

MODULE 1

OVERVIEW OF THE HIV/AIDS EPIDEMIC IN ZIMBABWE

Contents

Background

- Objectives
- Current status of the HIV/AIDS Epidemic in Zimbabwe
- Zimbabwe HIV trends over time
- Other Data Sources
- Discussion
- Conclusions and recommendation

Learning Objectives

When you have completed this module you should:

- Know the population of Zimbabwe
- Know current status of the HIV Epidemic in Zimbabwe
- Know Zimbabwe HIV trends over time

Background

Zimbabwe has a population of approximately 11.6 million.

58% of the population resides in the rural areas

32% of the population is urban based

10% in areas not classified as strictly urban or rural

Females constitute 51% of the population

The first AIDS case was identified in Zimbabwe in 1985 while AIDS case surveillance began in 1987

Sentimental surveillance of pregnant women receiving antenatal (ANC) service has been ongoing since 1990

Regular national estimates of people living with HIV/AIDS are needed to assess levels and trends in the overall magnitude of the epidemic and its current and future impact on health care services and other sectors of the economy

Estimates also help us measure progress towards the targets established at UNGASS

Objectives

The objectives of this module are to present the national HIV/AIDS estimates for Zimbabwe in 2003, specifically

- ❖ The total number of people living with HIV/AIDS at the end of 2003
- ❖ The number of adults between the age of 15 and 49 living with HIV/AIDS at the end of 2003 was estimated to be 33.7%
- ❖ The number of children aged 0 to 14 living with HIV/AIDS at the end of 2003
- ❖ The number of AIDS deaths among adults and children in 2003
- ❖ The number of children orphaned by AIDS in 2003

Current Status of HIV/AIDS epidemic in Zimbabwe

This section describes the current status of the HIV/AIDS epidemic in Zimbabwe. An estimated prevalence of 24.6% for adults 15 to 49 years at the end of 2003 was obtained using ANC data.

Table 1. Estimated number of people living with HIV/AIDS in Zimbabwe at the end of 2003

	Estimated Number
Total (adults and children)	1,820,000
Adults(15-49)	1,540,000
Women(15-49)	870,000
Children (0-14)	165,000
Adult Prevalence (15-49)	24.6%

Among adults aged 15 to 49 years living with HIV/AIDS, over half (56.5%) were women.

Table 2. Estimated number of new HIV infections during 2003

	Estimated Number
Adults(15-49)	166,000
Women (15-49)	88,000
Children (0-14)	40,000

Of the estimated 166,000 new adult (15-49) infections during 2003, over half (53,0%) were women. An estimated 40 000 new HIV infections were in children.

Table 3. Estimated number of new AIDS cases during 2003

	Estimated Number
Adults (15-49)	138,000
Women (15-49)	78,000
Children (0-14)	36,000

Over half (56.5%) of the estimated new adult AIDS cases in 2003 were in women

Table 4. Estimated number of AIDS death during 2003

	Estimated Number
Adults (15-49)	135,000
Women (15-49)	77,000
Children (0-14)	36,000

Of the estimated adult AIDS deaths 57.0% were women.

Table 5. Estimated number of HIV/AIDS orphans* (aged 0-14 years) at the end of 2003

	Estimated Number
HIV/AIDS Orphans (0-14)	761,000

Children who have lost one or both parents to HIV/AIDS

The number of orphans who lost their mother to HIV/AIDS was greater than the number of orphans who lost their father to HIV/AIDS.

Table 6. Estimated adult (aged 15-49 years) HIV/AIDS prevalence by census status at the end of 2003

Census Strata	Estimate
Urban	28,1%
Rural	20,9%
Other	34,9%

Rural- communal lands, small scale commercial farms, resettlements

Other- Large scale commercial farms, administrative centers, growth points, other urban

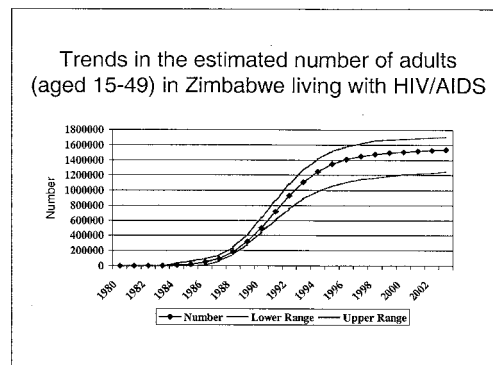
areas (e.g. mines), state land (e.g. national parks), special category (e.g. army camps)

HIV/AIDS prevalence was highest among those residing in “other” areas and lowest in rural areas.

Zimbabwe HIV/AIDS Trends over Time

Trends in no. of Adults Living with HIV/AIDS

Figure 2.



The estimated number of adults living with HIV/AIDS in Zimbabwe increased from zero in 1980 to 1,540,000 in 2003.

Trends in the estimated number of Adults (aged 15-49) in Zimbabwe living with HIV/AIDS

Discussion

The impact on women in Zimbabwe is evident from these estimates.

More than half of the estimated number of adults living with HIV/AIDS, the estimated number of new infections and the estimated number of AIDS-related death were in women.

Area of residence is an important consideration when making national HIV/AIDS estimates.

Conclusions

The overall estimate of HIV/AIDS prevalence among adults in 2003 was 24.6%.

Trends – additional years of data are needed to see whether trends in adults is leveling off.

Sex – the estimated number of adult women (aged 15 to 49 years) living with HIV/AIDS has been higher than the number of men since 1989.

Residence- Unique working and living conditions in “other areas” have likely contributed to “other” areas having the highest estimated adult HIV/AIDS prevalence (34.9%) compared with urban (28.1%) and rural (20.9%) areas in 2003. This has been the case since 1995.

MODULE 1A

OVERVIEW OF OPPORTUNISTIC INFECTIONS

Contents

- Introduction
- The normal immune response
- The life cycle of HIV
- Respiratory infections
- Gastrointestinal infections
- Neurologic manifestations
- Cryptococcosis
- Cancers associated with HIV infection

Learning Objectives

When you have completed this module you should:

- Know that a large number of infections occur in persons with HIV infection
- Understand why opportunistic infections occur in persons with HIV infection
- Be able to list the common opportunistic infections and their causes
- Understand the life cycle and pathogenesis of HIV infection
- Understand that HIV affects many organs and systems in the body
- Understand that certain types of cancers occur more frequently in immunosuppressed persons

1.1 INTRODUCTION

Immunity:

HIV infection disables the immune system resulting in the individual suffering from opportunistic infections and other illnesses including malignancies.

The human body is continuously exposed to pathogens that exist in the environment. The body comes into contact with pathogens through;

- the air that is breathed,
- through the ingestion of food and water,
- through direct contact with skin and mucous surfaces.

The body has a mechanism to resist and overcome most pathogens that it is exposed to. The

process of resistance to infection is known as **IMMUNITY**. The normal human immune system is able to detect substances that are foreign to the body and then to process and dispose of such substances. However the body's defense mechanisms may be overcome if

- the dose of the invading pathogens is large,
- the body has not been previously exposed to the invading pathogens,
- if the immune system is suppressed
- or if there is a breach in the barriers that protect against invasion.

Persons with weak immune responses become prone to developing infections that they would normally resist. If infection that the normal human body is capable of resisting causes disease in persons with weak immunity, this phenomenon is known as opportunistic infection.

Immune deficiency may be the result of congenital abnormalities (congenital immune suppression) or the result of conditions that occur after birth (acquired immune suppression). Acquired causes of immune suppression include:

- **Infections such as malaria, measles, influenza, HIV**
- **Metabolic causes such as diabetes, malnutrition**
- **Haematologic causes leukaemias, lymphomas**
- **Drugs such as steroids, cytotoxic agents, immunosuppressants**
- **Normal pregnancy and infancy**

The acquired immune deficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV). In persons with HIV infection the immune system is gradually destroyed, the resulting immune suppression makes affected individuals prone to infections that may normally be overcome if the immune system was intact and functioning normally. Immunosuppressed individuals are also more prone to repeated attacks of bacterial and viral infections that may not be true opportunistic infections. In addition they are more likely to develop certain cancers.

