



KEMENTERIAN KESIHATAN MALAYSIA

AIDS

series 3

**GUIDELINES FOR
THE MANAGEMENT OF
HIV INFECTION IN MALAYSIA**

Published by the
Ministry of Health Malaysia



KEMENTERIAN KESIHATAN MALAYSIA

**GUIDELINES FOR
THE MANAGEMENT OF
HIV INFECTION IN MALAYSIA**

AIDS/STDs Section
Ministry of Health Malaysia
KUALA LUMPUR

PREFACE

Before the availability of zidovudine for use in AIDS patients, the lifespan of a patient with AIDS was approximately 18-24 months from the onset of the first AIDS-defining illness. However, the management of HIV infection has evolved tremendously in the past decade with the licensing of zidovudine in 1987 for use in AIDS patients. Since then, other antiretrovirals such as ddC and ddI have been used in combination with zidovudine.

Until recently, combination therapy was only advocated in those patients who were intolerant to or developed resistance to zidovudine; however, current thinking is to use combination therapy as the first line in treating patients with AIDS.

Newer drugs like 3TC (lamivudine) and saquinavir, in combination with zidovudine, have been shown to be more effective in maintaining good quality of life in AIDS patients.

Phase 1 studies of HIV-1 protease inhibitors have demonstrated that there is an acceptable safety profile and antiviral activity.

The results of vaccine trials, currently conducted by the World Health Organization (WHO), to prevent the spread of HIV infection will only be available in the next 5-10 years.

Recent information indicates the use of zidovudine in HIV-infected pregnant mothers can prevent vertical transmission of HIV to infants.

In summary, with the availability of these drugs for use in AIDS patients, and others still under various stages of clinical trials, HIV infected individuals and AIDS patients should be given easy access to health care and proper followup, especially with the use of these toxic drugs.

PREFACE

CHAPTER 1 : Introduction & Objectives

CHAPTER 2 : Clinical Definition & Classification

CHAPTER 3 : Transmission
Sexual Transmission
Parenteral Transmission
Perinatal Transmission

CHAPTER 4 : Clinical Manifestations: (signs & symptoms)

CHAPTER 5 : Management of Asymptomatic HIV infection

CHAPTER 6 : Management of Advanced HIV disease (including antiretroviral therapy)

CHAPTER 7 : Management of Opportunistic Infections

CHAPTER 8 : Management of Occupationally-Acquired sharps injuries

Appendices & References

- *Inoculation Accidents*
- *Inoculation Accidents Surveillance Form (IAS-1)*
- *Inoculation / Sharp Accidents Record Book*

CHAPTER 1

INTRODUCTION AND OBJECTIVES

1. Introduction

Acquired Immunodeficiency Syndrome (AIDS) is caused by a retrovirus known as the Human immunodeficiency Virus (HIV). To date there are two types of HIV; HIV-1 and HIV-2. HIV-1 is known to cause AIDS, however HIV-2 may eventually lead to an immunodeficiency state; however, perhaps the development of severe immunodeficiency due to HIV-2 may require a longer latent period. It is thought that 80% of people infected with HIV-1 will progress to clinical AIDS within 10 years.

Management of HIV infection will require a prolonged period of follow-up and monitoring of these HIV-infected individuals. The chronic nature of the infection and the social stigma associated with AIDS makes management of HIV infection more than just providing medical care to these patients. Not only are we, the medical professionals, providing medical care to them, we may also have to be their confidante, for seldom will they have anyone else to confide in regarding issues related to the illness, their jobs, fears, anxieties, etc. Therefore, it is necessary to have a multidisciplinary approach to the care of HIV-infected patients. In order to develop this, we need dedicated people working in this area as care givers, and also to provide support to our other colleagues working in this area.

2. Objectives:

- 2.1. To identify early HIV infection
- 2.2. To provide continuous care to asymptomatics
- 2.3. To provide early intervention
- 2.4. To provide adequate medical care with therapy when required
- 2.5. To delay progression to full-blown AIDS

CHAPTER 2

DEFINITION OF ACQUIRED IMMUNODEFICIENCY SYNDROME

Acquired Immunodeficiency Syndrome (AIDS) is a conglomerate of signs and symptoms arising from the development of opportunistic infections and unusual tumours which arise as a result of a failing immune system. Therefore, any definition will centre around the identification of the causative agent, the effects of a failing immunity, and the quantitative determination of the specific target cells.

3. Clinical definition of AIDS requires the following:

1. A positive test for HIV antibodies by the ELISA and or Particle Agglutination test(s), and a positive supplementary test (done at a reference centre)
2. AIDS Defining Diagnosis as in modified Appendix B (attached)
3. A CD4+ T cell lymphocyte count of less than 200/uL

4. Classification of HIV Infection in Adults:

For surveillance purposes, the classification of HIV disease can be divided into:

1. Asymptomatic HIV Infection (white form*)
2. Symptomatic HIV disease(AIDs) (pink form*)

***N.B.** These coloured forms are used to facilitate reporting to the Ministry of Health.

However, for ease of managing HIV disease by clinicians, it is necessary to classify HIV disease into:

3. Clinical Classification:
 - i. Group 1- Acute Seroconversion illness

- ii. Group 2 - Asymptomatic HIV infection
- iii. Group 3 - Persistent Generalised Lymphadenopathy (PGL)
- iv. Group 4 - AIDS

N.B. Groups 1 and 2 - Asymptomatic HIV Infection (white form) Groups 3 and 4 - Symptomatic HIV disease (AIDS) (pink form).

4. For treatment strategies, a clinician should be able to classify HIV disease into:
- i. Asymptomatic HIV infection
 - ii. Advanced HIV disease
 - iii. Opportunistic Infections
 - iv. AIDS-related tumours and Neuro-Psychiatric disease

5. Notification

It is a requirement for all doctors to notify the nearest Medical Officer of Health in the following situations:

- 1. An HIV infected asymptomatic individual (white form)
- 2. First AIDS-related illness (pink form)
- 3. Subsequent change of clinical status/ subsequent AIDS-defining diagnosis
- 4. Death of an HIV-infected person

CHAPTER 3

TRANSMISSION

Human Immunodeficiency Virus can be isolated from virtually all body fluids of HIV-infected persons including blood, sweat, tears, saliva, semen, vaginal fluids and breast milk. The virus has been found in abundance in infected blood and semen. So far only blood, semen, vaginal fluids and breast milk have been implicated in transmission.

Modes of transmission:

1. Sexual
2. Parenteral
3. Perinatal

Sexual Transmission

Worldwide, sexual transmission remains the most common mode of transmission of HIV. The virus may be effectively transmitted from an infected person to his or her sexual partner (man to woman, man to man, or woman to woman). Transmission between woman to woman has also been reported.

Parenteral Transmission

This may occur in the following circumstances:

1. Transfusion of blood and blood-related products.
2. Sharing of contaminated needles and syringes.
3. Contaminated sharps/inoculation injuries.
4. Recipients of body organs/semen/other body tissues from an HIV-infected donor.

Perinatal Transmission

This is transmission from mother to child which may occur during pregnancy, at delivery or shortly after birth. The risk of transmission perinatally has been reported to be between 20% to 40%.

