevent infection from mother to child transmission. OSSHHM's position is to support countries to achieve the ***Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping Their Mothers Alive (UNAIDS,2011)***. The efforts should include a particular focus on the gendered aspects of Pacific social structures that increase the risk to women and the increased vulnerability to HIV acquisition associated with the extreme rates of other sexually transmissible infections.

The prevention of unintended pregnancy in women with HIV has already been underlined in these recommendations in relation to the potential teratogenicity of the recommended first- line antiretroviral regimen for the region (see 'Women with HIV who wish to become pregnant). OSSHHM emphasises that all people living with HIV should be engaged with regular clinical follow-up and that this follow-up should include provision of appropriate and effective contraceptive measures for positive women of childbearing potential who do not expressly wish to become pregnant.

## 10.1 Counselling and testing for HIV and other STIs among pregnant women and their male partners

OSSHHM recommends that all women who are pregnant should be routinely counseled on HIV and offered an HIV antibody test with fully informed consent. The test should be offered as early as possible in pregnancy. Ideally the regular male partners of pregnant women should also be provided with counseling and offered testing at the same time. Women with identified high risk of HIV transmission at booking should be re-tested for HIV serology as early as possible to establish the HIV status for women.

Additionally, very high rates of other sexually transmissible infections were documented among antenatal women in Second Generation Surveillance studies conducted in 2008 (SPC, 2008) as well as routine surveillance for most PICTs. Serological testing for syphilis and hepatitis B, and nucleic acid testing for ***Chlamydia***, and gram stain, culture and sensitivity for ***Gonorrhea*** to pregnant women as a routine part of antenatal care. Where it's possible, regular male partners of pregnant women should also offer testing for STIs including HIV. Once sexually transmitted infections are diagnosed they should be appropriately treated.

## 10.2 Managing women who have a reactive HIV screening test during pregnancy

It is important to emphasise that some women who have a reactive screening test for HIV during pregnancy may not, in fact, have HIV but may be showing false positive on the screening test.

Thus it is critical to manage reactive screening test results very carefully. The aim must be both to minimize the potential trauma to the woman and her family and to still ensure that optimal precautions are taken to minimize the risk of HIV transmission to the infant if the woman is really HIV infected.

Laboratories should immediately establish confirmatory diagnostic test for all specimens that are positive in screening test using national standard testing algorithm. The confirmatory result should be available within a week, provided the optimal means of transport and reference laboratory protocols are utilized. The OSSHHM network and regional laboratory support officers should be utilised to overcome any barriers operating against the transporting of the specimen on the next scheduled flight and its urgent testing at the reference laboratory.

The action to be taken while awaiting confirmation depends on the dates of the pregnancy. These dates must be accurately and urgently established, utilising ultrasonography if there is any doubt.

Antiretroviral therapy should be initiated and action taken as if the woman were definitely known to have HIV, following the approach described below.

## 10.3 Antiretroviral therapy for the mother

There is a great benefit for using ART in pregnant women as it significantly reduces HIV disease progression, and decreases morbidity and mortality in pregnant women. ART is also the most effective method of preventing MTCT and, by improving the health of the mother, improves the chances of survival of her child. Thus, treating a pregnant woman living with HIV not only addresses her individual health needs but also dramatically reduces the risk of MTCT, particularly for a woman with advanced disease and a higher risk of transmission.

OSSHHM advocates discussing with pregnant women with HIV in Pacific Island countries and territories the full range of options for the use of antiretroviral drugs to prevent mother- to-child transmission, including the advantages and disadvantages of each approach.

Women commencing antiretroviral therapy because they are pregnant require the same preparation and assessment as everyone starting treatment. It is important, however, that the woman and her core HIV care team consider the welfare of the foetus as well as the mother in reaching a conclusion about whether antiretroviral therapy should be commenced.

### Antiretroviral drugs for treating pregnant women for their own health and to prevent HIV infection in their infants

**Table 10.1:** Key recommendations in starting ART in HIV infected pregnant women

| When is ART indicated |
|---|
| Initiation of ART is recommended to all positive pregnant women with CD4 cell counts of ≤350 cells/mm3, irrespective of the WHO clinical staging, and for all women in WHO clinical stage 3 or 4, irrespective of the CD4 cell count. |
| **When to start ART in pregnancy** |
| Regardless of gestational age, HIV-infected pregnant women in need of ART for their own health should start ART as soon as possible and continue throughout pregnancy, childbirth, breastfeeding<br><br>(if breastfeeding), and thereafter. |
| **What ART regimen to initiate** |
| See select appropriate option (A, B, B+) in table 10.3. |
| **What ARV prophylaxis to give infants of HIV-infected women receiving ART** |
| All infants (regardless of whether breastfeeding or receiving only replacement feeding) born to<br><br>HIV-infected women receiving ART for their own health should be given daily NVP or twice-daily AZT from birth or as soon as feasible thereafter until 4 to 6 weeks of age. |

*Source: (WHO, 2010)*

### ART eligibility criteria for pregnant women

The criteria for initiating ART for pregnant women are the same as for non-pregnant women. OSSHHM strongly recommends to all PICTs to initiate ART in all pregnant women in need of ART for their own health.

The criteria for initiating ART in pregnant women are based on the CD4 cell count and WHO clinical staging. Where it is possible, assessment in pregnant women for determining eligibility to ART using CD4 cell count is strongly recommended. CD4 cell counts guide decisions about when to initiate ART as well as when to switch ART. In settings where CD4 cell counts are not available, evaluation of the WHO clinical stage alone can be used to determine ART eligibility.

The initiation of ART for the health of the HIV-infected pregnant woman is recommended for those with CD4 cell counts of ≤350 cells/mm$^{3,}$ irrespective of WHO clinical staging, and for women in WHO clinical stage 3 or 4, irrespective of the CD4 cell count. The eligibility criteria are described in table 10.2.

Pregnant women eligible for ART for their own health should start treatment as soon as feasible irrespective of gestational age and continue in pregnancy, delivery, during breastfeeding (if breastfeeding) and throughout life. Women be informed and understand on the potential benefits and implications of beginning ART for both themselves and their babies.

Table 10.2: Eligibility criteria for initiating antiretroviral treatment or prophylaxis in HIV infected pregnant women based on CD4 cell count and WHO clinical stage

| | CD4 cell count not available | CD4 cell count available | |
|---|---|---|---|
| | | CD4 ≤350 cells/mm3 | CD4 >350 cells/mm3 |
| WHO clinical stage 1 | ARV prophylaxis | ART | ARV prophylaxis |
| WHO clinical stage 2 | ARV prophylaxis | ART | ARV prophylaxis |
| WHO clinical stage 3 | ART | ART | ART |
| WHO clinical stage 4 | ART | ART | ART |

*Source: (WHO, 2010)*

## ART regimens for pregnant women

The recommended first-line ART regimens for eligible HIV-infected pregnant women are the same as for non-pregnant women. However, selected regimens should be considered on the following issue such as, potency, the safety profile, future treatment options, anticipated adherence, availability of fixed-dose combinations, and coexisting health conditions (e.g. TB, HBV or HCV).

Table 10.3: Three options for PMTCT programmes

| | **Woman receives:** | | **Infant receives:** |
|---|---|---|---|
| | **Treatment (for CD4 count ≤350 cells/mm3)** | **Prophylaxis (for CD4 count >350 cells/mm3)** | |
| ***Option A***(a) | Triple ARVs starting as soon as diagnosed, *continued for life* | ***Antepartum*:** AZT starting as early as 14 weeks gestation<br>***Intrapartum*:** at onset of labour, single-dose NVPand first dose of AZT/3TC<br>***Postpartum*:** daily AZT/3TC through 7 days postpartum | Daily NVP from birth until 1 week after cessation of all breastfeeding; or, if not breastfeeding or if mother is on treatment, through age 4–6 weeks |
| ***Option B***(a) | *Same initial ARVs for both*(b)*:* | | Daily NVP or AZT from birth through age 4–6 weeks regardless of infant feeding method |
| | Triple ARVs starting as soon as diagnosed, *continued for life* | Triple ARVs starting as early as 14 weeks gestation and *continued intrapartum and through childbirth if not breastfeeding or until 1 week after cessation of all breastfeeding* | |
| ***Option B+*** | *Same for treatment and prophylaxis*(b)*:* | | Daily NVP or AZT from birth through age 4–6 weeks regardless of infant feeding method |
| | Regardless of CD4 count, triple ARVs starting as soon as diagnosed (c) *continued for life* | | |

**Note:** "Triple ARVs" refers to the use of one of the recommended 3-drug fully suppressive treatment options. For the drug abbreviations in the table: AZT (azidothymidine, zidovudine [ZDV]); NVP (nevirapine); 3TC (lamivudine).
(a) Recommended in WHO 2010 PMTCT guidelines
(b) True only for EFV-based first-line ART; NVP-based ART not recommended for prophylaxis (CD4 >350)
(c) Formal recommendations for Option B+ have not been made, but presumably ART would start at diagnosis.

*Source: (WHO, 2012)*

### Advantages of option B+

The Option B+ approach of lifelong ART for all HIV-infected pregnant women, regardless of CD4 count, has important advantages over both Options A and B (if viral suppression is maintained) but needs to be evaluated in programme and field settings.

These recommended regimens have been shown to be acceptable to pregnant women and clinicians. Furthermore, acceptability of the regimen will also depend on ease of formulation and dosing (e.g. fixed-dose combination), ease of packaging and availability. Wherever possible, fixed-dose combinations or co-packaged formulations are recommended. The choice of regimen should be guided by the experience, availability, feasibility, and potential toxicity of the regimens in pregnancy.

Two specific concerns when using the first-line regimen:

1. Increased NVP hepatotoxicity in women with higher CD4 counts, and

2. Potential teratogenicity of EFV.

If the benefits of using NVP outweighed the risks of not initiating ART. Close clinical monitoring (and laboratory monitoring, if feasible) during the first 12 weeks of therapy is recommended when NVP is initiated in women with a CD4 cell count of 250 to 350 cells/mm3.

Due potential risk of tube defect, EFV should not be initiated in the first trimester of pregnancy. But it may be initiated in the second and third trimesters. Prospective data currently are insufficient to provide an assessment of neural tube defect risk with first-trimester EFV exposure, except to rule out a potential tenfold or higher increase in risk (i.e. an increase in risk from 0.1% to >1%). Since neural tube closure occurs by approximately 28 days of gestation and very few pregnancies are recognized by this time, the potential risk with the use of EFV is primarily in women who become pregnant while already receiving the drug.

## 10.4 Recommendations for the choice of ART regimen in pregnant women who require treatment and have had prior exposure to antiretroviral for PMTCT

Resistance to NNRTI drugs is a main concern for PMTCT regimens. A non-NNRTI-based ART regimen (e.g. a LPV/r-based regimen) is recommended for women who require ART for their own health who have received, within 12 months of initiating treatment, sd-NVP (single dose NVP) alone or in combination with other drugs ***without*** an NRTI tail.

If a non-NNRTI-based regimen is not available, an NNRTI-based regimen may be started, but it is recommended that viral load testing (if available) be performed after 6 months of ART and, if the viral load is greater than 5000 copies/ml a switch to a boosted PI regimen (e.g. LPV/r) is recommended. The selection of choice is stated in table below

**Table 10.4:** Choice of ART regimen for HIV-positive women with prior exposure to PMTCT prophylaxis

| Characteristics of previous PMTCT ARV exposure | Recommendation |
|---|---|
| sd-NVP (+/- short-course AZT) with no NRTI tail within the last 12 months | • Initiate a non-NNRTI regimen<br>• 2 NRTIs + PI preferred over 3 NRTIs |
| sd-NVP (+/- short-course AZT) with an NRTI tail within the last 12 months | • Initiate an NNRTI regimen<br>• If available, check viral load at 6 months and if >5000 copies/ml, switch to second-line ART with PI |
| sd-NVP (+/- short-course AZT) with or without an NRTI tail more than 12 months before | • Initiate an NNRTI regimen<br>• If available, check viral load at 6 months and if >5000 copies/ml, switch to second-line ART with PI |
| All triple ARV regimens, irrespective of duration of exposure and time since exposure | • Initiate NNRTI regimen<br>• If earlier triple ARV regimen was NNRTI based and was stopped without administration of an NRTI tail, check viral load at 6 months, if available, and if >5000 copies/ml, switch to second-line ART with PI |

*Source: (WHO, 2010)*

## 10.5 ART regimens for women of child-bearing age receiving treatment for their own health

Women of childbearing age receiving ART should continue treatment and monitoring as recommended in adult. Contraceptive counseling is essential component of care for HIV-infected women of reproductive age. Effective contraceptive should be provided taken in to consideration of potential interactions of antiretroviral drugs with hormonal contraceptives.

## 10.6 Women receiving ART and planning to become pregnant

As part of the contraceptive counseling, additional information should be also included in the counseling, the risk of infant HIV infection, risk factors and PMTCT, potential drug toxicity for mother and infant, safer sexual practices to prevent STIs, and other general health messages.

Women who are planning to become pregnant should use a regimen that does not include EFV, in order to avoid the highest risk period of in utero EFV exposure (conception to day 28 of gestation). Fully suppressive ART before conception, maintained during pregnancy, labour, delivery and breastfeeding is recommended.

## 10.7 Women receiving ART who become pregnant

Women who are already taking antiretroviral therapy when they become pregnant should continue it.

Since the neural tube closes at approximately 28 days of gestation, fetal exposure to EFV during the risk period for neural tube defects will have occurred before the recognition of pregnancy in the vast majority of women. If a woman receiving EFV is recognized as pregnant before 28 days of gestation, EFV should be stopped and substituted with NVP or a PI. If a woman is diagnosed as pregnant after 28 days of gestation, EFV should be continued.

There is no indication for abortion in women exposed to EFV in the first trimester of pregnancy.

Appropriate antenatal counseling, which should cover the risk of infant HIV infection, risk factors and PMTCT, potential drug toxicity for mother and infant, safer sexual practices to prevent STIs, and other general health messages is very important.

## 10.8 Antiretroviral prophylaxis for infants born to women receiving ART

Aiming to reduce HIV transmission from mother to child in peripartum and postpartum, short duration of antiretroviral prophylaxis (for 4-6 weeks) is indicated for all infants born to HIV infected women receiving ART. Regardless of infant feeding choice, infant prophylaxis provides added protection from early postpartum transmission, particularly in situations where women have started ART late in pregnancy, have less than optimal adherence to ART and have not achieved full viral suppression.(Lallemant et al, 2000)

**Table 10.5:** Considerations for choice of infant prophylaxis when mother receives ART for her own health

| Infant prophylaxis | Dose and duration | Feasibility and operational considerations | Safety considerations |
|---|---|---|---|
| AZT | 15 mg per dose twice daily if birth weight >2500 g (or 10 mg per dose twice daily if birth weight ≤2500 g) from birth until 4 to 6 weeks of age | • Twice-daily regimen<br>• Substantial experience among infants receiving replacement feeding | • Potential risk of anaemia (reversible) |
| NVP | 15 mg once daily if birth weight >2500 g (or 10 mgonce daily if birth weight ≤2500 g) from birth until 4 to 6 weeks of age | • Once-daily regimen<br>• Limited safety monitoring required<br>• Substantial experience among breastfeeding infants<br>• No evidence assessing the efficacy among infants receiving replacement feeding for any duration beyond a single dose at birth<br>• NVP is not recommended for infants born to mothers infected solely with HI V-2 | • Risk of acquired drug resistance for infants becoming infected despite interventions<br>• Potential risk for NVP toxicity if mother receives NVP-based ART regimen during breastfeeding (there is some passage of NVP to the infant through breast milk) |

Note: Infants should receive either twice-daily AZT or daily NVP from birth (within 6-12 hours) or as soon as feasible thereafter until 4 to 6 weeks of age.

*Source: (WHO, 2010)*

**Table 10.6:** Clinical scenarios and recommendations for antiretroviral treatment and infant

| Clinical scenario | Woman / infant regimen | Recommended drug regimen |
|---|---|---|
| Pregnant women tested HIV-infected and eligible for ART | Woman | AZT + 3TC + NVP or<br>TDF + 3TC (or FTC) + NVP or<br>AZT + 3TC + EFV or<br>TDF + 3TC (or FTC) + EFV |
| | Infant | AZT or NVP |
| Pregnant women eligible for ART but exposed to sd-NVP without dual NRTI tail in last 12 months | Woman | Non-NNRTI regimen |
| | Infant | AZT or NVP |
| Pregnant women eligible for ART who have clinically significant or documented severe anaemia (Hb <7g/dl) | Woman | TDF + 3TC (or FTC) + EFV or<br>TDF + 3TC (or FTC) + NVP |
| | Infant | AZT or NVP |
| Pregnant women eligible for ART with HIV-2 infection alone | Woman | AZT + 3TC + ABC or<br>AZT + 3TC + LPV/r |
| | Infant | AZT |
| Pregnant women eligible for ART with TB co-infection | Woman | AZT + 3TC + EFV or<br>TDF + 3TC (or FTC) + EFV |
| | Infant | AZT or NVP |
| Pregnant women eligible for ART with HBV coinfection requiring HBV treatment | Woman | TDF + 3TC (or FTC) + EFV or<br>TDF + 3TC (or FTC) + NVP |
| | Infant | AZT or NVP |
| Non-pregnant women of childbearing age who are eligible for ART and who may become /plan to become pregnant | Woman | AZT + 3TC + NVP or<br>TDF + 3TC (or FTC) + NVP |
| | Infant | AZT or NVP |
| Women receiving ART who become pregnant | Woman | Continue same ART |
| | Infant | AZT or NVP |

*Source: (WHO, 2010)*

## 10.9 Prophylaxis to prevent MTCT for HIV-infected pregnant women who do not need treatment for their own health

Although women with higher CD4 counts may not yet require ART for their own health and are at lower risk of transmitting HIV to their infants. However, they need an efficacious ARV regimen to prevent infection in their infants.

ARV prophylaxis should start from as early as 14 weeks of gestation (i.e. during the second trimester of pregnancy), or as soon as possible thereafter.

For women presenting late, prophylaxis can be started in the second trimester, labour or at delivery, or even postpartum, but the principle that should be followed is that ***as much as possible of the full prophylaxis regimen should be given.***

## Table 10.7 Key recommendations

| Eligibility for ARV prophylaxis |
|---|
| HIV-infected pregnant women who are not in need of ART for their own health require effective ARV prophylaxis to prevent HIV infection in their infants. ARV prophylaxis should be started from as early as 14 weeks of gestation (second trimester) or as soon as feasible during pregnancy, labour and delivery or thereafter. |
| **What ARV prophylaxis regimen to give women and their infants** |
| **Three options are recommended:**<br>Option A: maternal AZT + infant ARV prophylaxis:<br>Option A consists of antepartum twice-daily AZT, plus sd-NVP at the onset of labour 1, plus twice daily<br>AZT + 3TC during labour and delivery and continued for 7 days postpartum.<br>In breastfeeding infants, daily administration of NVP to the infant from birth until 1 week after all exposure to breast milk has ended, or for 4 to 6 weeks if breastfeeding stops before 6 weeks (but at least 1 week after the early cessation of breastfeeding), is recommended.<br>In infants receiving only replacement feeding, daily administration of NVP from birth or sd-NVP at birth plus twice-daily AZT from birth until 4 to 6 weeks of age is recommended.<br>Option B: maternal triple ARV prophylaxis<br>Option B consists of antepartum daily triple ARV prophylaxis until delivery, or, if breastfeeding, until 1 week after all exposure to breast milk has ended. Recommended regimens include<br>AZT + 3TC + LPV/r,<br>AZT + 3TC + ABC,<br>AZT + 3TC + EFV, or<br>TDF + 3TC (or FTC) + EFV.<br>In infants, regardless of infant feeding practices (breastfeeding or replacement feeding), the maternal triple ARV prophylaxis should be combined with the daily administration of NVP or twice-daily AZT to the infant from birth until 4 to 6 weeks of age.<br>Option B+: maternal triple ARV prophylaxis<br>*Same for treatment and prophylaxis, but* approach of lifelong ART for all HIV-infected pregnant women, regardless of CD4 count |
| *Source: (WHO, 2010)* |

## Table 10.9: Extended simplified infant NVP dosing recommendations*

| Infant age | NVP daily dosing |
|---|---|
| Birth** to 6 weeks | |
| • Birth weight 2000-2499g | 10 mg once daily |
| • Birth weight ≥2500g | 15 mg once daily |
| >6 weeks to 6 months | 20 mg once daily |
| >6 months to 9 months | 30 mg once daily |
| >9 months to end of BF | 40 mg once daily |
| Note:<br>* Based on the dosing required to sustain exposure in the infant of >100 ng/ml with the least dose changes.<br>** Low birth weight infants should receive mg/kg dosing, suggested starting dose is 2 mg/kg once daily. Therapeutic drug monitoring is recommended | |
| *Source: (WHO, 2010)* | |

**Table 10.10:** Simplified infant AZT dosing recommendations

| Infant age | AZT daily dosing |
|---|---|
| Birth to 6 weeks<br>• Birth weight 2000-2499 g<br>• Birth weight ≥2500 g | <br>10 mg twice daily<br>15 mg twice daily |
| * Low birth weight infants should receive mg/kg dosing. | |
| *Source: (WHO, 2010)* | |

For infants receiving replacement feeding, peripartum and post-exposure prophylaxis should be carry out for 4-6 weeks with either daily-NVP or sd-NVP plus twice-daily AZT. There is a strong quality of evidence that 6 weeks of daily infant AZT prophylaxis in conjunction with maternal antepartum AZT prophylaxis for more than 4 weeks significantly prevents the risk of HIV transmission around the time of delivery (Lallemant et al, 2000).

**Table 10.11:** Considerations for the choice of maternal triple ARV prophylaxis for HIV infected pregnant women who are not in need of treatment for their own health

| Recommended regimens | Dosing | Feasibility considerations | Safety considerations |
|---|---|---|---|
| AZT + 3TC + LPV/r | AZT 300 mg twice daily<br>3TC 150 mg twice daily<br>LPV/r 400/100 mg twice daily | • Extensive experience with AZT + 3TC backbone in pregnancy<br>• Hb assessment is recommended (but not necessary) before use of AZT<br>• Relatively high cost of regimen<br>• High pill burden | • Risk of anaemia with AZT |
| AZT + 3TC + ABC | AZT 300 mg twice daily<br>3TC 150 mg twice daily<br>ABC 300 mg twice daily | • Regimen could be provided as a fixed-dose combination<br>• Hb assessment is recommended (but not necessary) before use of AZT | • Risk of anaemia with AZT<br>• Risk of hypersensitivity reaction with ABC |
| AZT + 3TC + EFV | AZT 300 mg twice daily<br>3TC 150 mg twice daily<br>EFV 600 mg once daily | • Extensive experience with AZT + 3TC backbone in pregnancy<br>• Hb assessment is recommended (but not necessary) before use of AZT<br>• Effective contraception after delivery is required with use of EFV to prevent (subsequent) pregnancy<br>• EFV use is recommended for women presenting with TB | • Risk of anaemia with use of AZT<br>• Potential risk (probably <1 %) of neural tube defect with use of EFV in first month of pregnancy (before 6 weeks |

| | | | |
|---|---|---|---|
| TDF + 3TC (or FTC) + EFV | TDF 300 mg once daily<br>3TC 150 mg twice daily<br>EFV 600 mg once daily | • Effective contraception after delivery is required with use of EFV to prevent (subsequent) pregnancy<br>• EFV use is recommended for women presenting with TB<br>• TDF + 3TC use is recommended for women with hepatitis B infection requiring HBV treatment | • Risk of nephrotoxicity with use of TDF<br>• Limited data available on potential maternal and infant bone toxicity with use of TDF<br>• Potential risk (probably <1 %) of neural tube defect with EFV use in first month of pregnancy (before 6 weeks of gestation)<br>• Potential risk of hepatic flare in HBV-coinfected women after TDF + 3TC is discontinued after weaning |
| TDF + FTC + EFV | TDF 300 mg once daily<br>FTC 200 mg once daily<br>EFV 600 mg once daily | • Could be given as once daily regimen in a fixed-dose combination<br>• Effective contraception after delivery is required with use of EFV to prevent (subsequent) pregnancy<br>• EFV use is recommended for women presenting with TB<br>• TDF + FTC use is recommended for women presenting with hepatitis B infection requiring HBV treatment<br>• Relatively high cost of regimen | • Risk of nephrotoxicity with use of TDF<br>• Limited data available on potential maternal and infant bone toxicity with use of TDF<br>• Potential risk (probably <1 %) of neural tube defect with use of EFV in first month of pregnancy (before 6 weeks of gestation)<br>• Potential risk for hepatic flare in HBV-coinfected women after TDF + FTC is discontinued after weaning |
| | | | *Source: (WHO, 2010)* |

**Table 10.12:** Clinical scenarios and recommendations for the use of antiretroviral prophylaxis

| Clinical scenario | **Option** | Woman /infant regimen | Preferred recommended drug regimen and dosing |
|---|---|---|---|
| Pregnant woman tested HIV-infected and not in need of treatment; infant is breast-fed | Option A | Woman | AZT<br>sd-NVP *<br>AZT + 3TC * |
| | | Infant | NVP |
| | Option B | Woman | AZT + 3TC + LPV/r or<br>AZT + 3TC + ABC or<br>AZT + 3TC + EFV or<br>TDF + 3TC (or FTC) + EFV |
| | | Infant | AZT or NVP |
| Pregnant woman tested HIV-infected and not in need of treatment; infant receives replacement feeding only | Option A | Woman | AZT<br>sd-NVP *<br>AZT + 3TC * |
| Infant<br>Sd-NVP plus NVP or<br>AZT | | | |
| | Option B | Woman | AZT + 3TC + LPV/r or<br>AZT + 3TC + ABC or<br>AZT + 3TC + EFV or<br>TDF |
| | | Infant | AZT or NVP |
| Pregnant woman requiring prophylaxis with clinically significant or documented severe anaemia (Hb <7g/dl) | | Woman | TDF + 3TC (or FTC) + EFV |
| | | Infant | AZT or NVP |
| Pregnant woman requiring prophylaxis infected with HIV-2 alone | Option A | Woman | AZT |
| | | Infant | AZT |
| | Option B+ | Woman | Women taken regimen in option A or B. However, the treatment should continue for life |
| | | Infant | AZT or NVP |

*Source: (WHO, 2010)*

## 10.10 Women diagnosed during labour or immediately postpartum

Women diagnosed with HIV infection during labour or immediately postpartum has missed the ART for antepartum care. In this case, intrapartum-postpartum components of option A or B prophylaxis or the postpartum component of option A or B prophylaxis alone can reduce MTCT and should be provided immediately.

### 1. Women diagnosed with HIV infection in labour

***Option A (Maternal AZT plus infant ARV prophylaxis)***

**Mother:** sd-NVP as soon as possible during labour and AZT + 3TC twice daily for 1 week

**Infant (if breastfeeding):** daily NVP from birth until 1 week after all exposure to breast milk has ended, or for 4 to 6 weeks if breastfeeding ceases before 6 weeks (always continue for 1 week after all exposure to breast milk has ended).

**Infant (not breastfeeding):** sd-NVP plus twice daily AZT or daily NVP from birth until 4 to 6 weeks of age.

A clinical assessment should be done postpartum and a CD4 count obtained. Women who are found to require ART for their own health should be started on an appropriate life-long ART regimen.

***Option B (Maternal triple ARV prophylaxis, relevant only if breastfeeding)***

**Mother:** Triple ARV prophylaxis during labour until 1 week after all exposure to breast milk has ended.

A clinical assessment should be done postpartum and a CD4 count obtained. Women who are found to require ART for their own health should not discontinue their triple drug ARV regimen but continue on an appropriate life-long ART regimen.

**Infant:** daily NVP from birth until 6 weeks of age (since the infant is breastfeeding and immediate protection is desirable, NVP would be the preferred infant prophylaxis and given for a full 6 weeks).

### 2. Women diagnosed with HIV infection immediately postpartum

***Option A (infant ARV prophylaxis)***

**Infant:**

- **Infant (if breastfeeding):** daily NVP from birth until 1 week after all exposure to breast milk has ended, or for 4 to 6 weeks if breastfeeding ceases before 6 weeks.
- **Infant (not breastfeeding):** sd-NVP plus twice daily AZT or daily NVP from birth until 4 to 6 weeks of age.

**Mother:**

- A clinical assessment and CD4 count should be done postpartum.
- Women who are found to require ART for their own health should be started on an appropriate life-long ART regimen.

Infant should continue daily NVP until the mother has received at least 6 weeks of ART before discontinuing infant prophylaxis.

***Option B (maternal triple ARV prophylaxis, relevant only if breastfeeding)***

**Mother:**

- Triple ARV prophylaxis until 1 week after all exposure to breast milk has ended, or for 4 to 6 weeks if breastfeeding ceases before 6 weeks (always continue for 1 week after all exposure to breast milk has ended).
- A clinical assessment should be done postpartum and a CD4 count obtained. Women who are found to require ART for their own health should not discontinue their triple drug ARV regimen but continue on an appropriate life-long ART regimen.

**Infant:**

- Daily NVP from birth until 6 weeks of age (since the infant is breastfeeding and immediate protection is desirable, NVP would be the preferred infant prophylaxis and given for a full 6 weeks).

## 10.11 Clinical and laboratory monitoring of pregnant women receiving art for their own health and their infants

Clinical and laboratory monitoring of HIV-infected pregnant women should be done the same way as non infected women, and should be part of the comprehensive care package. Special consideration should be given to pregnant women to detect for any signs of clinically significant anemia. (Dabis et al, 1999)

Women should be routinely observed for potential disease progression based on WHO clinical stage. Using weight to determine clinical stage for women may be difficult. However, health-care providers may need to take into consideration her expected weight gain in relation to the gestational age of the pregnancy and her potential weight loss from HIV.

The monitoring of immunological status using CD4 cell count is not essential for monitoring patients on ART, but can be used to confirm clinical treatment failure (Dabis et al,1999 & Lallemant et al, 2004). Health care workers should aware that the absolute CD4 cell count decreases during pregnancy because of pregnancy-related haemodilution; after delivery, body-fluid changes normalize to the non-pregnant state, and

CD4 levels may rise by 50-100 cells/mm3(Chi et al, 2007; Lockman et al, 2009; Coffie et al,2008 & Kuhn et al,2009). A decrease in the absolute CD4 count of a pregnant woman from her CD4 values before pregnancy should therefore be interpreted with caution.

In addition, adverse reactions related to antiretroviral drugs should be closely monitored. Any new symptoms in pregnant women receiving NRTIs should be evaluated thoroughly. Good adherence to antiretroviral drug is one of the key successes for treatment as well as effective prevention of HIV transmission to infant.

## 10.12 Special considerations

### Women who acquire primary infection during pregnancy or breastfeeding

Women who become infected with HIV during pregnancy or while breastfeeding have a very high risk of transmitting the virus to their infants (Dunn et al, 1992). Retesting of women late in pregnancy is important in order to identify, establish the HIV status, and provide treatment and care to women on time. Standard ARV prophylaxis regimens for PMTCT should be used in this scenario.

### Women with anaemia

In resource limited settings, anaemia is common in pregnant women, particularly among HIV-infected pregnant women. **Some factors such as** malaria, worm infections, nutritional deficiencies and pregnancy itself, can severely exacerbate anaemia in women. Severe anaemia (Hb <7g/dl) in turn increases the risk of an adverse maternal outcome of delivery. Therefore, it is very important to screen and treat for all pregnant women for anaemia as part of antenatal care.

Pregnant or breastfeeding women eligible for ART who have clinically significant or severe anaemia should be started on a non-AZT-containing regimen while anaemia is being corrected. In such cases, AZT can be replaced with TDF or d4T. (WHO, 2010)

### Women with HIV-2 infection

HIV-2 has the same modes of transmission as HIV-1 but has been shown to be much less transmissible from mother to child (transmission risk 0-4%). (Adjorlolo-Johnson et al, 1994 & French Collaborative Study Group, 1994)

NNRTI drugs, such as NVP and EFV, are not effective against HIV-2. (Ren et al, 2002) For women who are infected with HIV-2 alone and eligible for treatment (based on the same eligibility criteria as for HIV-1), a triple NRTI regimen is recommended as the first-line ART regimen (e.g. AZT + 3TC + ABC). (WHO, 2010)

Women with HIV-1 and HIV-2 co-infection should receive one of the ART regimens recommended for women with HIV-1 infection alone.

Pregnant women living with HIV-2 alone who are not eligible for treatment for their own health should receive an ARV prophylaxis intervention consisting of AZT from 14 weeks of pregnancy (or as soon thereafter as possible) and continuing during labour and delivery.

### Women with active tuberculosis

The risk of active TB is approximately 10 times higher in HIV-infected pregnant women than in HIV-uninfected women and has been reported to account for about 15% of maternal mortality in some settings. (Pillay et al, 2004)

HIV-infected pregnant women with active TB should start ART, irrespective of the CD4 cell count. The TB treatment should be started first, and followed by ART as soon as clinically possible (within 8 weeks after the start of TB treatment). Drug interactions between rifampicin and some of the antiretroviral drugs (i.e. the boosted protease inhibitors) complicate simultaneous treatment of the two diseases.