Modes of HIV Transmission:

HIV infection can be transmitted through Blood, semen, vaginal fluid and breast-milk. Thus HIV can be acquired through:

- Having sex with an infected person
- Exposure to blood and blood products from an infected person e.g. accidents, needle sticks while injecting patients, unclean razors, blood transfusions and others.
- During pregnancy, birth or breast feeding from an infected mother to child.

Contact with saliva, tears or urine has not been shown to transmit the virus HIV is not transmitted by food, water, toilets, swimming pools, sharing eating utensils. Mosquitoes do not transmit HIV. Mosquitoes suck blood from human beings but do not deposit blood into its victim.

Everybody must know how HIV is and not transmitted in order to reduce the risk of transmission.

Groups at risk of HIV

- 1) **People on the move;** long distance truck drivers are among the first group to be identified to have HIV infection in Africa. Men living away from their families in search of work e.g. mine workers are also at risk.
- 2) **People in conflict;** Rape is often used as a weapon of war to humiliate and control behaviour of civilian populations or to weaken an enemy by destroying the bonds of family and society.
- 3) **Women;** Culturally, women are generally not in a position to question their husbands about extramarital affairs, negotiate for condom use or refuse to have sex etc. This is often enforced by domestic violence. This increases women's vulnerability to infection. Women are also more vulnerable to acquiring the HIV virus by virtue of their anatomy.
- 4) **Poverty;** AIDS tends to settle more among the less educated and the poor because of their lack of exposure to information for behaviour change and inability to acquire what is necessary to prevent HIV transmission.

Opportunistic infections are the main cause of illness in people living with HIV infection and AIDS (PLHA). In immunosuppressed persons the following occur:

- **Opportunistic infections occur more frequently, are more severe and less responsive to recommended treatment regimens**
- **Other “non-opportunistic” bacterial, viral, fungal and parasitic infections occur more frequently and often relapse after treatment**
- **Tuberculosis occurs commonly and is often recurrent**
- **Certain cancers occur more frequently**

Infections and other conditions that occur more frequently in PLHA are shown in Table 1.1.

Table 1.1: Infections and other conditions that occur more frequently in immunosuppressed persons

Bacterial infections	Viral infections	Fungal infections	Other infections	Cancers
Tuberculosis	Herpes simplex virus disease	Candidiasis	Cryptosporidiosis	Kaposi's sarcoma
Bacterial respiratory infections	Varicella zoster virus disease	Cryptococcosis	Microsporidiosis	Carcinoma of the cervix
Bacterial enteric infections	Human papilloma virus infection	Histoplasmosis	Isosporiasis	Lymphoma
	Molluscum contagiosum	Pneumocystis pneumonia	Scabies	Squamous cell cancer of the genital tract
	Cytomegalovirus disease		Toxoplasmosis	Squamous cell cancer of the conjunctiva

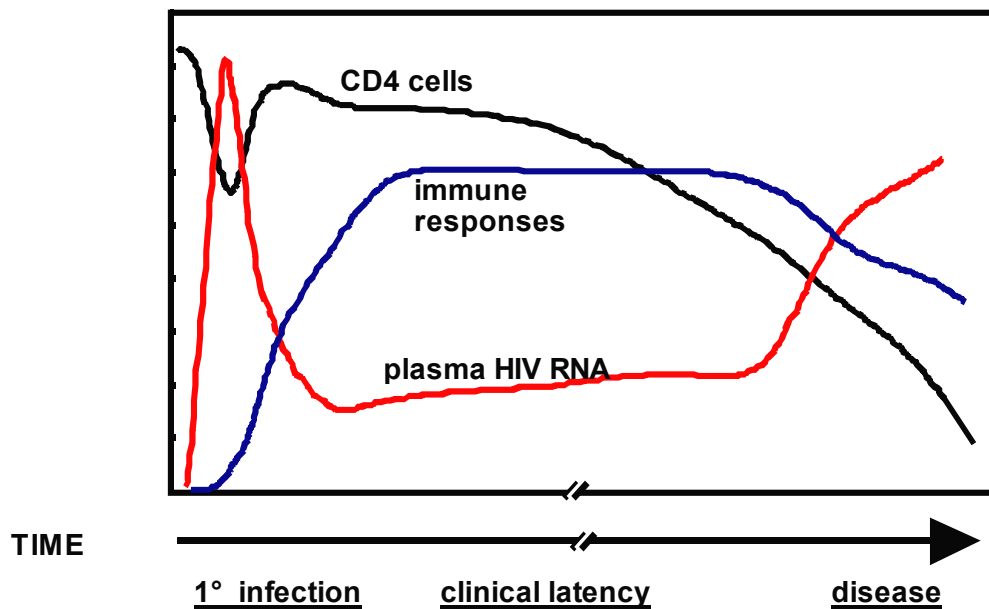
The pattern of infections that occur in PLHA depends on the prevalence of infections in the area that they live in.

Apart from the “true” opportunistic infections, a number of illnesses, termed opportunistic diseases, occur in immunosuppressed persons. Some of these illnesses may have a direct causal relationship with a pathogen while in others a causal relationship has not been firmly established. Other conditions associated with immunosuppression caused by HIV infection include progressive multifocal leukoencephalopathy, vacuolar myelopathy, cranial nerve palsies, peripheral neuropathy, and Guillain Barre Syndrome.

The onset of opportunistic infection and other opportunistic diseases is dependent on the level of immunosuppression and the prevalence of opportunistic pathogens in the environment. Hence the pattern of diseases encountered varies tremendously from place to place.

In Figure 1.1 the relationship between HIV plasma viral load, the peripheral blood CD4+ lymphocyte counts and the anti-HIV antibody levels is shown.

Figure 1.1: Relationship between HIV plasma viral load, CD4+ lymphocyte counts and anti-HIV antibody levels



It is known that soon after infection with HIV occurs is rapid replication of the virus and plasma viral loads reach high levels (plasma HIV RNA in figure). Once antibody to HIV develops (immune response) viral load levels diminish and may stabilize to lower levels. Later as HIV disease progresses and the CD4+ lymphocyte counts decrease, the viral load increases. Symptoms may occur early during the course of the infection and then the infection may enter a latent phase. HIV-related illness and opportunistic infections develop as the CD4+ lymphocyte counts decrease.

Activity 1.1

This is an individual exercise

1. List the modes of transmission of HIV
2. List three infections that transiently suppress immunity
3. How do you as a health worker prevent being becoming infected?
 - a) in your work please
 - b) in your personal life
4. How would you prevent other patients from getting HIV infection

There will be a discussion when this exercise has been completed

1.2 THE NORMAL IMMUNE RESPONSE

The normal immune response is dependent on the activation of lymphocytes in the circulation. With the entry into the body of a substance recognised as foreign, circulating macrophages bind the substance and transport it to the CD4+ lymphocyte. The substance is transferred to the surface of the CD4+ cell and this triggers off a series of cellular and chemical reactions. HIV enters and destroys CD4+ lymphocyte resulting in a reduction of the number of circulating CD4+ lymphocytes. Before destroying the CD4+ lymphocyte HIV replicates within the cell.

Within the body are a large number of different types of white blood cells. The cells responsible for providing immunity are the lymphocytes. There are two main types of lymphocytes in the circulation, the B cells and the T cells. The B lymphocytes produce natural antibodies. The antibodies are proteins known as immunoglobulins.

The T lymphocytes are responsible for cell-mediated immunity. There are a large number of different types of T lymphocytes. The majority of these T lymphocytes have a cluster of differentiation (CD) molecule on their surface. Each of these CD molecules reacts with an antigen or a chemical produced by other cells. The T lymphocyte bearing the CD4 molecule is known as the CD4+ lymphocyte. This cell, also known as the helper cell, plays a crucial role in the immune response. However, the CD4+ lymphocyte is the target for HIV, and HIV enters the cell and eventually destroys it. With the reduction in peripheral blood circulating

CD4+ lymphocytes immune suppression ensues and affected persons become prone to develop opportunistic infections.

The normal range of CD4+ lymphocytes in the peripheral blood varies tremendously. It has been demonstrated that when the peripheral blood CD4+ lymphocyte count falls below 200/mm³, the incidence of opportunistic infections increases. It has also been shown that in persons with HIV-related symptoms, the peripheral blood total lymphocyte count of less than 1200/ml is an approximate indication of peripheral blood CD4+ lymphocyte level of 200/mm³. As the CD4+ lymphocyte count falls a number of HIV-related infections and diseases develop. This correlation is shown in Table 1.2.