Breast milk has been implicated as a mode of transmission although reports still vary worldwide as to its effectiveness, In Malaysia, HIV-infected mothers are advised to refrain from breast feeding and alternative feeding supplements are advocated.

CHAPTER 4

CLINICAL MANIFESTATIONS OF HIV DISEASE

The human immunodeficiency virus, upon entry into the human body seeks out the CD4+ receptors on T-helper lymphocytes and other cells with CD4+ molecule. The virus then enters into the cell and incorporates itself into the cellular genome eventually causing cell death. With the decline in CD4+ T-lymphocytes, the body's defence mechanism will be compromised. This will allow opportunistic organisms to cause life-threatening infections. Atypical tumours may also develop. HIV infection is a chronic infection which causes the immune system to fail. The period from the onset of the infection to the development of AIDS-defining illnesses varies from 7 - 11 years. During this period the HIV-infected individual is asymptomatic; however he is infectious and can transmit the virus to others.

The HIV infection can be classified into 4 stages:

1. Acute Seroconversion Phase or Primary HIV-1 infection

This seroconversion phase occurs in approximately 60-90% of patients; however this phase may be difficult to identify because most of our patients may not remember the flu-like illness, or may attribute it to the ordinary common cold. This glandular fever type illness may be encountered 2 to 6 weeks after exposure. The symptoms and signs are indistinguishable from that of a flu-like illness. However this mononucleosis-like illness differs from the common cold in that the symptoms are more prolonged and may last 2-4 weeks. Sometimes neurological manifestations may occur during this phase.

An acute encephalitis-like illness with reversible encephalopathy (disorientation, impairment of consciousness and cognitive functions etc) has been described during seroconversion, as has acute meningitis, myelopathy and neuropathy.

Recovery is complete and the patient will feel well. Occasionally the acute seroconversion illness may be completely asymptomatic.

2. Asymptomatic HIV infection

Most HIV-infected patients in the early stages are asymptomatic. With the progressive fall of CD4+ T-lymphocyte count characteristic of the disease,

various symptoms and signs will become apparent. This phase may vary from 2 to 7 years before the appearance of constitutional symptoms which may herald the onset of AIDS.

3. Persistent Generalised Lymphadenopathy (PGL)

As the CD4+ T-lymphocytes progressively decline, symptoms may appear. The commonest symptoms and signs encountered in the early stages are:

- *Malaise*
- *Lethargy*
- *Loss of appetite*
- *Loss of weight*
- *Diarrhoea*
- *Intermittent fever*

These symptoms may be non-specific and are referred to as constitutional symptoms but efforts must be made to ensure that they are not part of the symptomatology of an underlying disease or infection.

Over time, the patient may develop progressive weight loss of more than 10% the ideal body weight, prolonged fevers of more than 3 months, persistent generalised lymphadenopathy of more than two groups of lymph nodes. The appearance of multi-dermatomal herpes zoster, oral candidiasis and oral hairy leukoplakia may herald the progression to AIDS.

Previously, this phase was known as AIDS-Related Complex (ARC).

Progression to AIDS can be predicted by doing certain laboratory tests during this phase.

Laboratory abnormalities:

- *Lymphopenia*

- *Leukopenia*
- *Thrombocytopenia*
- *Anaemia*
- *Reduced CD4+ T-lymphocyte count*
- *Decrease ratio of CD4+/CD8+*
- *Raised gamma-globulins*
- *Cutaneous Anergy*

The useful markers commonly used in predicting progression to AIDS are:

- *Absolute platelet counts*
- *Total Lymphocyte count*
- *CD4+ T-lymphocyte count (cells/uL)*
- *CD4+/CD8+ Ratio*
- *p24 antigen*
- *beta 2-microglobulins*
- *Serum Neopterin*
- *PCR-RNA-HIV*

4. Acquired Immunodeficiency Syndrome (AIDS)

Almost all HIV-infected individuals will progress to AIDS. The time from seroconversion to the development of AIDS may vary from 2 to 15 years. The rapid progressors are those individuals who harbour HIV that induces syncytium formation and cause clumping of cells, leading to death of the cells; the slow progressors are those with non-syncytium inducing variants of HIV.

Appendix A is the 1993 revised classification system for HIV infection and expanded surveillance Case Definition for AIDS among adolescents and adults. This expansion includes the addition of three clinical conditions:

- *pulmonary tuberculosis*
- *recurrent pneumonia, and*
- *invasive cervical cancer*

Together with the 23 clinical conditions in the AIDS surveillance case definition published in 1987.

This revised classification also includes the use of CD4+ T-lymphocyte counts as an added criteria in making the diagnosis of AIDS.

With declining immunity, patients can develop opportunistic infections and atypical tumours.

There are a spectrum of infections mainly of opportunistic organisms that may occur in an infected individual. As such the symptomatology and clinical findings are varied depending on the prevailing clinical situation.

It is imperative that clinicians caring for HIV-infected patients be aware of these clinical signs and symptoms as and when they arise in order that therapeutic options be maximized.

Kaposi's Sarcoma (KS)

HIV-infected patients are also prone to develop tumours and malignancies. Examples of these are Kaposi's Sarcoma, Lymphoma and Squamous cell Carcinoma.

Kaposi's sarcoma is a tumour of the blood vessel. Classical KS occurs commonly among elderly males of Mediterranean descent. These tumours are usually confined to the lower limbs. However, the appearance of KS in previously healthy young males will suggest the presence of concomitant HIV infection. In such situations, the lesions are usually numerous and fairly extensive. The lesions of Kaposi's sarcoma are not only confined to the skin, any organ in the body may be involved. Involvement of the lungs with KS may cause hemorrhagic pleural effusion.

Single lesions can be successfully excised, however extensive or disfiguring lesions may have to be treated with superficial X-ray therapy or by using cytotoxic drugs.

Opportunistic Infections

Opportunistic infections caused by bacteria, viruses, fungi and protozoa are common in immunocompromised patients. These infections usually occur with declining CD4+ T-cell counts. The most common opportunistic infection occurring in HIV-infected individuals is *Pneumocystis carinii* pneumonia (PCP). Other infections such as toxoplasmosis, candidiasis, herpes can occur.

It is important that doctors recognise the various signs and symptoms in order that various interventional therapy may be instituted. The symptoms however, may be rather non-specific initially.

(Details in Chapter 7)

CHAPTER 5

MANAGEMENT OF HIV INFECTION

Clinical management of HIV infection will depend on the stage at which the disease process has developed. This can be broadly classified into 2 clinical stages:

1. *Asymptomatic HIV infection*
2. *Advanced HIV disease, including,*
3. *AIDS-related Opportunistic Infections and Tumours.*
4. *Neuropsychiatric illness*

In the process of assessing the possibility of HIV infection, the following steps are recommended.

1. *Risk Assessment*
2. *Establish Diagnosis*
3. *Ascertain Stage*
4. *Useful laboratory tests*
5. *Initiate antiretroviral therapy*
6. *Initiate PCP prophylaxis*

1. RISK ASSESSMENT

In the initial evaluation of a patient, a full history including a detailed sexual and drug history should be obtained.