As for all adults, EFV is the preferred NNRTI for HIV/TB co-infected pregnant women (starting after the first trimester). For those HIV/TB co-infected women not able to tolerate EFV, an NVP-based regimen or a triple NRTI regimen (e.g. AZT + 3TC + ABC or AZT + 3TC + TDF) can be used.

### Women with hepatitis B or hepatitis C virus co-infection

ART should be started in all pregnant women co-infected with HIV and HBV when treatment is required for the HBV infection, irrespective of the CD4 cell count or the WHO clinical stage. (WHO, 2009)

If co-infected pregnant women do not require HBV treatment, ART or ARV prophylaxis should follow the general recommendation for HIV-infected pregnant women.

### Pregnant women living with HIV who are injecting drug-users

Pregnant women require counseling about the effects of alcohol and other drugs on the growth and development of the fetus and the benefit of harm reduction services. Comprehensive care is required throughout the continuum of pregnancy and postpartum, addressing HIV, obstetrical and IDU-related needs through the co-management of services and referrals. Drug interactions may result in decreased methadone levels or raised ARV levels, increasing the risk of methadone withdrawal or ARV-related side-effects. NNRTIs significantly decrease the methadone level and can precipitate withdrawal symptoms.

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# Chapter 11: Managing potential exposures to blood-borne viruse including HIV in health care settings

The term post-exposure prophylaxis (PEP) is generally understood to mean the medical response given to prevent the transmission of blood-borne pathogens.

The risk of exposed to blood to blood-borne pathogen including HIV could be derived from:

- Occupational post-exposure within the health care setting, and
- Non-occupational exposure outside the work setting. This term predominantly refers to potential exposure through sexual assault. Other forms of potential non-occupational exposure include those arising from needle-sharing among injecting drug users and potential exposure through consensual sex.

## 11.1 Occupational post-exposure within the health care setting

Health care workers are most vulnerable to accidental exposure to blood and other body fluids or tissues while performing their work duties. (Rapiti et al, 2005) Such exposures may put the person at risk of acquiring a blood-borne infection including HIV.

PEP may never be considered 100 % effective. Therefore imperative that post-exposure prophylaxis policies and standard infection control practices is the first line of protection for health care workers to prevent the risk of getting infection. PEP for HIV should never be provided in isolation, but should always form a part of a wider strategy for preventing exposure to HIV. It is also associated with measures to prevent other blood borne diseases, such as hepatitis B and C.

### Prevention of occupational exposures

Prevention of exposure through safer practices, barrier precautions and other methods is the most effective strategy to reduce the risk of infection with HIV and other blood-borne pathogens in health care settings.

There are three significant priorities in prevention:

1. All health care workers need to be trained, and be able to demonstrate competency, in the implementation of standard precautions;
2. All staff needs to be provided with the necessary materials and protective equipment;
3. Operational protocols and systems at health care facilities should be designed and refined to minimize the risk of occupational exposure.

OSSHHM recommends defining these priorities and articulating them in infection control policies and guidelines for every health care facility.

Health care workers should also be knowledgeable about the risks of acquiring HIV and HBV sexually. They should have ready access to condoms, as well as confidential HIV and STI counseling, testing and treatment services.

Recommended practices to reduce the incidence of occupational exposures include:

- not recapping needles;
- not disconnecting needles from syringes after use;
- always transporting sharp objects in a kidney dish or puncture proof container;
- always placing used sharps in puncture proof containers for proper disposal (preferably by incineration);
- ensuring sharps containers are readily available in the immediate vicinity of where sharp instruments are used; and
- not placing sharps containers on the floor or low surfaces where they may be accessed by young children.

### Systems for management of occupational exposures

OSSHHM recommends that health care employers ensure that:

- an efficient local system is established for reporting and managing potential exposures of health care workers to blood and body substances;
- confidentiality of injured health care workers is maintained;
- expert advice is available to all health care workers 24 hours a day and processes are in place to facilitate rapid assessment, which is essential to ensure timely administration of specific prophylaxis if appropriate; and
- all occupational exposures are fully documented to ensure that procedures can be reviewed and strengthened.

### Risks of transmission associated with particular occupational exposures

Occupational exposures include:

- percutaneous injuries or cuts with used instruments (such as solid or hollow bore needles or scalpel blades) involving blood or other body substances;
- contamination of fresh cuts or abr asions with blood or other body substances; and
- contamination of the eyes or other mucous surface with blood or other body substances. From the pooled data from several studies of health care workers exposed to HIV in the workplace, it appears that the risk of HIV transmission after percutaneous exposure to HIV- infected blood is approximately 0.3 per cent (Panlilio et al, 2005).

### The following exposure characteristics are associated with relatively higher levels of risk:

- a deep injury;
- visible blood on the 'sharp' device causing the injury;
- injury by a needle that has previously been used in the patient's vein or artery; and
- expose to the infected person who has high viral load.

The risk of transmission from a 'sharp' object contaminated with other infected body fluids or tissues is believed to be lower than for exposure to infected blood.

After a mucous membrane (eye, nose or mouth) exposure to HIV-infected blood, the risk is approximately 0.09 per cent. (OARAC, 2008)

For a person unvaccinated against HBV, the risk after percutaneous exposure is 23 to 37 per cent if the 'source' person is hepatitis B 'e' antigen (HBeAg) negative, and 37 to 62 per cent if the 'source' is HBeAg positive. Infection with hepatitis B is possible following mucous membrane exposure but has not been quantified. (CDC, 2001)

The risk for HCV infection after percutaneous exposure to infected blood is approximately 1.8 per cent. Infection with HCV following mucous membrane exposure has not been quantified but is thought to be rare. (WHO, 2006)

## Eligibility criteria

### Type and risk of exposure

All potential risk for HIV transmission should be offered for post exposure prophylaxis.

The potential exposure includes exposure of non-intact skin (through percutaneous sharps injury or skin abrasion) or mucous membranes (through sexual exposure or splashes to the eyes, nose or oral cavity) to a potentially infected body fluid from a source that is HIV positive or has unknown HIV status. Body fluids that may transmit HIV include blood, genital secretions and cerebrospinal, amniotic, peritoneal or pleural fluids.

### Chronic exposure

Post-exposure prophylaxis is not appropriate in the context of chronic exposure to HIV.

In health care setting, distinguishing between chronic and episodic exposure can be difficult. Having more than one potential episode of exposure is not essentially linked with evidence that chronic exposure. For example, medical-waste workers experiencing repeated sharps injuries have episodic rather than chronic exposure. Greater emphasis on prevention is essential for individual who more likely repeated or chronic exposure.

### Timing of post-exposure prophylaxis

When the eligible has been indentified, post-exposure prophylaxis should be initiated as soon as possible, within hours and no later than 72 hours following the potential exposure.

According to the results of animal studies, initiating PEP within 12, 24 or 36 hours of exposure is more effective than initiating it 48 or 72 hours following exposure. (Martin et al, 1993)

### Negative indications for post-exposure prophylaxis

Post-exposure prophylaxis is not indicated:

- if the exposed person is HIV-positive from a previous exposure;
- in chronic exposure;
- if the exposure does not pose a risk of transmission, that is, after:

- exposure of intact skin to potentially infectious body fluids
- sexual intercourse using a condom that remains intact
- any exposure to non-infectious body fluids such as faeces, saliva, urine and sweat
- exposure to body fluids from a person known to be HIV-negative, unless this person is identified as being at high risk for recent infection and thus likely to be within the window period; and

- if the exposure occurred more than 72 hours previously.

## Immediate step for post exposure prophylaxis

### First aid

First aid is a term describing the set of actions that should be taken immediately after potential exposure occurs. The aim of first aid is to reduce contact time with the source person's blood, body fluids or tissues and to clean and decontaminate the site of the exposure.

First aid practices recommended for the broken skin injury that caused by needle or sharp instruments:

- Do not squeeze or rub the injury site;
- Wash the site immediately using soap or a mild disinfectant solution that will not irritate the skin;
- If running water is not available, clean the site with a gel or other hand-cleaning solution whatever is customarily available; and
- Do not use strong solutions, such as bleach or iodine, to clean the site as these may irritate the wound and make the injury worse.

First aid practices recommended after a splash of blood or body fluids:

After a splash contacts unbroken skin, do the following:

- Wash the area immediately
- If running water is not available, clean the area with a gel or other hand- rub solution, whatever is customarily available
- Do not use strong disinfectants

After a splash contacts the eye, do the following:

- Irrigate the exposed eye immediately with water or normal saline
- Do not use soap or disinfectant on the eye
- Sit in a chair, tilt the head back and have a colleague gently pour water or normal saline over the eye, pulling the eyelids up and down to make sure the eye is cleaned thoroughly
- If contact lenses are worn, leave these in place while irrigating the eye, as they form a barrier over the eye and will help protect it. Once the eye has been cleaned, remove the contact lenses and clean them in the normal manner.

After a splash contacts the mouth

- Spit the fluid out immediately
- Rinse the mouth thoroughly, using water or saline, and spit again. Repeat this process several times
- Do not use soap or disinfectant in the mouth

### Reporting exposure

Individual exposed worker should report the incident to the designated person soon after the first aid complete. A designated person should oversee the investigation of both reporting and exposure incidents, as specified in local protocols. Complete an exposure report, which should contain the following information:

- the name of the staff member involved;
- the area where the incident occurred, such as the ward, operating room or emergency room;
- a description of the incident;
- the name of the 'source' person whose blood or body substances were involved in the incident (if known); and
- if the source of the blood is unknown, this must also be documented.

Send a copy of the exposure report to the institutional infection control professional. The exposed health care worker's supervisor should be made aware of any risks or lapses in standard precaution procedures in a confidential, sensitive and non judgmental way.

## Assessment

### Medical assessment after occupational exposures

A medical risk assessment involves taking and recording the history and details of the occupational exposure to assess the risk of the exposed person acquiring HIV, HBV and HCV from the 'source' person. A trained professional should make this assessment immediately after first aid is attended, regardless of what time of day the occupational exposure occurs.

Information to be examined during the assessment includes:

- date, time and location of the exposure;
- duty being performed at time of the exposure;
- how the exposure occurred;
- protective clothing, such as gloves, being worn at the time of the incident;
- nature of exposure such as percutaneous, mucous membrane, non-intact skin;
- type and volume of blood or other body fluids involved;
- duration of contact with blood or other body fluids;
- if the exposure was a sharps injury: the type of implement involved, whether it was visibly contaminated with blood, the depth of injury and whether bleeding occurred;
    - if the exposure was a needle stick injury: the gauge of needle, size of syringe, purpose for which needle was used;
    - if the exposure involved non-intact skin: the condition of skin;
    - HIV, HBV and HCV status of the 'source' person (if known); and
    - HBV immunity and vaccination history of the exposed person.

### The exposure and the 'source' patient

The exposure should be evaluated for its potential to transmit a blood-borne pathogen based on body substance and severity of exposure. Source identification and testing are only necessary if the results will change the clinical management of the exposed worker.

- If the exposure is assessed as having no or low risk of HIV transmission, then medication for post-exposure prophylaxis against HIV is not indicated. This applies regardless of whether the source person is known to be HIV positive or not. In low-risk exposures, testing of the source is not necessary.
- When testing of a 'source' patient of unknown status is appropriate, it should only occur with the person's informed consent.
- The 'source' person should receive appropriate pre test counseling and a plan for referral for care, treatment and support.
- Confidentiality must be maintained throughout the process.

### Assessment for exposed health care worker

Medical assessment constitutes an emergency for the exposed health care worker. Assessment should include baseline tests on a venous blood specimen from the health care worker, with fully informed consent, to ascertain whether the exposed person was already infected with a blood-borne pathogen from previous exposure before the incident:

- Baseline testing should occur as soon as possible following exposure (after first aid has been completed), and certainly within 72 hours
- Pre-test counseling for HIV should occur before any blood is taken for testing
- Baseline tests are usually HIV antibody, hepatitis B surface antigen (HBsAg) and surface antibody (HBsAb), as well as hepatitis C antibody where this test is available
- The health care worker's tetanus immunisation status should be considered
- Follow-up re-testing for HIV, HBV and HCV (where available) should occur at six weeks, three months and six months

Clinical evaluation and baseline testing of the exposed health care worker should proceed only after pre-test counseling and with informed consent. Pre-test counseling should always include:

- giving a realistic assurance of privacy and confidentiality;
- reviewing and, if necessary, further explaining HIV, HBV and HCV infection and their consequences;

- explaining testing, possible results and confirmatory testing;
- assessing risk related to past and current sexual and other behaviours, as well as any previous occupational exposures;
- assessing risk related to the occupational exposure in question;
- explaining the transmission risk for HIV associated with occupational exposure;
- assessing anxiety level and coping mechanisms;
- obtaining informed consent for testing;
- obtaining informed consent for a pregnancy test (if indicated);
- planning for precautions while awaiting test results (and while taking post-exposure prophylaxis medication, if indicated), including consideration of safer sexual practices or abstinence, cessation of breastfeeding if lactating and any required modification of occupational duties (this would only be necessary for health care workers whose work includes exposure-prone procedures – that is, procedures that involve the use of sharp instruments in confined spaces such as the mouth, vagina, or the chest or abdominal cavities);
- providing information about the potential adverse effects of antiretroviral medications;
- addressing any other risks identified by sexual and behavioural history;
- arranging support while awaiting results, and while taking post-exposure prophylaxis medication (if indicated); and
- reviewing the sequence of events that preceded the exposure, and providing exposure risk reduction education in a sensitive and non-judgmental way.

## Drug use for post-exposure prophylaxis for occupational exposure

PEP is treatment to reduce the likelihood of HIV, HBV and tetanus infection in health care workers after possible occupational exposure. There is no PEP available for HCV.

## Post-exposure prophylaxis for HIV

There are no prospective trials to prove the effectiveness of PEP for HIV in humans. Our understanding of the pathogenesis of HIV infection suggests that antiretroviral drugs should further reduce the already low rate of infection following occupational exposure, provided treatment is initiated early enough. A retrospective case-control study suggested that the use of zidovudine is associated with a reduction in risk of approximately 80 per cent. (Cardo et al, 1997) Clinical trials of the use of antiretroviral drugs for prevention of mother-to-child transmission of HIV consistently demonstrate good efficacy following perinatal exposure, even in babies who do not receive treatment until after birth. Although these results are encouraging, protection of newborns is not absolute and the relevance of this situation to occupational exposure cannot be guaranteed.

Where PEP is indicated, it should be offered immediately without waiting for the results of HIV testing from the 'source' of the exposure. PEP for HIV should be provided using a combination of two antiretroviral drugs as soon as possible after exposure to a 'source' person with confirmed HIV (or where it is medically likely that the 'source' person is infected with HIV). When the injury involves an increased risk of infection (an injury caused by a large-bore hollow needle, associated with a deep puncture, or caused by a device visibly contaminated with blood or a device that has been in a patient's artery or vein), the regimen should be expanded to include a third antiretroviral drug.

Table 11.1 and 11.2 summaries current indications for HIV PEP and prescribed regimens.

Nevirapine should not be used for PEP because of a very substantial risk of skin and liver toxicity in people with normal immune function.

Routine use of three drugs is not recommended for all exposed people. The disadvantages of adding a third drug are that it increases the probability that adverse events will occur, further complicates antiretroviral drug adherence and reduces the chance that the full four- week course of PEP will be completed.

If prophylaxis is commenced and the 'source' person is subsequently determined to be HIV negative, antiretroviral drugs should be discontinued.

**Table 11.1:** Indications for prophylaxis against HIV infection after percutaneous injury or mucosal exposure, according to infection status of the 'source' person

| Risk posed by exposure* | Infection status of the 'source' person** | | | | |
|---|---|---|---|---|---|
| | HIV positive, class 1 | HIV positive, class 2 | Unknown status | Unknown 'source' person | HIV negative |
| Lower | Basic two-drug PEP is recommended. | Expanded (three-drug) PEP is recommended. | Generally PEP is not warranted but basic two-drug PEP can be considered if the 'source' person has risk factors for blood- borne virus infections.† | Generally prophylaxis is not warranted but basic two-drug prophylaxis can be considered in settings where it is likely that the 'source' may have had a blood-borne virus . | PEP is not warranted. |
| Higher | Expanded (three-drug) PEP is recommended. | Expanded (three-drug) PEP is recommended. | Generally PEP is not warranted but basic two-drug PEP can be considered if the 'source' person has risk factors for blood- borne virus infections.† | Generally prophylaxis is not warranted but basic two-drug prophylaxis can be considered in settings where it is likely that the 'source' may have had a blood-borne virus . | PEP is not warranted. |

Notes:

* Injuries caused by solid needles and superficial injuries pose a lower risk of infection; those involving a large-bore hollow needle, a deep puncture, a device visibly contaminated with blood, or a needle used in a patient's artery or vein pose a higher risk of infection. PEP with antiretroviral drugs is not indicated for contact between intact skin and blood or other body fluids contaminated by HIV.

** Class 1 HIV positive status is defined by asymptomatic HIV infection or, if known, a viral load <30,000 copies per ml; Class 2 HIV positive status is defined by symptomatic HIV infection, acute seroconversion illness, or a viral load >30,000 copies per ml.

† If the 'source' person has risk factors for HIV infection, prophylaxis is optional and should be based on an individualised decision made jointly by the exposed health care worker and the treating doctor.

**Table 11.2: Antiretroviral regimens for post-exposure prophylaxis**

| Regimen | Doses | Principal adverse effects |
|---|---|---|
| Basic PEP (for lower-risk exposure) | | |
| zidovudine<br>plus lamivudine | One 300 mg tablet twice daily for four weeks<br>One 150 mg tablet twice daily for four weeks | Anaemia, neutropenia, nausea, headache, insomnia, muscle pain, weakness<br>Abdominal pain, nausea, diarrhoea, rash, pancreatitis (all very rare) |
| Expanded PEP (for higher-risk exposure) – Basic two-drug regimen plus | | |
| efavirenz | One 600 mg tablet at bed time for four weeks | Rash (including Stevens-Johnson syndrome), insomnia, somnolence, dizziness, trouble concentrating, abnormal dreaming; potentially teratogenic in 1st trimester of pregnancy |
| Expanded PEP (for higher-risk exposure in health care workers in the first trimester of pregnancy) – Basic two-drug regimen plus | | |
| lopinavir/ritonavir | 400 mg/100 mg twice daily for four weeks | Diarrhoea, nausea, abdominal pain, weakness, rash |

*Source: (CDC, 2001)*

## Post-exposure prophylaxis for hepatitis B

Childhood vaccination against HBV is included in the expanded programme of immunisation in Pacific Island countries and territories. OSSHHM recommends that health care institutions institute a programme to offer immunisation for HBV to all health care workers.

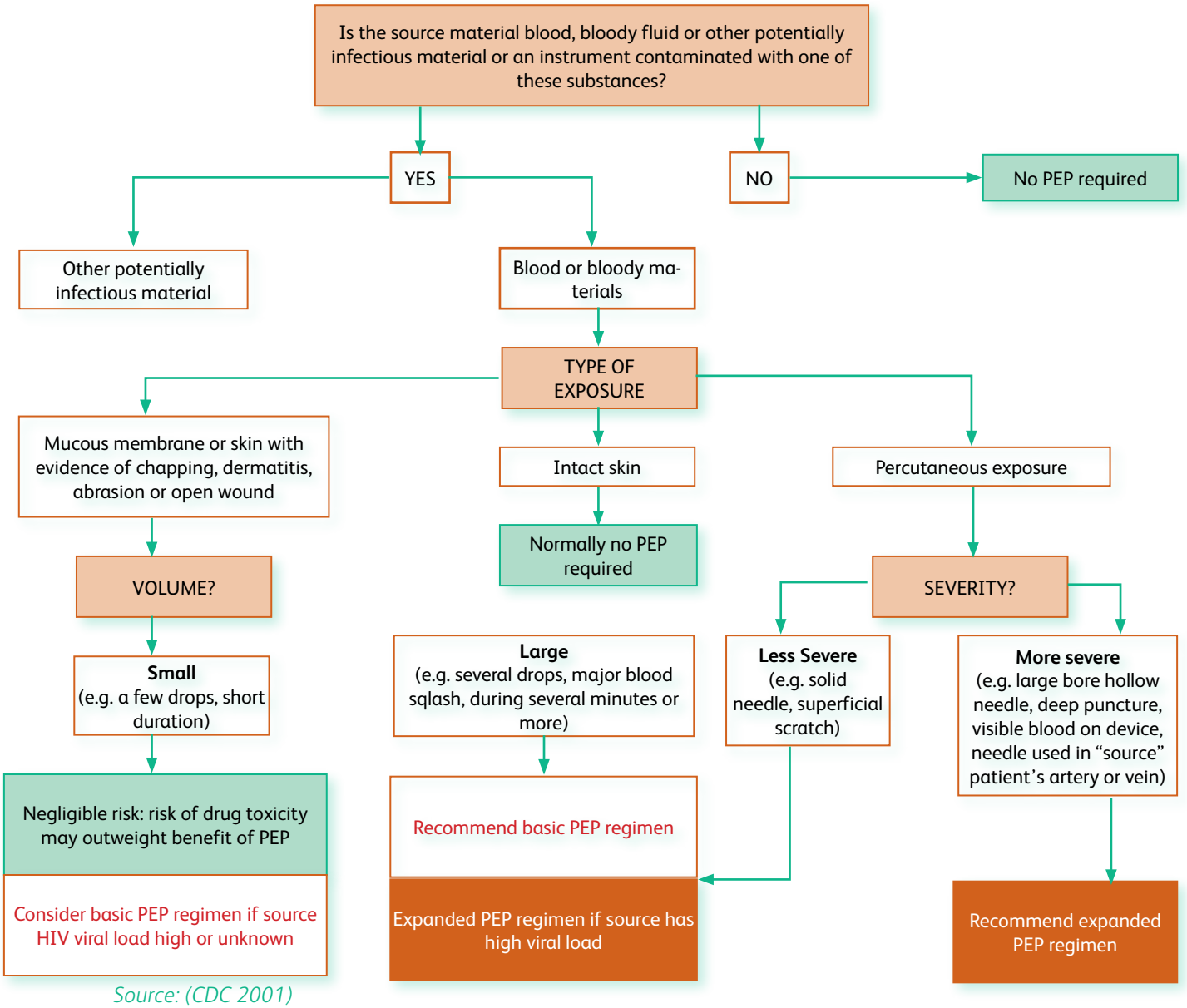
Laboratories in some Pacific Island countries and territories are unable to offer testing for HBV. Table 10.3 below summarises the recommended actions to protect health care workers against HBV after occupational exposure, where testing and hepatitis B immunoglobulin (HBIg) are available.

## Post-exposure prophylaxis for tetanus

Although exposure from discarded needles found in public places such as beaches are thought to pose a very low risk of blood-borne virus transmission, tetanus prophylaxis should be considered in these circumstances. Where the exposure constitutes a tetanus-prone injury, recommended prophylaxis depends on the exposed person's past history of tetanus

- If it is less than five years since immunisation, then no tetanus immunoglobulin or tetanus toxoid is necessary.
- If it is 5 to 10 years since immunisation, a tetanus toxoid or adult diphtheria immunisation and tetanus combined booster is recommended.
- If it is longer than 10 years since immunisation, both tetanus immunoglobulin and tetanus toxoid or adult diphtheria and tetanus immunisation (in different limbs) are recommended.

**Figure 11.1:** US Centers for Disease Control and Prevention algorithm for evaluating the risk of HIV transmission following occupational exposure




*Source: (CDC 2001)*

## Post-exposure prophylaxis for hepatitis C

Few Pacific small island countries and territories can currently test for hepatitis C and there is no HCV prophylaxis to offer at this time. Immunoglobulin is ineffective for HCV. Potential PEP agents such as ribavirin and interferon are not currently recommended because they are potentially very toxic and unlikely to be available.

## Clinical follow-up and counseling

In addition to HIV antibody testing at the time of the injury, exposed health care workers should be offered repeat testing at six weeks, three months and six months after exposure.

Health care workers who take PEP should use condoms (or abstain from sex) until serology is negative at six months post-exposure. Female health care workers who are lactating may consider stopping breastfeeding. Health care workers whose work includes exposure-prone procedures (those involving the use of sharp instruments in confined spaces such as the mouth, vagina, and the chest or abdominal cavities) should consider with their clinician whether they need to modify their practice until seronegativity is confirmed at six months following the exposure.

**Table 11.3:** Post-exposure prophylaxis for hepatitis B (where serological testing, HBIg and HBV vaccine are available)

| | | | 'Source' patient | |
|---|---|---|---|---|
| | | | **HBsAg positive** | **Unknown** |
| Health care worker | Unvaccinated | | HBIg x 1 dose<br><br>plus<br><br>Hepatitis B vaccine x 3 doses | Hepatitis B vaccine x 3 doses |
| | Vaccinated | Serological<br><br>'responder' (HBsAb >10 mIU/ml) | No treatment | No treatment |
| | | Serological<br><br>'non-responder' (HBsAb <10 mIU/ml) | HBIg x 1 dose<br><br>plus<br><br>Hepatitis B vaccine x 3 doses | If higher-risk exposure: HBIg x 1 dose plus<br><br>Hepatitis B vaccine x 3 doses |
| | | Antibody status unknown | Test health care worker for anti-HBs if available<br>If anti-HBs >10 mIU/ml: No treatment<br><br>If anti-HBs <10 mIU/ml: HBIg x 1 dose<br><br>plus<br><br>Hepatitis B vaccine x 3 doses | Test health care worker for anti-HBs if available<br><br>If anti-HBs >10 mIU/ml: No treatment<br><br>If anti-HBs <10 mIU/ml: Hepatitis B vaccine x 3 doses |

*Source: (CDC, 2001)*

If the health care worker is infected with HIV, they will usually develop an acute retroviral syndrome two to six weeks after exposure. This syndrome is an illness that resembles glandular fever with fevers, sweats, malaise, lethargy, anorexia, nausea, myalgia, arthralgia, headache, sore throat, diarrhoea, lymphadenopathy and rash.

Occupational exposure to HIV is a frightening experience. Some psychological morbidity (anxiety, depression, insomnia) and even post-traumatic stress disorder are relatively common among health care workers following such an exposure. Early and frequent follow- up appointments for counseling and clinical review is essential.

Should the health care worker become HIV positive, clinical management should follow these recommendations and ongoing counseling and support will be essential.

### Special considerations

Where the 'source' person is already taking antiretroviral therapy (especially a second-line or other drug combination), the possibility of HIV drug resistance should be considered. In this situation, and in all other complex circumstances, treating clinicians should seek advice from more experienced colleagues through the OSSHHM network as soon as possible.

## 11.2 Post-exposure prophylaxis for non-occupational exposure

OSSHHM recommends appropriate use of post-exposure prophylaxis following non- occupational exposure (PEP-NOE) to HIV as a potential method of preventing HIV infection.

The recommendations in this section are based on a comprehensive review of the literature pertaining to PEP-NOE.

The recommendations for PEP-NOE may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgment of the service provider and with consideration of individual client circumstances and wishes.

## Risks of HIV transmission

### Background

Studies indicate that once HIV crosses a mucosal barrier, it may take up to 48 to 72 hours before HIV can be detected within regional lymph nodes and up to five days before HIV can be detected in blood (Miller et al, 2000; Pinto et al, 1997 & Spira et al, 1996).

### Risks of HIV transmission

Risk of HIV transmission = Risk that source is HIV positive × Risk of exposure

(including co-factors such as sexually transmissible infections, high viral load and bleeding)

The risk of HIV transmission is dependent on the exposure characteristics, the infectivity of the source and host susceptibility. The risk of HIV transmission may be increased by:

- a high plasma viral load in the source (transmission may still be possible with low or undetectable viral loads. (Gray et al, 2011; Cardo et al, 1997; Quinn et al, 2007 & Deeks et al, 2000)
- breaches in the mucosal barrier such as abrasions and genital ulcer disease, following sexual assault or intercourse. (Rothenberg et al, 1998; Haase et al, 2002 & Rottingen et al, 2001)

**Table 11.4:** The risk of HIV transmission following an exposure from a source known to be HIV positive

| Type of exposure | Estimated risk of HIV transmission per exposure (%) |
|---|---|
| Blood transfusion (one unit) | 90–100 [30] |
| Receptor of anal intercourse | 0.1–3.0 [31,32] |
| Receptor of vaginal intercourse | 0.1–0.2 [32–37] |
| Penetrator of vaginal intercourse | 0.03–0.09 [23] |
| Penetrator of anal intercourse | 0.06 [38] |
| Receptor of oral sex (fellatio) | 0–0.04 [38] |
| Needle/stick injury | 0.3 (95 CI 0.2–0.5) [39–41] |
| Sharing injecting equipment | 0.67 [42] |
| Mucous membrane exposure | 0.09 (95 CI 0.006–0.5) [43] |
| *Source: (Mayer et al, 2006)* | |

## Calculating the risk of HIV transmission

Table 11. 5 gives examples of estimates of an individual's risk of contracting HIV through a source who is known to be HIV positive and through a source of unknown status, according to type of exposure.

**Table 11.5:** Calculating the risk of HIV transmission

| Population group and type of exposure | Risk of HIV transmission | |
|---|---|---|
| | Source unknown for HIV | Source known HIV positive |
| Unprotected receptor for anal intercourse | 15 % x 3 % = 0.45 %<br>1 in 222 | 1 x 3 % = 3 %<br>1 in 33 |
| Unprotected receptor for vaginal intercourse | 0.1 % x 0.09 % = 0.00009 %<br>1 in 100,000 | 1 x 0.09 % = 0.09 %<br>1 in 1111 |
| Intravenous drug user sharing injecting equipment | 4.7 % x 0.67 % = 0.031 %<br>1 in 3226 | 1 x 0.67 % = 0.67 %<br>1 in 149 |
| Note: Risk is calculated using data from Table 4 according to the formula: Risk of HIV transmission=Risk that source is HIV positive x Risk of exposure. | | |
| *Source: (Mayer et al, 2006)* | | |

## Evidence to support post-exposure prophylaxis

From a retrospective case-control study among health care workers occupationally exposed to HIV infection, it was demonstrated that a 28-day PEP course of zidovudine is protective. (Cardo et al, 1997) However, in some instances PEP has failed to prevent HIV infection following occupational exposure. (Roland et al, 2005) In a Brazilian study, none of the individuals who received PEP within 72 hours following sexual assault seroconverted, but seroconversion did occur in 2.7 per cent of individuals who took PEP after the 72-hour window. (Benn et al, 2001) This result shows that PEP may be less effective or ineffective if initiated after 72 hours of the exposure. In the sexual exposure setting, 'failures' of PEP-NOE have been attributed to late initiation, poor adherence, and repeated exposure to HIV. (CDC, 2001)

The availability of PEP-NOE may make individuals complacent to primary prevention strategies and consequently may result in more frequent high-risk behavior. ( Mayer et al, 2006) Some studies show that the availability of PEP-NOE increases risk behaviour especially among the younger and less educated gay men. (Winston et al, 2005) while other studies show no increase in risk behaviour. If the possible exposure to HIV causes a state of acute anxiety, the provision of PEP-NOE may help alleviate such anxiety.

A risk–benefit analysis should be undertaken for every individual presenting following an exposure. The decision to initiate PEP-NOE should be made on a case-by-case basis.

## Recommendations for prescribing PEP-NOE

OSSHHM recommends that PEP-NOE should be regarded as a last option where conventional, proven methods of HIV preventions have failed. PEP-NOE should be considered only if an individual presents within 72 hours of exposure.

The following tables provide more specific recommendations based on the HIV status and area of origin of the source. Table 6 first provides PEP recommendations in cases where the source is known to be HIV positive.

**Table 11.6:** Consideration of PEP-NOE with potential exposure risk if source is known to be HIV positive

| Type of exposure | Recommendation |
|---|---|
| Receptor of anal sex | PEP-NOE recommended |
| Inserter of anal sex | PEP-NOE recommended |
| Receptor of vaginal sex | PEP-NOE recommended |
| Inserter of vaginal sex | PEP-NOE recommended |
| Fellatio with ejaculation (receptor) | PEP-NOE considered |
| Splash of semen into eye | PEP-NOE considered |
| Fellatio without ejaculation (receptor) | PEP-NOE not recommended |
| Cunnilingus (receptor) | PEP-NOE not recommended |
| *Source: (Mayer et al, 2006)* | |

If the source is not known to be HIV positive, then try – where possible – to establish the HIV status of the source individual using voluntary confidential counseling and testing (VCCT) principles as soon as possible. Table 11. 7 list the PEP-NOE recommendations where the HIV status of the source is unknown.

High prevalence groups to which the recommendations in Table 11.8 apply are those where there is a significant likelihood of the source individual being HIV positive, such as men who have sex with men,

sex workers and people from areas of high HIV prevalence (particularly sub-Saharan Africa). HIV transmission is likely to increase following aggravated sexual intercourse (anal or vaginal), such as that experienced during sexual assault, hence PEP- NOE may be recommended readily in such situations.