Table 1.2: Occurrence of HIV-related illnesses and infections as the CD4+ lymphocyte count falls

CD4+ lymphocytes (per mm ³)*	Infections**	Non-infectious illnesses**
More than 500	Acute retroviral infection	Generalised lymphadenopathy, Myopathy, Aseptic meningitis, Guillain Barre syndrome
200-500	Bacterial pneumonias, Pulmonary TB, Zoster, Oro-pharyngeal candidiasis, Cryptosporidiosis, Oral hairy leukoplakia, Kaposi's sarcoma	Cervical cancer, Lymphoma, Anaemia, Thrombocytopaenia, Lymphocytic interstitial pneumonitis
Less than 200	Pneumocystis carinii pneumonia, Miliary TB and extrapulmonary TB, Disseminated histoplasmosis, Progressive multifocal leukoencephalopathy	HIV associated wasting syndrome, Polyneuropathy, Encephalopathy and dementia, Cardiomyopathy, Vacuolar myelopathy
Less than 100	Disseminated herpes simplex, Cryptococcosis, Toxoplasmosis, Cryptosporidiosis, Microsporidiosis, Disseminated cytomegalovirus infection, Oesophageal candidiasis	Primary CNS lymphoma

* This is a rough approximation, the incidence of opportunistic infections increases as the CD4+ lymphocyte counts fall.

** The pattern of opportunistic infections and diseases varies from place to place

*** CD4+ lymphocytes in children

Infants and young children normally have higher CD4+ lymphocyte counts than

adults when they develop opportunistic infections. The normal CD4+ lymphocyte count in children varies with age and is equal to the adult value by the time the child is six years old.

Activity 1.2

This is a group exercise

1. What are major routes of HIV transmission?
2. List the causes of immune suppression.
3. Give examples of three fungi that may cause opportunistic infection.

There will be a discussion when this exercise has been complete

1.3.1 HIV

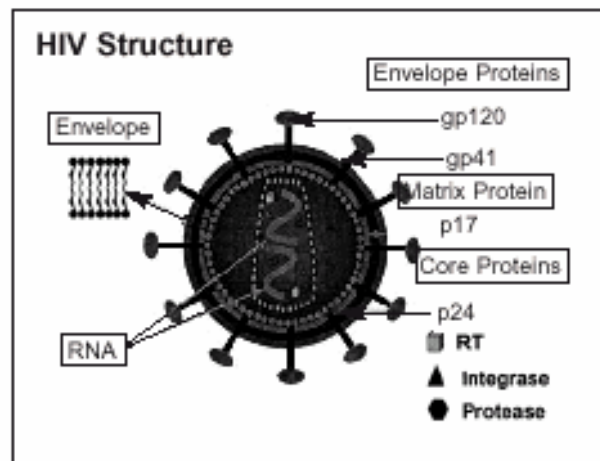


Figure 3. The Human Immunodeficiency Virus

HIV is an RNA virus. HIV has three principle genes that code its functional and structural components. The gag gene which encodes core proteins, the pol gene which encodes the enzyme reverse transcriptase protease and integrase and finally the ENV gene which encodes the HIV structural components known as glycoproteins. Other important genes that are necessary for replication include rev, nef, vif, vpr or vpx.

As many as ten million virions (individual viruses) per day may be produced by some individuals.

1.3.2 HIV Types

There are two types of HIV that cause AIDS and these are HIV-1 and HIV –2. HIV-1 divides very rapidly and this has a high chance of mutating. More than 10 subtypes of HIV-1 have been described. Subtype C is what is mainly found in Southern Africa.

1.3.3 HIV Diagnostic Tests:

The (ELISA) Enzyme Linked Immunosorbent Assay is a screening test-which is performed on the patient's serum or blood and identifies antibodies to HIV. False positives may occur with this test in certain viral infections or haematologic malignancies and pregnancy. Another test is required to confirm the ELISA test. Usually two ELISA tests with clinical symptoms can be used to diagnose HIV. The (Western Blot) is an expensive test which can also be used to confirm HIV infection. If the Western Blot remains indeterminate after 6 months the patient does not have HIV infection.

Rapid Tests for HIV are also in use. These tests are done on serum or blood and identify antibodies. Some rapid tests have been found to perform well and may be used to diagnose HIV.

Polymerase Chain Reaction (PCR) for DNA or RNA of the HIV virus, not generally available for diagnostic purposes in Zimbabwe because of their cost.

Viral Culture is not available.

1.4 THE LIFE CYCLE OF HIV

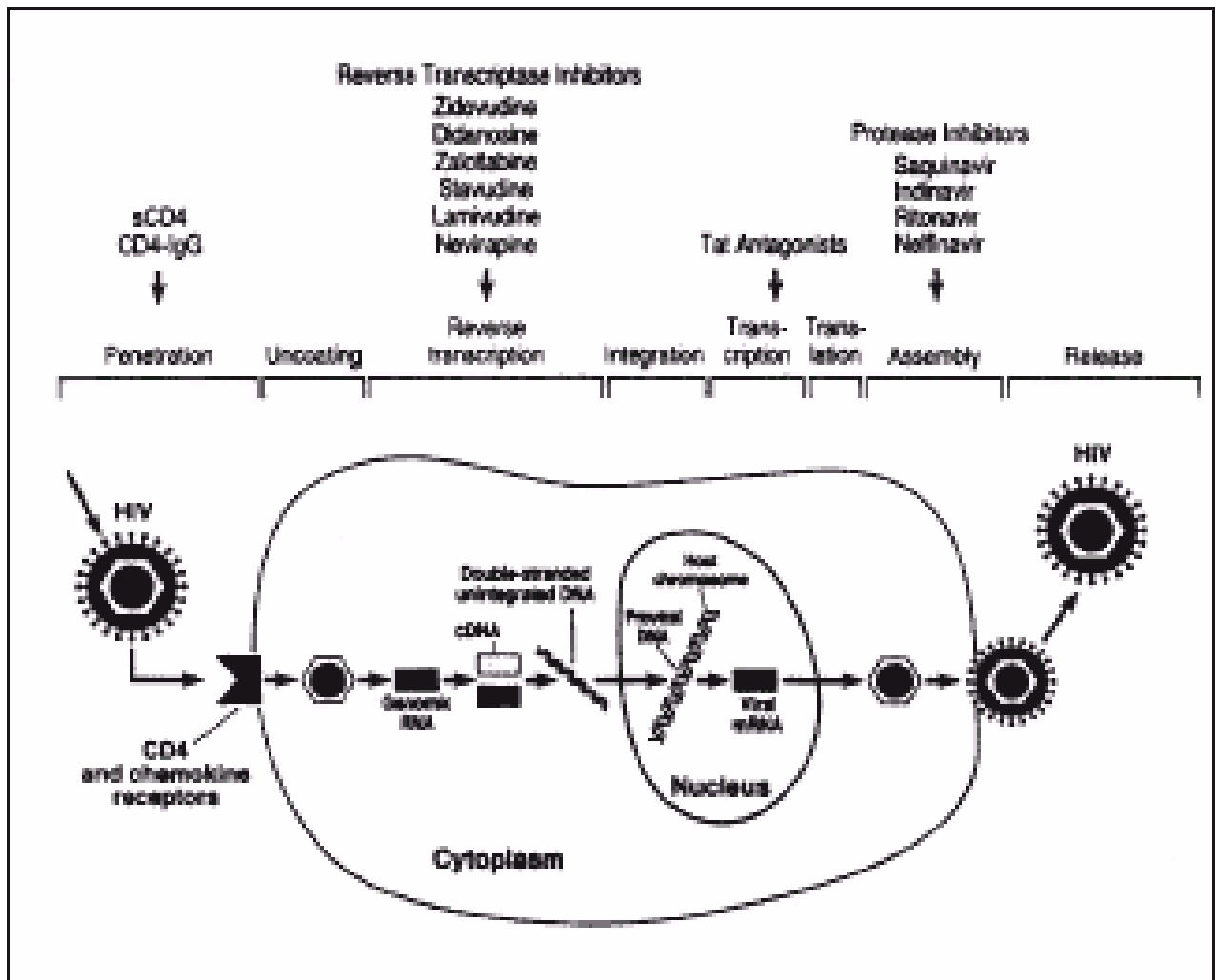


Figure 4. The HIV Lifecycle and Sites of Action of Some Antiretroviral Agents

Figure 4 is from the HIV nursing curriculum produced by Baylor College of Medicine and describe the life cycle of HIV in the lymphocyte and the points where drugs work.