Questions asked should be:

1. *Open-ended Questions*

2. *Non-Judgemental*
3. *Not to stigmatise*

A complete physical examination has to be done to look specifically for relevant signs that might indicate the stage of the disease.

Initial laboratory tests will include:

- a. A Full Blood Count with differential count, particular attention to be given to platelet and lymphocyte counts
- b. A Mantoux Test with 1 Tuberculin unit intradermally
- c. A Chest Radiograph

2. ESTABLISH DIAGNOSIS

- 2.1 HIV antibody Testing:
ELISA and or Particle agglutination tests
Confirmed by supplementary test

These tests can be done on a:

- a. voluntary basis
 - b. anonymously or
 - c. confidential basis
- 2.2 Pre-test Counselling should be given and consent obtained from the patient. Whether the test is positive or negative, post-test counselling should follow. During the post-test counselling, discussion on partner notification should be done by the physician or counsellor*. However if the patient is from out of town and there is no way in getting the partner to be seen by the counsellor or physician, then the medical officer of Health of that state should be notified and followup and counselling will be done by the health department.

*N.B. Patient confidentiality should be maintained at all times, however, where the possibility of a spouse or regular sexual partner may be at risk of being infected, the physician/counsellor should discuss the need for the patient to inform the partner and further counselling given.

3. ASCERTAIN STAGE

To ascertain the stage of the disease process, a complete history and physical examination and the initial investigations are helpful; however certain other tests may help with staging the disease. The most commonly used surrogate marker to assess progression of the disease is by measuring the CD4+ Tlymphocyte count and percentage. Therefore, it is recommended that all HIV infected individuals should have a baseline CD4+ count done at the initial follow-up, when he is found to be HIV positive.

Infants born of HIV-infected mothers may be ELISA positive. If the infant is not HIV infected, the ELISA titres will fall within 18 months after birth. Therefore, a better indicator of HIV infection in an infant younger than 18 months will be the measurement of p24 antigen, by doing a polymerase chain reaction (PCR) test, or detection of the virus itself.

SPECTRUM OF HIV INFECTION

The spectrum of HIV infection can be classified into:

1. Group 1 HIV disease (acute seroconversion illness)

This phase is usually difficult to elicit. Therefore, most times, by the time the patient is seen initially, he might be in the asymptomatic (Group 2) or symptomatic (Group 3 and 4) disease.

Acute seroconversion illness is also known as:

- a. *seroconversion phase,*
- b. *acute retroviral syndrome,*
- c. *acute primary HIV-1 infection*

Acute seroconversion illness usually presents as acute flu-like illness, or mononucleosis-like illness which presents 2-4 weeks after the initial HIV infection. The symptoms include:

- *fever*
- *arthralgia*
- *malaise*
- *myalgia*
- *headache*
- *photophobia*
- *maculopapular rash*
- *GI disturbances and*
- *neurological manifestations*

Acute neurological disease during the seroconversion phase may manifest with symptoms of:

- *meningitis*
- *encephalitis*
- *olyneuritis*
- *myelopathy*
- *brachial neuritis*
- *Guillian Barre syndrome*

The acute seroconversion phase usually lasts 2-4 weeks; during this phase investigations may show a low platelet and lymphocyte counts, and a low CD4+ T-lymphocyte counts, with a reversed CD4+/CD8+ ratio. Then the patient goes into the asymptomatic phase which can last for 3-7 years before

symptomatic HIV disease sets in. In the asymptomatic phase the CD4+ Tlymphocyte counts will rise to almost normal levels (600-1200/uL).

2. Asymptomatic Phase (Group 2) disease

The asymptomatic phase can last for 3-7 years from the initial HIV infection. During this phase the patient feels and looks well. Their CD4+ T-cell counts can be normal. It is recommended that these individuals be counselled towards change of behaviour, maintain good health and practise behaviour that will prevent further transmission of HIV.

The patient is also referred to a physician for assessment as to the need for antiretroviral therapy (ref: appendix 12.5 surveillance book). The recommended follow-up periods is every 6 months with 6-monthly CD4+ T cell count.

3. Symptomatic Phase (Group 3 and 4) disease

Clinical management of HIV disease will depend on the stage of the disease. Therefore early detection, clinical assessment, regular followup, and continuous monitoring of the patients are very important to detect early development of symptomatic HIV disease (AIDS). The aim of early intervention is to delay progression of the disease. This will allow an HIVinfected patient to continue working and be useful to society and have a good quality of life.

When the patient is symptomatic, there are a number of preliminary investigations that are recommended:

- *Chest X-ray*
- *Full blood count and differential count, ESR*
- *Stool examination for cryptosporidia/ isospora (when diarrhoea is present)*
- *Blood cultures for MAI/Mtb, Cryptococcus, Salmonella sp.*
- *Toxoplasma, Cytomegalovirus, Herpes Antibody titres.*
- *Sputum for PCP*

Immunological markers such as CD4+ T-cell counts, CD4+/CD8+ ratio and CD4+ percentage should be done.

Viral markers such as p24 antigen, polymerase chain reaction (PCR) and occasionally p24 antibody can be done when indicated. These markers are usually done only on specific situations, such as in babies born of HIV-infected mothers; in health care workers with occupational exposure to HIV-infected body fluids, where there is a high suspicion that he may seroconvert, or for research purposes.

It is difficult to predict how soon an HIV-infected person will develop AIDS; however there are clinical predictors that can be used as a guide:

- *herpes zoster (multi-dermatomal)*
- *oral candidiasis*
- *oral hairy leukoplakia*
- *Prolonged fever, night sweats*
- *Progressive weight loss*

Laboratory predictors of progression to AIDS:

- *thrombocytopenia*
- *falling CD4+ T. cell counts*
- *high p24 antigen*

The Centers for Disease Control (CDC) in Atlanta USA has revised the clinical definition of AIDS to include the AIDS defining conditions (see appendix) to incorporate the measurements of CD4+ T. cell counts.

CHAPTER 6

MANAGEMENT OF ADVANCED HIV DISEASE

USE OF ANTIRETROVIRAL AGENTS:

Without treatment, an AIDS patient will face death sooner than when antiretrovirals are used.

Zidovudine (ZDV), or previously known as azidothymidine (AZT) a nucleoside analogue, when it is phosphorylated inside HIV-infected cell, inhibits reverse transcriptase. It was approved by FDA for use in symptomatic HIV patients in the USA in 1987. Initial trials showed that ZDV used in symptomatic patients improved survival, delays progression to AIDS, decreases frequency of opportunistic infections, and cuts down length of hospital stay. However the results of the Concorde trial which was released in 1993 showed that ZDV cannot delay progression to AIDS, however, it does improve quality of life in AIDS patients and decreases the frequency of occurrence of opportunistic infections.

Early observations in 1989 showed that some patients with advanced HIV disease became less sensitive to zidovudine. It was later noted that resistance was due to the development of resistant strains of HIV-1. These mutations in HIV-1 reverse transcriptase (RT) which become resistant to zidovudine occur at 5 locations in the gene. Zidovudine is effective against replicating virus and can inhibit replication of sensitive strains.