**Table 11.7:** Consideration of PEP-NOE with potential exposure risk if source is of unknown HIV status but from group with high HIV prevalence

| Type of exposure | Recommendation |
|---|---|
| Receptor of anal sex | PEP-NOE recommended |
| Inserter of anal sex | PEP-NOE considered |
| Receptor of vaginal sex | PEP-NOE considered |
| Inserter of vaginal sex | PEP-NOE considered |
| Fellatio with ejaculation (receptor) | PEP-NOE considered |
| *Source: (Mayer et al, 2006)* | |

Table 11.8: Consideration of PEP-NOE with potential exposure risk if source is unknown and not from a group with high HIV prevalence

| Type of exposure | Recommendation |
|---|---|
| Receptor of anal sex | PEP-NOE considered |
| Inserter of anal sex | PEP-NOE not recommended |
| Receptor of vaginal sex | PEP-NOE not recommended |
| Inserter of vaginal sex | PEP-NOE not recommended |
| Fellatio with ejaculation (receptor) | PEP-NOE not recommended |
| *Source: (Mayer et al, 2006)* | |

## Recommendations for drug regimens to be used

Zidovudine (AZT) is the only drug to date that has been studied in regard to PEP and for which there is evidence of reduction of risk of HIV transmission following occupational exposure. It is for this reason that zidovudine is included in all first choice PEP regimens, unless there is evidence that the source virus is resistant to this drug.( Department of Health UK, 2004 & Tapsall et al., 2001) Nevirapine is not recommended due to hepatotoxicity. (Lert et al, 2000 & Kalichman et al., 1998)

## Recommended combinations

2NRTI + PI (boosted PI)

Given that, for optimal efficacy, PEP-NOE should be commenced as soon as possible after exposure, 24-hour access should be available including during weekends and public holidays (Winston et al., 2005). As with PEP following occupational exposure, local policies and pathways must be established to enable this level of accessibility. OSSHHM recommends that, in each Pacific small island countries and territories, one or more PEP officers are identified for the provision of PEP. Each officer must be experienced in the management of antiretroviral therapy and have expertise in HIV testing and transmission.

It is recommended that individuals presenting for PEP-NOE are referred to the PEP officer and seen by them as early as possible – whether or not PEP-NOE is offered or accepted. PEP-NOE should not be withheld until such expertise is available.

**Table 11.9:** Antiretroviral regimens for post-exposure prophylaxis for non-occupational exposure

| Regimen | Doses |
|---|---|
| PEP-NOE for lower-risk exposure | |
| Zidovudine plus Lamivudine | One 300 mg tablet twice daily for four weeks<br>One 150 mg tablet twice daily for four weeks |
| PEP-NOE for higher-risk exposure – Basic 2-drug regimen plus | |
| Efavirenz | One 600 mg tablet at bed time for four weeks |
| *Source: (ASHM, 2005)* | |

## Assessment and initial management of the individual presenting for PEP-NOE

When an individual presents for PEP-NOE, an appropriate risk assessment should be performed. At presentation, and prior to administration of PEP-NOE, the following issues must be discussed with the individual:

- the rationale for PEP-NOE;
- the potential risks and side effects of PEP following sexual exposure to HIV; and
- the arrangement for early follow-up with a PEP officer.

Keep documentation to demonstrate that the above issues have been discussed. It is mandatory that individuals for whom PEP-NOE is considered have an HIV VCCT screening test (with rapid result) prior to or shortly after initiating therapy. If this test detected any previously undiagnosed HIV infection, this finding would significantly alter the management.

Those presenting for PEP-NOE must be seen by the PEP officer at the earliest opportunity, who will then address the following issues:

- pre-test counseling;
- the need for compliance with the four-week course of PEP-NOE if the baseline result is negative, with discussion including the side effects of the drugs

and the support available in the clinic and in the community to help adherence;

- the need to have a follow-up HIV test at three and six months;
- the need for safer sex for the following three months; and
- planning for coping strategies.

## Follow-up arrangements for individuals presenting for PEP after Sexual Exposure

Regular follow-up, ideally on a weekly basis at first, is necessary for individuals receiving PEP-NOE to monitor compliance and possible adverse effects of the medications. This approach is designed to improve adherence to the treatment regimen and allow prompt management of any concerns or complications.

All individuals who receive PEP (and those who decline but have had significant risk of exposure to HIV) should be re-tested for HIV antibodies at three and six months.

All individuals presenting for PEP-NOE should be offered comprehensive screening for other STIs at an appropriate time, in accordance with the guidelines on screening for STIs. Hepatitis B vaccination (and immunoglobulin) should also be considered to PEP-NOE.

The opportunity should be taken for appropriate behaviour modification and risk-reduction counseling with individuals presenting for PEP-NOE.

## Management of individuals who repeatedly present for PEP after Sexual exposure or with ongoing risk behaviour

Repeat users of PEP-NOE warrant attention. Consider repeat courses of PEP-NOE according to the risk of HIV acquisition at the time of presentation, particularly if the circumstances suggest this to be appropriate (commercial sex workers, serodiscordant couples, inability to control the preventative behaviour of their partners). Individuals who present more than once a year for PEP-NOE, who do not otherwise have prevailing circumstances for doing so, should be referred for counseling. PEP-NOE should be considered if the current risk circumstances clearly indicate a need for this.

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# Chapter 12: HIV in Dentistry

As the HIV disease progresses and immune status decreases it allows other diseases to affect the patient. New pathogens can more easily cause disease, due to the immune-compromised state patients. The people living with HIV may present symptoms more severe than a person whose immune system is good.

Pre-existing conditions that remained latent or under the control of a functioning immune system can become re-activated and cause disease. These pathologies are defined as opportunistic infections. Oral lesions may be present at all stages of HIV infection. However, it should be emphasised that HIV-associated oral lesions are not pathognomonic, as it is possible to find the conditions in immunocompetent people without HIV infection.

Similar to systemic HIV-associated pathology, the oral lesions presenting during HIV infection are more likely to occur with a high VL or a reduced CD4 cell count. Oral manifestations of the seroconversion illness may include oral ulcers, oral candidiasis, oral herpes and tonsillitis, and uncommonly gingivitis and stomatitis.

The failure of normal immune surveillance throughout the course of HIV infection also increases the risk of neoplasia.

## Impact of HIV treatment on oral conditions

Oral manifestations may occur with the progression of HIV infection in patients without medical treatment or intervention. The impact of ART generally results in a marked reduction in viral load, which in turn enables reduces the oral manifestations.

Occasionally, some conditions such as aphthous ulceration may persist while HIV-related periodontal diseases may recur, even in the presence of adequate viral control. However, co-factors such as stress and smoking have been suggested to have a role in their re-emergence.

Introduction of ART often improves oral health and stabilizes or cures existing oral conditions. Some oral complications may result from the initiation of therapy. There seems to be a few significant oral side effects associated with any particular medication. However, the combination of potent antiretroviral drugs with other medications may commonly result in xerostomia and dry lips. Often persistent cracking will occur at the anterior commissure, which appears to have no causative fungal or obvious pathogen involvement. Dryness of the mouth can often cause rapid dental decay, which is significant if pre-existing HIV related periodontal diseases have caused significant damage to root structure.

**Oral Conditions associated with HIV infection and the development of advanced HIV disesase can be aetiologically divided into five major groups:**

1. Fungal, bacterial and viral infections
2. Oral Neoplasias
3. Neurological COnfitions
4. Lesions of uncertain aetiology
5. Oral Conditions associated with HIV treatment

**Other co-infections and conditions associuated with HIV infection, which are significant to dentists are:**

1. Syphilis
2. Tuberculosis
3. Persistent generalized lymphadenopathy
4. Gastro-Oesophageal reflux disease (GORD)
5. Odynophagia

*Source: (ASHM, Dentist and HIV publication, 2011)*

## Fungal Infections:

Fungal Infections are the most common infections seen in the PICT's. The main fungal pathogen involved in oral disease is Candida Albicans.

Fungal infections may appear at any time throughout the HIV infection, though they are more prevalent when the CD4 count is less than 500cells/mm3, 90 % of patients with AIDS are affected with oral candidiasis at some point during their disease. It has been seen that the introduction of ART has reduced the incidence of oral candida.

## Erythematous candidiasis

**Figure 1:** Erythematous candidiasis on the of the tongue. *Source: (ASHM 2011)*

**Description:** patchy red or erythematous areas that may become diffuse and atrophic

**Location:** commonly found on the hard palate and the dorsum of the tongue and occasionally on the buccal mucosa

**Symptom:** none or mild-to-moderate pain or burning

**Duration:** usually intermittent, however may be chronic. The chronic form is often associated with dentures

**Diagnosis:** clinical, with a swab for microscopy and culture when there is an uncertain diagnosis or poor response to treatment

**Treatment:** Antifungals Nystatin 100,000 units 4 times a day after food for 7 days / Fluconazole 200mg daily for 7-14 days/ Ketoconazole 200mg daily for 14days (depending on availability in the region)

## Pseudomembranous candidiasis

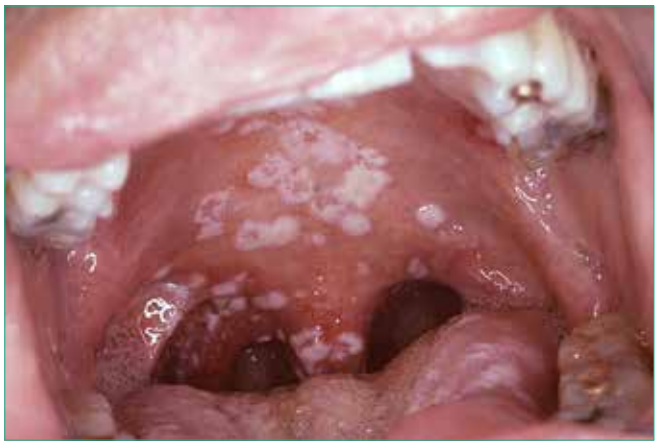

**Figure 2: Pseudomembranous candidiasis affecting palate, tongue and buccal mucosa**

*Source: (CDC Website)*

**Description:** creamy white or yellow plaques which, when scraped, reveal an erythematous or bleeding mucosal surface

**Location:** may be found on any of the intra-oral surfaces

**Symptoms:** none or mild-to-moderate pain or burning

**Duration:** usually intermittent, however may be chronic

**Diagnosis:** clinical, with a swab for microscopy and culture when the diagnosis is uncertain or there is a lack of response to treatment

**Treatment:** Antifungals as mentioned above

## Angular cheilitis

**Figure 3:** Angular cheilitis affecting the corner of the mouth. *Source: (Medical Pictures Infor web site)*

Angular cheilitis is commonly associated with a concurrent infection with *Staphylococcus aureus*.

**Description:** erythema and red or white fissures or ulcers at the corners of the mouth

**Location:** found at the labial commissures

**Symptoms:** none or mild-to-moderate pain or burning

**Duration:** usually intermittent but can be chronic

**Diagnosis:** clinically diagnosis is done in most comment practice. However, taking a swab for microscopy and culture may be appropriate if there is an uncertain diagnosis or the lesion does not respond well to therapy.

**Treatment**: Antifungals as mentioned above and Miconazole 2 % cream or gel topically for four times a day for at least 14 days. If not, Nystatin cream topically2-3 times a day to the angles of the mouth for at least 14 days.

## Chronic hyperplastic candidiasis

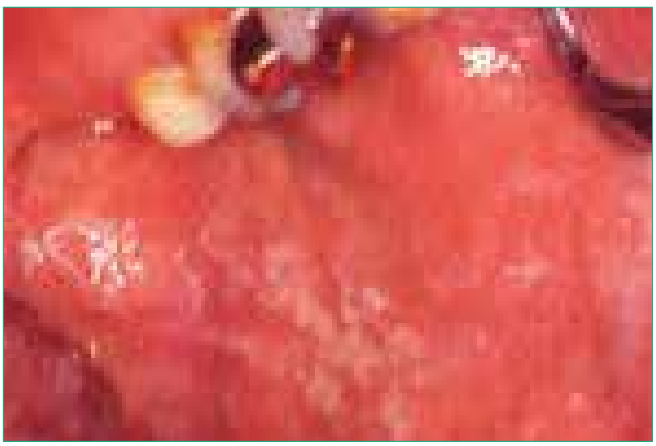

**Figure 4:** Hyperplastic candidiasis of the palate
*Source: (Oral Disease and Conditions web site)*

This condition has an association with smoking. It is generally considered premalignant and the lesion may demonstrate dysplasia.

**Description:** homogenous white patches that are rough and irregular and cannot be wiped off. Clinically indistinguishable from leukoplakia and can be confused with oral hairy leukoplakia

**Location:** most commonly found on the buccal mucosa near the labial commissures with less frequent involvement of the palate or tongue

**Symptoms:** usually symptomless but speckled lesions may produce discomfort

**Duration:** chronic

**Diagnosis:** Clinical diagnosis is done in most practices. A swab for microscopy and culture is needed when there is an uncertain diagnosis or poor response to treatment, though difficult to do in a resource limited setting, as the PICT's.

## Linear gingival erytema (LGE)

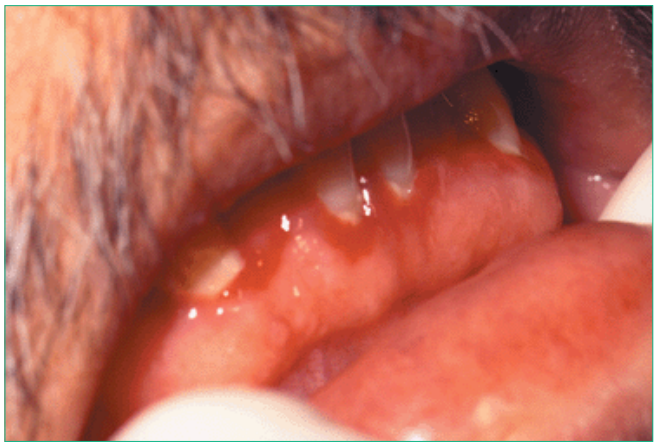

**Figure 6:** Linear gingival erythema
*Source: (A Clinical Guide to Supportive and palliative care for HIV/AIDS Website)*

Linear gingival erythema is a gingival condition of immunosuppressed people. Evidence supports the theory of a fungal origin for this condition. It is classified as a disease of fungal aetiology. The lack of response of linear gingival erythema to oral hygiene measures and conventional periodontal therapy is important in diagnosis.

**Description:** initially discrete petechiae that may coalesce into a 1-3 mm wide, intensely erythematous band on the marginal gingivae. This condition is unlike gingivitis induced solely by dental plaque in that the erythema associated with linear gingival erythema is disproportionate to any local factors, such as plaque and calculus.

**Location:** found along the gingivae and may be localized or generalized

**Symptoms:** usually no significant symptoms, however the gingival may be tender and bleed easily

**Diagnosis:** clinical

## Bacterial Infections

There is a wide range of bacterial pathogens that cause oral disease in patients with HIV infection. This section will deal with bacterial periodontal infections associated with HIV infection as well as syphilis and tuberculosis.

## Periodontal Infections

For dentists, the most significant oral manifestation of HIV-associated bacterial infections is periodontal pathology. These pathologies fall into three groups:

i. Linear gingival erythema

ii. Necrotising periodontal diseases and

iii. accelerated progression of chronic periodontitis

## Necrotising ulcerative gingivitis

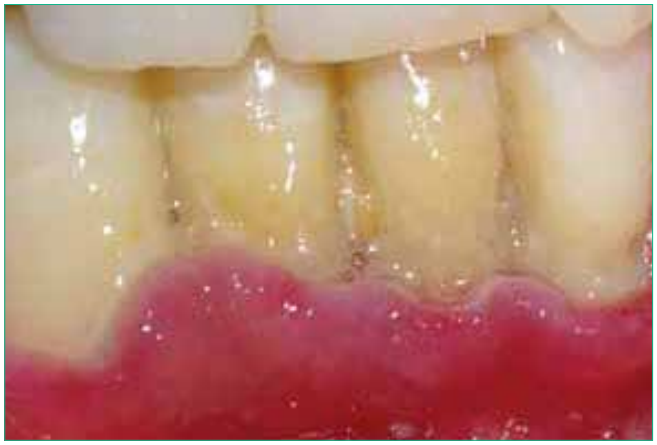

**Figure 7:** Necrotising ulcerative gingivitis
*Source: (ASHM Publications, 2010)*

Necrotising ulcerative gingivitis presents with pain, ulceration and gingival bleeding. The lesion does not involve the alveolar bone.

**Description**: the characteristic lesion is a punched out, ulcerated and erythematous interdental papilla covered by a greyish necrotic slough

**Location:** gingival tissues particularly the interdental papillae

**Symptoms:** moderate-to-severe pain, bleeding and fetor oris. Systemic

features such as fever, malaise and lymphadenopathy may be present

**Duration:** sudden onset and rapidly deteriorating

**Diagnosis:** mainly by clinical

## Necrotising ulcerative periodontitis

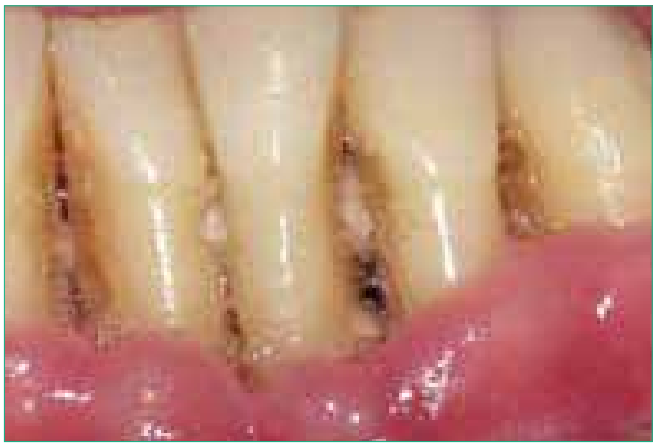

**Figure 8:** Necrotising ulcerative periodontitis

*Source: (ASHM Publications, 201)*

Necrotising ulcerative periodontitis presents identically to necrotising ulcerative gingivitis with pain, ulceration and gingival bleeding except the lesion involves the alveolar bone.

**Description:** ulcerated erythematous gingival tissues, particularly the interdental papilla, covered by a greyish necrotic slough. There may be exposed bone, gingival recession and tooth mobility

**Location:** the interdental papilla extending into the deeper periodontal tissues

**Symptoms:** moderate-to-severe pain, bleeding and fetor oris. Systemic features such as fever, malaise and lymphadenopathy may be present

**Duration:** sudden onset and rapidly worsening

**Diagnosis:** Clinically diagnosis

## Necrotising ulcerative stomatitis

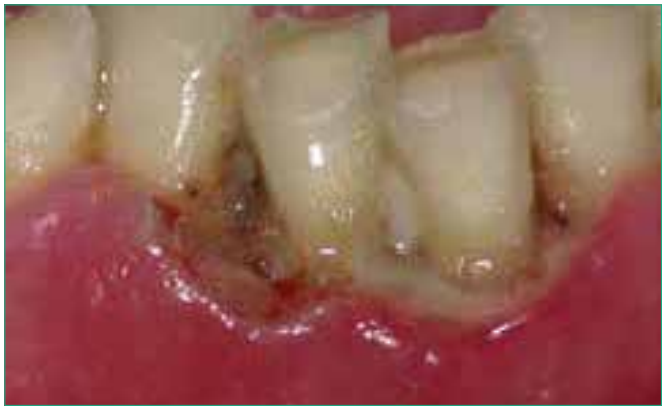

**Figure 9:** Necrotising ulcerative stomatitis

*Source: (ASHM publications,2010)*

**Description:** extensive area of ulceration, tissue necrosis and erythema that extends from gingival into the adjacent mucosa and may involve bone leading to osteonecrosis and sequestration

**Location:** periodontal tissues and may extend into the maxillary or mandibular bone

**Symptoms:** moderate-to-severe pain, bleeding, fetor oris. It is usually associated with systemic symptoms of fever, malaise and lymphadenopathy

**Duration:** sudden onset and rapidly worsening

**Diagnosis:** clinical

**Treatment:** There is no evidence showing management of LGE and other periodontal infections, but it should be treated like a patient without HIV, Oral hygiene is recommended, irrigation, rinsing using Chlorhexidine mouth wash 0.12 % -0.2 % ,15ml rinsed in the mouth for 1 minute for 8-12hrly for 5 days and Metronidazole 400mg orally for 12hours for 5 days would.

## Non- Peridontal Infections:

### i. Syphilis:

Syphilis in its tertiary stage can affect the oral cavity- Gumma, which may occur in the mouth and the lesions range in size from microscopic to a number of centimeters in diameter. Gummas are chronic, asymptomatic, indurated nodular or ulcerative lesions. Atrophic glossitis and syphilitic leukoplakia are other oral manifestations of tertiary syphilis.

### ii. Tuberculosis:

TB may present as granulomas, which form chronic ulcers with a grey-yellow slough in the mouth. There may also be lymphadenopathy in the head and neck.

### iii. Viral Infections:

HIV patients co-infected with any of the viruses are at increased risk of developing oral conditions. The viral groups are those mentioned in the previous chapter. In a person with HIV infection, co-infection with these viruses may manifest in the oral cavity in a typical manner no different from the pattern of infection seen in an immune-competent person.

**Treatment would be as mentioned in the Opportunistic Infection Chapter**

## Oral Neoplasias:

There are mainly two common malignancies associated with HIV infection that may have oral involvement:

1 Kaposi's Sarcoma (KS)

2 Non-Hodgkins Lymphoma(NHL)

There is another which has shown a connection- HIV and Squamous Cell Carcinoma though there is insufficient evidence to show a direct relationship.

## Kaposi's Sarcoma:

Most common malignancy associated with HIV infection, though rates have decreased over the years secondary to ARV Therapy. In 22% of the cases oral manifestations are the initial presentation and majority will have oral involvement at some point in time. It starts as an asymptomatic red macule which enlarges to form a red blue plaque and these plaques may grow into lobulated nodules that may ulcerate and sometimes cause pain. These lesions are usually painless, diagnosis can be made clinically followed by a biopsy.

Treatment: Often commencement of ARV therapy can lead to spontaneous resolution of these lesions. Otherwise Systemic chemotherapy, intra lesional chemotherapy and radiotherapy can be use an option for therapy. Though difficult in resource limited settings.

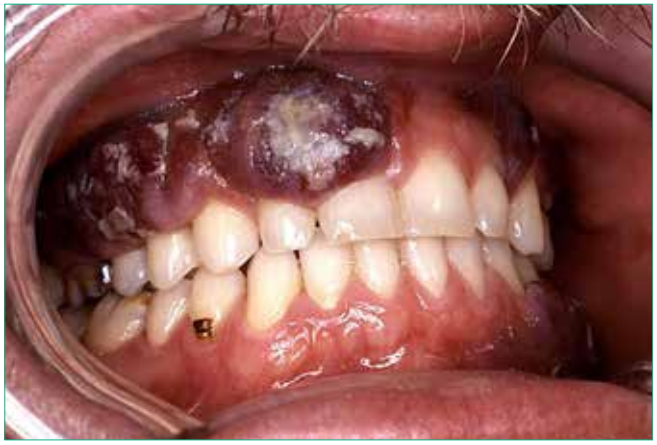

**Figure 10:** Kaposi's Sarcoma lesion

*Source : (CDC Web site)*

## Non-Hodgkins Lymphoma

The rates of NHL also decreased after ARV therapy has come into the picture; however there has been still a continual increase in NHL not related to advanced HIV infection. HIV infection in association with Ebstein Barr Virus can induce NHL.

It may be diffuse, rapidly proliferating, slightly purplish mass in the mouth, and patient may present with generalized symptoms of fever, night sweats, and weight loss. It can become chronic without treatment and usually diagnosis is made clinically followed by biopsy.

Usual treatment for NHL is via medical specialists, where they may include surgical or chemotherapy, radiotherapy or palliative care depending on patient's general condition. In the process of radiotherapy and chemotherapy.

## Oral conditions associated with HIV treatment:

### i. Taste Alterations:

Multiple medications can often cause a taste disturbance.

### ii. Dry Lips:

Protease Inhibitors can cause dry lips in patients taking ARV therapy. Lip ointments may help relieve this problem.

### iii. Other Conditions associated with HIV treatment include:

a) Xerostomia

b) Oral Ulceration

c) Erythema multiforme- Steven Johnsons Syndrome

d) Lichenoid reactions

e) Hyperpigmentation

The possibility of drugs prescribed by dentists may react with ARV therapy; therefore the interactions should be discussed with the HIV clinician prior to prescription.

## HIV and Tooth Decay:

Dental caries can cause a significant burden of disease and affect quality of life for people with HIV infection. All HIV patients regardless the stage of the disease, they should have a yearly check with their dentists.

Xerostomia is the most important factor in the development of dental caries that can be directly linked to HIV infection or its treatment. The most serious complication of dental caries is the occurrence of a potentially life-threatening infection, which is an important consideration in immune-compromised people.

## Prevention of Tooth Decay is Important:

Oral Hygiene, dietary factors and dental factors need to be looked at holistically with a patient who has an immune-compromised status.

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# Part 2:

# Sexually Transmitted Infections

STIs remain a public health problem of major significance in many parts of the world, the Pacific is no exception. Failure to diagnose and treat STIs at an early stage may result in serious complications and sequelae, including pelvic inflammatory disease, infertility, ectopic pregnancy (Low et al.,2006), increased likelihood of cervical cancer anogenital cancers (Safaeian, 2006), stillbirth or neonatal death (Martin, 1982), as well as neonatal conjunctivitis and/or pneumonia (Mardah, 2002). The individual and national expenditure on STI care can be substantial. Additionally, there is a strong link between the spread of STIs and HIV transmission. Both ulcerative and non-ulcerative STIs have been found to increase the risk of sexual transmission and acquisition of HIV infection.

Globally, herpes simplex virus type 2 (HSV-2) infections have become the leading causative etiology of genital ulcer disease (GUD). Evidence of HSV-2 infection cases has been reported in many Pacific islands countries and territories. However, there is a paucity of data related to this disease. Clinical diagnosis is the main method used to diagnose HSV-2 in the Pacific Region.

Antimicrobial resistance of some sexually transmitted pathogens has increasingly become a critical public health problem. There is widespread resistance to penicillin's, early generation cephalosporins, such as cephalexin and cefuroxime and quinolones. The penicillin group of agents remains the recommended treatment in a few island countries in the Western Pacific Region. (WHO, 2011)

The third edition of the OSSHHM recommendations emphasise the identification of: STI syndromes; the various causative agents; providing appropriate treatment for STI patients and their partner(s); management of genital ulcer disease including herpes simplex virus type 2 (HSV-2); anorectal infection; and the management of STIs in children and adolescent populations. It also focuses on the relevant components such as selecting the best antimicrobials available for treatment, patient education and counseling including VCCT and provider initiated counseling and testing for HIV (PICT), condom promotion and other safer sexual practices, and identification and management of sex partner(s) to enhance STI management. The third edition is an evolving document and is a review of the 2nd OSSHHM recommendations and is updated to be in-line with the 2011 WHO guidelines for the management of STIs. The recommendations need to be reviewed from time to time to maintain its relevance and applicability to situations in the Pacific region.

This section outlines what OSSSHHM considers as essential aspects or considerations in the management of STIs in the context of the Pacific. They are in line with best practice and are recommended by the WHO.

# Chapter 13: Comprehensive STI case management

In line with the WHO recommendations of 2011 this chapter focuses on ensuring that STI case management is delivered in light of both, internationally recognized best practice for STI case management, utilizes public health principles and finally is based on the 2011 STI update provided by WHO. It is a recommendation what when each client is seen by a health worker that the following key components of care are in place or are maintained (in addition to the 8 principles of discussed below) in all settings and by all health workers:

- user-friendly environment ensuring privacy;
- history taking including an appropriate sexual history;
- conduct physical examination, including detailed genital examination;
- syndromic or laboratory-based diagnosis of presenting complaint;
- investigation of other asymptomatic STIs if suspected;
- effective curative or palliative therapy;
- patient education and counseling – issues include: importance of notifying and treating partner, risk reduction and prevention of further transmission, HIV risk perception, assessment and VCCT screening;
- contact tracing and partner notification; and
- follow-up if relevant or referral if indicated.

## There are eight (8) key principles that OSSHHM recognizes as essential in STI case management.

### 1. Standard treatment guidelines

Correct and effective treatment of STIs at the first contact between patients and health-care providers is an important public health measure in the control of STIs. It is strongly recommended that countries establish and use national standardized treatment protocols for STIs. Standardization ensures that all patients receive adequate treatment at all levels of health-care services and that care is delivered consistently regardless of who or where a client is seen in the Pacific.

### 2. Case management

STI case management is the care of a person with an STI or STI-related syndrome or with a positive test for one or more STIs. Comprehensive STI Case Management includes: history taking; clinical examination; correct diagnosis; effective treatment; advice on safer sexual behavior; promotion and/or provision of condoms; the notification and appropriate treatment of sexual partners; case reporting; and clinical follow-up as appropriate. Thus, effective case management consists not only of antimicrobial therapy to obtain cure and reduce infectivity, but also comprehensive assessment and care of the patient's reproductive health and that of their sexual partners. In the case of adolescent[5] patients, the approach must be appropriate and user-friendly as there is the potential to influence future sexual behaviour and treatment-seeking practices at a critical stage in their development.

### 3. Syndromic management

Health care providers in many settings have had problems with conducting aetiological diagnosis of STIs as it places constraints on their time, human resources, financial resources, and delays treatment. Where laboratory facilities are available, staff must be qualified and have adequate skills to perform the laboratory procedures, furthermore external quality control must be made mandatory. Additionally, many health care facilities in PICTs lack the equipment and trained personnel required for etiological diagnosis of STIs.

To overcome this problem, a syndrome-based approach to the management of STI patients has been adopted in large number of PICTs. The syndromic management approach is based on the identification of consistent groups of symptoms, and the provision of treatment that will address the majority of or the most serious organisms responsible for producing the syndrome. This approach has been found to be cost-effective and uses flowcharts us a guidance tool for diagnosis and treatment.

### 4. Risk factors for STI-related cervicitis

Abnormal vaginal discharge could be found in vaginal infection or cervical infection (gonococcal and/or chlamydial). In some cases, diagnostic of cervical infection could be found by clinical observations of the presence of cervical mucopurulent discharge, cervical erosions, cervical friability and bleeding between menses or during sexual intercourse.

The behavioural risk factors have also been frequently associated with cervical infection. Some of those factors are: being less than 25 years old[6]; not married; having more than one sexual partner in the previous three months; having a new partner in the previous three months; and having a current partner with an STI.

## 5. Selection of drugs

Provision or less effective drugs may result in unacceptable rates of treatment failure, possible risk of transmission and complications, and may erode people's confidence in health services. The drugs used for STI treatment in all health care facilities should have an efficacy of at least 95 %.

**Medicines selected for treating STIs should meet the following criteria:**

- high efficacy (at least 95 %);
- low cost;
- low toxicity levels;
- organism resistance unlikely to develop or likely to be delayed;
- single dose;
- oral administration; and
- not contraindicated for pregnant or lactating women.

## 6. Client education, counseling and behavior modification. Behavioural assessment during sexual history taking from the index client is essential to provide leads to issues that need to be addressed during the education session. The following issues should be included in client education:

- the nature of infection, including the importance of completing the course of treatment and of attending the follow-up visits or referral;
- harm reduction issues in relation to possibility of drug use, where appropriate;
- informing and educating index client and partner(s) on ways of minimising or lowering their risks of contracting and transmitting HIV and other STIs, including through safer sexual practices such as abstinence, having one faithful sexual partner, and consistent condom use.

## 7. Voluntary confidential counseling and testing (VCCT) for HIV and testing for other STIs

**Testing should be targeted in particular to:**

- STI clients (investigating for their current symptoms and also screening for other STIs); people who have been newly diagnosed with HIV;antenatal women, where detection and treatment would benefit the neonate; and
- anyone who volunteers to be screened for STIs and HIV.

**Comprehensive screening tests for STIs should ideally include:**

- Blood for all consenting males and females:
  - syphilis: RPR or VDRL titre and treponemal test;
  - hepatitis B: hepatitis B surface antigen (no need if the client is known to have a chronic infection); and
  - HIV: HIV antibody following proper VCCT.
- For symptomatic and asymptomatic females:
  - first void urine for chlamydia testing (note: most PICTs are now able to test for chlamydia);
  - endocervical swab-- culture and sensitivity;
  - Vaginal swab-- microscopy, culture and sensitivity;
  - pap smear (note: swabs must be taken before pap smear); and
  - throat swabs (if indicated) if history of oral sex.
- For symptomatic and asymptomatic male:
  - urethral swab for microscopy, culture and sensitivity if discharge is noted;
  - first void urine for chlamydia (note: majority of male with chlamydia are asymptomatic); and
  - rectal swabs if indicated.

## 8. Contact tracing and management of sexual partners

Contact tracing and management of sex partner(s) is an essential component of STI management. It should be done in a way that keeps information confidential (despite the difficulty of such a task in the small communities of the Pacific Island region).

Contacting the sex partner(s) of an index client is often challenging. The index clients needs appropriate counselling, and the process of identifying and notifying sex partner(s) should be voluntary and non-coercive. The main aim of this process is to identify the sex partner(s), and to ensure that they are referred for evaluation and treated appropriately, regardless of whether they are symptomatic or not.