HIV begins its infection of a susceptible host cell by binding to the CD4 receptor on the host cell (process facilitated by glycoprotein (gp) 120). CD4 molecules are present on the surface of many lymphocytes and are a critical part of the body's immune system. A number of drugs are being developed to prevent infection by blocking fusion of HIV with its host cell. These drugs are known as **fusion inhibitors**.

Following fusion of the virus with the host cell (process facilitated by glycoprotein (gp) 41), HIV enters the cell. The genetic material of the virus, which is RNA, is released and is converted to DNA within the cell. An enzyme in HIV called reverse transcriptase is necessary to catalyze this conversion of viral RNA into DNA. Drugs are available to block the action of reverse transcriptase.

These drugs are called **reverse transcriptase inhibitors** and three classes of these drugs exist for the treatment of HIV. These are:

- **Nucleoside reverse transcriptase inhibitors**
- **Non-nucleoside reverse transcriptase inhibitors**
- **Nucleotide reverse transcriptase inhibitors**

Examples of reverse transcriptase inhibitors include zidovudine, didanosine, stavudine, lamuvidine and nevirapine.

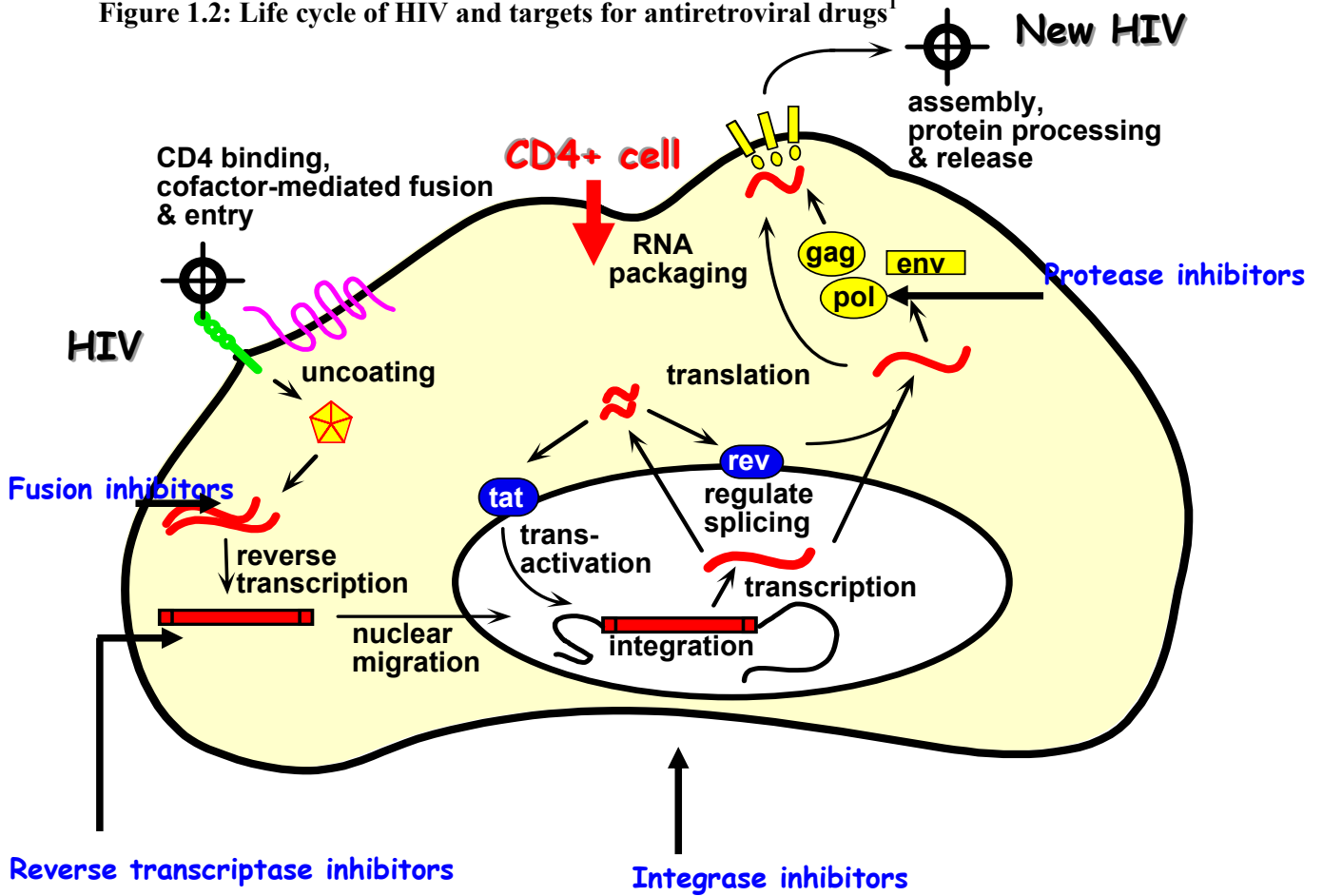
Once the genetic material of HIV has been changed into DNA, this viral DNA enters the host cell nucleus where it can be integrated into the genetic material of the cell. The enzyme integrase catalyzes this process, and **integrase inhibitors** are under study as a new way to block HIV replication.

After the viral DNA is integrated into the genetic material of the host, it is possible that HIV may persist in a latent state for many years. This ability of HIV to persist in certain latently infected cells is the major barrier to eradication or cure of HIV.

Activation of the host cells results in the transcription of viral DNA into messenger RNA (mRNA), which leads to the production of viral proteins. The new viral RNA forms the genetic material of the next generation of viruses. The viral RNA and viral proteins assemble at the cell membrane into a new virus. Amongst the viral proteins is HIV protease, which is required to process other HIV proteins into their functional forms. **Protease inhibitors**, one of the most potent types of anti-viral medications, act by blocking this critical maturation step. Examples of protease inhibitors include saquinavir, indinavir, ritonavir and nelfinavir. Following assembly at the cell surface, the virus then buds off from the cell and is released to infect other cells.

Unless the HIV lifecycle is interrupted by treatment, the virus infection spreads throughout the body and results in the destruction of the body's immune system. With current anti-viral medications, such as reverse transcriptase inhibitors and protease inhibitors, HIV infection can be contained. These facts are summarised in the diagram in Figure 1.2

Figure 1.2: Life cycle of HIV and targets for antiretroviral drugs¹



1.7 WHO CLASSIFICATION OF HIV IN ADULTS

CD4+ lymphocyte counts are not currently available in Zimbabwe thus major and minor signs and symptoms may be used. One major signs or symptoms plus two minor signs or symptoms define symptomatic HIV infection.

¹ Adapted from: R. Collman. Princess Marina Hospital, Gaborone, Botswana. May 2002

Major signs/Diseases in Adults

- Weight loss of 10% or more of body weight.
- Prolonged fever for 1 or more months
- Chronic diarrhoea
- Tuberculosis

Minor signs/Diseases in Adults

- Oropharyngeal candidiasis
- Persistent cough for over one month
- Body weakness
- Night sweats
- Loss of appetite
- Generalised skin infections
- Herpes zoster
- Chronic herpes simplex infection
- Pneumonia

Alternative WHO Classification for Adults

For adults, the WHO has also developed a system to categorize the immunosuppression of adults by their total lymphocyte counts (Table 1). Finally, the WHO staging system (Table 1) applies to adults, and several studies have shown its reliability for predicting morbidity and mortality in infected individuals.