Although development of ZDV resistance occurs with prolonged use of the drug, zidovudine is still considered the gold standard in HIV management.

The decision to start antiretroviral therapy on an HIV-infected person should be considered with care and consideration. Discussions with the patient and perhaps a close relative may be necessary (especially in an HIV-infected child or a patient with AIDs-related dementia). This is important because the drug is toxic and requires close follow-up and monitoring, compliance and cooperation of the patient.

When to start Zidovudine therapy?

Clinical assessment by the attending physician is essential before starting therapy (Chart 1). The assessment includes

1. current weight of the patient,
2. any evidence of opportunistic infections (which should be treated first before commencing on ZDV therapy),
3. immunological status (as evidence by the level of CD4+ T-lymphocyte counts or CD4+/CD8+ ratio).

If possible CD4+ counts should be taken on 2 occasions at 2 weeks interval to give allowance for any variations in the counts. It has been recommended that if the CD4+ counts are below 200/uL, the patient should be offered zidovudine at 500-600mg per day in 2 or 3 divided doses (250mg b.i.d. or 200mg t.i.d). The patient should be informed of the adverse effects of the drug and its toxicity. If at the initial encounter with the patient, the CD4+ counts are 200 or less, then chemoprophylaxis against *Pneumocystis carinii* pneumonia (PCP) should also be given.

Close monitoring of the patient is essential; an initial 2-week follow-up to assess side effects and monitor the full blood count (CBC), with special attention to hemoglobin levels, MCV, white blood count and platelet levels. (Chart 2 & 3)

When the full blood count monitoring is stable, follow-up monthly with CBCs for 3 months, then every three months; CD4+ counts should be done every 36 months. This is necessary in order to decide on the use of chemoprophylaxis against PCP when the CD4+ counts fall to 200 or less.

Side effects of Zidovudine:

1. General symptoms (first few weeks of therapy)
 - Headache
 - Nausea
 - Diarrhoea
 - Myalgia
 - Anorexia
 - Vomiting

- Malaise
- Fatigue

2. Haematologic

- Macrocytosis
- Anaemia
- Neutropenia

3. Others

- Proximal myopathy
- Encephalomyelopathy
- Hepatotoxicity
- Nail pigmentation

Management of adverse reactions to Zidovudine

1. Anaemia

Check mean corpuscular volume (MCV), vitamin B12 and folate. If MCV is more than 108fL (normal 76-96fL), monthly intramuscular injections of cyanocobalamin 1000mcg. may help reverse the macrocytosis. Folic acid supplements may be necessary.

Blood transfusions can be given if the haemoglobin is below 8gm%. Sometimes reducing or interrupting the dosage will reverse the bone marrow suppression.

2. Neutropenia

Regular monitoring and reducing or interrupting the dosage is necessary if the neutrophil count is below 1000/ul. When the neutrophil count is between 600-800/ul, it is sufficient to decrease the zidovudine dose; if the counts are

below 500/ul then ZDV should be stopped and resumed when the neutrophil count rises.

3. Intolerable headache and nausea

This can be reduced by interrupting or decreasing the dosage of ZDV.

Use of Zidovudine in HIV-infected pregnant women

Recent data has shown that vertical transmission of HIV-1 from a pregnant infected mother to her unborn baby can be decreased by 2/3 with the use of zidovudine administered to the mother during gestation. Transmission rates can be reduced from 25% to 8% when oral zidovudine is given to the infected mother during pregnancy, intravenously during labour and oral suspension to newborns from birth to age 6 weeks.

Use of Zidovudine in HIV-infected children

Zidovudine can be used in symptomatic HIV-infected children, however, the dosage will have to be adjusted to the weight and surface area. Close monitoring will be necessary. Prevention of opportunistic infections, maintaining proper growth and development and treatment of current bacterial infections will be the mainstay in the management of HIV infection in children.

COMBINATION THERAPY

Rationale:

Zidovudine, the first antiretroviral nucleoside analogue, has been shown to improve quality of life and decrease the frequency of occurrence of opportunistic infections. However, it is toxic and it has been shown that using zidovudine alone as a single drug therapy has caused the development of resistant strains. Therefore the current strategy in the management of HIV infection is in the use of combination therapy.

1. Combination therapy may have
2. additive or synergistic effects
3. decrease toxicity
4. prevent the development of resistant strains, and

5. may have different attack points on the HIV.

Various combinations have been on different stages of the phase 1, 2 and 3 trials. The most studied clinical trials are:

1. ZDV and ddI
2. ZDV and ddC
3. ZDV and 3TC.

Clinical trials are ongoing in the use of protease inhibitors.

FOLLOW-UP MANAGEMENT OF AIDS PATIENTS

Regular out-patient follow-up of HIV-infected patients is the key in providing good medical and health services. Follow-up management requires dedicated health care professionals who will provide continuity of care and link-up with other services that the patient requires. The concept of "holistic medicine" and "total care" should be provided to people with HIV and AIDS. Supportive counselling and medical care will help detect problems earlier.

In the medical follow-up management of AIDS patients, it is useful to monitor the following:

Clinical

Weight gain
General well-being
Free from infections

Laboratory

Full Blood Count & ESR
CD4+ cells

A Karnofsky score chart (chart 4) is useful in the clinical assessment and monitoring of disability due to disease.

CHAPTER 7

MANAGEMENT OF OPPORTUNISTIC INFECTIONS:

Introduction

In immunocompromised patients are prone to various opportunistic infections. Fungal, bacterial, viral and parasitic infections are very common in patients with AIDS. In predicting the development of opportunistic infections, a useful guide is by monitoring the CD4+ T-lymphocyte counts (chart 5).

1. Pneumocystis carinii pneumonia (PCP)

Pneumocystis carinii pneumonia (PCP) is a common opportunistic infection occurring in HIV infected individuals. In 80% of cases it is the first indicator of the development of AIDS. Usually these patients will have a CD4+ T-lymphocyte counts of less than 200/uL or a CD4+/CD8+ ratio of less than 20%.

Early PCP may be asymptomatic, therefore a high index of suspicion should be developed in physicians caring for HIV-infected individuals. Symptoms of PCP may include dry cough of more than 5 days, fever and difficulty in breathing. Physical examination may show minimal signs. More advanced infection will include acute breathlessness, cyanosis and presence of respiratory rales. The chest X-ray may be normal.

Investigations:

- a) Tracheal secretions for Pneumocystis carinii
 - collected by induction of sputum production with inhaled 3% saline.
 - or - by doing a bronchial lavage,
 - or - occasionally by bronchoscopy and lung biopsy.

- b) Arterial Blood gases - this may indicate oxygen desaturation

Management of mild PCP can be done on an outpatient basis, if the patient is compliant, however in moderately severe infections it is advisable to admit the patient to the hospital for more intensive management.

If the patient is not acutely ill, oral cotrimoxazole, 4 tablets 6 hourly for 14 days is adequate.

In severe PCP infection, intravenous cotrimoxazole, 20 mg trimethoprim and 100 mg sulphamethoxazole/kg/day (diluted 1:25 in 0.9% saline or 5% dextrose) should be given for 14 days.