Contact tracing and sex partner(s) notification can be carried out either by **client referral or health provider referral or in combination**. In client referral, the index client is encouraged to notify the sex partner(s) of their possible infection. With health **provider referral**, a

health care worker notifies the sex partner(s), after the index client has accurately identified the partner(s). **Table 13.1** outlines all possible explanations, partner treatment requirements, and counseling messages for selected syndromes.

Management of sex partner(s) depends on the diagnosis of the index client's STI, either using the syndrome approach or through laboratory diagnosis.

The following are some of the suggested strategies for the treatment of partners:

- offer immediate epidemiological treatment, based solely on the index client's diagnosis. No laboratory investigation is done on the sex partner(s); and
- offer immediate epidemiological treatment but obtain specimens from the partner(s) for subsequent confirmation from the laboratory (Offer screening tests as well).

**Table13.1:** Possible explanations, partner treatment requirements, and counselling messages for selected syndromes

| Syndrome | Possible explanations | Partner treatment requirements | Counselling message |
|---|---|---|---|
| Urethral discharge (men) | STI very likely | Treat partners for same conditions (female partners as for cervical infection) | STI prevention counselling |
| Genital ulcer | STI very likely | Treat partners for same conditions | STI prevention counselling |
| Inguinal bubo | STI very likely | Treat partners for same conditions | STI prevention counselling |
| Scrotal swelling | STI very likely if urethral discharge present Other causes possible | Treat partners for same organisms (female partners as for cervical infection) | STI prevention counselling if urethral discharge present If no urethral discharge: partner treatment a precaution to reduce complications |
| Lower abdominal pain (women) | Pelvic inflammatory disease, often STI. But other genitourinary or gastrointestinal causes possible | Treat male partners as for urethral discharge | Partner treatment a precaution to reduce complications |
| Vaginal discharge | Endogenous (non-STI) infection most likely cause of vaginitis | No partner treatment unless relapse (then give treatment for trichomoniasis) | Usually not sexually transmitted |
| | If cervical infection judged present or likely, presume STI | Treat male partners as for urethral discharge | STI prevention counselling |
| Neonatal conjunctivitis | Often caused by STI, but other causes possible | Treat mother for cervical infection, and her partner(s) as for urethral discharge | Partner treatment a precaution to reduce complications |

# Chapter 14: Treatment of STI associated syndromes

The basis of this approach is to identify groups of symptoms and easily recognised signs (syndromes), and to provide treatment that addresses the majority of organisms, or the most serious among them, that are responsible for producing that syndrome.

**Table 14.1** outlines the syndromes associated with STIs, the potential causative organisms and conditions for which treatment should be provided and/or considered. Successful management of STIs requires members of staff to be respectful of patients and not to be judgmental. Clinical examination must take place in an appropriate location which will ensure privacy and confidentiality for all patients. When dealing with adolescents, the health care provider should be reassuring, experienced and conversant with the changes in anatomy and physiology associated with the different maturation stages, e.g. the menarche in girls or nocturnal emissions in boys.

**Table 14.1**: Syndromes, potential causative organisms/conditions, and flowcharts*

| Syndrome | Most common organism responsible in Pacific Island region | Other organisms (conditions) for which treatment should be considered** |
|---|---|---|
| Urethral discharge (in men) | Neisseria gonorrhoeae<br>Chlamydia trachomatis | Trichomonas vaginalis (persistent or recurrent cases) |
| Vaginal discharge | Bacterial vaginosis<br>Trichomonas vaginalis | Neisseria gonorrhoeae<br>Chlamydia trachomatis<br>Candida albicans |
| Lower abdominal pain (in females) | Neisseria gonorrhoeae<br>Chlamydia trachomatis<br>Anaerobic bacteria | |
| Neonatal conjunctivitis | Neisseria gonorrhoeae<br>Chlamydia trachomatis | |
| Genital ulcers | Treponema pallidum (syphilis) | Herpes simplex virus 2<br>Haemophilus ducreyi (chancroid)<br>Klebsiella granulomatis (granuloma inguinale/ donovanosis)<br>Chlamydia trachomatis serovars L1-3 (lymphogranulomavenereum) |
| Inguinal bubo | Chlamydia trachomatis serovars L1–3 (lymphogranuloma venereum)<br>Haemophilus ducreyi (chancroid) | |

**Note:**
*The flow chart in this recommendation has been adapted from the Comprehensive STI case management for the Pacific region
** Consideration of other organisms/conditions should be based on local epidemiology and/or an individuals' symptoms or signs as described in the flowcharts.

## 14.1 Urethral discharge

Male patients complaining of urethral discharge and/or dysuria should be examined for evidence of urethral discharge or any other urethral infection. If no abnormal discharge, or other sign of infection, is seen, the urethra should be gently massaged from the ventral part of the penis towards the meatus to express any exudates that may not be evident.

The main sexually transmitted pathogens causing urethral discharge are *Neisseria gonorrhoeae* (*N. gonorrhoeae)*, and *Chlamydia trachomatis* (*C. trachomatis*). Additional causes of urethral discharge are *Mycoplasma genitalium (M. genitalium), and Trichomonas vaginalis ((T. vaginalis)*. In the syndromic management, treatment of a patient with urethral discharge should adequately cover the first two organisms. *T. vaginalis* and *M. genitalium* and should be suspected in cases of persistent urethral discharge.

If microscopy is available, examination of the urethral smear may show an increased number of polymorphonuclear leukocytes and a Gram stain may demonstrate the presence of intra-cellular Gram-negative diplococci suggestive of gonorrhoea. In the male, more than 5 polymorphonuclear leukocytes per high power field (x 1000) are indicative of urethritis. If the microscopic examination is conducted competently and no suggestion of gonococcal infection is seen, consideration may be given to treating for chlamydial infection only. If in doubt, however, then treatment should be given for both gonococcal and chlamydial infections.

Azithromycin should not be used as a stand-alone therapy for gonorrhoea because of the rapid emergence of resistance.

**Recommended syndromic treatment of urethral discharge**

| | | |
|---|---|---|
| Therapy for uncomplicated gonorrhoea | **PLUS** | Therapy for chlamydia |

**Note:** Patients should be advised to return if symptoms persist 7 days after start of therapy

**Table 14.2**: Treatment recommendation for Urethral discharge

| Condition | First line | Second line |
|---|---|---|
| Treatment options for gonorrhoea | Ciprofloxacin 500 mg orally, single dose* **OR**<br>Cefixime 400 mg orally, single dose<br>**OR**<br>Ceftriaxone 250 mg intramuscularly, single dose<br>**OR**<br>Amoxicillin 2.5 g **Plus**<br>Amoxicillin/Clavulanic acid 500mg/125mg plus<br>Probenecid 1 g orally all as single supervised dose** | Gentamicin† 240 mg IM single dose<br>**OR**<br>**Special situations**<br>Spectinomycin 2 g IM as a single dose:<br>- In pregnant or penicillin-allergic patients<br>- For multi-drug resistant infection. |
| Treatment options for Chlamydia | Azithromycin 1 gram single oral dose **OR**<br>Doxycycline 100 mg twice daily for 7 days* | |

**Note:**

*Not to use in pregnancy and lactation

** In countries were gonococcal sensitivity to Penicillin is less than 95 % this treatment is not recommended.

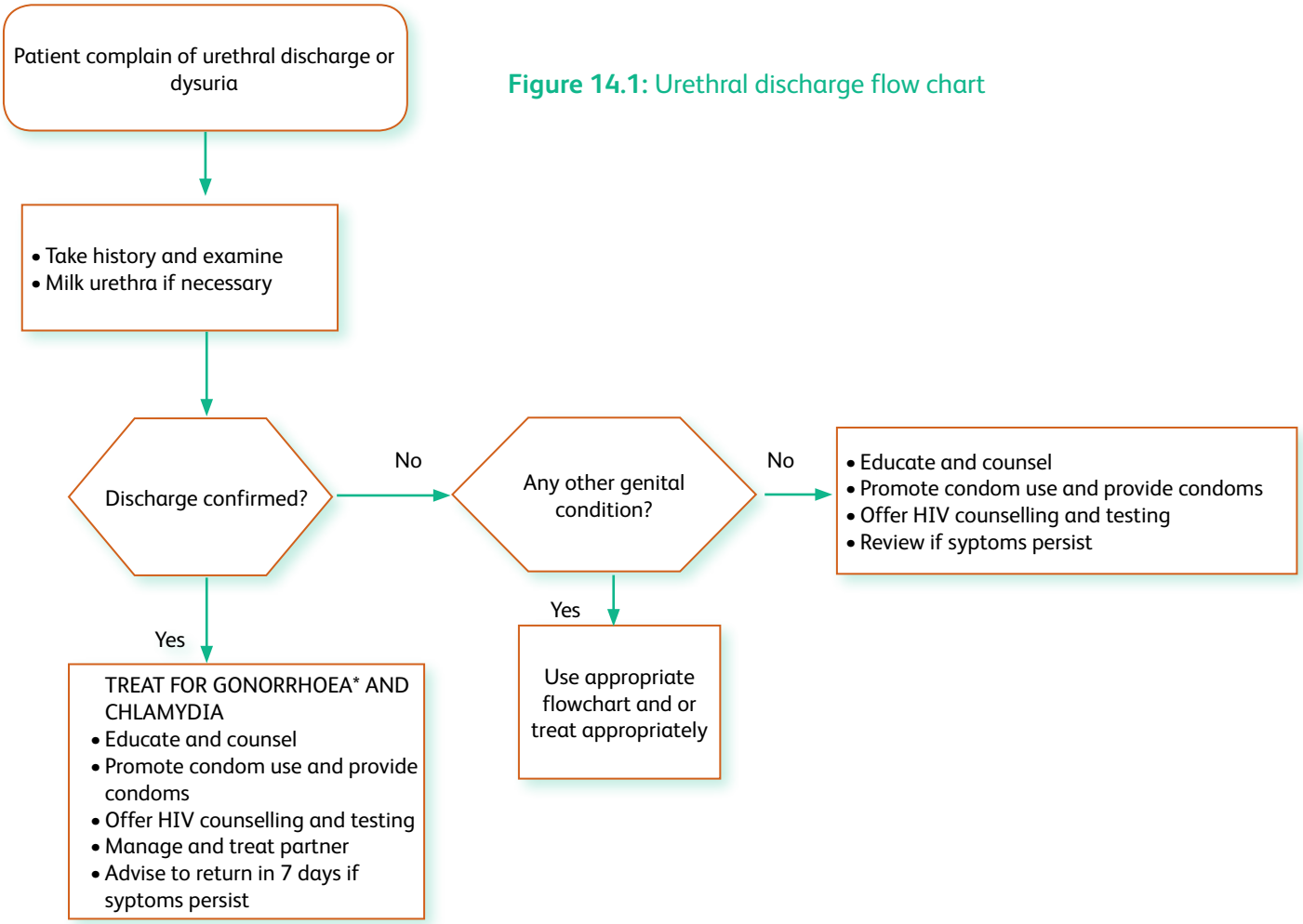



**Figure 14.1:** Urethral discharge flow chart

## 14.2 Persistent or recurrent Urethral discharge

Persistent or recurrent symptoms of urethritis may result from drug resistance, poor compliance or re-infection. In some cases there may be infection with *T. vaginalis* or with *M. genitalium*. Where symptoms persist or recur after adequate treatment for gonorrhoea and chlamydia in the index patient and the sexual partner(s), the patient should be treated for *T. vaginalis* and/or for *M. genitalium*, if the local epidemiological pattern so indicates. If the symptoms still persist at follow-up the patient must be referred for further discussion on the management of *T. Vaginalis*.

**Figure 14.1**: Flow chart of Persistent urethral discharge in men

N.B. This flow chart assumes that the patient has received and taken effective therapy for gonorrhoea and chlamydia prior to this consultation

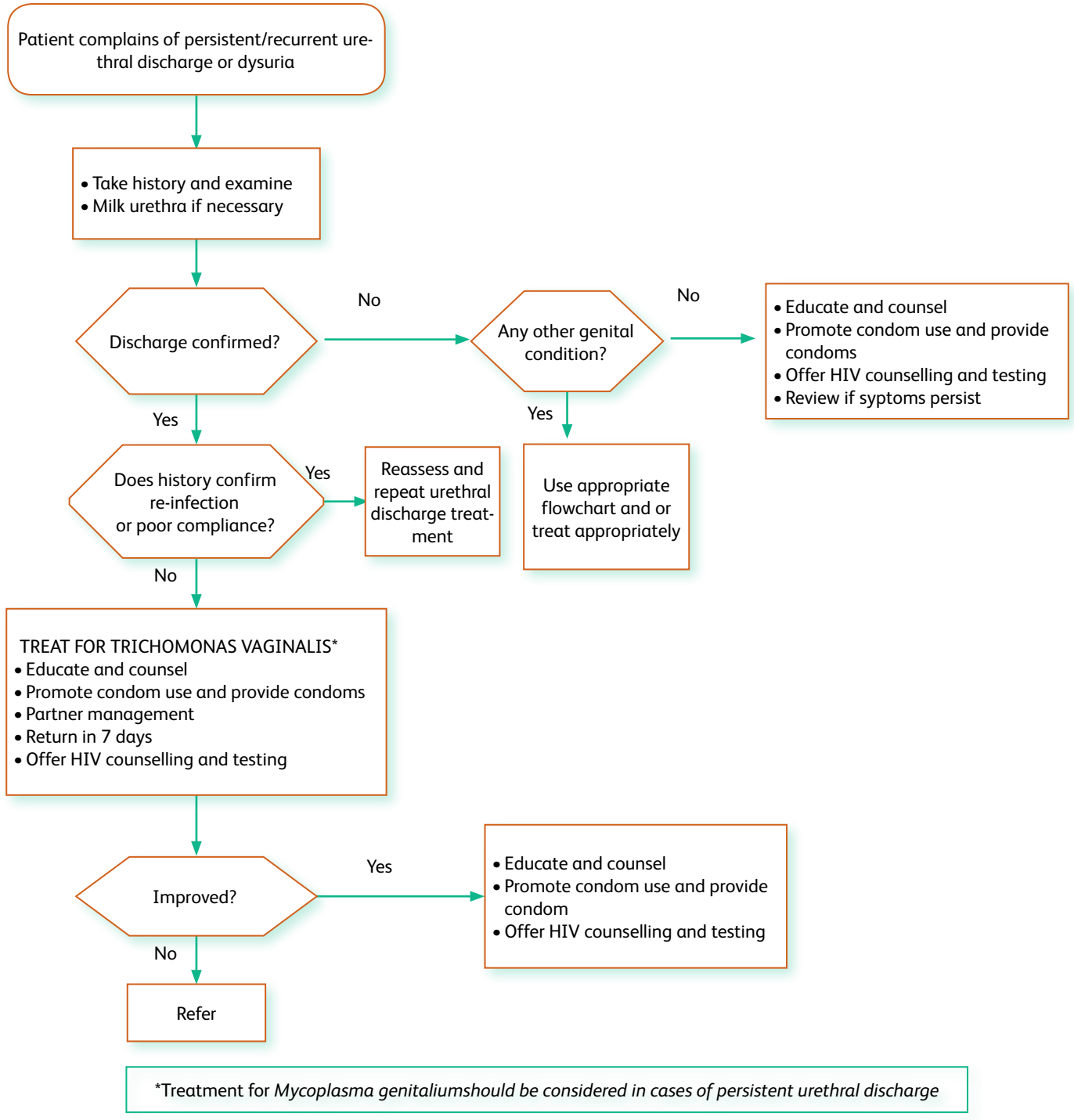


**Table 14.3:** Treatment options for recurrent or persistent urethral discharge, covering Trichomonas vaginalis

| Treatment recommendation | Alternative treatment |
|---|---|
| • Metronidazole, 2 g orally, in a single dose<br>OR<br>• Tinidazole, 2 g orally, in a single dose | • Metronidazole, 400 mg or 500 mg orally, twice daily for 7 days<br>OR<br>• Tinidazole, 500 mg orally, twice daily for 5 days |
| Note:<br>• Other 5-nitroimidazoles are also effective, both in single and in multiple dose regimens.<br>• Patients taking Metronidazole or other imidazoles should be cautioned not to consume alcohol while they are taking the drug, and up to 24 hours after taking the last dose.<br>• Asymptomatic women with trichomoniasis should be treated with the same regimen as symptomatic women. | • Infants with symptomatic trichomoniasis or with urogenital colonization persisting past the fourth month of life should be treated with metronidazole. |

## 14.3 Genital ulcer disease

Following confirm the presence of genital ulceration via examination, treatment appropriate to local etiologies and antimicrobial susceptibility patterns should be given.

Laboratory-assisted differential diagnosis is also rarely helpful at the initial visit, as mixed infections are common. In areas of high syphilis prevalence, a reactive serological test may only be a reflection of a previous infection and give a misleading picture of the patient's present condition, and a negative test does not necessarily exclude an ulcer of primary syphilis as seroreactivity may take 2–3 weeks to develop.

### Genital ulcers and HIV infection

There have been a number of anecdotal reports in the literature suggesting that the natural history of syphilis may be altered as a result of concomitant HIV infection.

In immunosuppressed individuals, herpes simplex lesions may present as persistent multiple ulcers that require medical intervention. Anti-herpes treatment is particularly important in such instances, to be given therapeutically or prophylactically to offer comfort to the patient. Adequate education and counselling need to be given to the patient as well an explanation of the nature and purpose of treatment and in order to avoid false expectations of cure, and to minimize further transmission to sex partners.

**Table 14.4:** Recommended syndromic treatment of GUD

| Genital Ulcer Disease Management | Herpes Simplex Management |
|---|---|
| Treat for syphilis, and, depending upon local epidemiology, either chancroid, granuloma inguinale or lymphogranuloma venereum<br><br>Aspirate any fluctuant glands (surgical incision should be avoided)<br><br>Educate and counsel on risk reduction<br><br>Offer syphilis serologic testing and HIV serologic testing<br><br>Review if lesion not fully healed in 7 days | Advise on basic care of the lesion (keep clean and dry)<br><br>Provide or prescribe specific antiviral herpes treatment according to local policy<br><br>Educate and counsel on compliance, risk reduction and natural history of HSV-2 infection<br><br>Offer syphilis and HIV serologic testing<br><br>Promote and provide condoms<br><br>Advise to return in 7 days if lesion is not fully healed, and sooner if there is clinical deterioration; if so, treat for other causes of GUD as per guidelines |

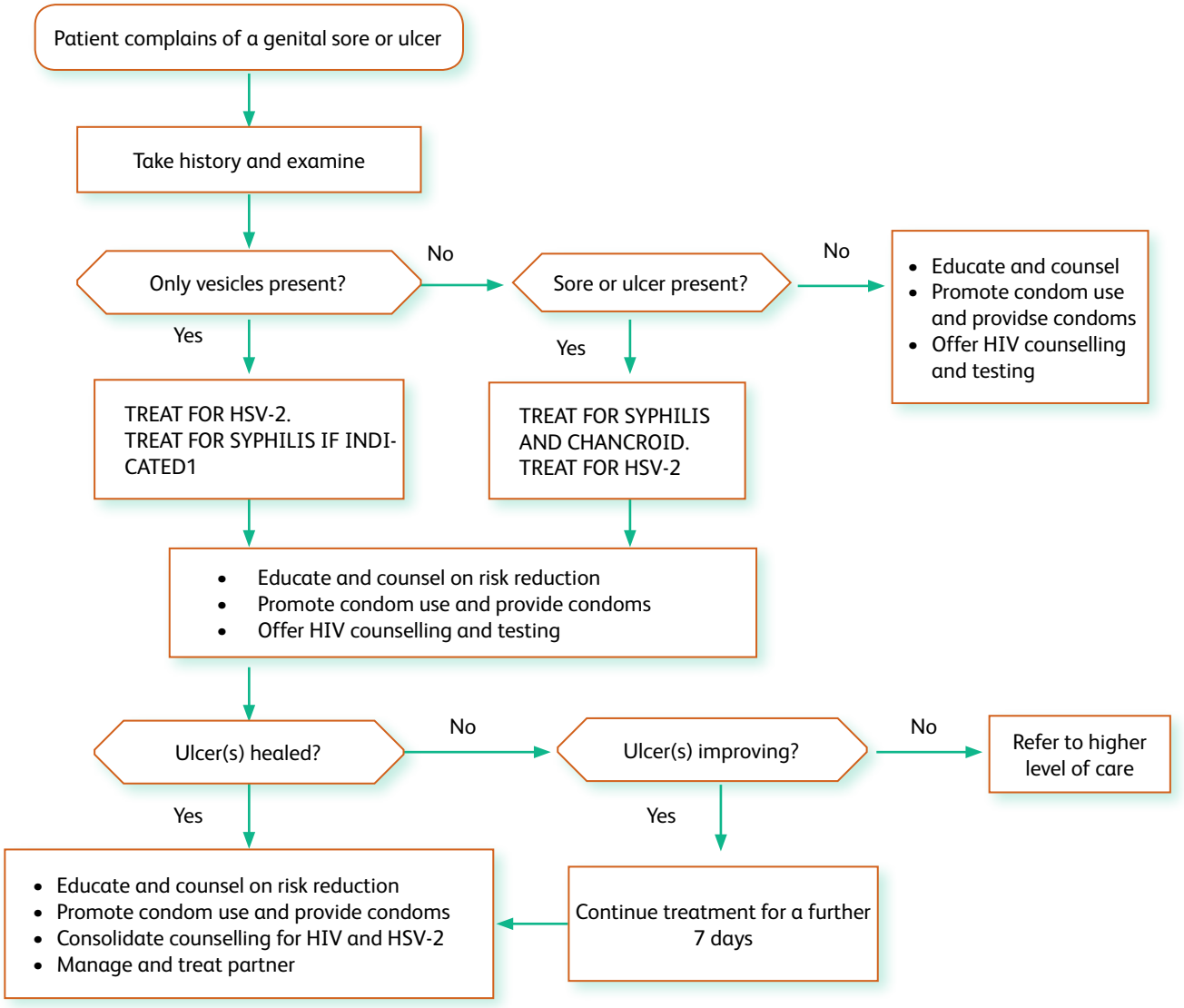
**Table 14.2**: Treatment recommendation for GUD

| Condition | First line | Second line |
|---|---|---|
| **Syphilis (early syphilis)*** | Benzathine penicillin, 2.4 megaUnits IM, single dose | Procaine benzylpenicillin, 1.2 mega Unit IM x 10 daily doses, **OR** Doxycyline 100 mg orally twice daily for 14 days |
| **Syphilis (late syphilis)*** | Benzathine Benzylpenicillin, 2.4 mega Units IM x 3 weekly doses | Procaine benzylpenicillin, 1.2 mega Unit IM x 20 daily doses, **OR** Doxycycline 100 mg twice daily, orally for 30 days |
| **Chancroid** | Ciprofloxacin, 500 mg orally, twice daily for 3 days, **OR** Erythromycin, 500 mg orally, 4 times daily for 7 days, **OR** Azithromycin, 1 g orally, single dose | Ceftriaxone, 250 mg IM, single dose |
| **Granuloma Inguinale (Donovanosis)** | Azithromycin, 1 g orally stat, then 500 mg once daily until healed, **OR** Doxycycline, 100 mg orally, 2 times daily until healed | Erythromycin, 500 mg orally, 4 times daily, **OR** Tetracycline, 500 mg orally, 4 times daily, **OR** Trimethoprim 160 mg/ Sulfamethoxazole 800, 2 times daily for 14 days minimum |
| **LGV** | Doxycycline, 100 mg orally, 2 times daily for 14 days, **OR** Erythromycin, 500 mg orally, 4 times daily for 14 days | Tetracycline, 500 mg orally, 4 times daily for 14 days |
| **Genital herpes (first clinical episode)** | Acyclovir, 200 mg orally, 5 times daily for 7 days, **OR** Acyclovir, 400 mg orally, 3 times daily for 7 days, **OR** Valaciclovir, 1 g orally, 2 times daily for 7 days, **OR** Famciclovir, 250 mg orally, 3 times daily for 7 days | |
| **Special considerations in treatment of genital ulcer disease** | | |
| **Condition** | **Penicillin allergy in pregnancy** | **Penicillin allergy and non-pregnant** |
| **Syphilis** | Erythromycin, 500 mg 4 times daily for 14 days, **OR** Azithromycin 2 g orally single dose | Doxycycline, 100 mg orally, twice daily for 14 days, **OR** Tetracycline, 500 mg orally, 4 times daily for 14 days |

Note.

- The decision to treat for chancroid, granuloma inguinale or LGV depends on the local epidemiology of the infections.
- Specific treatment for herpes genitalis is recommended as it offers clinical benefits to most symptomatic patients. Health education and counselling regarding the recurrent nature of genital herpes lesions, the natural history, sexual transmission, probable perinatal transmission of the infection and available methods to reduce transmission, are an integral part of genital herpes management. There are some indications that treatment for herpes genitalis in HIV infected individuals may improve ulcer healing and possibly reduce shedding of HIV. In GUD patients who are HIV infected, or whose HIV status is unknown, specific treatment for herpes genitalis should be given as part of syndromic management of GUD.
- *Classification of syphilis is base on the STI case definition recommended by the Pacific Regional STI technical Working Group

**Figure 14.2:** Flowchart of genital Ulcer disease in men and women




[1]Indications for syphillis treatment:
- RPR positive; or
- Patient has not been treated for syphillis recently.

## 14.4 Inguinal Bubo

Inguinal and femoral buboes are localised enlargements of the lymph nodes in the groin area, which are painful and may be fluctuant. They are frequently associated with LGV and chancroid. In many cases of chancroid an associated genital ulcer is also visible together with the presence of a bubo. Non-sexually transmitted local and systemic infections, such as infections of the lower limb or tuberculous lymphadenopathy, can also cause swelling of inguinal lymph nodes and need to be considered in the differential diagnosis.

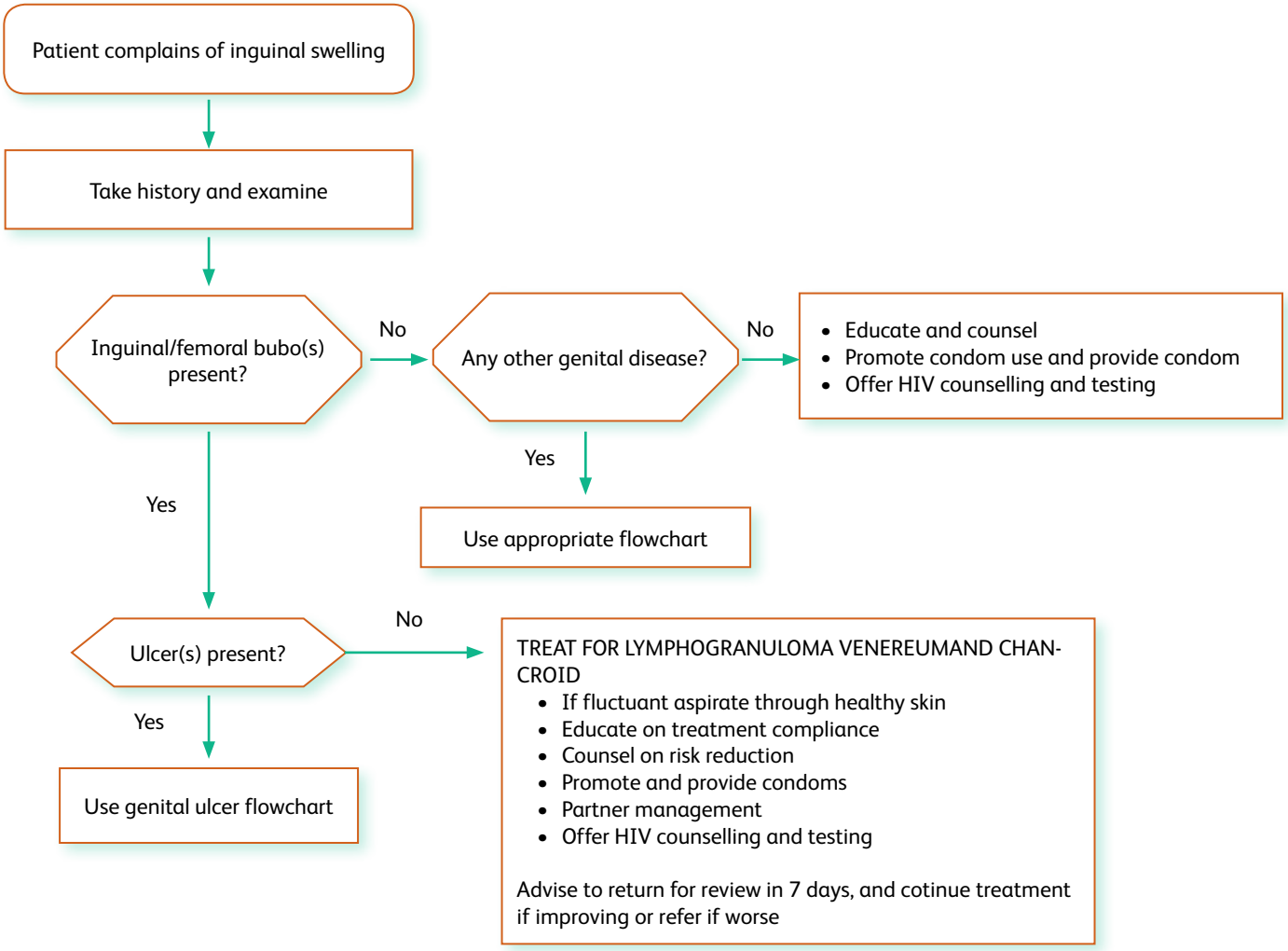
### Recommended syndromic treatment

| | | |
|---|---|---|
| Ciprofloxacin, 500 mg orally, twice daily for 3 days | AND | Doxycycline, 100 mg orally, twice daily for 14 days OR<br><br>Erythromycin, 500 mg orally, four times daily for 14 days |

**Note:**

Some cases may require longer treatment than the 14 days recommended above. Fluctuant lymph nodes should be aspirated through healthy skin. Incision and drainage or excision of nodes may delay healing and should not be attempted. Where there is doubt and/or treatment failure, referral for diagnostic biopsy is advisable.

**Figure14. 3:** Flowchart for Inguinal bubo




## 14.5 Scrotal swelling

Inflammation of the epididymis (epididymitis) is usually obvious itself by acute onset of unilateral testicular pain and swelling, often with tenderness of the epididymis and vas deferens, and occasionally with erythema and oedema of the overlying skin. In men under 35 years is more frequently caused by sexually transmitted organisms than in those over 35 years. When the epididymitis is accompanied by urethral discharge, it should be presumed to be of sexually transmitted origin, commonly gonococcal and/or chlamydial. The adjacent testis is often also inflamed (orchitis), giving rise to epididymo-orchitis.

In pre-pubertal males, epididymitis is frequently due to non-sexually transmitted pathogens, such as *Pseudomonas* infection or coliform bacteria, e.g. *Escherichia coli*, and structural abnormalities of the urinary tract are frequently found as predisposing factors.

In post-pubertal men, complication of mumps is common (epididymo-orchitis). It is usually noted within a week of parotid enlargement. Adolescents with epididymitis should have a sexual history taken and appropriate evaluation done to exclude sexually transmitted pathogens.

In older men, where there may have been no risk of a sexually transmitted infection, other general infections may be responsible, for example, *Escherichia coli*, *Klebsiella* spp. or *Pseudomonas aeruginosa*. A tuberculous orchitis, generally accompanied by an epididymitis, is always secondary to lesions elsewhere, especially in the lungs or bones. In brucellosis, usually caused by *Brucella melitensis* or *Brucella abortus*, an orchitis is usually clinically more evident than an epididymitis.

Trauma, testicular torsion and tumour should also be considered as important causes of testicular pain. Sudden onset of scrotal pain most frequently is due to testicular torsion which is a surgical emergency that needs urgent referral.

If not effectively treated, STI-related epididymitis may lead to infertility.