Table 1. WHO Staging System for HIV Infection and Disease: Laboratory Classification*

Lymphocytes	CD4+/ mm ³	Clinical stage 1 Asymptomatic	Clinical stage 2Early	Clinical stage 3 Intermediate	Clinical stage 4 Late
>2000	>500	1A	2A	3A	4A
1000-2000	200-500	1B	2B	3B	4B
<1000	<200	1C	2C	3C	4C

WHO Staging System for HIV Infection and Disease: Clinical Classification*
Clinical Stage 1
<ul style="list-style-type: none"> • Asymptomatic • Persistent generalized lymphadenopathy • Performance scale 1: asymptomatic, normal activity
Clinical Stage 2
<ul style="list-style-type: none"> • Weight loss, <10% body weight • Minor mucocutaneous manifestation (seborrhoeic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, and angular cheilitis). • Herpes zoster, within last 5 years • Recurrent upper respiratory infections (i.e., bacterial sinusitis) • And/ or performance scale 2: symptomatic, normal activity
Clinical Stage 3
<ul style="list-style-type: none"> • Weight loss, <10% body weight • Unexplained chronic diarrhoea, >1 month • Unexplained prolonged fever (intermittent or constant), >1 month • Oral candidiasis (thrush) • Oral hairy leukoplakia • Pulmonary tuberculosis, within the past year • Severe bacterial infections (i.e. pneumonia, pyomyositis) • And/ or performance scale 3: bed-ridden <50% of the day during the last month
Clinical Stage 4
<ul style="list-style-type: none"> • HIV wasting syndrome (weight loss of >10%, plus either unexplained chronic diarrhoea > 1 month, or chronic weakness and unexplained prolonged fever > 1 month) • <i>Pneumocystis carinii</i> pneumonia • Toxoplasmosis of the brain • Cryptosporidiosis with diarrhoea, >1 month • Cryptococcosis, extrapulmonary • Cytomegalovirus (CMV) disease of an organ other than liver, spleen or lymph nodes • Herpes simplex virus (HSV) infection, mucocutaneous >1 month, or visceral and duration • Progressive multifocal leukoencephalopathy (PML) • Any disseminated endemic mycosis (i.e.) histoplasmosis, coccidioidomycosis • Candidiasis of the esophagus, trachea, bronchi or lungs • Atypical mycobacteriosis, disseminated • Non-typhoid Salmonella septicemia • Extrapulmonary tuberculosis • Lymphoma • Kaposi's Sarcoma (KS) • HIV encephalopathy (Clinical findings of disabling cognitive and/ or motor dysfunction interfering with activities of daily living, progression over weeks or months, in the absence of a concurrent illness or condition other than HIV infection that could explain findings) • And/ or Performance scale 4: bed – ridden, >50% or the day during the last month.

1.3.4 HIV diagnosis in infants and children

HIV is mainly acquired through parent to child transmission. The risk of mother to child transmission of HIV can be reduced by the use of ARVs. Because of maternal antibodies that persist in infants up to 18 months the ELISA and Western Blot tests are positive if mother is positive regardless of whether the infant is infected or not. DNA PCR or viral culture are the best tests. Most infants present with an AIDS defining illness commonly pneumocystic pneumonia. Other common signs include diarrhoea or enlarged liver or spleen. Presence of these signs and a positive ELISA test indicate HIV infection. Children over 18 months of age can be diagnosed using an ELISA test.

Widespread use of highly active antiretroviral therapy targeting different sites in the replication cycle of HIV has been associated with a considerable reduction in mortality and morbidity from AIDS. Effective combination therapy leads to resolution of opportunistic infections and opportunistic diseases.

Activity 1.3

This is a group exercise

1. What are the main functions of T and B lymphocytes?
2. What are the phases of the HIV life cycle?
3. List 5 infections which may occur when CD4 cell counts are less than 200.

There will be a discussion when this exercise has been completed

1.4 RESPIRATORY INFECTIONS IN PERSONS WITH HIV

Infections of the lower respiratory tract are commonly encountered in immunocompetent persons and do not necessarily indicate immunosuppression from HIV infection. However, in persons with HIV associated immunosuppression these infections are more frequent and often more severe.

Individual infections are discussed in later modules in this course; in this section a general overview is given of the commoner infections encountered in clinical practice.

1.4.1 Bacterial respiratory infections

A large number of bacteria may cause infection of the lower respiratory tract in persons with HIV infection. These include,

- *Streptococcus pneumoniae*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus*
- *Haemophilus influenzae*

Pneumonia caused by *Streptococcus pneumoniae* may often be the first indication of HIV infection. Patients with bacterial pneumonia present with cough, fever, systemic symptoms of myalgia, headache and loss of appetite, they often have chest pain, difficulty in breathing and tachypnoea, and they may also have haemoptysis. Patients may present with classic lobar pneumonia, bronchopneumonia or with unresponding atypical pneumonia.

1.4.2 Pneumocystis pneumonia

Pneumocystis pneumonia (PCP) is an opportunistic infection. It is commonly encountered in immunosuppressed persons with HIV infection and causes death in persons with AIDS. Patients usually present with cough, shortness of breath and fever. Often patients with PCP have features of respiratory failure. Symptoms may be very severe and an attack of PCP may lead to the death of the patient if untreated early and effectively.

1.4.3 Other causes of lower respiratory tract infections in immunosuppressed persons

Besides bacterial pneumonia and *Pneumocystis pneumonia*, lower respiratory tract infections in HIV infected immunosuppressed persons may be the result of fungal and viral infections. These are difficult to diagnose without sophisticated laboratory facilities and difficult to treat without effective agents. Viral pneumonias may be caused by herpes simplex virus, varicella zoster virus, and cytomegalovirus. Fungal pneumonia may be due to *Histoplasma capsulatum*, *Cryptococcus neoformans* and *Aspergillus fumigatus*. However, it should be remembered that tuberculosis is probably the commonest opportunistic infection encountered amongst immunosuppressed persons with HIV infection in the developing world.

1.4.4 Tuberculosis

About one third of the world's population is infected with *Mycobacterium tuberculosis*. There has been a global increase in the annual incidence of tuberculosis (TB). The World Health Organization estimates that about 9 million new cases of TB occur each year and each year 3 million deaths occur from TB globally.

HIV infection fuels the TB epidemic. Immunosuppressed persons may reactivate an old tuberculous infection or may become infected *de novo* with *Mycobacterium tuberculosis*. In persons with HIV infection both pulmonary and extrapulmonary TB can occur. Patients may present with classic features of pulmonary disease as seen in non-HIV infected individuals or may have atypical pulmonary TB. Disseminated tuberculous infection may manifest itself as generalised lymphadenopathy, meningitis, pericarditis, pleural effusion, abdominal and peritoneal disease and renal and bone disease. Rarely adrenal and genital tract involvement may occur.

TB is a frequent first indication of HIV infection in Zimbabwe and the diagnosis should always be considered in immunosuppressed persons. TB is readily curable using the standard anti-TB treatment regimens. The implementation of the directly observed, short course treatment strategy (DOTS) recommended by WHO is highly effective in treating HIV infected individuals co-infected with TB.

The typical symptoms and signs of pulmonary TB are cough with or without fever, night sweats and weight loss. Chest x-ray may show upper lobe infiltrates with or without cavitation. In immunosuppressed persons the diagnosis may be difficult to make as TB in such hosts may present with atypical symptoms, lack of typical symptoms and minimal changes on chest x-ray. In addition in persons with AIDS the presence of other opportunistic infections and extrapulmonary TB may complicate the diagnosis. Sputum should always be examined for the presence of acid-fast bacilli (AFBs) indicative of mycobacteria. Sputum may also be cultured for mycobacteria and cultured colonies can be tested for antimicrobial resistance.

Activity 1.4

This is an individual exercise

1. List the clinical features in a person with HIV infection that may indicate the presence of TB
2. What facilities do you have in your place of work for making a diagnosis of TB?

There will be a discussion when this exercise has been completed

1.5 GASTROINTESTINAL INFECTIONS

1.5.1 Introduction

Gastrointestinal infections are commonly encountered in persons with HIV infection. Infections may be bacterial, viral, fungal, protozoan and helminthic. Infection of the gastrointestinal tract may involve the lips, the mouth, oesophagus, stomach, small and large intestines and the rectum and anus. The HIV-associated mucosal lesions are described in the next section.

HIV can cause an enteropathy leading to acute, acute-on-chronic or chronic diarrhoea. Patients with HIV enteropathy often also have weight loss fever and oro-pharyngeal candidiasis. Weight loss can be quite severe. Malabsorption as a result of sub-total villous atrophy may also occur, though this is commoner in children.