In patients with severe PCP infection, a short course of steroids can be used together with the cotrimoxazole. Prednisolone is used when the pA02 is less than 70 mm.Hg.

When using high doses of cotrimoxazole, the side effects may include: nausea, fever, rashes, which may lead to Steven-Johnson's syndrome, raised liver enzymes, bone marrow suppression, and hyponatremia.

Other drugs:

1. A combination of dapsone and trimethoprim
2. Clindamycin 600-900 mg six hourly with primaquine 15-30 mg six hourly can be used.
3. Atovaquone 750 mg three times a day given orally is found to be effective.

Second line therapy:

In patients who do not respond to cotrimoxazole, or who develop adverse reactions to this drug, a second line therapy can be used.

1. Intravenous or inhaled pentamidine isethionate can be used. This is given in the dosage of 4mg/kg/day in 250mls of dextrose 5% by slow infusion for 14-21 days.
2. Intravenous pentamidine although better than inhaled pentamidine is not usually used because of the danger of forming sterile abscesses when extravasation of the drug occurs. Inhaled pentamidine can only kill the Pneumocystis in the lung tissue. It has no effect on systemic pneumocystosis .

Side effects include hypoglycemia, abscess formation, hepatitis, renal failure, and bone marrow suppression.

Prophylaxis against PCP

CD4+ T-lymphocyte counts are also used to guide the initiation of PCP prophylaxis. HIV-infected persons with CD4+ cell counts below 200/uL are at increased risk for PCP. Therefore CD4+ T-lymphocyte counts of below 200/uL indicates that the patient should be given prophylaxis for PCP.

In the past, PCP prophylaxis was given to patients who had the first episode of PCP. However, current thinking is to give primary prophylaxis against PCP to HIV-infected individuals whose CD4+ is below 200/uL or CD4+/CD8+ ratio of less than 20% even if the patient is clinically well. At such level of his immune status, there is impending progression to AIDS. The Centers for Disease Control recommends that PCP prophylaxis be offered to these patients. At this point too zidovudine therapy should be offered to the patient.

For PCP prophylaxis,

trimethoprim/suphamethoxazole (cotrimoxazole)

2-tablets 3 times a week is effective to prevent the development of PCP.

Other drugs that can be used in the prophylaxis against PCP are:

1. Dapsone 100mg. daily or
2. Fansider 1 tab weekly

2. Toxoplasmosis

The most common opportunistic infection affecting the central nervous system in HIV-infected individuals is toxoplasmosis. Patients can present with headache, fever, confusion, and convulsions. Physical examination may reveal minimal signs, or the patient may have focal neurological signs. A positive toxoplasma antibody titres may not be helpful, however, a computerised tomography (CT) of the brain may show a single or multiple hypodense lesions with ring enhancement. The use of magnetic resonance

imaging (MRI) of the brain is more sensitive in detecting lesions in the brain. These findings may suggest a primary brain lymphoma or toxoplasma infection in the brain. A therapeutic trial of anti-toxoplasmosis therapy for 2 weeks may be helpful to differentiate between the 2 pathologies. After completion of the course, a repeat CT scan is necessary. If the CT scan shows a decreasing size of The lesion, it is recommended that the therapy be extended for 6 weeks. The presence of persistent hypodense areas in the brain tissue may suggest lymphoma.

The recommended therapy is:

sulphadiazine 4gm daily (or 150mg/kg/day) orally, **PLUS**

pyrimethamine 25 - 50 mg /day, (or 50mg. loading dose followed by 25 mg/day) (or consider 4 tabs stat, followed by 2 tabs daily for 6 weeks),
AND

Folinic acid 5 - 10 mg daily, orally.

The duration of therapy is usually for 3 - 6 weeks.

The side effects include bone marrow suppression. Recurrence of toxoplasmosis can occur; therefore regular followup is essential.

Alternatively,

a combination of pyrimethamine 50 - 100mg/day with clindamycin 2.4 - 4.8gm/day can be used,

OR pyrimethamine 50 - 100mg/day

PLUS clarithromycin 2gm/day

Other drugs:

Atovaquone, and Azithromycin have been used.

Prophylaxis for toxoplasmosis is not well documented. However drugs such as trimethoprim and sulphamethoxazole, dapson and pyrimethamine, or sulphadiazine and pyrimethamine combinations have been used. It is said that the regular use of trimethoprim/sulphamethoxazole prophylaxis against PCP will also protect the patient from recurrence of toxoplasmosis.

3. Fungal Infections

Fungal infections are common in patients infected with the Human Immunodeficiency Virus (HIV-1). Severe systemic fungal infections such as cryptococcosis and aspergillosis which can be life threatening, occur when the CD4+T-lymphocyte counts are very low.

The incidence of systemic mycoses has been on the increase in recent years. In a significant number of immunocompromised patients these infections have caused morbidity and mortality. Patients with organ transplants, cancer patients on chemotherapy and patients with Acquired Immunodeficiency Syndrome are more at risk for systemic fungal infections. The most common fungal infection in AIDS patients is oral/esophageal candidiasis, however, cryptococcal meningitis has been recognised more frequently now. In those patients who are severely immunocompromised, invasive aspergillosis is a recognised complication. The infections with aspergillus species in AIDS patients are seen when their CD4 + T-lymphocyte counts are below 100/uL. With prolonged survival of these patients due to better management, use of antiretroviral agents and prophylactic drugs, there will be a higher chance of them acquiring systemic fungal infections, like aspergillosis, cryptococcal meningitis and *Penicillium marneffeii* infections. Therefore, a high index of suspicion should be maintained when managing these patients.

Antifungal

Drugs:

Before the advent of AIDS, the most widely used antifungal therapy was intravenous amphotericin B and 5-flucytosine. These drugs are toxic and the patients require hospitalisation and close monitoring for side effects. In AIDS patients, this combination therapy was not entirely satisfactory, with high incidence of failure and relapses.

The introduction of triazole antifungals, itraconazole and fluconazole, in the last decade, have been shown to be effective, well tolerated and easily administered.

a. Candidiasis

Opportunistic fungal infections is common in immunocompromised patients. The most common fungal infection is candidiasis caused by *Candida albicans*. In the early stages of the progression to AIDS, the patient may complain of painful lesions in the mouth, subsequently the symptoms become worse with burning pain in the throat during swallowing. By this stage the patient is likely to have oro-pharyngeal candidiasis. Oroesophageal candidiasis is a recognised AIDS-defining illness. At this stage the CD4+ T-

lymphocyte count would be below 400/uL. Candidal infection can also affect other organs like the gut, liver, central nervous systems and the respiratory system.

There is no "ideal" antifungal agent for the treatment of oroesophageal candidiasis. The use of nystatin, clotrimazole, amphotericin B and miconazole will alleviate the symptoms, but not sufficient to attain a cure, and recurrence can occur. Nystatin suspension in a dosage of 100,000 IU 6 hourly can be given as a gargle. Short term use of ketoconazole, itraconazole or fluconazole can be given to treat oral or oropharyngeal candidiasis for 2 weeks. Treatment of oropharyngeal or esophageal candidiasis may need to be treated for 4 weeks to prevent recurrence. Longterm therapy with ketoconazole is not advisable because of the hepatic and endocrine toxicities.