## Recommended syndromic treatment

The treatment of uncomplicated acute epididymitis, particularly when associated with a urethral discharge, should be approached in the same manner as uncomplicated urethral infection. However, therapy may have to be given for a longer period for chlamydial infection. In addition, the management of acute epididymitis should also include bed rest, scrotal support and analgesics for the pain until local inflammation and fever subside. Patient should re-evaluate on the third day of treatment and continue with treatment if improvement is reported. If there is no improvement or the condition is worse, then alternative diagnoses must be considered, including a surgical indication, such as testicular torsion.

| Therapy for uncomplicated gonorrhoea | **PLUS** | Therapy for chlamydia |
|---|---|---|

**Table 14.6**: Recommendation treatment for scrotal swelling

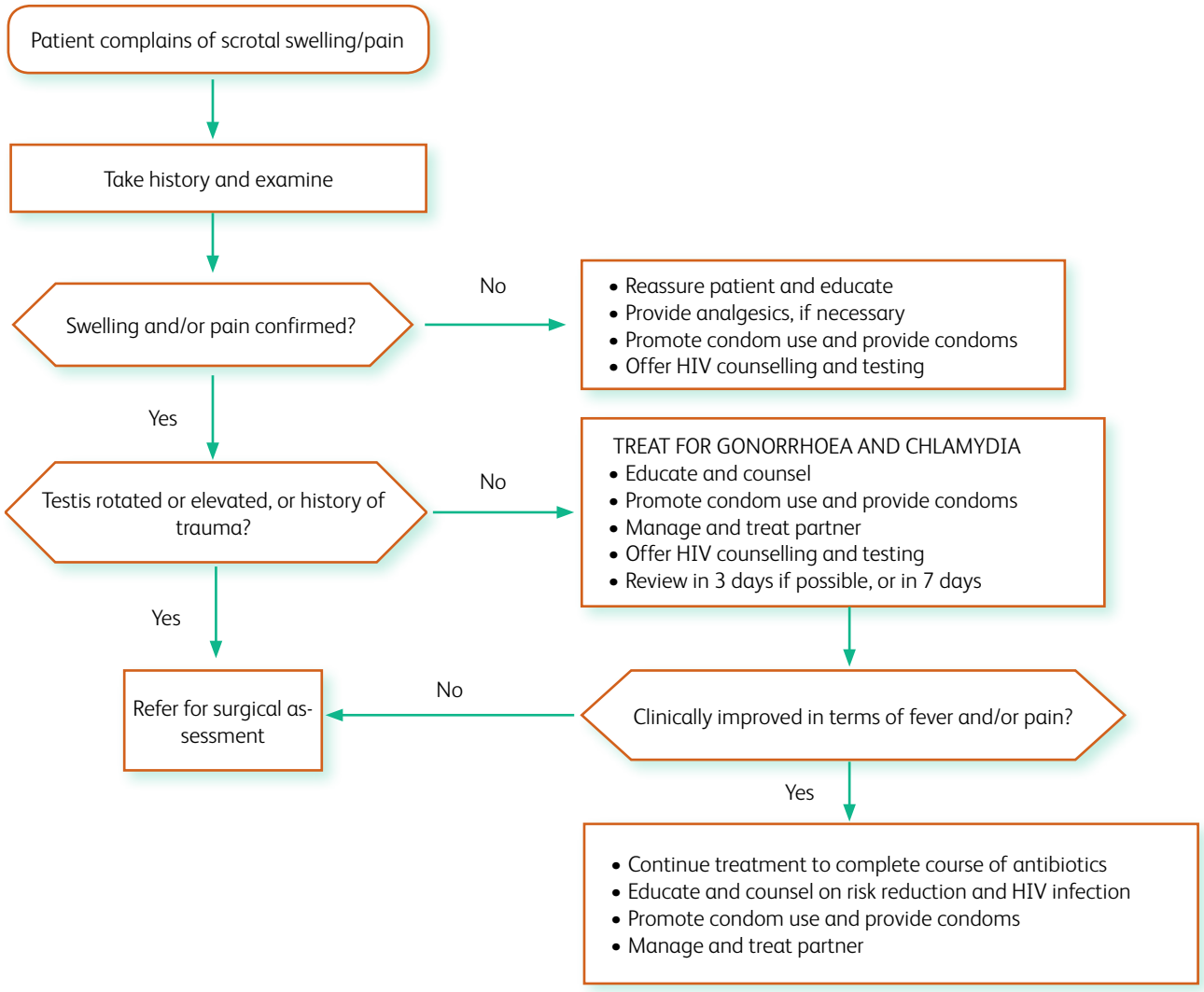
| Condition | First line | Second line |
|---|---|---|
| Treatment options for gonorrhoea | Ciprofloxacin 500 mg orally, single dose*,<br>**OR**<br>Cefixime 400 mg orally, single dose, **OR**<br>Ceftriaxone 250 mg intramuscularly, single dose,<br>**OR**<br>Amoxicillin 2.5 g **plus**<br>Amoxicillin/Clavulanic acid 500mg/125mg **plus**<br>Probenecid 1 g orally all as single supervised dose** | Gentamicin† 240 mg IM single dose,<br>**OR**<br>**Special situations**<br>Spectinomycin 2 g IM as a single dose:<br>- In pregnant or penicillin-allergic patients<br>- For multi-drug resistant infection. |
| Treatment options for Chlamydia | Azithromycin 1 gram single oral dose, **OR**<br>Doxycycline 100 mg twice daily for 7 days* | |

**Note:**

*Not to use in pregnancy and lactation

** Treatment recommendations do not apply to countries where sensitivity of gonococcus to Penicillin is less than 95 %.

**Figure14.4**: Flowchart for Scrotal swelling




## 14.6 Vaginal discharge

A complaint of abnormal vaginal discharge (in terms of quantity, colour or odour) expressed spontaneously by the patient most commonly indicates an infection in either the vagina or the cervix. A vaginal infection (vaginitis) due to bacterial vaginosis (multiple organisms) or yeast infection (Candida albicans) is not always an STI, while trichomoniasis (Trichomonas vaginalis) usually is. Since symptomatic infection with T. vaginalis is not common in men, a health-care provider should consider giving treatment for T. vaginalis in male sex partners of women with confirmed T. vaginalis infection or with recurrent vaginal discharge.

All females presenting with abnormal vaginal discharge should receive treatment for bacterial vaginosis and trichomoniasis. Additional treatment for yeast infection is indicated when clinically apparent (white, curd-like discharge, redness of the vulva and vagina, and itching). Given that vaginitis is usually not due to sexually transmitted organisms, treatment of partners is not recommended (at least not initially; it may become necessary if symptoms recur or do not resolve).

Large proportions of women with gonococcal or chlamydial cervical infection are asymptomatic. The symptom of abnormal vaginal discharge is highly indicative of vaginal infection, but poorly predictive for cervical infection. In a minority of cases abnormal vaginal discharge can be caused by mucopurulent STI-related cervicitis, attributable to *N. gonorrhoeae* and/or *C. Trachomatis*.

In the context of high prevalence of Chlamydia in the Pacific, it is a stronger justification for treatment for cervicitis. Women with a positive risk assessment have a higher likelihood of cervical infection than those who are risk negative. Women with vaginal discharge and have a positive risk assessment should, therefore, be offered treatment for gonococcal and chlamydial cervicitis. Where resources permit, the use of laboratory tests to screen women with vaginal discharge for other STIs should be considered.

## Recommended treatment for vaginal discharge

| VAGINAL INFECTION | CERVICAL INFECTION |
|---|---|
| Therapy for *T. vaginalis*<br>**PLUS**<br>Therapy for BV<br>**AND, where indicated**<br>Therapy for *C. albicans* | Therapy for uncomplicated gonococcal infection<br>**PLUS**<br>Therapy for chlamydial infection |

**Table 14.7**: Drugs recommended for vaginal infection

| Condition | First line | Second line |
|---|---|---|
| ***Trichomonas vaginalis*** | Metronidazole 2 grams orally, single dose,<br>**OR**<br>Tinidazole 2 grams orally, single dose | Metronidazole, 400 mg or 500 mg orally, twice daily for 7 days<br>**OR**<br>Tinidazole, 500 mg orally twice daily for 5 days |
| **Bacterial vaginosis** | Metronidazole 400-500 mg orally, twice daily for 7 days | Metronidazole 0.75 % gel 5 grams intravaginally, for 5 days,<br>**OR**<br>Clindamycin 2 % cream 5 grams intravaginally, for 7 days,<br>**OR**<br>Clindamycin 300 mg orally, twice daily for 7 days |
| **Vaginal candidiasis** | Fluconazole, 150 mg orally, as a single dose,<br>**OR**<br>Miconazole 200 mg vaginal suppository, one a day for 3 days,<br>**OR**<br>Clotrimazole vaginal pessaries, 200 mg intravaginally, at night for 3 nights,<br>**OR**<br>Clotrimazole vaginal pessaries, 500 mg at night, single dose,<br>**OR**<br>Clotrimazole 10 % vaginal cream, 5 grams as a single dose at night | Nystatin 100,000 IU intravaginally, daily for 14 days |

**Special considerations**

| Condition | Precautions |
|---|---|
| **Metronidazole** | Patients taking metronidazole and tinidazole should avoid alcohol during treatment and for 24 hours and 72 hours, respectively after completion of treatment.<br>Use of metronidazole in the first trimester of pregnancy is not recommended unless the benefits outweigh the potential hazards. |
| **Oil-based vaginal creams** | Clindamycin and clotrimazole creams are oil based and might weaken latex condoms and diaphragms for up to 5 days after use. Clients should be advised to use alternative protective precautions against pregnancy and STIs. |

**Table14.3**: Drugs recommended for cervical infection

| Condition | First line | Second line |
|---|---|---|
| Treatment options for gonorrhoea | Ciprofloxacin 500 mg orally, single dose,<br>**OR**<br>Cefixime 400 mg orally, single dose,<br>**OR**<br>Ceftriaxone 250 mg intramuscularly, single dose | Gentamicin† 240 mg IM single dose, **OR**<br>**Special situations**<br>Spectinomycin 2 g IM as a single dose:<br>- In pregnant or penicillin-allergic patients<br>- For multi-drug resistant infection. |
| Treatment options for Chlamydia | Azithromycin 1 gram single oral dose, **OR**<br>Doxycycline 100 mg twice daily for 7 days | Erythromycin 500 mg orally 4 times daily for 7 days, if tetracyclines are contraindicated |
| **Special considerations** | | |
| Tetracyclines, such as doxycycline, and quinolones, such as ofloxacin or ciprofloxacin, are contraindicated in pregnancy. | | |

**Figure14.5**: Flowchart of **Vaginal discharge syndrome**

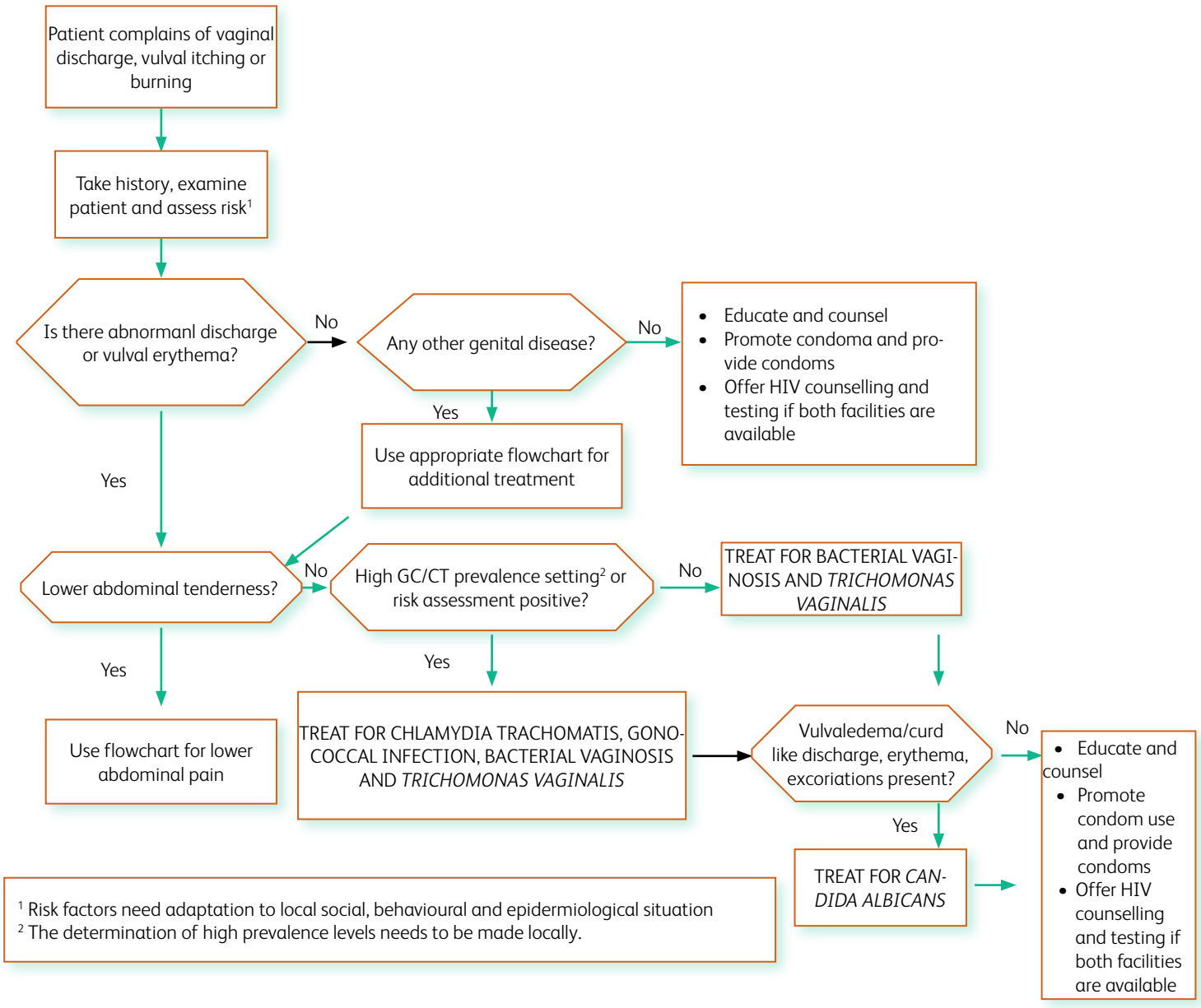
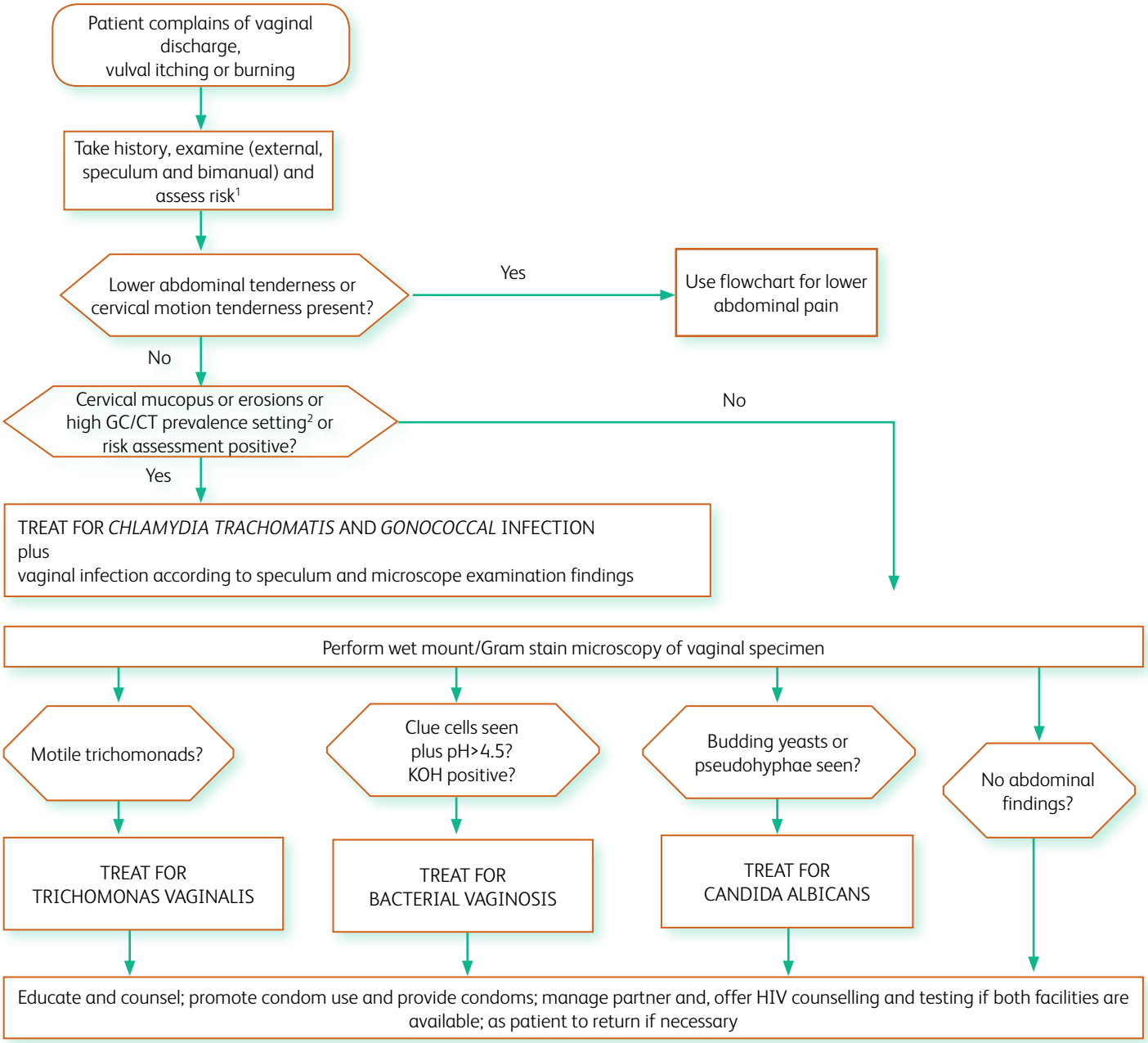


**Figure 14.6:** Flowchart for vaginal discharge with speculum/microscopy




[1] Risk factors need adaptation to local social, behavioural and epidemiological situation.
[2] The determination of high prevalence levels needs to be made locally

## 14.7 Anorectal infections

Infections of the anogenital region can be divided into:

**anal infections**: infections of the external anus and anal canal, involving the stratified squamous epithelium – a common site for pathogens such as the human papillomavirus (HPV), herpes simplex virus (HSV) and syphilis;

**proctitis:** infections from the dentate line to the rectosigmoid junction – a common site for gonococcal and chlamydial infections and HSV;

**proctocolitis:** infections of the rectum and colon – a common site for *Shigella*, *Campylobacter*, *Salmonella*, cytomegalovirus and amoebiasis.

Symptoms associated with ano-rectal infections include pain, itching, discharge, bleeding, sensation of rectal fullness, tenesmus, constipation, and mucus streaking of stools.

Symptomatic ano-rectal infections are thought to be uncommon, although data are rare. Populations most at risk for asymptomatic ano-rectal infections are men who have sex with men (MSM), male and female sex workers, male-to-female transgendered individuals, and men and women who have had receptive anal intercourse with men with STIs. Specific risk sexual

behaviours associated with ano-rectal infections include receptive anal sex, oro-anal contact, fisting, fingering, nudging, dipping, and sharing of sex toys.

Drug choice, dosage, and duration of treatment are, in general, not different from those for infections at other anatomical locations.

### Recommended syndromic treatment of ano-rectal infections

| | | | | |
|---|---|---|---|---|
| Therapy for uncomplicated gonorrhoea | **PLUS** | Therapy for chlamydia | **PLUS** | Antiherpes virus treatment for HSV infection. |

Note: If painful ano-rectal ulcers are detected or herpes proctitis is suspected, management should be the same as for those with genital ulcer disease for the ulcers.

**Table 14.9:** Drugs recommended for Anorectal infections

| Condition | First line | Second line |
|---|---|---|
| Anorectal infections | Ciprofloxacin 500 mg orally, single, **OR**<br>Cefixime 400 mg orally, single dose,<br>**OR**<br>Ceftriaxone 250 mg intramuscularly, single dose | Gentamicin 240 mg IM single dose,<br>**OR**<br>**Special situations**<br>Spectinomycin 2 g IM as a single dose:<br>- In pregnant or penicillin-allergic patients<br>- For multi-drug resistant infection. |
| Treatment options for Chlamydia | Azithromycin 1 gram single oral dose,<br>**OR**<br>Doxycycline 100 mg twice daily for 7 days* | |
| **Special considerations** | | |
| * Treatment with doxycycline 100 mg twice daily should be extended to 21 days if a NAAT is positive for *Chlamydia*, and this would cover lymphogranuloma venereum (LGV) as well.<br>**Inclusion of treatment for herpes simplex infection should be considered in patients with suspected or documented ano-rectal herpes virus infection, following the GUD algorithm.** | | |

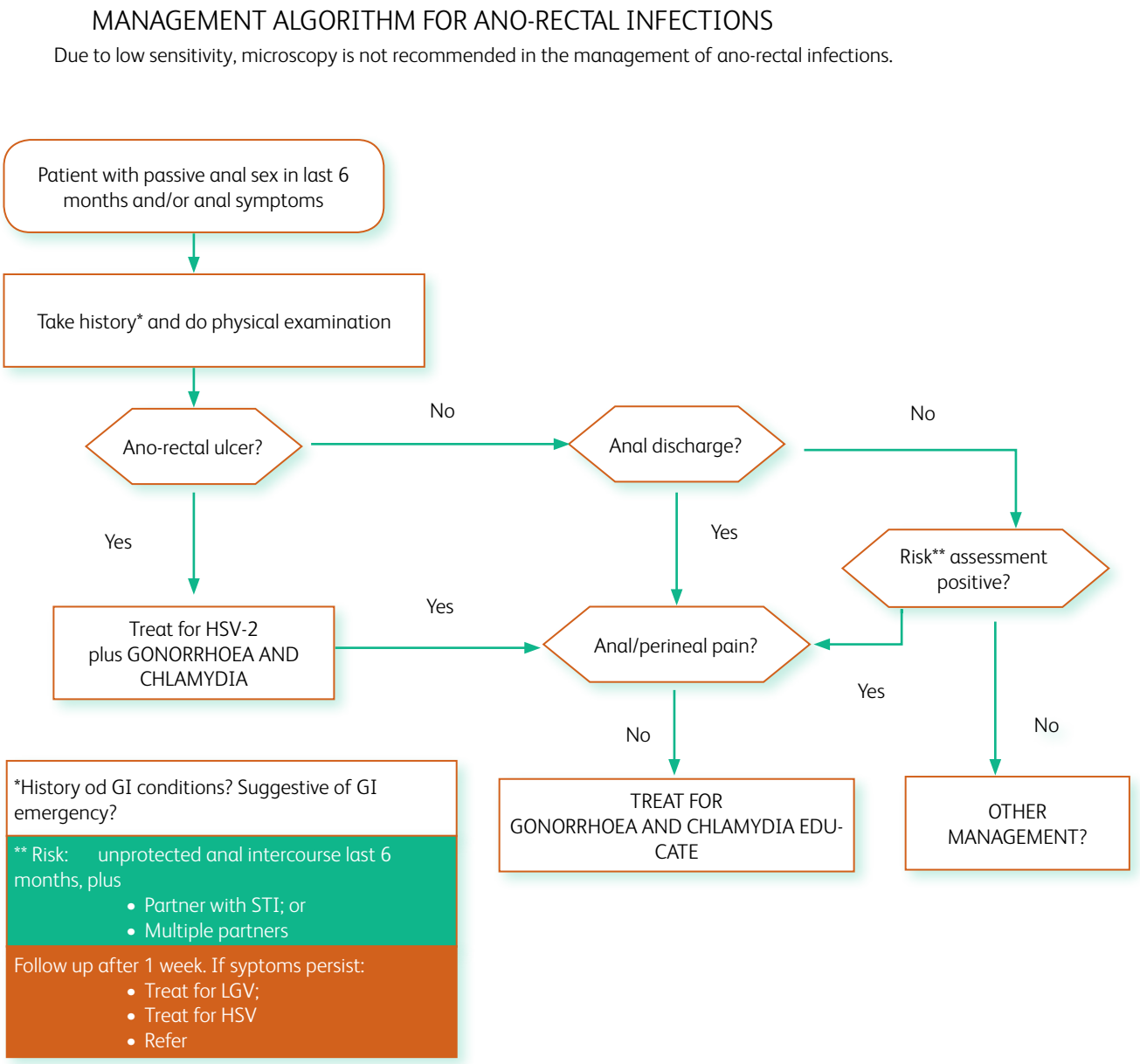
## 14.8 Lower abdominal pain

All sexually active women presenting with lower abdominal pain should be carefully evaluated for the presence or elements of pelvic inflammatory disease (PID) such as, salpingitis, pelvic peritonitis and/or endometritis. In addition, routine bimanual and abdominal examination should be carried out on all women with a presumptive STI since some women with PID or endometritis will not complain of lower abdominal pain. Women with endometritis may present with complaints of vaginal discharge and/or bleeding and/or uterine tenderness on pelvic examination. Symptoms suggestive of PID include abdominal pain, dyspareunia, vaginal discharge, menometrorrhagia, dysuria, pain associated with menses, fever, and sometimes nausea and vomiting.

PID is difficult to diagnose because clinical manifestations are varied. PID becomes highly probable when one or more of the above symptoms are seen in a woman with adnexal tenderness, evidence of lower genital tract infection, and cervical motion tenderness. Enlargement or induration of one or both fallopian tubes, a tender pelvic mass, and direct or rebound tenderness may also be present. The patient's temperature may be elevated but is normal in many cases.

Hospitalization of patients with acute PID should be seriously considered when:

**Figure 14.7**: Flowchart for **Anorectal infections**




- the diagnosis is uncertain;
- surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded;
- a pelvic abscess is suspected;
- severe illness precludes management on an outpatient basis;
- the patient is pregnant;
- the patient is unable to follow or tolerate an outpatient regimen; or
- the patient has failed to respond to outpatient therapy.

Outpatients with PID should be followed up no later than 72 hours after starting treatment (24 hours for females with fever) and admitted to hospital if their condition has not improved. Patients should show substantial clinical improvement (absence of fever, reduction in abdominal tenderness, and reduction in uterine, adnexal and cervical motion tenderness) within three days of starting treatment. Patients who do not improve within this period may require hospitalization. Aetiological agents include sexually transmitted pathogens, especially *N. gonorrhoeae* and *C. trachomatis*, as well as non-sexually transmitted anaerobic bacteria (*Bacteroides* spp. and Gram-positive cocci). Facultative Gram-negative rods and *Mycoplasma hominis*, *Mycoplasma genitalium* and *Ureaplasma urealyticum* have also been associated with some cases of PID. As it is impossible to differentiate between any of these causes clinically, and a precise microbiological diagnosis is difficult, the treatment regimens must be effective against this broad range of pathogens. The regimens recommended below are based on this principle.

**Recommended in Out-patient therapy for PID**

| | | | | |
|---|---|---|---|---|
| Single-dose therapy for uncomplicated gonorrhoea | **PLUS** | Doxycycline, 100 mg orally, twice daily for 14 days | **PLUS** | Metronidazole, 400–500 mg orally, twice daily for 14 days |

**Note:**

Patients taking metronidazole should be cautioned to avoid alcohol.

Tetracyclines are contraindicated in pregnancy.

### Recommended in In-patient therapy for PID

| | | | | |
|---|---|---|---|---|
| Ceftriaxone, 250 mg by intramuscular injection, once daily | PLUS | Doxycycline, 100 mg orally or by intravenous injection, twice daily | PLUS | Metronidazole, 400–500 mg orally or by intravenous injection, twice daily, **OR**<br><br>Chloramphenicol, 500 mg orally or by intravenous injection, 4 times daily. |
| Clindamycin, 900 mg by intravenous injection, every 8 hours | PLUS | Gentamicin, 1.5 mg/kg by intravenous injection every 8 hours | | |
| Spectinomycin 1 g by intramuscular injection, 4 times daily | PLUS | Doxycycline, 100 mg orally **OR**<br><br>by intravenous injection, twice daily, | PLUS | Metronidazole, 400–500 mg orally or by intravenous injection, twice daily,<br><br>**OR**<br><br>Chloramphenicol, 500 mg orally or by intravenous injection, 4 times daily |

**Note**

For all three options of regimen above, therapy should be continued until at least two days after the patient has improved and should then be followed by doxycycline, 100 mg orally, twice daily for 14 days.
Tetracycline hydrochloride 500 mg 4 times daily can be used if doxycycline is not available.
Tetracyclines, including doxycycline are contraindicated in pregnant women.
Patients taking metronidazole should be cautioned to avoid alcohol.

## 14.9 Neonatal conjunctivitis

Neonatal conjunctivitis (ophthalmia neonatorum) can lead to blindness. The most important sexually transmitted pathogens which cause ophthalmia neonatorum are *N. gonorrhoeae* and *C. trachomatis*. In developing countries, the common causes are *N. gonorrhoeae* and *C. trachomatis*). Other common causes are *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus* spp. and *Pseudomonas* spp. (WHO, 2001) Newborn babies are generally presented because of redness and swelling of the eyelids or "sticky eyes", or because of discharge from the eye(s).

As the clinical manifestations and possible complications of gonococcal and chlamydial infections are similar, in settings where it is impossible to differentiate between the two infections, treatment should be provided to cover both. This would include single-dose therapy for gonorrhoea and multiple dose therapy for chlamydia.

**Figure 14.8**: Flowchart for PID

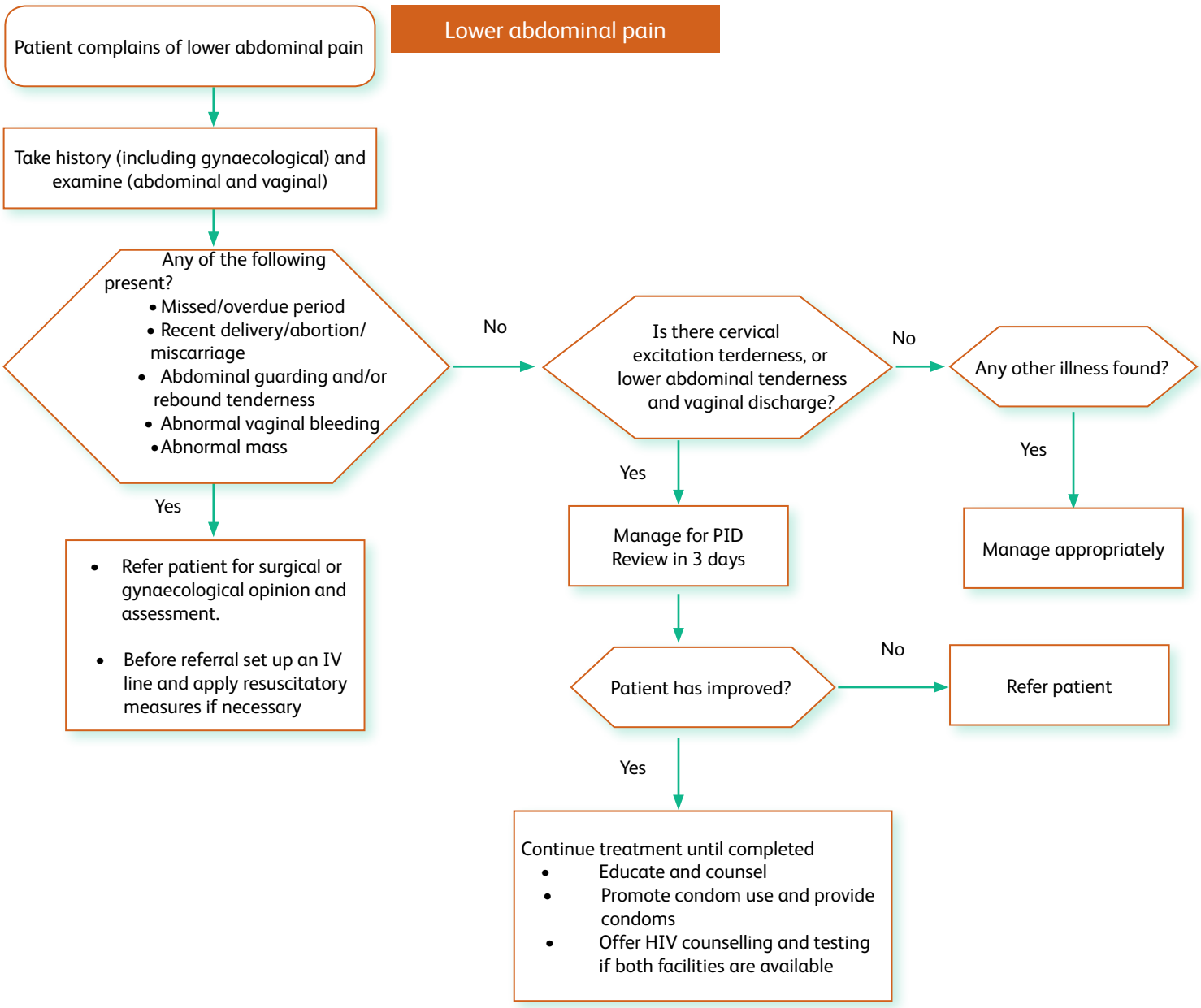
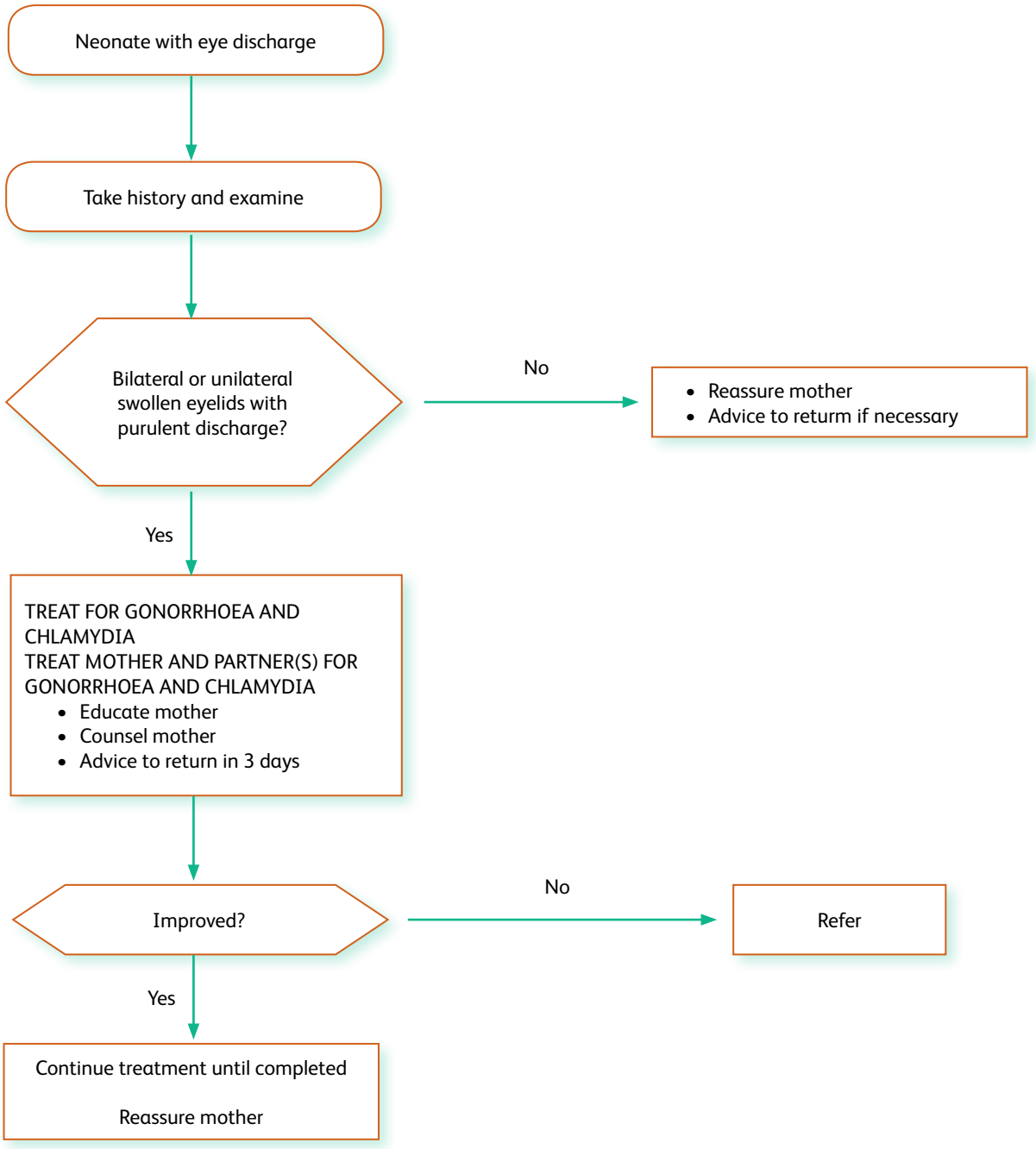



**Table 14.4**: Drugs recommended treatment for Neonatal conjunctivitis

| Condition | First line | Second line |
|---|---|---|
| Gonococcal ophthalmia neonatorum | Ceftriaxone 50 mg per kilogram body weight intramuscularly, single dose, to a maximum of 125 mg | Kanamycin 25 mg per kilogram body weight, as a single dose, to a maximum of 75 mg, **OR**<br>Spectinomycin 25 mg per kilogram body weight intramuscularly, single dose to a maximum of 75 mg. |
| Chlamydial ophthalmia neonatorum | Erythromycin syrup 50 mg per kilogram body weight per day, orally, divided into 4 doses for 14 days. | |
| **Special considerations** | | |
| Single dose ceftriaxone and kanamycin are of proven efficacy; therefore, addition of tetracycline eye ointment to these treatments is of no documented benefit.<br>Topical antibiotic treatment alone is inadequate for treatment of chlamydial infection, and it would not take care of infection in other sites such as chlamydial pneumonia.<br>The mothers of infants who have gonococcal or chlamydial conjunctivitis should be treated for these infections appropriately, and their sex partners should be evaluated and treated. | | |

**Figure14.9**: Flowchart for Neonatal conjunctivitis



# Chapter 15: Treatment of Specific Infections

Treatment of a specific STI should be based on laboratory confirmation and/or specific clinical presentations.