Perianal lesions such as bacterial skin infections, anal warts and herpes may occur. Persons with HIV infection may have anorexia, nausea and vomiting and are prone to gastrointestinal infection with a number of pathogens. These are shown in the Table 1.3.

1.5.2 Oropharyngeal and oesophageal candidiasis

The two main types of candidiasis are **localized disease** (e.g. of the mouth and throat, and of the vagina), and **systemic disease** (e.g. of the oesophagus, skin and nails and other viscera). The mouth and throat variant (oropharyngeal candidiasis) is believed to occur at least once in the lifetime in all HIV-infected patients. This does not lead to death but can cause pain and

odynophagia. The symptoms of oesophageal candidiasis are difficulty in swallowing and pain in the chest that increases with swallowing. Disseminated candidiasis causes fever and symptoms in the organs affected by the disease (for example, blindness when it affects the eyes).

The diagnosis of oro-pharyngeal candidiasis is made on clinical grounds. The diagnosis may be confirmed by the microscopic examination of material obtained from lesions. The diagnosis of oesophageal candidiasis is made by direct visualization of oesophageal lesions by upper gastrointestinal endoscopic examination. In other sites the diagnosis is confirmed by histologic examination of tissue biopsies.

See module 8 for the management of diarrhea

Table 1.3: Gastrointestinal pathogens in persons with HIV infection

	PATHOGEN	CLINICAL FEATURES
VIRUSES	Herpes simplex virus infection	Abdominal pain, diarrhoea. Diagnosis on biopsy or tissue culture.
	Cytomegalovirus infection	Abdominal pain, diarrhoea, obtundation. Diagnosis on biopsy
	Adenovirus	Watery diarrhea
BACTERIA	Non-typhoid salmonellosis	Fever, abdominal pain, diarrhoea, diarrhoea with blood, weight loss, anorexia, hepatosplenomegaly. Diagnosis on blood or stool culture
	Shigellosis	Fever, abdominal pain, bloody diarrhoea. Diagnosis on blood or stool culture
	Campylobacter infection	Fever, abdominal pain, diarrhoea, diarrhoea with blood, Diagnosis on stool microscopy
	Clostridial infection	Diarrhoea, abdominal pain, blood in stool, pseudomembranous colitis
	Mycobacterium avium intracellulare	Fever, night sweats, malaise, weight loss, abdominal pain, diarrhoea, hepatomegaly. Diagnosis on blood culture, bone marrow or lymph node or liver biopsy
PARASITES	Microsporidiosis	Watery diarrhoea, loss of appetite, afebrile. Diagnosis on stool microscopy.
	Cryptosporidiosis	Watery diarrhoea, loss of appetite, afebrile. Diagnosis on stool microscopy.
	Isosporiasis	Watery diarrhoea, loss of appetite, afebrile. Diagnosis on stool microscopy.
	Giardia lamblia Strongyloides stercoralis	Hyperinfection and diarrhoea

1.5.3 Oral lesions in persons with HIV infection

In persons with HIV infection a large number of other oral lesions may be found, including,

- Oral candidiasis
- Oral and labial herpes
- Aphthous ulcers
- Stomatitis
- Histoplasmosis
- Kaposi's sarcoma
- Oral hairy leukoplakia
- Gingivitis, pyorrhea and periodontitis
- Cheilitis

Each of these conditions should be looked for when managing persons with HIV infection.

1.6 NEUROLOGIC MANIFESTATIONS OF HIV INFECTION

HIV itself causes encephalopathy, myelopathy and peripheral neuropathy. Numerous neurologic syndromes have been ascribed to HIV including, cerebral atrophy and degeneration, AIDS dementia complex, cerebellar atrophy, vacuolar myelopathy, facial nerve paralysis, Guillain Barre syndrome and painful sensory and motor peripheral neuropathy. A number of opportunistic infections affect the central nervous system.

1.6.1 Cryptococcal meningitis

Systemic mycoses such as cryptococcosis probably cause up to 10% of all HIV-associated deaths worldwide. Cryptococcosis most often appears as meningitis, and occasionally as pulmonary or disseminated disease. Cryptococcal meningitis is the most frequent systemic fungal infection in HIV-infected persons. Patients present with headache, fever, neck stiffness, and may be comatose. Commonly fever is absent in patients with cryptococcal meningitis. Without treatment, life expectancy is probably less than a month.

1.6.2 Toxoplasmosis

This disease, though fairly frequently encountered in PLHA in industrialized nations, is diagnosed infrequently in developing countries. This is probably the result of the lack of

diagnostic facilities developing countries. The infection leads to the development of multiple cystic lesions in the brain. In HIV-infected persons toxoplasmosis mainly appears as encephalitis or as disseminated disease. Treatment is with high dose cotrimoxazole. Second line treatment is with pyrimethamine plus sulphadiazine or clindamycine

1.6.3 Herpes simplex virus

Herpes simplex virus infection (HSV), which causes sores around the mouth and genitals, can become disseminated in immunosuppressed subjects. Dissemination may lead to infection of the lungs, the oesophagus, and the brain. Herpes simplex virus may also cause meningoencephalitis.

1.6.4 Herpes zoster infections

Herpes varicella zoster virus often causes disseminated infection after initial exposure. In children initial infection results in the development of chicken pox, though most persons that become infected develop no symptoms and signs of infection. The virus lays dormant in the paraspinal ganglia for years and with immune suppression, from whatever cause, the virus replicates and produces lesions along the length of a cutaneous nerve in a dermatomal distribution. Dissemination can also occur at this time with involvement of skin, nervous system, lungs and mucous membranes. In immune suppressed persons zoster is often multidermatomal in distribution and is persistent and extensive. It is associated with severe pain and debility.

1.6.5 Cytomegalovirus infection (CMV)

Cytomegalovirus may affect multiple systems and organs in the body in immunosuppressed individuals. The incidence of CMV disease varies between geographical locations, but CMV causes significant suffering in HIV-infected persons worldwide. Symptoms include fever and diarrhoea from CMV colitis, dyspnoea from CMV pneumonitis, and blindness caused by CMV retinitis.

1.7 CANCERS ASSOCIATED WITH HIV INFECTION

A number of cancers are known to be associated with HIV infection. These include,

- **Kaposi's sarcoma**
- **Non-Hodgkins lymphoma**
- **Carcinoma of the cervix**
- **Squamous cell carcinoma of the genital tract**
- **Squamous cell carcinoma of the conjunctiva**
- **Intracranial lymphoma**
- **Burkitt-type lymphoma**

Kaposi's sarcoma is caused by the human herpes virus type 8 (HHV8), also known as the Kaposi's sarcoma herpes virus (KSHV). The incidence of Kaposi's sarcoma in persons with HIV infection varies from place to place, being high in Central and Southern Africa. In HIV associated immunosuppression Kaposi's sarcoma is more aggressive, disseminated and more rapidly progressive when compared with endemic disease found in non-HIV-infected persons. Lesions may be found anywhere on the body and on any mucosal surface. Skin lesions are hyperpigmented, blue or purplish papules or nodules and associated with lymphoedema. Lesions are commonly found on the palate, the gastrointestinal tract, lungs or lymph nodes. Pulmonary lesions are infiltrative and often lead to respiratory failure. In persons with pulmonary infiltrative Kaposi's sarcoma the outcome is poor and there is a high mortality.

Non-Hodgkins lymphoma and intracranial lymphoma have been described frequently in association with HIV infection. Non-Hodgkins lymphoma is often generalised and can only be diagnosed by histologic examination of biopsied material. Intracranial lymphoma is associated with advanced immune suppression and is diagnosed after examining biopsies of tumour found on CT scans or MRI scans of the brain.

Carcinoma of the cervix is associated with HIV infection and there has been an increase in the annual incidence of this cancer in areas where the prevalence of HIV infection is high. It is advisable therefore to perform annual Pap smears on all women with HIV infection. There is a strong aetiologic association between carcinoma of the cervix and human papilloma virus.

Recently a strong association has been noted between HIV infection and squamous cell carcinoma of the conjunctiva. This tumour can lead to destruction of the eye and blindness. The aetiology of the cancer is not known.