For persistent oral or oropharyngeal candidiasis, fluconazole or itraconazole can be given in a dose of 100 - 200 mg daily for 7 - 14 days. For the treatment of esophageal candidiasis, these triazoles can be used with a loading dose of 100-200mg followed by 100mg daily for 4 weeks. It has been shown to produce a significantly greater rates of endoscopic and clinical cures of candidal esophagitis than ketoconazole.

b. Cryptococcal Infections

Cryptococcal infections are common in immunocompromised patients especially when their CD4+ T cell counts are less than 100/uL. These infections are due to *Cryptococcus neoformans* which is usually isolated from the soil, but the most common source of the virulent strains are from pigeon droppings, which are uncapsulated and upon contact with human beings, rapidly develop capsules. The causative organisms are *C. neoformans var neoformans* and *var gatti*. The infection is probably well established in the lungs and other viscera before disseminating to the brain and meninges. Cryptococcosis is becoming more prevalent in patients with advanced AIDS with an incidence of 5-30 percent.

Cryptococcal meningitis:

In AIDS patients, disseminated cryptococcal infections is the 4th most common cause of life threatening illness, with meningeal infection being the most common affecting 5-30% of patients with advanced AIDS. Involvement of the central nervous system with cryptococcal meningitis is the most common, occurring in about 85% of those with cryptococcal infections, where the symptoms include fever, headaches, meningeal signs, altered mental status, cranial nerve palsies, motor abnormalities, cerebellar signs and

occasional fits. Diagnosis is by doing a lumbar puncture, collecting the cerebrospinal fluid (csf) for microscopic examination looking for the spores under India ink staining and culturing for the organism. Sometimes, cryptococcal antigen titres are done on the csf specimen. Assessment of response to therapy can be done by monitoring the csf and serum cryptococcal antigen titres. Cryptococcal infection especially of the central nervous system requires life-long therapy to suppress the replication of the fungus.

Pulmonary Cryptococcal Infection:

The respiratory infection is usually asymptomatic and may only be an accidental finding during a chest radiological examination; occasionally, pulmonary cryptococcal infection can manifest with chronic cough, weight loss, low grade fever, hemoptysis, dyspnoea, night sweats and malaise. Diagnosis requires a high index of suspicion; sputum can be sent for culture on Sabouraud's agar medium and on histology.

Less common are infections in the skin, bone, genitourinary tract, lymphnodes, liver, spleen, and adrenals.

Treatment:

In an immunocompromised patient with prolonged fever, systemic fungal infections should be excluded. Cultures of body fluids need to be taken. The gold standard for the treatment of cryptococcal meningitis is still intravenous amphotericin B and 5 flucytosine. Intravenous amphotericin B 0.4mg/kg/day, with flucytosine 100-200mg/kg/day orally or I/V infusion in divided doses, can be given in the initial phase until the csf cultures become negative. Because of the toxicity, this combination should be used in the first 2 weeks of therapy, or until the csf cultures are negative, then triazoles like fluconazole 200-400mg daily can be used to continue therapy for at least 6-8 weeks. The relapse rates are high with cryptococcal meningitis, therefore, lifelong maintenance therapy with fluconazole 200mg daily is recommended.

The prognosis of cryptococcal infections depends on the site of infection, whether therapy is initiated early or late, the efficacy of the drugs used and the underlying clinical and immunological status of the patient.

c. *Aspergillus* Infections:

Systemic aspergillosis is the most common invasive fungal infection in the immunocompromised host. The common pathogenic species are *Aspergillus fumigatus* and *A. flavus*. They are commonly found in the soil, water, organic debris and decaying vegetation, fireproofing materials, ventilation & airconditioning systems, and in marijuana.

Aspergillosis in AIDS patients:

Infection with aspergillus species can present in many ways such as allergic aspergillosis, aspergillomas (fungus balls) in the lungs, superficial (ears, eyes, skin) aspergillosis, chronic necrotising pulmonary aspergillosis and invasive aspergillosis with pulmonary involvement (90-95%) and extrapulmonary dissemination (25%). Recently a few cases of ulcerative tracheobronchitis has been reported, with initial mucosal lesions, extending into the submucosa and cartilage. Diagnosis is by biopsy and culture. Ulcerative tracheobronchitis makes up 20% of all reported cases of aspergillosis associated with AIDS and 10% of invasive aspergillosis. The more invasive forms of aspergillosis has been recognised in advanced AIDS when the CD4 cell counts are low.

The incidence of aspergillosis in autopsy findings of AIDS patients ranges from 0-9%, with increasing incidence of CNS involvement.

Invasive Aspergillosis: Predisposing factors:

The predisposing factors include prior episode of *Pneumocystis carinii pneumonia* in AIDS patients, neutropenia, organ and bone marrow transplantation, hematologic malignancies, chronic granulomatous disease, corticosteroid therapy. Invasive aspergillosis may be linked with use of marijuana.

Invasive pulmonary aspergillosis can be divided into

- (1) acute invasive, and
- (2) chronic invasive types.

The clinical manifestations of invasive pulmonary aspergillosis includes:

- (1) unremitting fever and new pulmonary infiltrates in spite of broad-spectrum antibiotic therapy,
- (2) dyspnoea,
- (3) non productive cough,
- (4) sudden pleuritic pain, fever, tachycardia and sometimes with a pleural rub, may mimic pulmonary embolism,
- (5) hemoptysis,
- (6) night sweats.

Sometimes the patients may be asymptomatic. However, because these symptoms are common in advanced AIDS, the diagnosis of aspergillosis may be overlooked and therefore there may be a delay in diagnosis and treatment.

Radiological findings can vary; the disease may be unilateral or bilateral involving the upper or lower lobes, or the X-rays may be normal. Sometimes cavitory, nodular or diffuse pulmonary disease can be seen. Pleural involvement may occur. Computerised tomographic findings can be normal especially in early disease, early findings heterogenous, or cavitation or "air crescent" sign on CT scan is highly suggestive.

Invasive Aspergillosis: Diagnosis:

The diagnosis of aspergillosis in AIDS patients can be difficult; a high index of suspicion and an aggressive approach to investigate the cause is necessary. The diagnosis of aspergillosis may be definitive or circumstantial. A definitive diagnosis requires a positive culture or tissue biopsy showing hyphae, or a percutaneous aspirate of the lesion with positive culture. A circumstantial or probable diagnosis of aspergillosis can be made on respiratory culture or microscopy positive, nasal/sinus culture, nodular infiltrates on chest-X-ray, or new cavitory infiltrate on chest x-ray or CT scan.

Treatments:

Early diagnosis and long term antifungal therapy is the mainstay in managing patients with aspergillosis. The triazole, itraconazole can be given initially at 200mg b.i.d, and subsequently reducing the dosage to 100mg b.i.d for a

period of 2-5 months. In disseminated aspergillosis, it is advisable to prolong the therapy for 12 months.