## 15.1 Gonococcal infections

### Transmission

Neisseria gonorrhoeae is basically transmitted through sexual contact. It can also be passed from mother's genital tract to the newborn during vaginal delivery causing ophthalmia neonatorum or systemic neonatal infection. Transmission through blood can cause disseminated gonococcal infection especially in the younger age group.

### Clinical features

In males, it may present as:

- asymptomatic infection (in some males);
- urethral discharge and dysuria;
- upper respiratory tract infection;
- rectal infection, which may cause anal discharge or perianal pain;
- acute epididymo-orchitis (more common in men aged over 35 years);
- fever, petechial or pustular skin lesions, asymmetrical arthralgia, septic arthritis, and tenosynovitis in disseminated infection; and
- very rarely, meningitis or endocarditis.

In females, it may present as:

- asymptomatic infection (more common than males);
- mucopurulent endocervical discharge, contact bleeding (cervicitis);
- altered vaginal discharge;
- acute lower abdominal pain and tenderness; and
- disseminated infection (as in males).

In newborns, it presents as:

- purulent conjunctivitis.

### Laboratory diagnosis

N. gonorrhoeae is a gram-negative intracellular, aerobic diplococcus that can be identified from genital, rectal, pharyngeal or ocular secretion of infected individuals; Methods involve gram staining/ methylene blue stain and microscopy by visualising the diplococci in leucocytes; Culture and sensitivity provide confirmation of gonococcal infection and sensitivity to antimicrobials.

### Treatment considerations

Some PICTs have reported a large proportion of resistant gonococcal isolates to penicillins, tetracyclines and quinolones. (Australia, 2000; WHO, 1996 & WPRO-WHO, 1999) Adding anti-chlamydia therapy for all patients with Gonorrhoea is strongly recommended because of the high prevalence of chlamydia in the region, dual infection is common and difficult to differentiate.

### Treatment for uncomplicated anogenital infections

Ciprofloxacin, 500mg orally in single dose **OR**

Ceftriaxone, 250 mg by intramuscular injection, as a single dose **OR**

Cefixime, 400 mg orally, as a single dose **OR**

Spectinomycin, 2 g by intramuscular injection, as a single dose, only to be used as an alternative

**Note:**

Spectinomycin should be reserved as an alternative in patients with documented treatment failure to cephalosporins, as well as an option for pregnant women allergic to penicillin in whom cross-reactivity with cephalosporins may be a concern.

### Treatment for disseminated gonococcal infections

Ceftriaxone, 1 g by intramuscular or intravenous injection, once daily for 7 days (alternative third-generation cephalosporins may be required where ceftriaxone is not available, but more frequent administrations will be needed) **or** Spectinomycin, 2 g by intramuscular injection, twice daily for 7 days.

**Note:**

For gonococcal meningitis and endocarditis the same dosages apply but for endocarditis the duration of therapy will need to be increased to 4 weeks.

Hospitalisation is advisable for initial therapy of patients with disseminated infection.

### Treatment for gonococcal ophthalmia

This is a serious condition that requires systemic therapy as well as local irrigation with saline or other appropriate solutions. Careful hand washing by personnel caring for infected patients is essential.

There is not much data on treatment of gonococcal conjunctivitis in adults. One published study was based on 12 study participants who were all cured with a single dose of ceftriaxone 1 gram intramuscularly. (Haimovici & Roussel, 1989) Based on this and the decreasing susceptibility of *N. gonorrhoeae*, the documented dose of 1 gram of ceftriaxone is recommended for adult gonococcal conjunctivitis.

### Treatment for adult gonococcal conjunctivitis

| |
|---|
| Ceftriaxone, 1 g by intramuscular injection, as a single dose<br><br>**OR**<br><br>Spectinomycin, 2 g by intramuscular injection, as a single dose |
| **Note**: Spectinomycin 2-gram dose is also likely to be effective although there are no published data on its use in gonococcal ophthalmia |
| **Follow-up:** Careful monitoring of clinical progress is important. |

### Treatment for neonatal gonococcal conjunctivitis

| First regimen | Alternative regimens |
|---|---|
| Ceftriaxone, 50 mg/kg by intramuscular injection, as a single dose, to a maximum of 125 mg | Kanamycin, 25 mg/kg by intramuscular injection, as a single dose, to a maximum of 75 mg, **OR**<br><br>Spectinomycin, 25 mg/kg by intramuscular injection, as a single dose, to a maximum of 75 mg |
| **Note**<br><br>Single-dose ceftriaxone and kanamycin are of proven efficacy. The addition of tetracycline eye ointment to these regimens is of no documented benefit. | |
| **Follow-up**<br><br>Patients should be reviewed after 48 hours. | |

### Prevention of ophthalmia neonatorum

Gonococcal ophthalmia neonatorum is preventable with timely eye prophylaxis. The infant's eyes should be carefully cleaned immediately after birth. The application of 1 % silver nitrate solution or 1 % tetracycline ointment to the eyes of all infants at the time of delivery is strongly recommended as a prophylactic measure. Ocular prophylaxis provides poor protection against *C. trachomatis* conjunctivitis.

### Recommended regimen for infants born to mothers with gonococcal infection

| First regimen | Alternative regimens |
|---|---|
| Ceftriaxone 50 mg/kg by intramuscular injection, as a single dose,<br><br>to a maximum of 125 mg | Kanamycin, 25 mg/kg by intramuscular injection, as a single dose, to a maximum of 75 mg, **OR**<br><br>Spectinomycin, 25 mg/kg by intramuscular injection, as a single dose, to a maximum of 75 mg |

### Management of sexual partner(s)

Sexual partners should be treated for both gonococcal and chlamydial infections similar to those of the index patient's protocol. Categories of sexual contacts to be treated include:

- all sex partners within the preceding 14 days, or last partner if longer, for symptomatic
- index of gonorrhoea; and
- in asymptomatic cases, all partners within the preceding 90 days

## 15.2 Chlamydia trachomatis infections

**(Other than Lymphogranuloma venereum)**

### Transmission

Like gonococcal infections, chlamydia is basically sexually transmitted. Similarly, transmission from mother to newborn during vaginal delivery, causing neonatal conjunctivitis, is also possible.

### Clinical Features

Most of chlamydia infection in men and women are asymptomatic. The signs and symptoms are mainly of those secondary to cervicitis or urethritis and to complications. Chlamydial infection is symptomatic in about 30 per cent of women and 75 per cent of men. (Anony, 2001 & Mathew, 2005) In males, it may present as urethritis, prostatitis, or epididymitis.

In females, it may present as cervicitis and/or pelvic inflammatory disease (PID), or ectopic pregnancy.

In both sexes, it may present as:

- infertility;
- proctitis (rectal disease and bleeding); and
- reactive arthritis.

In newborns, it may present as conjunctivitis or lung infection.

## Laboratory diagnosis:

High sensitive technology Nucleic Acid Assay Test (NAAT) is now available in most PICTs. However, this technology may not be available in rural health services or outer islands.

## Treatment considerations

### Uncomplicated Anogenital infections

| Recommended regimens | Alternative regimens |
|---|---|
| Azithromycin, 1 g orally, in a single dose,<br><br>**OR**<br><br>Doxycycline, 100 mg orally, twice daily for 7 days | Amoxycillin, 500 mg orally, 3 times a day for 7 days, **OR**<br><br>Erythromycin, 500 mg orally, 4 times a day for 7 days, **OR**<br><br>Ofloxacin, 300 mg orally, twice a day for 7 days,<br><br>**OR**<br><br>Tetracycline, 500 mg orally, 4 times a day for 7 days |
| **Note**<br><br>Doxycyline and other tetracyclines are contraindicated during pregnancy and lactation.<br><br>Current evidence indicates that 1 g single-dose therapy of azithromycin is efficacious for chlamydial infection.<br><br>There is evidence that extending the duration of treatment beyond 7 days does not improve the cure rate in uncomplicated chlamydial infection.<br><br>Erythromycin should not be taken on an empty stomach. | |
| **Follow-up**<br><br>Compliance with the 7-day regimens is critical. Resistance of *C.trachomatis* to recommended treatment regimens has not been observed | |

| **Chlamydial infections during pregnancy (Recommended regimens)** |
|---|
| Azythromycin, 1g, orally in single dose, **OR**<br><br>Erythromycin, 500 mg orally, 4 times a day for 7 days, **OR**<br><br>Amoxycillin, 500 mg orally, three times a day for 7 days |
| **Note**<br><br>Doxycycline (and other tetracyclines) and ofloxacin are contraindicated in pregnant women.<br><br>Erythromycin estolate is contraindicated during pregnancy because of drug-related hepato-toxicity. Therefore, only erythromycin base or erythromycin ethylsuccinate should be used. |

## Neonatal chlamydial conjunctivitis

All newborn infants with conjunctivitis should be treated for both *N. gonorrhoeae* and *C. trachomatis*, because of the possibility of mixed infection.

| Condition | Recommended regimen | Alternative regimen |
|---|---|---|
| Gonococcal ophthalmia neonatorum | Ceftriaxone 50 mg per kilogram body weight, intramuscularly, single dose, to a maximum of 125 mg | Kanamycin 25 mg per kilogram body weight, as a single dose, to a maximum of 75 mg.<br>**OR**<br>Spectinomycin 25 mg per kilogram body weight intramuscularly, single dose to a maximum of 75 mg. |
| Chlamydial ophthalmia neonatorum | Erythromycin syrup 50 mg per kilogram body weight per day, orally, divided into 4 doses for 14 days. | |
| Note:<br>Single dose ceftriaxone and kanamycin are of proven efficacy; therefore, addition of tetracycline eye ointment to these treatments is of no documented benefit.<br>Topical antibiotic treatment alone is inadequate for treatment of chlamydial infection, and it would not take care of infection in other sites such as chlamydial pneumonia.<br>The mothers of infants who have gonococcal or chlamydial conjunctivitis should be treated for these infections appropriately, and their sex partners should be evaluated and treated. | | |

## Infantile pneumonia

| **Recommended regimen** |
|---|
| Erythromycin syrup, 50 mg/kg per day for 14 days |
| **Note** |
| The optimal duration of therapy has not been definitively established, but treatment should not be less than 14 days. |

## Management of sexual partner(s)

Counsel the index client on safer sexual practices, and the importance of contact tracing for treatment. Also ask them to abstain from sexual intercourse until they complete the seven-day drug regimen. Screen and treat the last sexual partner even if the last sexual contact was about two months prior to the index patient being diagnosed. (Mathew, 2005) There are limited published data on the treatment of LGV in the Pacific Region.

| Recommended regimen | Alternative regimen |
|---|---|
| Doxycycline, 100 mg orally, twice daily for 14 days, **OR**<br>Erythromycin, 500 mg orally, 4 times daily for 14 days | Tetracycline, 500 mg orally, 4 times daily for 14 days |
| **Note**<br>Tetracyclines are contraindicated in pregnancy. Fluctuant lymph nodes should be aspirated through healthy skin. Incision and drainage or excision of nodes may delay healing. Some patients with advanced disease may require treatment for longer than 14 days, and sequelae such as strictures and/or fistulae may require surgery. | |

## 15.3 Syphilis

### Transmission and clinical presentation

Syphilis is a systemic disease caused by the spirochaete, *Treponema pallidum* (*T. pallidum*). The infection can be classified as congenital or acquired. Congenital syphilis is transmitted from mother to child in-utero. Acquired syphilis is divided into early and late syphilis. Early syphilis comprises the primary, secondary and early latent stages. Late syphilis refers to late latent syphilis, gummatous neurological and cardiovascular syphilis.

Primary syphilis is characterized by an ulcer or chancre at the site of infection or inoculation. Secondary syphilis manifestations include a skin rash, condylomata lata, mucocutaneous lesions and generalised lymphadenopathy.

In the early phase of primary syphilis the cardiolipin/non-treponemal tests, such as the Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) test may be negative and should, therefore, not be interpreted as absence of syphilis infection.

Latent syphilis has no clinical manifestations. Early latent syphilis is infection of less than two years duration. An infection of more than two years duration without clinical evidence of treponemal infection is referred to as late latent syphilis. Early stages are more infectious but respond better to treatment. A few weeks after infection occurs, the body produces syphilis antibodies that can be detected by an accurate, safe and inexpensive blood test. A low level of antibodies will likely stay in the blood for months or years even after the disease has been successfully treated.

The syphilis bacterium can infect the baby of a woman during her pregnancy. Depending on how long a pregnant woman has been infected, she may have a high risk of having a stillbirth or neonatal death. An infected baby may be born without signs or symptoms of disease. However, if not treated immediately, the baby may develop serious problems within a few weeks. Untreated babies may become developmentally delayed, have seizures or die.

**Clinical features**

- Incubation period is 9 to 90 days;
- Many people infected with syphilis have no symptoms for years; and
- Some of the symptoms may not be clear.

### Primary stage

There is often a single painless sore (chancre) usually 1–2 cm, firm, round and raised on the genitalia, rectum or lips (but there may be multiple sores.) The chancre lasts for six weeks, and heals without treatment, if not adequately treated the infection progresses to the secondary stage. Untreated primary chancre will heal in three to eight weeks

### Secondary stage

Secondary syphilis is a systemic infection (in the blood) and may come and go over a year (occasionally up to two years) after initial infection. Skin rash and mucous membrane lesions characterize the secondary stage. The rash usually does not cause itching and it appears as rough, red or reddish brown spots both on the palms of the hands and the soles of the feet. However, rashes with a different appearance may occur on other parts of the body. Other symptoms of secondary syphilis may include fever, swollen lymph glands, sore throat, patchy hair loss, headaches, weight loss, muscle aches and fatigue. The signs and symptoms of secondary syphilis will resolve without treatment within one to two years, but without treatment the infection will progress to the latent and possibly late stages of disease.

### Latent stages

In the latent stage, untreated syphilis will manifest with signs or symptoms of syphilis.

(This stage usually occurs one to two years after the initial infection.)

Latent syphilis is often referred to as either:

- early latent syphilis (infection of less than two years); or
- late latent syphilis (infection of more than two years).

### Tertiary stage

The late stages of syphilis appear 10 to 20 years after infection was first acquired.

In the late stages of syphilis, the disease may subsequently damage the internal organs, including the brain, nerves, eyes, heart, blood vessels, liver, bones and joints.

Signs and symptoms of the late stage of syphilis include difficulty coordinating muscle movements, paralysis, numbness, gradual blindness and dementia. This damage may be serious enough to cause death.

## Neonatal Syphilis

Early signs are characteristic skin lesions, lymphadenopathy, hepatosplenomegaly, failure to thrive, blood-stained nasal discharge (snuffles), perioral fissures, meningitis, choroiditis, hydrocephalus, seizures, mental retardation, osteochondritis and pseudoparalysis.

Later signs are gummatous ulcers, periosteal lesions, paresis, tabes dorsalis, optic atrophy, interstitial keratitis, sensorineural deafness and dental deformities.

## Therapeutic considerations

A treponemacidal level of antimicrobials needs to be achieved in the serum and cerebrospinal fluid (CSF) to provide effective treatment for syphilis. Long-acting benzathine penicillin, at a dose of 2.4 million units, provides a treponemacidal penicillinaemia for up to three weeks and is recommended for late syphilis treatment.

Management of patients with cardiovascular syphilis should include consultation with a cardiologist. All patients with cardiovascular syphilis and neurosyphilis should be followed for many years. The follow-up should include clinical, serological, CSF and, based on the clinician's assessment of the individual patient's condition, radiological examinations.

## Follow-up of patients treated for syphilis

The clinical condition of the patients should be assessed to detect reinfection during the first year after therapy. Patients with early syphilis who have been treated with appropriate doses should be evaluated clinically and serologically, using a non-treponemal test, after three months, to assess the results of therapy. A second evaluation should be performed after six months and, if indicated by the results at this point, again after 12 months, to reassess the condition of the patient and detect possible reinfection.

All patients should be monitored following therapy until free of clinical disease and until titres are stable at negative or low (1:4 or less) levels.

## At all stages of the disease, repeat treatment should be considered when:

- clinical signs or symptoms of active syphilis persist or recur; and
- there is confirmed increase in the titre of a non-treponemal test.

## Management of sexual partner(s):

Generally, any person who has been exposed sexually to a person diagnosed with syphilis should be clinically and serologically evaluated. People who were exposed within the 90 days preceding the diagnosis of primary, secondary or early latent syphilis in a sex partner should be treated presumptively. People who were exposed more than 90 days before the diagnosis of primary, secondary or early latent syphilis in a sexual partner should be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.

For purposes of partner notification and presumptive treatment of exposed sexual partners, patients with syphilis of unknown duration who have high non-treponemal serologic test titres (i.e. >1:32) can be assumed to have early syphilis. However, serologic titres should not be used to differentiate early from late latent syphilis for the purpose of determining treatment. Long-term sexual partners of patients who have latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation findings.

## Syphilis and HIV infection

All patients with syphilis should be encouraged to undergo testing for HIV infection because of the high frequency of dual infection and its implications for clinical assessment and management. Neurosyphilis should be considered in the differential diagnosis of neurological disease in HIV-infected individuals.

In people who both are HIV positive and have syphilis, serologic responses are unusual. Thus, when clinical findings suggest syphilis but serological tests are non-reactive or unclear, undertake alternative investigative tests such as biopsy of the lesion, dark-field microscopy, and direct fluorescent antibody staining of lesion material.

Recommended therapy for early syphilis in HIV-infected patients is no different from that in patients not infected with HIV. However, where feasible, CSF examination should be carried out to determine response to treatment.

## Syphilis in pregnancy

Pregnant women should be regarded as a separate group, requiring close surveillance, in particular to detect possible reinfection after treatment has been given. Pregnant women who have reactive RPR or VDRL should be treated, even in absence of a confirmative test like the Treponema pallidum haemagglutination assay (TPHA). (CDC, 2006 & WHO, 2005) It is also important to treat their sexual partner(s). Pregnant patients at all stages of pregnancy, who are not

allergic to penicillin, should be treated with penicillin according to the dosage schedules recommended for the treatment of non-pregnant patients at a similar stage of the disease.

The effectiveness of erythromycin in all stages of syphilis is still questionable. Also, the efficacy in neurosyphilis is probably low. Penicillin desensitization of pregnant women with syphilis requires that the procedure be performed in a hospital setting. This is not feasible at most primary health care settings and cannot be recommended as a routine procedure.

## Follow-up

Following treatment, quantitated non-treponemal serological tests should be performed at monthly intervals until delivery, and re-treatment should be undertaken if there is serological evidence of reinfection or relapse.

## Congenital syphilis

Congenital syphilis is divided into early (first two years of life) and late (becomes apparent later in life).

Prevention of congenital syphilis is feasible. Programmes should implement effective screening strategies for syphilis in pregnant women. Screening for syphilis should be conducted at the first prenatal visit. Some programmes have found it beneficial to repeat the tests at 28 weeks of pregnancy and/or at delivery in populations with a high incidence of congenital syphilis.

Congenital syphilis may occur if the expectant mother has syphilis, but the risk is minimal if she has been given penicillin during pregnancy. All infants of seropositive mothers should be examined at birth and at monthly intervals for three months until it is confirmed that serological tests are, and remain, negative. Any antibodies passively transmitted from mother to baby usually disappear within three to four months of birth. However, in some cases antibody detection can persist up to a period of 18 months. In such cases repeat testing with titration should be done, and the baby treated for congenital syphilis if a 4-fold increase or more of titre of a non-treponemal or treponemal test is detected. Nevertheless, all infants born to seropositive mothers should be treated with a single intramuscular dose of benzathine benzylpenicillin, 50 000 IU/kg whether or not the mothers were treated during pregnancy (with or without penicillin). Hospitalization is recommended for all symptomatic babies born to mothers who were seropositive. Symptomatic infants and asymptomatic infants with abnormal CSF (up to two years of age) should be treated as for early congenital syphilis (see table 15.1).

Early congenital syphilis generally responds well, both clinically and serologically, to adequate doses of penicillin. Recovery may be slow in seriously ill children with extensive skin, mucous membrane, bone or visceral involvement. Those in poor nutritional condition may succumb to concurrent infections, such as pneumonia.

**Table 15.1**: Recommended treatment and alternate regimens for congenital syphilis

| Recommended regimen | Alternate regimen |
|---|---|
| **Early congenital syphilis (up to two years of age) and infants with abnormal CSF** | |
| Aqueous benzylpenicillin 100,000–150,000 IU/kg/day administered as 50,000 IU/kg/dose IV every 12 hours during the first seven days of life and every eight hours thereafter for a total of 10 days<br><br>Procaine benzylpenicillin 50,000 IU/kg IM daily for 10 days | |
| | Alternate regimen for penicillin-allergic patients, after first month of life:<br><br>Erythromycin 7.5–12.5mg/kg orally 4 times a day for 30 days |
| **Congenital syphilis of two years or more** | |
| Aqueous benzylpenicillin 200,000–300,000 IU/kg/day IV or IM, administered as 50,000 IU/kg/dose every 4–6 hours for 10–14 days | |
| Note: Antimicrobials other than penicillin are not recommended for congenital syphilis unless there is absolutely no other choice. Tetracyclines should not be used in young children. | |

## Diagnostic considerations of syphilis

**Dark-field microscopy:**

The treponemes could be detected under the dark-field microscopy examination of lesion exudates or tissue. This is the most specific method for the diagnosis of the early stages of syphilis. The dark-field examination must be performed immediately after specimen collection from primary chancres, moist secondary lesions or from lymph nodes. This method requires special equipment, skill personnel. The detection of spirochaetes depends on the number of live treponemes in the lesion sample. How ever, negative dark-field result does not exclude syphilis.

### Serology test

A presumptive diagnosis of syphilis can be made from serological tests for syphilis. Two types of serological tests exist as follows. **Non-treponemal tests**, such as the microscopic Venereal Diseases Research Laboratory (VDRL) and the macroscopic rapid plasma reagin (RPR) tests. These tests may be used as qualitative or quantitative tests detecting antibodies to lipoidal material released from damaged host cells or cardiolipin-like material from the treponemes. These antibodies can also be produced in some acute or chronic diseases in which tissue damage occurs in conditions such as acute febrile viral infections and some chronic autoimmune diseases.

Non-treponemal tests may be negative for up to 4 weeks after the chancre of primary syphilis first appears. Repeat tests at 1 & 3 months are recommended in suspect lesions with an initial negative test to exclude syphilis. A negative non-treponemal test at 3 months of onset of the primary chancre virtually excludes the diagnosis of syphilis.

The RPR generally rises early in a new infection, and will drop over time, or with treatment. The RPR will become non-reactive in only 25 per cent of people, so often people with either treated or untreated infection will have a low resting titre (1:1, 1:2, 1:4 and sometimes higher). In general, though, a titre of 1:8 or greater indicates that a person has acquired syphilis in the last two years. (see figure 15.1 below)

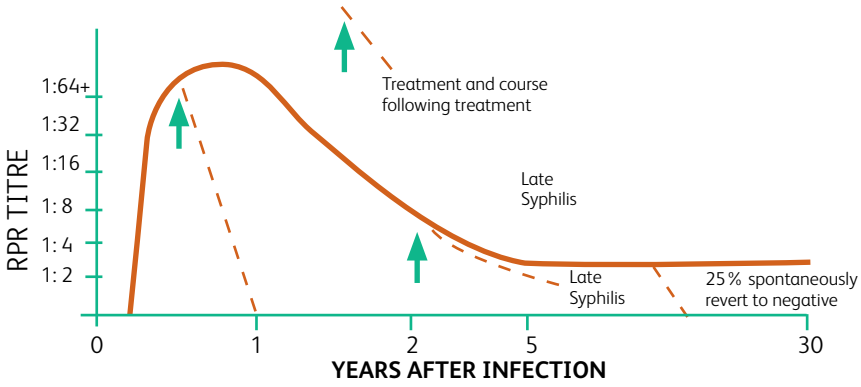
Non-treponemal tests is also used to monitor response to treatment by performing quantitative testing. Titres will decrease following effective treatment or increase in untreated active infection. A 4-fold change or higher in titre, equivalent to a change of at least two dilutions, for example, from 1:16 to 1:4 for effective positive response to treatment or from 1:8 to 1:32 for continued active infection, would be considered significant between two sequential non-treponemal test results using the same testing method (e.g. VDRL or RPR), preferably by the same laboratory.

**Note**: Venereal Disease Research Laboratory (VDRL) is a non-specific test that is no longer used in the region. (The terminology is still in use but should be phased out as it is misleading.)

**Specific test or Treponemal tests**, such as the *Treponema Pallidum* haemaglutination assay (TPHA), the *T. pallidum* passive particle agglutination assay (TP-PA) and the fluorescent treponemal antibody absorbed (FTA-ABS) tests. These tests detect antibodies formed specifically to the antigenic determinants of the treponemes. Classically, these tests are used as confirmatory tests to the non-treponemal tests. Characteristically, treponemal tests remain positive for the patient's lifetime regardless of outcome of treatment. Thus, a positive treponemal test does not distinguish between active infection and prior treated infection.

Lumbar puncture: In some patients with syphilis (especially in the latent or late stages), a lumbar puncture (spinal tap) must be done to check for infection of the nervous system.

**Figure 15.1**: Variation in RPR titre after infection




## Rapid diagnostic tests

The rapid diagnostic tests (RDTs) can give a result in 10 to 15 minutes, and they can be performed in any setting as opposed to the RPR which requires refrigeration facilities for storing reagents, a rotator and a centrifuge.

Some of the examples of the RDT's are:

- treponema-specific tests that use *T. pallidum* antigens to detect treponema-specific antibodies; and
- dual rapid tests provide both a screening (RPR equivalent) and confirmatory (TPHA/TPPA equivalent) component. However, these dual rapid tests are not yet sufficiently evaluated and field tested at this stage

**Table 15.3**: Recommended treatment and alternate regimens for early syphilis, late latent syphilis and neurosyphilis

| Recommended regimen | Alternative regimen |
|---|---|
| **EARLY SYPHILIS**<br>(primary, secondary, or latent syphilis of not more than two years' duration) | |
| Benzathine benzylpenicillin,[1] 2.4 million IU by intramuscular injection, at a single dosage.<br><br>Because of the volume involved, this dose is usually given as two injections at separate sites | Procaine benzylpenicillin,[2] 1.2 million IU by intramuscular injection, daily for 10 consecutive days<br>**OR**<br>Azithromycin 2 g orally, single dose. |
| | **For penicillin-allergic non-pregnant patients**<br>Doxycycline, 100 mg orally, twice daily for 14 days<br>**OR**<br>Tetracycline, 500 mg orally, 4 times daily for 14 days |
| | **For penicillin-allergic pregnant patients**<br>Erythromycin, 500 mg orally, 4 times daily for 14 days<br>OR<br>Azithromycin 2 g orally, single dose |
| **Note:**<br>Azithromycin is an effective treatment option for early.(Hook, E.W., et al., 2002; Hook, E.W., et al., 2010; Riedner.G., et al., 2005) However, attention should be paid to the emergence of resistance to this macrolide antibiotic in *T. pallidu*m with chromosomal mutations conferring resistance to it. Close follow up of patients treated with azithromycin is essential, with repeated testing and physical examination to detect treatment failures. | |
| **LATE LATENT SYPHILIS**<br>(infection of more than two years' duration without evidence of treponemal infection) | |
| Benzathine benzylpenicillin, 2.4 million IU by intramuscular injection, once weekly for 3 consecutive weeks | Procaine benzylpenicillin, 1.2 million IU by intramuscular injection, once daily for 20 consecutive days |
| | **Alternative regimen for penicillin-allergic non-pregnant patients**<br>Doxycycline, 100 mg orally, twice daily for 30 days<br>**OR**<br>Tetracycline, 500 mg orally, 4 times daily for 30 days |
| | **Alternative regimen for penicillin-allergic pregnant patients**<br>Erythromycin, 500 mg orally, 4 times daily for 30 days |
| **NEUROSYPHILIS** | |
| Aqueous benzylpenicillin,[3] 12–24 million IU by intravenous injection, administered daily in doses of 2–4 million IU, every 4 hours for 14 days | Procaine benzylpenicillin, 1.2 million IU by intramuscular injection, once daily,<br>**PLUS**<br>Probenecid, 500 mg orally, 4 times daily, both for l0–14 days<br>This regimen should be used only for patients whose outpatient compliance can be assured |
| | **Alternative regimens for penicillin-allergic non-pregnant patients**<br>Doxycycline, 200 mg orally, twice daily for 30 days<br>**OR**<br>Tetracycline, 500 mg orally, 4 times daily for 30 days |
| **Note**<br>The above alternatives to penicillin for the treatment of neurosyphilis have not been evaluated in systematic studies.The central nervous system may be involved during any stage of syphilis. Clinical evidence of neurological involvement (e.g. optic or auditory symptoms, or cranial nerve palsies) warrants examination of the CSF. However, examination of the CSF is also highly desirable in all patients with syphilis of more than two years' duration, or of uncertain duration, in order to evaluate the possible presence of asymptomatic neurosyphilis. Some experts recommend consulting a neurologist when caring for a patient with neurosyphilis. Careful follow-up is essential. | |

| CONGENITAL SYPHILIS | |
|---|---|
| **A. Early congenital syphilis (up to 2 years of age) AND Infants with abnormal CSF** | |
| Aqueous benzylpenicillin 100 000–150 000 IU/kg/day administered as 50 000 IU/kg/dose IV every 12 hours, during the first 7 days of life and every 8 hours thereafter for a total of 10 days<br>**OR**<br>Procaine benzylpenicillin, 50 000 IU/kg by intramuscular injection, as a single daily dose for 10 days | |
| **Note:** Some experts treat all infants with congenital syphilis as if the CSF findings were abnormal. Antimicrobials other than penicillin (e.g. erythromycin) are not indicated for congenital syphilis except in cases of severe allergy to penicillin. Tetracyclines should not be used in young children. | |
| **B. Congenital syphilis of 2 or more years' duration** | |
| Aqueous benzylpenicillin, 200 000–300 000 IU/kg/day by intravenous or intramuscular injection, administered as 50 000 IU/kg every 4–6 hours for 10–14 days | **Alternative regimen for penicillin-allergic patients, after the first month of life**<br><br>Erythromycin, 7.5–12.5 mg/kg orally, 4 times daily for 30 days |

## 15.4 Genital herpes infections

Two serotypes of herpes simplex virus (HSV) infect humans: HSV-1 and HSV-2. HSV-2 causes recurrent genital herpes which is usually life-long viral infection. The major public health importance of HSV-2 is in facilitating HIV transmission. (CDC, 2006) Most people with HSV may have mild, unrecognised infections but continue to shed the virus into the genital tract, thus may continue to transmit to another person without recognising or being aware of it. HSV-2 is almost always sexually transmitted.