Intraepithelial neoplasia of the uterine cervix, the anus, penis and vulva has also been described in association with HIV infection.

Activity 1.5

This is a group exercise

1. List the differences between primary and secondary prevention

There will be a discussion when this exercise has been completed

Important points to remember

- HIV is a very common infection in Zimbabwe
- HIV is a preventable disease
- Primary prevention of HIV through behaviour change and safer sexual activity remains the most important strategy in the prevention and control of the epidemic
- The main modes of transmission of HIV infection are sexual intercourse and mother to child transmission of infection
- HIV infection is a multi-system disease and its main impact is on cell mediated immunity
- With cell mediated immune suppression HIV infected persons develop opportunistic infections and are prone to developing certain types of cancers
- Infections that occur in persons with HIV infection may be bacterial, viral, fungal or parasitic in origin, and many of these may be adequately treated
- In parts of the world where antiretroviral agents form the mainstay of HIV therapy the incidence of opportunistic infections may be reduced and infected patients may enjoy a good quality of life
- In developing countries tuberculosis is common infection associated with HIV infection and immune suppression
- A number of infections may be prevented with the use of antibacterial and antifungal agents

MODULE 2

SPECIFIC OPPORTUNISTIC INFECTIONS

Contents

- Pneumocystis carinii
- Candidiasis
- Cryptococcosis
- Histoplasmosis
- Microsporidiosis
- Cryptosporidiosis

Learning Objectives

When you have completed this module you should:

- Understand that the major causes of death in persons with HIV infection are infections that can be treated or prevented
 - Be able to recognise clinical features suggestive of opportunistic infections
 - Recognise when to refer patients for investigations and specialist opinion
 - Know what treatment may be given to persons with certain opportunistic infections
-

2.1 PNEUMOCYSTIS JIROVECI PNEUMONIA

Pneumocystis pneumonia (PCP) is a common HIV-associated opportunistic infection. Patients usually present with cough, shortness of breath and fever. Usually patients with PCP have a sudden onset of severe dyspnoea but PCP may also present in persons with more chronic symptoms. Symptoms may be very severe and an attack of PCP may lead to death if not treated early and effectively.

Diagnosis

The diagnosis is often made on clinical grounds when a patient with HIV infection presents with shortness of breath. The patient may have a cough but the main feature is the extreme dyspnoea. Chest x-ray may be completely normal or there may be evidence of patchy infiltrates in both lung fields. The classic chest x-ray appearance of a ground glass

opacification in the middle zones of both lung fields may also be found. The diagnosis is confirmed upon the finding of cysts of *Pneumocystis* in sputum or in bronchial lavage aspirate.

Treatment

Patients with pneumocystis pneumonia usually are in respiratory failure and should ideally be admitted to hospital for management. Supportive therapy includes oxygen by facemask and adequate hydration. Intravenous fluids may be necessary but may lead to over hydration. Details of specific treatment are given in the table below:

PCP FIRST LINE TREATMENT				
Antimicrobial agent	Dose	Frequency	Route	Duration
Trimethoprim/sulphamethoxazole (Cotrimoxazole)	320mg/960mg	TID	PO	21 days

PCP SECOND LINE TREATMENT				
Antimicrobial agent	Dose	Frequency	Route	Duration
Clindamycin	600mg	QID	PO	21 days
PLUS				
Primaquine	15mg	OD	PO	21 days

Severely ill patients may require prednisolone 60mg PO daily for 5 days reducing to 40mg PO OD for 5 days and then to 20mg PO OD for 10 days. After successfully treating the acute episode of pneumocystis pneumonia it is necessary to continue secondary prophylaxis with trimethoprim 160mg/sulphamethoxazole 800mg on a long-term basis.

Some patients are sensitive to cotrimoxazole and may need desensitisation.

Rapid cotrimoxazole desensitization regimen (for PCP)

(suitable for prophylactic dose cotrimoxazole or high dose cotrimoxazole for treatment of PCP).

- Do not desensitize anyone who has had an anaphylactic reaction to cotrimoxazole or a severe skin rash such as a Stevens-Johnson syndrome. Usually about 60% effective. Rapid desensitization ideally should be performed during the day in a setting where emergency resuscitation can be provided and adrenaline can be given.
- Observations during rapid desensitization should be done every 30 minutes before each dose is given and include temperature, pulse and BP.
- If mild rash or pruritus only occur, administer antihistamine (e.g. chlorpheniramine or promethazine) and continue. If more serious side - effects occur such as severe wheeze, severe or symptomatic hypotension, severe rash etc, discontinue desensitization, manage appropriately and do not try to restart desensitization.
- Once cotrimoxazole has been started it can be continued indefinitely as long as no reactions are noted, but if the drug is stopped at any time, there may be a risk of reaction when it is restarted.

Desensitization process

Using a 1ml syringe put 0.5ml of paediatric cotrimoxazole 240mg/5ml syrup in 1000ml of 5% Dextrose and mix well. Give as follows:

Minutes	Quantity of above mixture given orally
0	1ml (use 10ml syringe)
30	10ml (use 10ml syringe)
60	100ml (use 10ml syringe)

The switch to paediatric cotrimoxazole 240mg / 5ml syrup.

Minutes	Quantity
90	0.5ml
120	5ml
150	480mg tablet
180	Start full prophylactic or therapeutic dose

Slow Desensitization regimen for adults allergic to cotrimoxazole (excluding those with Stevens-Johnson syndrome, acute anaphylaxis, and fixed drug reaction to cotrimoxazole)

Use a 1ml syringe and cotrimoxazole syrup 240mg/5ml

Day	Dose of cotrimoxazole syrup
1	0.05ml = 2.4mg
2	0.1ml = 4.8mg
3	0.2ml = 9.6mg
4	0.4ml = 19.2mg
5	0.6ml = 28.8mg
6	1.0ml = 48mg
7	2.5ml = 120mg = ½ teaspoon
8	5ml = 240mg = 1 teaspoon
9	480mg = 1 tablet
10	480mg = 1 tablet
11	960mg = 2 tablets

Stop cotrimoxazole at any point if there is evidence of a skin rash.

Activity 2.1

This is an individual exercise

A 37-year old man HIV positive man who has been well and has been attending regularly at the OIP Clinic attends 10 days before his scheduled appointment. At this visit he states that over the last 4 days he has been coughing and that today he has become short of breath. The shortness of breath is present even at rest.

- List the causes of shortness of breath in this patient.
- What further information would you want to obtain from this patient to assist you with the differential diagnosis?

There will be a discussion when this exercise has been completed

2.2 CANDIDIASIS

The two main types of candidiasis are localized disease (of the mouth and throat, and of the vagina), and systemic disease (of the oesophagus, skin and nails and other viscera). The mouth and throat variant (oropharyngeal candidiasis (OPC) is believed to occur at least once in the lifetime in all HIV-infected patients. The symptoms of oesophageal candidiasis are difficulty in swallowing and pain in the chest that increases with swallowing. Disseminated candidiasis causes fever and symptoms in the organs affected by the disease (for example, blindness when it affects the eyes).

Diagnosis

The diagnosis of oro-pharyngeal candidiasis is made on clinical grounds. The diagnosis may be confirmed by the microscopic examination of material obtained from lesions. The diagnosis of oesophageal candidiasis is made by direct visualization of oesophageal lesions by upper gastrointestinal endoscopic examination. In other sites the diagnosis is made by histologic examination of tissue biopsies.

Treatment

Localized disease is treated first with topical drugs such as aqueous GV paint, nystatin, miconazole, or clotrimazole. If there is a failure to respond to local treatment systemic antifungal agents may be used. In patients with disseminated candidiasis and in those in whom topical therapy has failed antifungal agents such as ketoconazole, itraconazole, fluconazole or amphotericin B may be given.