Invasive Aspergillosis: Prognosis

The prognosis of invasive aspergillosis is directly related to

- (1) early diagnosis and initiation of therapy,
- (2) the extent and duration of immunosuppression,
- (3) appropriate use of antifungal therapy. In general, the mortality rates are high in AIDS patients with invasive aspergillosis. Relapses may occur.

d. *Penicillium marneffe* Infection:

Recently, cases of *Penicillium marneffe* infections in AIDS patients have been documented. *Penicillium marneffe*, a dimorphic fungus, is a rare opportunistic pathogen. It can cause systemic and deep seated infection in immunocompromised patients. The disease is endemic in South East Asian countries. All cases reported in the literature were found in South East Asia and neighbouring countries or in patients who had a history of travelling in South East Asia.

Penicillium marneffe is identified by its dimorphic character, penicillium-like colonial morphology and the production of pink pigment which diffused into the medium around the colony. Microscopically, the isolate showed a typical penicillium-like structure.

P. marneffe is the only known dimorphic fungus in the genus *Penicillium* which causes both localized and systemic infection in humans. The common clinical manifestations are fever, weight loss, hepatomegaly, generalized lymphadenopathy, soft tissue abscesses and chronic skin ulcers. Infection with *P. marneffe* can manifest with popular skin-coloured lesions with umbilicated centre that may resemble molluscum contagiosum. The fungus is most often isolated from the skin, bone marrow, lymph nodes and blood. A high index of suspicion and early diagnosis and treatment will improve outcome of the infection.

The differentiation of *P.marneffe* from *Histoplasma capsulatum* in tissue sections may be difficult because both fungi show similar microscopic morphology and both are intracellular organisms. However, *P.marneffe*

multiply by schizogony but in contrast, *H. capsulatum* multiply by budding and this feature is helpful for differentiating the organisms. *Candida glabrata* may also complicate the diagnosis because of similar morphology - The most reliable method of diagnosis of *P. marneffei* is by culture on SDA at 30° Celsius. *P. marneffei* can be identified by its dimorphic nature and a mould-like colony with red pigment diffusing into the medium surrounding the colony. On blood agar at 37° Celsius, it appears as a yeast-like colony.

Amphotericin-B is the most effective treatment for *P. marneffei* infection. However, mortality rate remains high and the survival rate is about 20%. Favourable outcome of treatment depends on the early institution of therapy. Triazoles such as itraconazole has been shown to be effective in the treatment of *P. marneffei* infection.

4. Mycobacterial Infections:

Tuberculosis (TB) is endemic in this country. Therefore a diagnosis of pulmonary TB in an HIV-infected patient need not necessarily place the patient in the CDC AIDS defining diagnosis. A negative tuberculin test (with one tuberculin unit) given intradermally, and a positive test for HIV antibodies are necessary criteria for the diagnosis of AIDS to be made. In our local setting, only people who are HIV positive and have an added CD4+ counts of below 200/uL, should be classified as AIDS.

(details of guidelines for the management of TB with HIV/AIDS, please refer to: "Guidelines for the management check of Tuberculosis in HIV/AIDS" produced by National TB Centre MOH, Feb 1993.) (add this as appendix)

a. Mycobacterium tuberculosis infection:

Medical management for tuberculosis in HIV infected individuals is along similar lines as non HIV infected individuals.

The drugs used are: isoniazid 300 mg/day with rifampicin 600mg/day, pyrazinamide 20 - 30 mg/kg/day, and ethambutol 25 mg/kg/day; with an intensive phase lasting 2 months, and a maintenance phase for 4 months with isoniazid and rifampicin.

However in HIV infected patients with tuberculosis, life long therapy with isoniazid and rifampicin should be given.

Second line therapy with drugs such as PAS, fluroquinolone, amikacin, and the newer macrolides have been used.

Mycobacterium avium complex (MAC):

Typical as well as atypical mycobacterium infections are common among patients with AIDS. Their clinical presentations may be nonspecific fevers, weight loss or diarrhoea. A high index of suspicion is essential to make a correct diagnosis.

However, with the atypical mycobacterial infections, treatment is not satisfactory.

Infections caused by atypical mycobacteria such as *Mycobacterium avium* intracellular and *M.kansasii* are very common in HIV infected individuals when their CD4+ T lymphocytes fall below 100 uL. The presenting symptoms can be prolonged fevers, severe weight loss, and chronic diarrhoea. Diagnosis can be made from blood and stool cultures. The drugs used in the treatment of MAC infections are ciprofloxacin 750 mg/twice daily (or b.i.d.), clofazimine 100 mg/day, and amikacin may be added at 7.5 mg/kg/day for 4 weekly. Alternatively rifabutin (ansamycin) 300 - 600 mg/day, with clofazimine 100 mg/day, ethambutol 15 mg/kg/day, and isoniazid 300 mg/day can be used in combination.

Other drugs such as clarithromycin 1 - 2 gm/day either as monotherapy or in combination can be used. Azithromycin 500 mg/day can also be used as an alternative to clarithromycin.

Prophylaxis against tuberculosis in HIV infected individuals is necessary to prevent relapses. Rifabutin alone or clarithromycin with clofazimine can be used. ref (NTBC guidelines).

5. Cytomegalovirus infection:

Cytomegalovirus (CMV) infection is not very common in immunocompetent individuals, however, in immunocompromised HIV infected individuals, the virus can affect the eyes causing retinitis and subsequent blindness. Infection of the gastrointestinal tract can occur with symptoms of colitis, and severe weight loss. The respiratory system can also be affected with pneumonitis. Therapy against CMV infection in AIDS patients is not satisfactory; the drugs used are very toxic, and most of these patients are already on multiple drugs, like zidovudine, which has a marrow suppressive effect on its own.

a. Ganciclovir: (DHPG): 9 - (1,3 - dihydroxy - 2 - propoxymethyl

2.5 - 5 mg/kg/in 100 mls 0.9% N/S or D/W 12 hourly.
(each dose given over 1 hr) for 14 - 21 days.

Maintenance therapy may be needed, especially, for retinitis.

Side effects: Bone marrow suppression.

b. Phosphonoformate (Foscarnet)

I/V 0.05 - 0.16 mg/kg/min. given continuously for 14 - 21 days.

Side effect: Renal impairment

c. Intravitreal ganciclovir has been used for CMV infection of the eye.

Suppressive therapy:

a. Ganciclovir 5mg/kg/day

b. Foscarnet 90 -120 mg/day

Bacillary Angiomatosis: (Rochalimaea):

Rochalimaea hebselae (Rickettsia-like)

Firm nodular papular lesions

Hepatosplenomegaly, lytic bone lesions

Treatment: Erythromycin, Doxycycline, Rifampicin.

250 - 500mg. 4 times a day for 2 - 4 weeks.

2nd line therapy: Cotrimoxazole, Doxycycline, Rifampicin or soniazial

6. Viral Infections:

Viral infections are common in immunocompromised patients. Multidermatomal herpes zoster or simplex infections may be indicator diseases for progression to AIDS. Extensive genital warts in males has been

seen in AIDS patients. The detection of Human Papilloma virus (HPV) in the female cervix has been associated with HIV infection.