There is no known cure for genital herpes, but the course of symptoms can be modified if systemic therapy with acyclovir, or its analogues, is started as soon as possible following the onset of symptoms. Treatment can be expected to reduce the formation of new lesions, the duration of pain, the time required for healing, and viral shedding. Topical therapy with acyclovir produces only minimal shortening of the duration of symptomatic episodes and is not recommended.

### Recurrent infections

Most patients with a first episode of genital herpes infection will have recurrent episodes of genital lesions. Episodic or suppressive antiviral therapy will shorten the duration of genital lesions. Many patients who have recurrent disease benefit from episodic therapy if treatment is started during the prodrome or within one day after onset of lesions. If episodic treatment of recurrences occur, the patient should be provided with antiviral therapy, or a prescription for the medication, so that treatment can be initiated at the first sign of prodrome or genital lesions.

### Diagnosis

Clinical features

Multiple painful vesicular or ulcerative lesions

Laboratory diagnosis

In some developed countries, HSV could be detected through: cell culture, polymerase chain reaction (PCR), viral culture immunofluorescence which is used to detect viral antigens, and

serological testing

**Note:** In the Pacific region, clinical diagnosis is the main method used to diagnosed herpes simplex infection.

### Herpes in pregnancy

There is a high risk for transmission to the newborn from a pregnant woman who acquires genital herpes near the time of delivery.

Note: A caesarean section does not totally eliminate the risk of HSV transmission to the infant.

### Herpes and HIV co-infection

In people whose immunity is deficient, persistent and/or severe mucocutaneous ulcerations may occur, often involving large areas of perianal, scrotal or penile skin. The lesions may be painful and atypical, making a clinical diagnosis difficult. It is recommended that herpes treatment in HIV infected patients be initiated

as soon as possible after lesions occur or recur, and that treatment be continued for at least a week. Subsequently, patients may benefit from chronic suppressive therapy.

## Management of genital herpes

Counselling and health education regarding the natural history of genital herpes, sexual transmission, perinatal transmission, risk for HIV transmission or acquisition and general hygiene to keep any sores clean and dry form part of the clinical management of patients with herpes infection. Antiviral medication offers clinical benefits in partially controlling the signs and symptoms of herpes episodes, especially to treat primary genital herpes. Antiviral treatment can be given either as episodic when recurrent ulcerative episodes occur or as suppressive therapy on a daily basis. Daily suppressive therapy reduces the frequency of genital herpes recurrences by more than 75 % among patients who have frequent recurrences (six or more recurrences per year).

## Treatment options for genital herpes

| |
|---|
| **Recommended regimens for first clinical episode** |
| Acyclovir, 200 mg orally, 5 times daily for 7 days, **OR** |
| Acyclovir, 400 mg orally, 3 times daily for 7 days, **OR** |
| Famciclovir, 250 mg, 3 times daily for 7 days, **OR** |
| Alaciclovir, 1 g, twice daily for 7 days |
| **Recommended regimen for recurrent infection** |
| Acyclovir, 200 mg orally, 5 times daily for 5 days, **OR** |
| Acyclovir, 400 mg, 3 times daily for 5 days, **OR** |
| Acyclovir, 800 mg orally, twice daily for 5 days, **OR** |
| Famciclovir, 125 mg orally, twice daily for 5 days, **OR** |
| Valaciclovir, 500 mg orally, twice daily for 3 days, **OR** |
| Valaciclovir, 1000 mg orally, once daily for 5 days |
| **Note:** As indicated above, for best results episodic treatment of recurrent genital herpes should be initiated within one day of the onset of the lesion or when prodromal symptoms are experienced. Therefore, consideration should be given to providing the patient with a supply of antiviral medicines or a prescription for the medication with instructions to commence treatment immediately the symptoms begin. |
| **Recommended regimens for suppressive therapy** |
| Acyclovir, 400 mg orally, twice daily, continuously, **OR** |
| Famciclovir, 250 mg orally, twice daily, **OR** |
| Valaciclovir, 500 mg orally, once daily, **OR** |
| Valaciclovir, 1000 mg orally, once daily |
| **Note:** Some experts recommend discontinuing acyclovir after one year of continuous use so that the recurrence rate can be reassessed. The lowest continuous dose that will suppress recurrences in an individual can only be determined empirically. |
| **Recommended regimen for severe disease** |
| Acyclovir, 5–10 mg/kg IV, every 8 hours for 5–7 days or until clinical resolution is attained |
| **Recommended regimen in severe herpes simplex lesions with co-infection with HIV** |
| Acyclovir, 400–800 mg orally, 2–3 times daily until clinical resolution is attained. |
| **Recommended regimen for neonates** |
| Acyclovir, 20 mg/kg intravenously, 3 times a day for 14–21 days; the latter in the case of disseminated herpes or central nervous system involvement. |

## 15.5 Chancroid

Chancroid characteristically presents with one or more painful genital ulcers with or without inguinal lymphadenopathy. The causative organism is a Gram-negative facultative anaerobic bacillus, *Haemophilus ducreyi* (*H.ducreyi*). The effective treatments include macrolides, quinolones and ceftriaxone. Single-dose treatments are preferred to enhance compliance.

### Management of lesions

The lesion should be kept clean. Fluctuant lymph nodes should be aspirated as required through the surrounding healthy skin. Incision and drainage or excision of nodes may delay healing. Response to treatment can usually be reported within 3 days of commencing treatment with a reduction in pain and diminution of purulence of the ulcer exudates. Re-epithelialization of the ulcer base usually takes less than 10 days. Patients not showing such response within seven days should be regarded as treatment failures and alternative medication should be commenced.

### Follow-up

All patients should be followed up until there is clear evidence of improvement or cure. In patients infected with HIV, treatment may appear to be less effective, but this may be a result of co-infection with genital herpes or syphilis.

### Treatment options for chancroid

| Recommended regimens | Alternative regimen |
|---|---|
| Ciprofloxacin, 500 mg orally, twice daily for 3 days, **OR**<br><br>Erythromycin base, 500 mg orally, 4 times daily for 7 days, **OR** Azithromycin, 1 g orally, as a single dose | Ceftriaxone, 250 mg by intramuscular injection, as a single dose |

## 15.6 Granuloma inguinale (Donovonosis)

Donovanosis is caused by the intracellular gram-negative bacterium *Calymmatobacterium granulomatis*. The disease presents clinically as painless, progressive, ulcerative lesions without regional lymphadenopathy. The lesions are highly vascular and can easily bleed on contact. Treatment should be continued until all lesions have completely epithelialized.

### Treatment options for Donovanosis

| Recommended regimens | Alternative regimens |
|---|---|
| Azithromycin, 1 g orally on first day, then 500 mg orally, once a day **OR**<br><br>Doxycycline, 100 mg orally, twice daily | Erythromycin, 500 mg orally, 4 times daily **OR**<br><br>Tetracycline, 500 mg orally, 4 times daily **OR**<br><br>Trimethoprim 80 mg/ sulfamethoxazole 400 mg, 2 tablets orally, twice daily for a minimum of 14 days |
| **Note:** The addition of a parenteral aminoglycoside such as gentamicin should be carefully considered for treating HIV-infected patients. | |

### Follow-up

Patients should be followed up clinically until signs and symptoms have resolved.

## 15.7 Veneral (genital) warts

The human papillomavirus (HPV) is the causative agent for this common sexually transmitted condition. The removal of the lesion does not mean that the infection has been cured. No treatment is completely satisfactory. Podophyllin lotion (or podophyllotoxin) or trichloroacetic acid (TCA) is used to treat external genital and perianal warts. Cryotherapy with liquid nitrogen, solid carbon dioxide or cryoprobe is preferred by many physicians when available. Cryotherapy is non-toxic, does not require anaesthesia and, if carried out properly, does not result in scarring.

Sexual partner(s) should be examined for evidence of warts. Patients with anogenital warts should be made aware that they are contagious to sexual partners. The use of condoms is recommended to help reduce transmission. HPV type 16 and 18 may give rise to invasive cancer of the cervix, as well as other anogenital cancers such as cancer of the vulva and vagina in women and penile cancers in men.

### Prevention interventions for HPV infection

It is recommended practice to examine the cervix in all female STI patients, and to perform regular cervical smears in this population for Papanicolaou examination. Vaccines against HPV offering protection against HPV types 16 and 18, the types which cause 70% of cervical cancers. The current HPV vaccines can be administered to girls aged 11 to 12 years. The benefits of vaccination are greatest if administered before the onset of sexual activity. Current vaccines are administered in three doses over

a 6-month period, with the second and third doses given 1–2 months after the first dose and the last dose is given at 6 months after the first dose. Women who have been vaccinated against HPV infection still need to have routine cervical cancer screening because the vaccines do not cover all the oncogenic types of HPV.

### Recommended treatment regimens for venereal warts

#### A. Chemical

| Patient-applied | Provider-administered |
|---|---|
| Podofilox 0.5 % solution or gel, twice daily for 3 days, followed by 4 days of no treatment, the cycle repeated up to 4 times (total volume of podofilox should not exceed 0.5 ml per day) | Podophyllin 10–25 % in compound tincture of benzoin, applied carefully to the warts, avoiding normal tissue. External genital and perianal warts should be washed thoroughly 1–4 hours after the application of podophyllin. |
| **Note:** The safety of podofilox during pregnancy has not been established | |

#### B. Physical

| |
|---|
| **Vaginal or cervical cream**<br><br>Cryotherapy with liquid nitrogen, solid carbon dioxide, or a cryoprobe. Repeat applications every 1–2 weeks, **or** Electrosurgery, **or** Surgical removal |
| **Meatal warts**<br><br>Cryotherapy with liquid nitrogen **or** Podophyllin 10–25 % (for external meatal warts) |
| **Urethral warts**<br><br>Urethroscopy is necessary to diagnose intra-urethral warts, but they should be suspected in men with recurrent meatal warts. Some experts prefer electrosurgical removal |
| **Anal warts**<br><br>Cryotherapy with liquid nitrogen, **or** Trichloroacetic Acid 80–90 %, applied carefully to the warts and allowed to dry, repeated weekly, **or** Surgical removal |

## 15.8 Trichomonas vaginalis

The flagellated protozoon, *T. vaginalis*, is a common infection among sexually active adults. Although the majority of women infected with *T. vaginalis* tend to be asymptomatic, some have symptoms characterized by a diffuse, yellow-green, offensive vaginal discharge and vulval itching. Similarly most men infected with *T. vaginalis* are asymptomatic, but some present with urethral discharge.

### Management of sexual partners

Sexual partner(s) should be notified and treated, and patients should be advised against sexual intercourse until both the index patient and the partner(s) are treated.

### Trichomoniasis in pregnancy

*T. vaginalis* infection has been shown to be associated with adverse pregnancy outcomes, particularly premature rupture of membranes, pre-term delivery and low birth weight. (Smith, et al., 2002)

### Follow-up

Patients should be asked to return after seven days if symptoms persist. Reinfection should be carefully excluded. Patients not cured following initial treatment often respond favorably to repeat treatment with the seven-day regimen.

Patients not cured with the repeated course of metronidazole may be treated with a regimen consisting of metronidazole 2 g orally, daily, together with 500 mg applied intravaginally each night for 3–7 days.

### Recommended treatment regimens for trichomonas infection

| Recommended regimen for vaginal infections | Alternative regimens |
|---|---|
| **For vaginal discharge in women** | |
| Metronidazole, 2 g orally, in a single dose, **OR**<br>Tinidazole, 2 g orally, in a single dose | Metronidazole, 400 mg or 500 mg orally, twice daily for 7 days, **OR**<br>Tinidazole, 500 mg orally, twice daily for 5 days |
| **Note**<br>The reported cure rate in women ranges from 82 % to 88 % but may be increased to 95 % if sexual partners are treated simultaneously | **Note**<br>Other 5-nitroimidazoles are also effective, both in single and in multiple dose regimens.<br>Patients taking metronidazole or other imidazoles should be cautioned not to consume alcohol while they are taking the drug, and up to 24 hours after taking the last dose.<br>Asymptomatic women with trichomoniasis should be treated with the same regimen as symptomatic women. |
| **For urethral infections in men** | |
| Metronidazole, 400 mg or 500 mg orally, twice daily for 7 days **OR**<br>Tinidazole, 500 mg orally, twice daily for 5 days | |
| **Recommended regimen for neonatal infections** | |
| Metronidazole, 5 mg/kg orally, 3 times daily for 5 days | **Note**: Infants with symptomatic trichomoniasis or with urogenital colonization persisting past the fourth month of life should be treated with metronidazole |

## 15.9 Bacterial vaginosis

Bacterial vaginosis (BV) is a clinical syndrome resulting from a shift in the vaginal ecosystem in which the normal hydrogen peroxide ($H_2O_2$)-producing *Lactobacillus* species are replaced by high concentrations of anaerobic bacteria, such as *Gardnerella vaginalis*, *Mycoplasma hominis*, *Mobilincus* species and *Peptostreptococcus* species. The cause of the microbial alteration is not fully understood, but some triggers include multiple sexual partners, frequent sexual intercourse and douching. However, women who have never been sexually active can also be affected. Treatment of sexual partners has not been demonstrated to be of benefit.

### BV in pregnancy

There is evidence that BV is associated with an increased incidence of adverse pregnancy outcomes (e.g. premature rupture of membranes, preterm delivery and low birth weight). (Govender, et al., 1996) Symptomatic pregnant women should be treated, and those with a history of previous pre-term delivery should be screened to detect asymptomatic infections. Pregnant women with recurrence of symptoms should be re-treated. Screening of asymptomatic pregnant women without a prior history of preterm delivery is not recommended.

### Recommended treatment regimens for BV

| Recommended regimen | Alternative regimens |
|---|---|
| Metronidazole, 400 mg or 500 mg orally, twice daily for 7 days | Metronidazole 0.75 % gel, 5 g intravaginally, twice daily for 5 days, **OR**<br>Clindamycin 2 % vaginal cream, 5 g intravaginally, at bedtime for 7 days, **OR**<br>Clindamycin, 300 mg orally, twice daily for 7 days |
| **Note:** Patients taking metronidazole should be cautioned not to consume alcohol while they are taking the drug and up to 24 hours after taking the last dose. | |
| **Recommended regimens for pregnant women** | |
| Metronidazole, 200 or 250 mg orally, 3 times daily for 7 days, **OR**<br>Metronidazole 2 g orally, as a single dose, **OR**<br>Metronidazole 400 mg or 500 mg orally, twice daily for 7 days, **OR**<br>Clindamycin 300 mg orally, twice daily for 7 days. | |

## 15.10 Candidiasis

### Vulvo-vaginal candidiasis

In the majority of cases, vulvo-vaginal candidiasis is caused by *Candida albicans* (*C. albicans*). Up to 20 % of women with the infection may be asymptomatic. If symptoms occur, they usually consist of itching of the vulva, soreness and a non-offensive vaginal discharge, which may be curdy. Clinical examination may reveal vulval erythema (redness) or excoriations from scratching and oedema of the vulva.

Vulvo-vaginal candidiasis is usually not acquired through sexual intercourse. Although treatment of sexual partners is not recommended, however, it should be considered for women who have recurrent infection. Therapy generally involves topical application of any of a wide variety of imidazoles (e.g. miconazole, clotrimazole, econazole, butoconazole, terconazole) or nystatin.

Topical azoles should be used to treat pregnant women. Of those treatments that have been investigated for use during pregnancy, the most effective are miconazole, clotrimazole, butoconazole and terconazole.

### Vulvo-vaginal candidiasis in HIV infection

Candidiasis at several sites, including the vulva and vagina, is an important correlate of HIV infection. It is often quite severe and frequently relapses. Prolonged treatment is generally required and chronic suppressive therapy is frequently employed.

### Recurrances

It is recommended that predisposing factors such as antibiotic use, the use of antiseptic/antibiotic vaginal preparations or vaginal douching be reduced or eliminated. Other underlying factors for recurrent vulvo-vaginal candidiasis include uncontrolled diabetes mellitus, Immunosuppression and corticosteroid use.

### Balanoposthitis

Balanoposthitis refers to an inflammation involving the glands penis and the foreskin. When caused by *C. albicans* it is characteristically found in men with underlying immunosuppressive disease or uncontrolled diabetes mellitus.

### Recommended treatment regimens for Candida infection

| Recommended regimens | Alternative regimen |
|---|---|
| **For vulvo-vaginal candidiasis** | |
| Miconazole or clotrimazole vaginal pessaries, 200 mg intravaginally, daily for 3 days, **OR**<br><br>Clotrimazole vaginal pessaries, 500 mg intravaginally, as a single dose, **OR**<br><br>Clotrimazole 10 % vaginal cream, 5 grams, single dose, **OR**<br><br>Fluconazole, 150 mg orally, as a single dose | Nystatin, 100 000 IU intravaginally, daily for 14 days |
| **For balanoposthitis** | |
| Clotrimazole 1 % cream, twice daily for 7 days, **OR**<br><br>Miconazole 2 % cream, twice daily for 7 days | Nystatin cream, topically twice daily for 7 days |

## 15.11 Scabies

The causative mite, *Sarcoptes scabiei*, is transmitted by protracted direct body contact. In adults this is often through sexual contact. However, there are evidently situations in which scabies is transmitted through close body contact not related to sexual activities.

The mites can burrow into the skin of a contact person within one hour. Proteases (enzymes) in mite faecal matter generate a hypersensitivity reaction which leads to the characteristic symptom of pruritus (itch), usually 2–6 weeks after infestation.

### Special considerations

Lindane (gamma benzene hexachloride or hexachlorocyclohexane) in a 1 % lotion or cream has been used extensively in resource-constrained countries because of its low cost. However, it should not be used in children under the age of 10 years, pregnant or lactating women or immediately after a bath or in patients with extensive dermatitis because of its toxicity.

Oral ivermectin may be of particular advantage in refractory cases and in immunocompromised patients with crusted scabies who have a very high parasite load. The drug has been effectively used for scabies in doses of 200 µg/kg orally as a single dose, repeated in one to two weeks.

## Crusted scabies

This hyperkeratotic scabies, also known as Norwegian scabies, is characterised by thick scales containing large numbers of mites. The disease is frequently seen in immunodeficient or malnourished persons, persons on topical fluorinated steroids or on immunosuppressive therapy.

## Recommended treatment regimens for scabies

<table>
<tr><th>Recommended regimens</th><th>Alternative regimen</th></tr>
<tr><td colspan="2">For adults, adolescents and older children</td></tr>
<tr><td rowspan="2">Permethrin 5 % cream, applied to the whole body from neck down, and wash off after 8–12 hours, OR<br><br>Benzyl benzoate 25 % lotion, applied to the entire body from the neck down, Repeat the following day (without bathing in between). Wash off 24 hours after this last application,<br><br>OR<br><br>Sulphur 6 % in petrolatum, applied to the entire body from the neck down nightly for 3 nights; patients may bathe before reapplying the product and should bathe 24 hours after the final application,<br><br>OR<br><br>Ivermectin 200 µg/kg orally, single dose. Repeat 1 dose in 1–2 weeks</td><td>lindane 1 % lotion or cream, applied thinly to all areas of the body from the neck down and washed off thoroughly after 8 hours.</td></tr>
<tr><td>Note: Lindane is not recommended for pregnant or lactating women.<br><br>Resistance to lindane has been reported in some areas. Lindane is toxic to the central nervous system and should be used only if other treatments are not available.</td></tr>
<tr><td colspan="2">For infants, children under 10 years of age, pregnant or lactating women</td></tr>
<tr><td colspan="2">Crotamiton 10 %, as above, or Sulphur 6 %, as above, or Permethrin 5 % cream, applied in the same way as the sulphur regimen described above</td></tr>
<tr><td colspan="2">For Crusted scabies</td></tr>
<tr><td>Permethrin 5 % cream, full body application daily for 1 to 2 weeks, or Benzyl benzoate 25 % lotion, full body application daily for 1 to 2 weeks,<br><br>PLUS<br><br>Ivermectin 200 µg/kg orally, with duration determined on severity of infection, as three doses on days 1, 2 and 8 or five doses on days 1, 2, 8, 9 and 15 or seven doses on days 1, 2, 8, 9, 15, 22 and 29.</td><td>Note: Lindane should be avoided as frequent topical application and the denuded skin will increase percutaneous absorption and cause neurotoxicity.</td></tr>
</table>

## Contacts

Sexual contacts and close household contacts should be treated as above.

## Phthiriasis (pediculosis pubis)

The louse, *Pthirus pubis*, is the cause of pediculosis pubis (pubic lice). The infestation is usually transmitted by sexual contact. Patients usually seek medical care because of pruritus. The *Pthirus pubis* spreads predominantly through intimate sexual contact.

## Recommended treatment regimens for Pedeculosis Pubis

| Recommended treatment regimens | Alternative treatment regimens |
|---|---|
| Permethrin 1 % cream rinse applied to affected areas and washed off after 10 minutes,<br><br>**OR**<br><br>Pyrethrins plus piperonyl butoxide, applied to the infested and adjacent hairy areas and washed off after 10 minutes | Malathion 0.5 % lotion applied for 8–12 hours, then washed off, **or** Ivermectin 250 µg/kg orally, and repeat dose in 2 weeks, **OR**<br><br>lindane 1 % shampoo, applied for 4 minutes and then thoroughly washed off,<br><br>**OR**<br><br>lindane 1 % lotion or cream, rubbed gently but thoroughly into the infested area and adjacent hairy areas and washed off after 8 hours |
| **Note:** Lindane is not recommended for in children below 2 years of age, pregnant or lactating women and patients with extensive dermatologic conditions**.** The pubic louse survives for less than a day if not in contact with the host, therefore it is not necessary to fumigate or wash furniture and other potential fomites. After treatment, any clothes and bed linen used during the preceding 24 hours should be either washed, dry cleaned or not used for 72 hours. | |

## Special considerations

Pediculosis of the eyelashes should be treated by the application of an occlusive ophthalmic ointment to the eyelid margins daily for 10 days to smother lice and nits. The ointment should not be applied to the eyes.

(Footnotes)

1 Benzathine benzylpenicillin synonyms: benzathine penicillin G; benzylpenicillin benzathine; benzathine penicillin.

2 Procaine benzylpenicillin **synonyms**: procaine penicillin G.

3 Aqueous benzylpenicillin synonyms: Benzylpenicillin potasium; Benzylpenicillin sodium; Crystalline penicillin, Penicillin G potassium; Penicillin G sodium.

# Chapter 16: The Public Health approach to STI case management; prevention and control

The Public health approach to STI control involves more than just diagnosis and treatment. This chapter highlights the broader public health interventions required to provide for sustained STI control within a population.

## 16.1 Essentials for a Public Health approach

The WHO (2011) recommends that STI control and prevention be addressed using a broader public health approach. These WHO (2011) approaches ideally should include:

- promotion of safer sex behavior;
- condom programming – encompassing a full range of activities from condom promotion to the planning and management of supplies and distribution;
- promotion of health care-seeking behavior;
- integration of STI prevention and care into primary health care, reproductive health care facilities, private clinics and others;
- specific services for key populations at risk – such as female and male sex workers, men who have sex with men, adolescents and other locally defined population groups;
- comprehensive case management of STIs;
- prevention and care of congenital syphilis and neonatal conjunctivitis; and
- early detection of symptomatic and asymptomatic infections.

## 16.2 Essential components of STI control

There are four major components that should accompany STI control these are summarized here:

### 1. Information and education

Information, education and behaviour change strategies are central to preventing primary infections. Failing primary prevention strategies, at an individual level (through counseling) the focus should identify individual high risk behavior and strategies identified to lower the risk of onward transmission of infections and importantly prevent re-infections.

The prevention of STIs is based primarily on changing the sexual behaviours that put people at risk and on promoting the use of condoms, thus, breaking the chain of transmission of infections.

### Client education

All clients and their contacts should be informed, among other things, about the nature of the infection and the importance of taking the full course of medication. A consultation for an STI is a unique opportunity to provide information and education on the prevention of STIs including HIV infection to people who are at risk for these infections.

Health-care providers who treat patients with STIs should make resources available for the promotion of safer sexual behaviour. Behavioural assessment is an essential part of the STI history and patients should be educated in methods of lowering their risk of acquiring STIs and HIV, including abstinence, careful selection of partners and use of condoms.

Condoms should also be available and promoted in any health care facility providing services for the management of STIs.

### Counselling

A consultation for an STI provides an opportunity for the health worker to discuss and explore with the patient, on a one-to-one basis, his or her risk factors for STIs, including HIV infection, and other issues related to prevention and treatment. Frequently this consists of the provision of information about STIs and their prevention, condom use and partner notification. This is education for prevention and is an essential part of an STI consultation.

Issues that should be addressed in a counselling session include:

- understanding the nature of the infection and its natural history with or without treatment
- informing the partner(s) or spouse about the STI diagnosis (options: either the patient or the health care provider informs the partner(s) or spouse)
- assessing the patient's risk for HIV and deciding whether or not to undergo testing for HIV
- learning about, and coming to terms with, worrisome complications of STIs, such as infertility and congenital syphilis

- dealing with an incurable STIs, such as herpes genitalis, which may be transmitted to the partner(s) or spouse
- preventing future infections, including strategies to discuss and introduce condom use with partner(s) or spouse
- confidentiality, disclosure and the risk of violence or stigmatizing reactions from spouse, partner(s), family or friends
- enabling patients to take control of their own life and their responsibilities for disease prevention.

## 2. Detection of infection

Once and infection has occurred diagnosis is essential to preventing ongoing transmission, preventing the development of disease sequelae, allows for secondary prevention strategies, contact tracing and other essential infection control measures. There are two main approaches that OSSHHM recognizes in these recommendations that facilitate the detection of infections which are discussed in chapters 14 and 15 above notably the syndromic approach and the aetiological approach. These approaches facilitate the diagnosis (detection) of STIs and further facilitates the application of the 'comprehensive case management' approach, which should include the provision of antimicrobial treatment.

### Anitmicrobial treatment

Regardless of the means used for diagnosis - syndromic management flowcharts or laboratory-based tests - the availability and use of ***effective*** antimicrobials is an absolute requirement. The recommended medicines must be available at the first point of contact with a patient with an STI. Effective treatment must also be available and used in the private sector.

## 3. Effective management

Once a diagnosis is made, regardless of the approach, be it the syndromic or the aetiological approach management is key. It prevents the development of disease sequelae, halts ongoing transmission and through contact tracing prevents reinfection. of infected individuals seeking care; and

## 4. Notification and management of sexual partners for STIs

The sexual partners of STI patients are likely to be infected and should be offered empirical treatment. Further transmission of STIs and reinfection can be prevented by referral of sexual partners for diagnosis and treatment. Female partners of male STI patients may well be asymptomatic; thus, partner notification and management offers an opportunity to identify and treat people who otherwise would not receive treatment for STIs.

Partner notification should be conducted in such a way that all information remains confidential. The process should be voluntary and non-coercive. The aim is to ensure that the sexual partners of STI patients, including those without symptoms, are referred for evaluation and appropriate treatment. Notification can be by patient referral or by provider referral. In ***patient referral,*** an infected patient is encouraged to notify partner(s) of their possible infection without the direct involvement of health care providers while in ***provider referral,*** health care providers or other health care workers notify a patient's partner(s).

Management of sexual partners is based on knowledge of the index patient's diagnosis (syndromic or laboratory-based). The following three strategies can be adopted for the treatment of partners:

i. offer immediate epidemiological treatment (treatment based solely on the diagnosis of the index patient) without any laboratory investigation

ii. offer immediate epidemiological treatment, but obtain specimens for subsequent laboratory confirmation

iii. delay treatment until the results of definitive laboratory tests are available.

The strategy selected will depend on:

- the risk of infection
- the seriousness of the disease
- the availability of effective diagnostic tests
- the likelihood of a person returning for follow-up
- the available infrastructure for follow-up of patients
- the availability of effective treatment
- the likelihood of spread if epidemiological treatment is not given.

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# **Chapter 17:** Children[5], Adolescent and Sexually Transmitted Infections

In all Pacific countries sexual assault of children and adolescents exist. A strategic approach is required which should involve policy makers, essential professionals and a variety of social and health services who are trained at specifically addressing the needs of children and adolescents who have been subjected to sexual assault.

OSSHHM recognizes that there are serious psychosocial issues that need to be addressed however these recommendations will not do sufficient justice to cover all the essential aspects of this sensitive area. As this part of the recommendations is focused on STIs, this chapter will therefore look to provide readers with a standardized and methodical approach to making STI diagnosis with young people, so as to ensure that (as best as possible) young people are adequately provided with comprehensive STI case management. OSSHHM recommends that the health worker using these recommendations refer to national norms and standards when approaching such cases.

This chapter is a summarized version of the WHO (2011) guidelines focusing on adolescents and children.

## **17.1** Management of sexual abuse

The identification of a sexually transmissible agent in a child beyond the neonatal period, in the vast majority of cases, is suggestive of sexual abuse. Postnatal acquired gonorrhoea, syphilis or nontransfusion and nonperinatally acquired HIV are usually suggestive of sexual abuse.

However, exceptions do exist. For example, rectal or genital infection with *C. trachomatis* in young children may be caused by perinatally acquired infection, which may persist for up to three years. In addition, genital mycoplasma has been identified in both abused and non-abused children and genital warts, although suggestive of assault, are not specific for abuse without other corroborative evidence.

Psychological and social support services should be included for complete management of all sexual abuse cases. Health workers are reminded to keep excellent documentation of your interaction with clients as they may be useful for court proceedings.

## **17.2** Evaluation of STIs in children and adolescents

Examination of children and adolescents for sexual assault or abuse should be arranged so as to minimize further trauma. The decision to evaluate the individual for STIs must be taken on a case-by-case basis.

Health care workers dealing with children and adolescents must show respect and maintain confidentiality. They should be trained to elicit a good medical and sexual history and know how to overcome the patient's fear of pelvic examination.

Special care must be taken in collecting the required specimens in order to avoid undue psychological and physical trauma to the patient.

The scheduling of examinations should be based on the history of assault or abuse. If initial exposure is recent, a follow-up visit, approximately one week after the last sexual exposure will be needed to repeat the physical examination and to collect additional specimens, in order to allow sufficient time for infections to incubate. Follow-up visit at approximately 12 weeks after the last sexual exposure is also necessary to collect sera.

### Initial examination

An initial examination and any follow-up examination should include:

Screening for *N. gonorrhoeae* and *C. trachomatis* from specimens collected from the pharynx and anus in both sexes, the vagina in girls, and the urethra in boys. Cervical specimens should not be collected from prepubertal girls. In boys, a meatal specimen of urethral discharge is an adequate substitute for an intraurethral swab specimen when a discharge is present. Only standard culture systems for the isolation of *N. gonorrhoeae* should be used.

Wet-mount microscopic examination of a vaginal swab specimen for *T. vaginalis* infection.

Collection of a serum sample testing for *T. pallidum*, HIV and hepatitis B. The choice of agents for serological tests should be made on a case-by-case basis.

[5]WHO defines children as persons between the ages of 0 and 9 years.

### Examination at 12 weeks following assault

Follow up examination 12 weeks following the last sexual exposure is recommended. Repeat serological tests for the following agents should be considered: *T. pallidum*, HIV and hepatitis B virus.

## 17.3 Presumptive treatment for children with STIs

Presumptive treatment for children who have been sexually assaulted or abused is not widely recommended. However, some children or their parents/guardians may be very concerned about the possibility of contracting an STI, even if the risk is perceived to be low by the health-care providers.