1. Oral candidiasis

FIRST LINE TREATMENT

Oral candidiasis

Antifungal agent	Dose	Frequency	Route	Duration
Nystatin lozenges to suck	200 000 units	5 times a day	PO	14 days
OR				
Clotrimazole lozenges to suck	10mg	5 times a day	PO	14 days
OR Aqueous GV paint		5 times a day	PO	14 days

SECOND LINE TREATMENT

Oral candidiasis

Antifungal agent	Dose	Frequency	Route	Duration
Fluconazole	100mg	OD	PO	14 days
OR				
Itraconazole	100mg	OD	Gargle	21 days

2. Vaginal candidiasis

FIRST LINE TREATMENT

Vaginal candidiasis

Antifungal agent	Dose	Frequency	Route	Duration
Fluconazole	100mg	Single dose	PO	Single dose
OR				
Miconazole cream/pessaries	200mg	Once a day	Vaginal	3 days
OR				
Clotrimazole cream/pessaries	100mg	Twice daily	Vaginal	3 days

SECOND LINE TREATMENT

Vaginal candidiasis

Antifungal agent	Dose	Frequency	Route	Duration
Ketoconazole	200mg	BID	PO	3 days
OR				
Ketoconazole	200mg	OD	PO	7 days

3. Oesophageal candidiasis

FIRST LINE TREATMENT

Oesophageal thrush

Antifungal agent	Dose	Frequency	Route	Duration
Fluconazole	200mg to 400mg	OD	PO	14-21 days

SECOND LINE TREATMENT**Oesophageal thrush**

Antifungal agent	Dose	Frequency	Route	Duration
Ketoconazole	200mg-400mg	BID	PO	2-3 weeks
OR				
Itraconazole	200mg	OD	PO	2-3 weeks
OR				
Amphotericin B	0.3-0.5mg/kg	OD	IV	2-3 weeks

2.3 CRYPTOCOCCOSIS

Systemic mycoses such as cryptococcosis probably cause up to 10% of all HIV-associated deaths worldwide. Cryptococcosis most often appears as

- meningitis,
- occasionally as pulmonary or
- disseminated disease.

Cryptococcal meningitis is the most frequent systemic fungal infection in HIV-infected persons. Patients present with headache, fever, neck stiffness, and may be comatose. Commonly fever is absent in patients with cryptococcal meningitis. Without treatment, life expectancy is probably less than a month.

Diagnosis

Cryptococcosis is relatively easy to diagnose. The centrifuged deposit of the cerebrospinal fluid is examined microscopically after a drop of India skin is added. The yeasts are seen as organisms surrounded by a thick capsule.

Treatment

The treatment of cryptococcal meningitis is summarised in the tables below. Note that lifelong secondary chemoprophylaxis is necessary and this may be achieved with fluconazole 200mg orally daily for life. Alternate long term secondary prophylaxis may be achieved with itraconazole 200mg orally daily for life.

FIRST LINE TREATMENT**Cryptococcal meningitis**

Antifungal agent	Dose	Frequency	Route	Duration
Amphotericin B	0.7mg/kg	OD	IV	14 days
PLUS				
5-flucytosine	15-25mg/kg	QID	PO	14 days
THEN				
Fluconazole	400mg	OD	PO	8 weeks
THEN				
Fluconazole	200mg	OD	PO	For life

2.4 HISTOPLASMOSIS

This infection is caused by *Histoplasma capsulatum*, a fungus that can cause an acute or chronic illness. Intact cell mediated immunity is essential for preventing its dissemination. Reactivation of previous infection as well as acquisition of new infection can lead to dissemination. Infection occurs by inhalation of spores. The outcome of exposure depends on immune status of host as well as size of inoculum. The acute illness is influenza-like with fever, anorexia, arthralgia, myalgia, a dry cough and chest pain. Dissemination occurs soon after initial infection in immunosuppressed hosts who develop weight loss, chest symptoms, liver, spleen and lymph node enlargement and oral and skin lesions. The skin lesions may be follicular, maculopapular, pustular, erythematous, nodular or papulo-necrotic. While buccal lesions may be ulcers, nodules, or perforated palate.

Diagnosis

The diagnosis is made on clinical grounds and is confirmed on fungal cultures or histological examination of biopsied tissues. A chest x-ray in the acute illness may show hilar lymphadenopathy, scattered infiltrates and lower lobe nodules. Blood and skin tests have been developed for the diagnosis of histoplasmosis but these are not readily available.

Treatment

Acute histoplasmosis is self-limiting with normal immunity and does not require treatment. Immunosuppressed patients may be treated as follows:

FIRST LINE TREATMENT**Histoplasmosis**

Antifungal agent	Dose	Frequency	Route	Duration
Amphotericin B	0.7-1mg/kg	OD	IV	3-14 days
THEN				
Itraconazole	200mg	BID	PO	Long term

Long-term secondary prophylaxis may be achieved with itraconazole or fluconazole 200mg orally daily for life.

2.5 MICROSPORIDIOSIS

Microsporidia are intracellular protozoan parasites. There are over 1200 species of microsporidia, though human disease is caused by about 14 species. The pathogens produce resistant spores and at least three species that infect humans are found in domestic animals.

These include,

- **Encephalitozoon cuniculi**
- **Encephalitozoon intestinalis**
- **Encephalitozoon bieneusi**

Infection occurs with the ingestion of spores. The infection is an opportunistic disease, occurring mainly in immunocompromised patients. The clinical manifestations of microsporidiosis vary according to the causal species with diarrhoea being the most common manifestation. Infections of the eyes, respiratory tract, gall bladder, genitourinary tract and muscles have also been described.

Diagnosis

The diagnosis is made on finding the spores in stool smears stained by the Chromotrope 2R method.

Treatment

Albendazole has been found to be effective in treating ocular and intestinal infections. In

addition for ocular infection, topical fumagillin is recommended.

Important points to remember

- Fungal infections occur commonly in immunosuppressed persons
- The incidence of fungal opportunistic infections in persons with HIV infection increases as the cell mediated immunity decreases
- The type of fungal infections that occur varies geographically
- Candidial infections are probably the commonest fungal infections seen in HIV infected individuals
- Pneumocystis pneumonia (PCP) and cryptococcal meningitis are life threatening fungal infections and may be treated adequately in most patients but recurrences commonly occur and secondary prophylaxis with appropriate antimicrobial agents is necessary
- PCP and cryptococcal meningitis are common causes of death in HIV infected persons

2.6 CRYPTOSPORIDIOSIS

Cryptosporidiosis is a diarrhoeal disease caused by a *Cryptosporidium parvum*. It can live in the intestine of humans and animals and is passed in the stool of an infected person or animal. The parasite can form cysts allowing it to survive outside the body for long periods of time and makes it resistant to chlorine disinfection. Cryptosporidiosis is a common cause of waterborne disease. The organisms cause a secretory diarrhoea and malabsorption. Infection may ascend from the intestine to the biliary tree resulting in cholangitis

Symptoms include diarrhoea, abdominal pain with mild fever. The infection may remain completely asymptomatic. Symptoms usually start 2 to 10 days after infection and in immunocompetent hosts symptoms last about 2 weeks. The organisms (cysts) may be found in soil, food, and water, and on surfaces contaminated with faeces of infected persons.

Infected persons pass millions of cysts in the faeces. HIV infected persons who become infected develop repeated bouts of diarrhoea and a severe chronic illness and wasting. Infection is easily transmitted to family members of infected patients. Cholangitis, cholecystitis, hepatitis, pancreatitis and respiratory tract infections may also occur.

Diagnosis

The diagnosis is made on finding the organisms in stool smears stained by the modified acid fast staining method.

Treatment

HIV-infected persons should be educated and counseled about the ways that *Cryptosporidium* can be transmitted. Modes of transmission include having direct contact with infected adults and children, and infected animals; drinking contaminated water; and eating contaminated food. HIV-infected persons should avoid contact with human and animal feces. They should be advised to wash their hands after contact with human faeces (e.g., napkin changing), after handling pets, and after gardening or contact with soil. Supportive treatment is with oral rehydration fluid and codeine or loperamide. Drinking boiled water is advisable.

Recovery from cryptosporidiosis depends on the immune status. With effective antiretroviral therapy the incidence of infection has been reduced. Antiretroviral therapy usually results in a good response with session of the chronic diarrhea. The following may be used in treating the infection:

RECOMMENDED TREATMENT				
Antimicrobial agent	Dose	Frequency	Route	Duration
Paromomycin	1g	BID	PO	4 weeks
PLUS				
Azithromycin	600mg	OD	PO	4 weeks

Activity 2.3

This is an individual exercise

How would you assess dehydration in an adult?

There will be a discussion when this exercise has been completed