6.1 Herpes Zoster:

Acyclovir (zovirax) has been found to be effective in treating herpes infections; however it should be given as early as possible. Acyclovir, given during the first five days of the symptoms promotes viral shedding and shortens the disease process. Therefore, in treating herpes infections, it is recommended that acyclovir be given within the first 5 days of the appearance of signs and symptoms.

1. Acyclovir: Oral: 800 mg 5 times a day for 7 days,

I/V: 10 mg/kg 8 hrly (1 - 2 weeks) for severe Herpes zoster infections: for 1 - 2 weeks

or 500mg/m² I/V 3 x a day for 1 week

6.2 Herpes Simplex:

Herpes simplex infection occurs when the CD4+ T cell counts fall to below 400/uL. Lesions are usually erosive and in male homosexuals usually seen on the perianal region.

Acyclovir when given early in the course of the illness can abort the infection. In severe herpes infections, intravenous acyclovir has to be given. To prevent recurrence, suppressive therapy is advocated.

1. Acyclovir: Oral: 200 mg 5 times a day for 5 - 14 days.

For herpes encephalitis: I/V 5 - 10 mg/kg 8 hrly

Prophylaxis: (suppressive therapy):

suppression of Herpes simplex

200mg. 6 hrly. daily initially, gradually tail down, to 200mg 12 hrly.

7. Isosporiasis:

Isospora belli is a unicellular parasite. It can affect the gut causing profuse diarrhoea. Symptoms of weight loss and malabsorption may be seen.

Weight loss due to isospora infection can be very severe, and the patient may present with emaciation and severe dehydration. Acute management of isospora infection entails the use of antidiarrhoeal agents such as codeine phosphate or lomotil, for symptomatic relief; and hydration with either oral hydration salts or intravenous replacement is essential. High dose trimethoprim and sulphamethoxazole (bactrim) 4 tablets every 6 hourly for a duration of ten days is sufficient to clear the infection. However recurrences do occur. Therefore it might be necessary to maintain the patient on longterm prophylaxis with bactrim 2 tablets daily.

8. Cryptosporidiosis:

Cryptosporidia is also a unicellular parasite that can cause profuse diarrhoea in immunocompromised patients. Severe weight loss and dehydration can occur. There is no definitive treatment for this infection; therefore prompt diagnosis and symptomatic treatment is essential to prevent morbidity.

Conclusion:

Management of AIDS has become more challenging with advances in the use of antiretrovirals singly or in combination, and the availability of prophylaxis against PCP. Patients with advanced AIDS are living longer, therefore there would be an increased susceptibility to opportunistic viral and invasive fungal infections. Therefore, a high index of suspicion and vigilant investigative procedures have to be done to make the diagnosis. Early effective treatment will reduce morbidity, mortality and ensure a better quality of life.

The aim of management in HIV disease is to delay progression to AIDS and to prevent the occurrence of opportunistic infections, thereby ensuring a good quality of life and prolonged survival.

CHAPTER 8

MANAGEMENT OF OCCUPATIONALLY ACQUIRED SHARPS INJURIES

With increasing prevalence of HIV infection in our community, the health care workers (HCWs) will be faced with increasing risks of occupational exposure to potentially infected body fluids. Therefore it is essential that all HCWs be very vigilant in taking precautions when handling potentially infected materials.

Definition of Inoculation Accidents: penetration or puncture of skin or mucous membrane by any sharp objects which have been used on patients during the course of duty. The sharp objects include: used needles/lancets/scalpel blades, scissors, intravenous catheters and used Pasteur pipettes.

Daily activities in hospital that may result in inoculation accidents:

(a) Daily activities in ward/ clinic/OT/labs:

- venesection
- administering of medication via parenteral injection
- assembly/disassembly of i/v tubing
- surgical procedures (major/minor)
- laboratory glassware breakages

(b) Clean-up and disposal-related injuries: - recapping of needles - introduction of sharps into disposal containers - handling of linen or rubbish - cleaning of used glasswares containing clinical specimens - accidental stabbing by a colleague.

APPENDIX 1

INNOCULATION ACCIDENT SURVEILLANCE FORM (IAS-1)*

SHARPS/NEEDLE STICK INJURY SURVEILLANCE

Date _____ Unit _____

1. Name of staff member _____

Grade of staff member : Doctor () Attendant ()

Nurse () Technician () Student Nurse ()

2. Account of accident (describe):

Type of sharp involved

Incident date _____ Time _____

Place of accident (ward/clinic/O.T. A&E):

3. Hepatitis B status: Vaccinated () Non-vaccinated () Unknown ()

4. Tetanus immunization: Date/Year () Unknown ()

5. Patient contact known? Yes () No ()

If "Yes", please specify:

Patient's name _____ R.N. _____

Ward _____ Diagnosis _____

Was the patient in a "high risk" group? Yes () No () Unknown ()

If "Yes", specify: _____

6. Immediate action:

Health Care Worker

a. 5ml of blood taken for testing: Yes () No ()

If "No", please specify:

b. **Patient contact (if unknown)**

5ml of blood taken for testing: Yes () No ()

If "No", please specify:

Form completed by: Name _____ Signature _____

I agree to HIV testing: Signature _____

* This has been implemented at the University Hospital

APPENDIX II

INNOCULATION /SHARP ACCIDENT RECORD BOOK

Unit/Ward/Clinic: _____

Following every report of accidental sharps injury (eg. used needles/lancets/scalpel blades, scissors, intravenous catheters and used pasteur pipettes), please enter the relevant information into this record book.

			If patient contact (source) is known		Date blood was taken for HIV / Hep B	
Incident date & time	Name of staff	Account of accident & type of sharp involved	Name of Patient	R.N.	From staff	Patient

INOCULATION ACCIDENTS

SHARPS INJURIES PROCEDURE:

1. Cuts and puncture wounds should be washed out at once with soap and water.
 2. Inform immediate superior and
 - a) Complete an Inoculation Accident Surveillance form IAS-1
 - b) Inform the consultant (office hours).
 - c) Enter information in Inoculation/Sharp Accident record book (to be kept at ward/clinic/unit).
 3. It is essential to:
 - a) identify "sharp" and the patient contact
 - b) obtain 5 ml blood sample from the staff member and the patient (if known) involved.
 4. Immediately attend Staff Health Clinic between 08.00 and 16.00 hours on weekdays, or outside these hours attend Accident & Emergency for:
 - a) wound dressing
 - b) antitetanus, if necessary
 - c) collect 5 ml blood specimen (in plain tube) for HIV and Hepatitis B testing.
- If this not possible, contact the Medical Staff in the Medical Department.
5. Surveillance Form (IAS-1), blood specimens from the staff involved and the source patient (if known) should be delivered to The Department of Medical Microbiology immediately together with request forms (pink virology form) duly completed with full details and marked "Urgent Inoculation accident". Use labels stating "Danger of Infection" or Biohazard Tapes.

6. Refer to Guidelines for Health Care Workers if the patient is a known HIV carrier.
7. The results of the blood test will be available within 48 hours. If further treatment is recommended this will be arranged through Staff Health Clinic.

It is your responsibility to ensure that you get the necessary follow-up treatment.

This procedure has been implemented at the University Hospital Kuala Lumpur. (Please refer to your local guidelines in your hospital)