**Table 17.1:** Considering presumptive treatment options for children and adolescents

| **STI** | **Children**<br>All single-dose antibiotics are highly effective. Choose one from each box (= three or four drugs) | **Adolescents** |
|---|---|---|
| Syphilis | Benzathine penicillin 50,000 units/kg of body weight by single intramuscular injection,<br>**OR**<br>Erythromycin 12.5 mg/kg of body weight orally four times a day for 14 days | >45 kg, use adult protocol |
| Gonorrhoeae/ chancroid | Cefixime 8 mg/kg of body weight as a single dose,<br>**OR**<br>Ceftriaxone 125 mg by intramuscular injection,<br>**OR**<br>Spectinomycin 40 mg/kg of body weight (maximum 2 g) by intramuscular injection | >45 kg, use adult protocol |
| Chlamydia/ LGV | Erythromycin 12.5 mg/kg of body weight orally four times a day for seven days | 12 years or older, use adult protocol |
| Trichomoniasis | Metronidazole 5 mg/kg of body weight orally three times a day for seven days | 12 years or older, use adult protocol |

**Table 17.2:** STI presumptive treatment options for adults

| **STI** | **Option 1**<br>All single-dose, highly effective. Choose one from each box (= three or four drugs). | **Option 2**<br>Effective substitutes – possible resistance in some areas, or require multiple dosage | If patient is pregnant, breastfeeding or under 16 years old. Choose one from each box (= three or four drugs). |
|---|---|---|---|
| Syphilis | Benzathine penicillin 2.4 million units by single intramuscular injection | Doxycycline 100 mg orally twice a day for 14 days | Benzathine penicillin 2.4 million units by single intramuscular injection |
| Gonorrhoea/ Chancroid | Cefixime 400 mg orally as a single dose,<br>**OR**<br>Ceftriaxone 125 mg by intramuscular injection | Ciprofloxacin 500 mg orally as a single dose,<br>**OR**<br>Spectinomycin 2 g by intramuscular injection | Cefixime 400 mg orally as a single dose,<br>**OR**<br>Ceftriaxone 125 mg by intramuscular injection |
| Chlamydia/ LGV | Azithromycin 1 g orally as single dose | Doxycycline 100 mg orally twice a day for seven days,<br>**OR**<br>Tetracycline 500 mg orally four times a day for seven days | Azithromycin 1 g orally as single dose,<br>**OR**<br>Erythromycin 500 mg orally four times a day for seven days |
| T. vaginalis | Metronidazole 2 g orally as a single dose | Tinidazole 2 g orally as a single dose | Metronidazole 2 g orally as a single dose,<br>**OR**<br>400–500mg three times a day for 7 days |

## 17.4 Medical and psycho-social support for survivors of sexual assault

Survivors of sexual assault should be rapidly evaluated to determine whether they need emergency medical, psychological or social intervention.

It is important to remember that the trauma of the event may make parts of the examination difficult.

Explain carefully the steps that will be taken and obtain written informed consent from the patient before proceeding with examination, treatment, notification or referral for legal reasons.

History and examination findings must be well documented.

It is the client's right to decide whether to be examined.

Treatment can be started without examination if that is the patient's choice.

For minors under the age of consent, usually parental consent is required. If at all possible, do not deny adolescents immediate access to medical services.

Where facilities or referral for a more complete examination are not available, the following minimal information should be collected:

- date and time of assault;
- date and time of examination;
- patient's statement; and
- results of clinical observations and any examinations conducted.

Such information should be collected or released to the authorities only with the survivor's consent. Be aware of legal obligations that will follow if the assault is reported and goes to legal proceedings. Ideally, a trained health care provider of the same sex should accompany the survivor during the history taking and examination.

A careful written record should be made of all findings during the medical examination.

Pictures to illustrate findings may help later in recalling details of the examination.

The medical management of the survivor includes treatment of any injuries sustained in the assault, and initial counseling. Emergency contraception and STI prophylaxis should be offered early to survivors of sexual violence. For many women, the trauma of the event may be aggravated and prolonged by fear of pregnancy or infection. Knowing that the risks can be reduced may give immense relief.

### Emergency contraception

Emergency contraceptive pills can be administered immediately, preferably within 72 hours but not after five days after unprotected intercourse.

A second option for emergency contraception (for adolescents and women only) is insertion of a copper-bearing intrauterine device (IUD) within five days of the rape. The IUD may be removed during the woman's next menstrual period or left in place for continued contraception. Even if an IUD is inserted, full

STI treatment should still be given as recommended.

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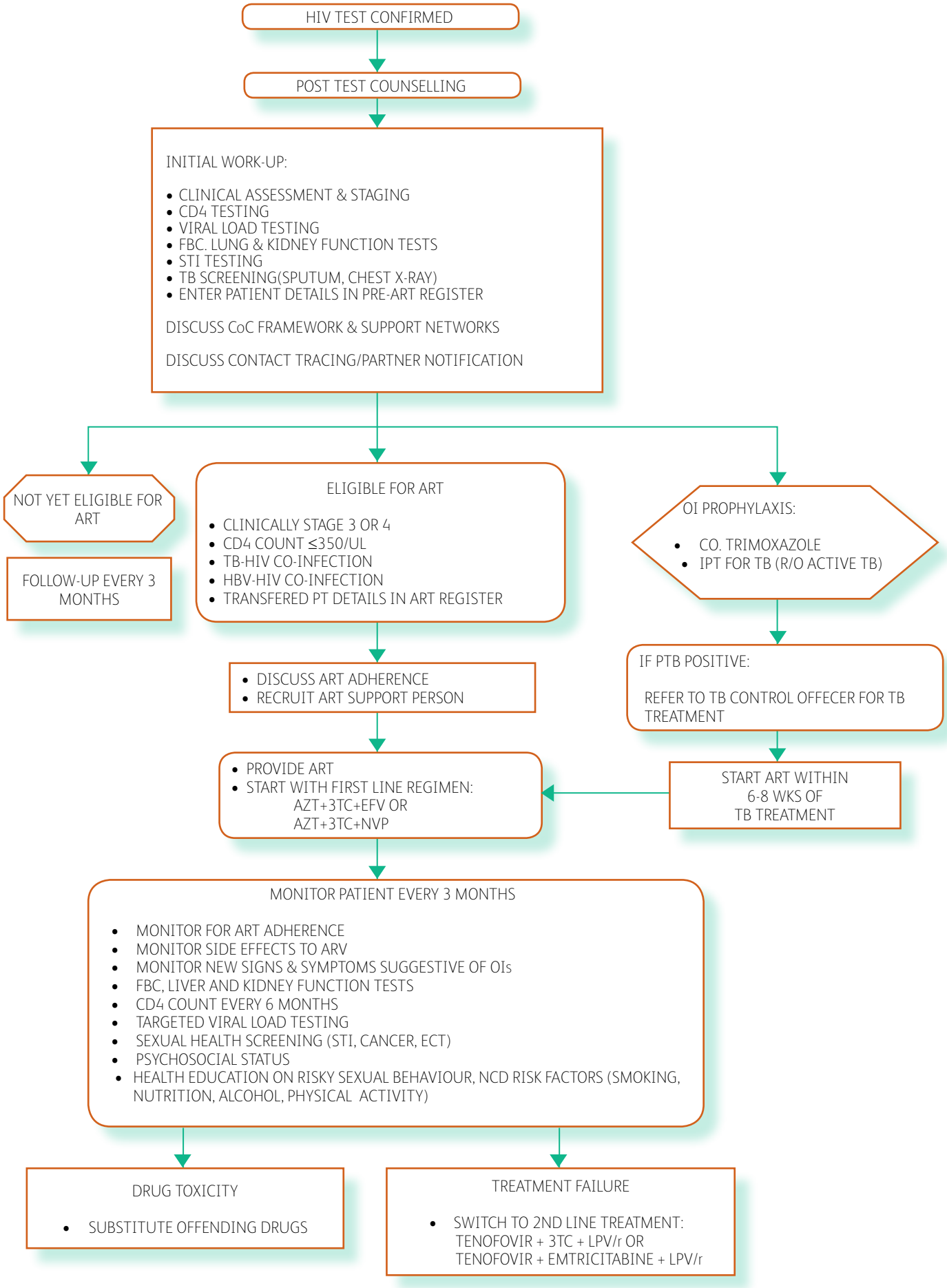
# Appendices

## Appendix A: WHO Clinical Staging of HIV/AIDS for Adults and Adolescents

| Primary HIV Infection |
|---|
| • Asymptomatic |
| • Acute retroviral syndrome |
| Clinical Stage 1 |
| • Asymptomatic |
| • Persistent generalized lymphadenopathy |
| Clinical Stage 2 |
| • Moderate unexplained weight loss (<10% of presumed or measured body weight) |
| • Recurrent respiratory infections (sinusitis, tonsillitis, otitis media, and pharyngitis) |
| • Herpes zoster |
| • Angular cheilitis |
| • Recurrent oral ulceration |
| • Papular pruritic eruptions |
| • Seborrheic dermatitis |
| • Fungal nail infections |
| Clinical Stage 3 |
| • Unexplained severe weight loss (>10% of presumed or measured body weight) |
| • Unexplained chronic diarrhea for >1 month |
| • Unexplained persistent fever for >1 month (>37.6°C, intermittent or constant) |
| • Persistent oral candidiasis (thrush) |
| • Oral hairy leukoplakia |
| • Pulmonary tuberculosis (current) |
| • Severe presumed bacterial infections (e.g., pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia) |
| • Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis |
| • Unexplained anemia (hemoglobin <8 g/dL) |
| • Neutropenia (neutrophils <500 cells/μL) |
| • Chronic thrombocytopenia (platelets <50,000 cells/μL) |

| Clinical Stage 4 |
| --- |
| • HIV wasting syndrome, as defined by the CDC (see Table 1, above) |
| • *Pneumocystis* pneumonia |
| • Recurrent severe bacterial pneumonia |
| • Chronic herpes simplex infection (orolabial, genital, or anorectal site for >1 month or visceral herpes at any site) |
| • Esophageal candidiasis (or candidiasis of trachea, bronchi, or lungs) |
| • Extra pulmonary tuberculosis |
| • Kaposi sarcoma |
| • Cytomegalovirus infection (retinitis or infection of other organs) |
| • Central nervous system toxoplasmosis |
| • HIV encephalopathy |
| • Cryptococcosis, extra pulmonary (including meningitis) |
| • Disseminated nontuberculosis mycobacteria infection |
| • Progressive multifocal leukoencephalopathy |
| • Candida of the trachea, bronchi, or lungs |
| • Chronic cryptosporidiosis (with diarrhea) |
| • Chronic isosporiasis |
| • Disseminated mycosis (e.g., histoplasmosis, coccidioidomycosis, penicilliosis) |
| • Recurrent nontyphoidal *Salmonella* bacteremia |
| • Lymphoma (cerebral or B-cell non-Hodgkin) |
| • Invasive cervical carcinoma |
| • Atypical disseminated leishmaniasis |
| • Symptomatic HIV-associated nephropathy |
| • Symptomatic HIV-associated cardiomyopathy |
| • Reactivation of American trypanosomiasis (meningoencephalitis or myocarditis |

# Appendix B: Flow chart in HIV care after seroconversion



# Appendix C: OSSHHM Core team training content guide

## OSSHHM-endorsed content for basic core HIV care team training

Training is conducted as six half-day sessions.

### Session 1: Introduction to support for HIV care under the Pacific Regional HIV Strategy

Pre-test to assess participants' knowledge in advance of training

#### Presentation covering the following topics:

- Introductory discussion on HIV epidemiology and the 'state of play' with HIV services in the country
- Introduction to the Pacific Regional HIV Strategy Implementation Plan (PRSIP) including:
  - » partners involved
  - » countries covered
  - » funding streams
- Key messages about antiretroviral therapy:
  - » It does not have to be expensive and is currently available under regional funding streams.
  - » It does not just delay death but can keep people well for the long term.
  - » HIV is a chronic manageable illness.
- Provision of antiretroviral therapy under the PRSIP:
  - » regional procurement mechanism in Suva
  - » drugs are WHO pre-approved
  - » country eligibility for funding streams
  - » pharmacist-to-pharmacist support for stock management
  - » training, technical support and mentorship for clinical teams from SPC in medium term, plus WHO and OSSHHM
- Nine criteria for effective and sustainable antiretroviral therapy (ART):

1. National decision-making bodies are committed to providing ART in the country.
2. An assigned central unit, with an identified leader, is responsible for provision of medical care to people receiving ART.
3. People living with HIV have been involved in development of care services.
4. Ongoing supply of ART has been secured and at least six months' supply is available in country.
5. A technically sound ART protocol has been developed and is available.
6. A local partnership of public health services, clinical services and community organisations exists to ensure a continuum of care and support for people taking treatment, including support for ART adherence.
7. A core multidisciplinary HIV care team has received appropriate training.
8. Diagnostic services are available to perform HIV antibody tests and essential routine tests to monitor for drug toxicity.

» An adequate patient record system exists.

#### Tea break

Group work to assess the site against the nine criteria and plan action needed to ensure they are met in the near future.

### Session 2: The biology of HIV and HIV treatment

Presentation covering the following topics:

HIV life cycle (demonstrated using an animated film):

- fusion
- reverse transcription
- integration
- transcription and polyprotein synthesis

- protease activity
- assembly
- budding
- Resistance
- application of evolutionary theory
- relationship between resistance and adherence
- clinical implications

### Tea break

Group work on the factors that bear on adherence and strategies to enhance it.

## Session 3: Introduction to the spectrum of HIV disease

Presentation covering the following topics:

- The dynamic nature of HIV infection in terms of production and destruction of HIV and CD4 lymphocytes (bucket and tap analogy)
- Likely impossibility of eradication due to long-lived cells with integrated proviral DNA
- 'AIDS' – discussion of history and current meaning

Monitoring people with HIV not yet on treatment (including 'prevention with positives')

- Physical examination
- CD4 count
- Viral load
- Common course of HIV infection
- Common HIV-related conditions, their management and prophylaxis:
  - » skin problems
  - » candidiasis
  - » oral hairy leukoplakia
  - » acute necrotising ulcerative gingivitis
  - » Kaposi's sarcoma
  - » aphthous ulcers
  - » CMV retinitis
  - » pneumocysis pneumonia
  - » tuberculosis
  - » wart virus infections
  - » herpes simplex
  - » varicella zoster
  - » tinea

### WHO clinical staging of HIV

### Tea break

Interactive case discussion:

1. A young woman presenting with recurrent vaginal thrush turns out to have HIV.
2. A 35-year-old man who is known to have HIV diagnosed overseas presents for a 'check up'.

## Session 4: Prevention of mother-to-child transmission of HIV

Presentation covering the following topics:

- Prevalence and mechanisms of mother-to-child transmission (MTCT) of HIV

Risk factors for MTCT:

- Overall
- specific to transmission during pregnancy
- specific to transmission during labour and delivery
- specific to transmission during breastfeeding

The four elements of preventing MTCT under the WHO/UNICEF guidelines:

1. primary prevention of HIV in women
2. prevention of unintended pregnancy in women with HIV
3. measures to reduce risk of transmission from HIV-positive mothers to their babies
4. treatment, care and support services for women with HIV, their babies and their families, including:

- antenatal care and HIV testing
- antiretroviral therapy
- labour and delivery
- neonatal prophylaxis
- infant feeding
- diagnosis of HIV in infants
- care of infants born to mothers with HIV

### Tea break

### Interactive case discussion

- A 20-year-old woman presents to antenatal clinic at 30 weeks' gestation by dates. She is found to have gonorrhoea and also tests positive for HIV.

## Session 5: Antiretroviral therapy

Presentation covering the following topics:

- Fusion inhibitors: mode of action (illustrated by animated film)
- Nucleoside reverse transcriptase inhibitors (NRTI):
  - » names, codes and combinations
  - » mode of action (illustrated by animated film)
  - » adverse effects
  - » final common pathway of most NRTI
  - » toxicity:
  - » structure and function of mitochondria
  - » consequences of mitochondrial failure
  - » peripheral lipoatrophy
- Non-nucleoside reverse transcriptase inhibitors (NNRTI):
  - » names and codes
  - » mode of action (illustrated by animated film)
  - » adverse effects
- Protease inhibitors:
  - » names and codes
  - » mode of action (illustrated by animated film)
  - » adverse effects
- Drug interactions
  - » When to start?
  - » Choice of starting regimen
  - » Monitoring people taking antiretroviral therapy
  - » Antiretroviral failure and second-line regimens
  - » Continuum of care and engaging other health and welfare services

### Tea break

Interactive case discussion

1. A 26-year-old man, diagnosed HIV positive two years ago, presents with weight loss and falling CD4 – preparation for starting therapy and early follow-up (including role plays).

2. A 36-year-old woman, on treatment with stavudine/didanosine/nevirapine overseas for several years, presents with mitochondrial adverse effects – diagnosis and management.

Post test to assess effectiveness of training

## Session 6: Next steps and clinical mentorship

**Interactive discussion** covers any issues that remain unclear and identifies the next steps for implementation.

This session is also utilised to provide direct mentorship of clinicians in clinic if patients are available to be seen.

# Appendix D: Severity grading of selected clinical and laboratory toxicities most commonly seen with recommended antiretroviral drugs for children

| Parameter | Mild | Moderate | Severe | Severeandpotentiallylife-threatening |
|---|---|---|---|---|
| Gastrointestinal[c] | | | | |
| Laboratory | | | | |
| ALT(SGPT) | 1.25–2.5 x ULN | 2.6–5.0 x ULN | 5.1–10.0 x ULN | >10.0 x ULN |
| AST (SGOT) | 1.25–2.5 x ULN | 2.6–5.0 x ULN | 5.1–10.0 x ULN | >10.0 x ULN |
| Bilirubin (>2 weeks of age) | 1.1–1.5 x ULN | 1.6–2.5 x ULN | 2.6–5.0 x ULN | >5.0 x ULN |
| Lipase | 1.1–1.5 x ULN | 1.6–3.0 x ULN | 3.1–5.0 x ULN | >5.0 x ULN |
| Pa creatic amylase | 1.1–1.5 x ULN | 1.6–2.0 x ULN | 2.1–5.0 x ULN | >5.0 x ULN |
| Clinical | | | | |
| Diarrhoea<br><br>≥1 year of age<br><br><br><br><br><br><br><1 year of age | Transient or intermittent episodes of unformed stools OR increase of<br><br>≤3 stools over<br><br>baseline per day<br><br><br><br>Liquid stools (more unformed than usual) but usual number of stools | Persistent episodes of unformed to watery stools OR increase of 4–6 stools over baseline per day<br><br><br>Liquid stools with increased number of stools OR mild dehydration | Grossly bloody diarrhoe OR increase of ≥7 stools per day OR intravenous fluid replacement indicated<br><br><br>Liquid stools with moderate dehydration | Life-threatening consequences (e g hypotensive shock)<br><br><br>Liquid stools resulting in severe dehydration with aggressive rehydration indicated OR hypotensive shock |

\Source: Adapted from Division of AIDS, National Institute of Allergy and Infectious Diseases, Table for grading the severity of adult and paediatric adverse events, Bethesda, Maryland, USA; December 2004

[a] Usual social and functional activities in young children include those that are appropriate to their age and culture

(e g social interactions, play activities, learning tasks)

[b] Activities that are appropriate to age and culture (e g feeding self with culturally appropriate eating implement, walking or using hands)

[c] Values are provided for children in general except where age groups are specifically noted

| Parameter | Mild | Moderate | Severe | Severeandpotentiallylife-threatening |
|---|---|---|---|---|
| Nausea | Transient (<24 hours) or intermittent nausea with no or minimal interference with oral intake | Persistent nausea resulting in decreased oral intake for<br><br>24–48 hours | Persistent nausea resulting in minimal oral intake for<br><br>>48 hours OR aggressive rehydration indicated (e g intravenous fluids) | Persistent nausea with no or minimal oral intake resulting in dehydration with aggressive rehydration indicated |
| Pancreatitis | Not applicable | Symptomatic AND hospitalization not indicated (other than emergency treatment) | Symptomatic AND hospitalization indicated | Life-threatening consequences (e g circulatory failure, haemorrhage, sepsis) |
| Vomiting | Transient or intermittent vomiting with no or minimal interference with oral intake | Frequent episodes of vomiting with no or mild dehydration | Persistent vomiting resulting in orthostatic hypotension OR aggressive rehydration indicated (e g intravenous fluids) | Life-threatening consequences (e g hypotensive shock) |
| Allergic/dermatological | | | | |

Source: Adapted from Division of AIDS, National Institute of Allergy and Infectious Diseases, Table for grading the severity of adult and paediatric adverse events, Bethesda, Maryland, USA; December 2004

[a] Usual social and functional activities in young children include those that are appropriate to their age and culture

(e g social interactions, play activities, learning tasks)

[b] Activities that are appropriate to age and culture (e g feeding self with culturally appropriate eating implement, walking or using hands)

[c] Values are provided for children in general except where age groups are specifically noted

| Parameter | Mild | Moderate | Severe | Severeandpotentiallylife-threatening |
|---|---|---|---|---|
| Acute systemic allergic reaction | Localized urticaria (weals) lasting a few hours | Localized urcaria with medical intervention indicated OR mild angio-oedema | Generalized urticaria OR angio-oedema with medical intervention indicated OR symptomatic mild bronchospasm | Acute anaphylaxis OR life-threatening bronchospasm or laryngeal oedema |
| Cutaneous reaction – rash | Localized macular rash | Diffuse macular, maculopapular, or morbilliform rash OR target lesions | Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae OR superficial ulcerations of mucous membrane limited to one site | Extensive or generalized bullous lesions OR Stevens-Johnson syndrome OR ulceration of mucous membrane involving two or more distinct mucosal sites OR toxic epidermal necrolysis (TEN) |
| Neurological | | | | |
| Alteration in personality, behaviour or mood[b] | | | | |
| Alteration causing no or minimal interference with usual social and functional activities[b] | | | | |
| Alteration causing greater than minimal interference with usual social and functional activities[b] | | | | |
| Alteration causing inability to perform usual social and functional activities [b] AND intervention indicated | | | | |
| Behaviour potentially harmful to self or others OR life-threatening consequences | | | | |

Source: Adapted from Division of AIDS, National Institute of Allergy and Infectious Diseases, Table for grading the severity of adult and paediatric adverse events, Bethesda, Maryland, USA; December 2004

[a] Usual social and functional activities in young children include those that are appropriate to their age and culture

(e g social interactions, play activities, learning tasks)

[b] Activities that are appropriate to age and culture (e g feeding self with culturally appropriate eating implement, walking or using hands)

[c] Values are provided for children in general except where age groups are specifically noted

| Parameter | Mild | Moderate | Severe | Severeandpotentiallylife-threatening |
|---|---|---|---|---|
| Altered mental status | Changes causing no or minimal interference with usual social and functional activities[b] | Mild lethargy or somnolence causing greater than minimal interference with usual social and functional activities[b] | Onset of confusion, memory impairment, lethargy, or somnolence causing inability to perform usual social and functional activities[b] | Onset of delirium, obtundation or coma |
| Neuromuscular weakness (including myopathy and neuropathy) | Asymptomatic with decreased strength on examination OR minimal muscle weakness causing no or minimal interference with usual social and functional activities[b] | Muscle weakness causing greater than minimal interference with usual social and functional activities[b] | Muscle weakness causing inability to perform usual social and functional activities[b] | Disabling muscle weakness causing inability to perform basic self-care functions OR respiratory muscle weakness impairing ventilation |
| Neurosensory alteration (including painful neuropathy) | Asymptomatic with sensory alteration on examination OR minimal paraesthesia causing no or minimal interference with usual social and functional activities | Sensory alteration or paraesthesia causing greater than minimal interference with usual social and functional activities | Sensory alteration or paraesthesia causing inability to perform usual social and functional activities | Disabling sensory alteration or paraesthesia causing inability to perform basic self-care functions[c] |

Source: Adapted from Division of AIDS, National Institute of Allergy and Infectious Diseases, Table for grading the severity of adult and paediatric adverse events, Bethesda, Maryland, USA; December 2004

[a] Usual social and functional activities in young children include those that are appropriate to their age and culture

(e g social interactions, play activities, learning tasks)

[b] Activities that are appropriate to age and culture (e g feeding self with culturally appropriate eating implement, walking or using hands)

[c] Values are provided for children in general except where age groups are specifically noted

| Parameter | Mild | Moderate | Severe | Severeandpotentiallylife-threatening |
|---|---|---|---|---|
| OtherlaboratoryparametersStandardinternationalunitsarelistedinitalics | | | | |
| Cholesterol (fasting, paediatric <18 years old) | 170 – < 200 mg/dl<br>4 40–5 15 mmol/l | 200–300 mg/dl<br>5 16–7 77 mmol/l | >300 mg/dl<br>>7 77 mmol/l | Not applicable |
| Glucose, serum, high:<br>non-fasting | 116–<161 mg/dl<br>6 44–<8 89 mmol/l | 161–< 251 mg/dl<br>8 89–<13 89 mmol/l | 251–500 mg/dl<br>13 89–27 75 mmol/l | >500 mg/dl<br>>27 75 mmol/l |
| Glucose, serum, high: fasting | 110–<126 mg/dl<br>6 11–<6 95 mmol/l | 126–< 251 mg/dl<br>6 95–<13 89 mmol/l | 251–500 mg/dl<br>13 89–27 75 mmol/l | >500 mg/dl<br>>27 75 mmol/l |
| Lactate | <2 0 x ULN without acidosis | ≥2 0 x ULN without acidosis | Increased lactate with pH<br><7 3 without<br>life-threatening consequences or related condition present | Increased lactate with pH <7 3 with life-threatening consequences (e g neurological<br>findings, coma) or related condition present |
| Triglycerides (fasting) | Not applicable | 500–<751 mg/dl<br>5 65–<8 49 mmol/l | 751–1200 mg/dl<br>8 49–13 56 mmol/l | >1200 mg/dl<br>>13 56 mmol/l |

Source: Adapted from Division of AIDS, National Institute of Allergy and Infectious Diseases, Table for grading the severity of adult and paediatric adverse events, Bethesda, Maryland, USA; December 2004

[a] Usual social and functional activities in young children include those that are appropriate to their age and culture

(e g social interactions, play activities, learning tasks)

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[c] Values are provided for children in general except where age groups are specifically noted

# Appendix E: Cotrimoxazole Desensitization Protocol

## Background

Trimethoprim-sulfamethoxazole (TMP-SMX), also known as Septra, Bactrim, and cotrimoxazole, is a key antibiotic for prophylaxis and treatment of several HIV-related illnesses. It is the most effective prophylaxis and the first-line treatment for *Pneumocystis jiroveci* pneumonia (PCP). In addition, it is effective in preventing toxoplasmosis encephalitis in severely immunocompromised patients who have evidence of previous exposure, and it is effective against certain bacterial infections. TMP-SMX is quite inexpensive, which is a rarity in the field of HIV treatment. Because of its effectiveness and availability, it is used widely throughout the world. However, adverse reactions to TMP-SMX and other sulfa drugs occur in a high proportion of HIV-infected patients (roughly 25 % ), and such reactions may limit treatment options.

When a patient with HIV experiences a side effect related to cotrimoxazole, often the drug is continued (treating-through) or reintroduced at a later date, either using increasingly larger doses (desensitization), or immediately starting at the full dose (rechallenge).

Desensitization to TMP-SMX should be considered when there are no reasonable or available alternatives and the patient has not experienced severe (Grade 4) reactions (e.g., Stevens-Johnson syndrome or toxic epidermal necrolysis) to sulfa drugs. It can be attempted two weeks after a non severe (grade 3 or less) reaction.

Several methods of desensitizing patients with previous reactions to TMP-SMX have been tried. These methods vary in starting dosage and length of dosage escalation, but success rates are around 80 % in most cases and may be higher in patients with CD4 counts of <200 cells/µL.

## S: Subjective

The patient reports a previous adverse reaction to sulfa drugs, such as erythema, pruritus, or rash. The patient has no history of anaphylaxis, Stevens-Johnson syndrome, or toxic epidermal necrolysis, i.e. Grade 4 reactions.

### Cotrimoxazole Toxicity Grading Scale for Adolescents and Adults:

| TOXICITY | CLINICAL DESCRIPTION | RECOMMENDATION |
|---|---|---|
| Grade 1 | Erythema | Continue cotrimoxazole prophylaxis with careful and repeated observation with follow-up. Provide symptomatic relief, e.g. antihistamines if available |
| Grade 2 | Diffuse macula-papular rash, dry desquamation | Continue cotrimoxazole prophylaxis with careful and repeated observation with follow-up. Provide symptomatic relief, e.g. antihistamines if available |
| Grade 3 | Vesiculation, mucosal ulceration | Cotrimoxazole should be discontinued until adverse effects have completely resolved( usually 2weeks), and then reintroduction or desensitization can be attempted. |
| Grade 4 | Exfoliative dermatitis, Steven-Johnsons syndrome, erythema multiforme, moist desquamation | Cotrimoxazole should be permanently discontinued |

## O: Objective

CD4 count <200 cells/µL, or other important indication for TMP-SMX.

## A: Assessment

Reaction to sulfa, possibly reversible with desensitization protocol.

## P: Plan

Begin 9- to 13-day desensitization protocol, starting with pediatric oral suspension, which contains 40 mg of TMP and 200 mg of SMX per 5 mL (1 teaspoon). Gradually increase the dosage according to the protocol.

If there is any concern about the severity of a previous reaction, have the patient take the initial morning dose in the clinic so that the patient may be monitored for 3-4 hours before going home. (This assumes that emergency treatment, including IV access materials, IV fluids, epinephrine, antihistamines, and steroids, are readily available.)

Many experts recommend treatment with an antihistamine medication starting 1 day before initiation of the desensitization regimen and continuing daily until the dosage escalation is completed.

## Desensitization Regimen

Use commercially available pediatric suspension (containing TMP 8 mg and SMX 40 mg per mL [40 mg/200 mg per 5 mL]), followed by double-strength tablets, as follows:

### Table 1. Sulfa Desensitization Regimen

| Days | Dosage (TMP/SMX) | Volume or Tablet |
|---|---|---|
| **1-3** | 8 mg/40 mg | 1 Ml |
| **4-6** | 16 mg/80 mg | 2 ml |
| **7-9** | 40 mg/200 mg | 5 mL (or 1/2 single-strength tablet) |
| **9-12** | 80 mg/400 mg | 1/2 double-strength tablet (or 1 single-strength tablet) |
| **13 and thereafter** | 160 mg/800 mg | 1 double-strength tablet |

**Note**: These day ranges are approximate; patients can be advanced more quickly or more slowly, depending on their reactions to the dosages.

**In the event of mild reaction**: If the patient experiences a mild reaction or itching (i.e., mild morbilliform rash without fever, systemic symptoms, or mucosal involvement), the dose can be reduced to the last tolerated step or continued at the same dosage for an additional day, while simultaneously treating the rash or reaction. Antihistamines or antipyretics may be used to treat symptoms of mild reactions. If the reaction diminishes, the patient may advance to the next dosage (consider more gradual increase of dosages); if the reaction worsens or if systemic symptoms develop, TMP-SMX should be discontinued.

**In the event of severe reaction**: The desensitization regimen should be discontinued and the patient should be treated appropriately for the reaction.

### More rapid desensitization protocols are available for patient's urgently needing treatment with TMP-SMX:

**Table 2:**

| STEP | DOSE |
|---|---|
| DAY 1 | 80 mg sulfamethoxazole + 16 mg trimethoprim (2 ml of oral suspension) |
| DAY 2 | 160 mg sulfamethoxazole + 32 mg trimethoprim (4 ml of oral suspension) |
| DAY 3 | 240 mg sulfamethoxazole + 48 mg trimethoprim (6 ml of oral suspension) |
| DAY 4 | 320 mg sulfamethoxazole + 64 mg trimethoprim (8 m of oral suspension) |
| DAY 5 | One single-strength sulfamethoxazole-trimethoprim tablet (400 mg sulfamethoxazole + 80 mg trimethoprim) |
| DAY 6 ONWARDS | Two single-strength sulfamethoxazole-trimethoprim tablets or one double strength tablet (800 mg sulfamethoxazole + 160 mg trimethoprim) |

## Patient Education

### For home desensitization regimen

- Explain the benefits of using TMP-SMX. Be sure the patient understands and is able to follow these instructions:
- The patient should measure the dose carefully and take it each morning, followed by a glass (6-8 oz) of water. (The patient should do a demonstration, if possible, using an oral syringe that will be used for the actual measuring at home.)
- TMP-SMX can cause severe illness unless close attention is paid to any problems that may occur. It is extremely important for the patient to check his/her body temperature each afternoon. If the temperature is more than 100.5°F by mouth, the patient should stop taking the drug and contact the clinic. Note: If shaking chills occur, the body temperature should be checked as soon as the shaking stops, and the patient should contact the clinic.
- If the patient develops a rash, blisters on the skin or in the mouth, or vomiting, he or she should stop taking TMP-SMX and go the clinic or emergency room immediately. The skin should be checked each evening, and any time itching occurs.
- If mild itching or a faint rash occurs, diphenhydramine (Benadryl) 25-50 mg PO can be taken Q4H as needed. If itching or rash persists, continue with the same dosage for an additional day; the patient should contact the clinic if there are questions or concerns.
- The patient should contact the clinic for alternative dosage instructions in the event of persistent itching without rash.

Other adverse events should be reported immediately.

### For all desensitized patients

- Desensitization may be effective only as long as the allergic individual is continuously exposed to the drug. After desensitization is complete, continue with the daily dosage. If the drug is stopped (even for a few days), the entire regimen may have to be repeated, as patients may have a recurrence of the adverse reaction.

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