National HIV/AIDS
Clinical Care
A Reference Guide for Physicians
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Ministry of Health & Population
National AIDS Program
Arab Republic of Egypt

National HIV/AIDS Clinical Care

A Reference Guide for Physicians
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The upgrading of health services offered to the Egyptian people for the care and treatment of individuals with the Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) is a major priority area for the Ministry of Health and Population (MOHP).

Due to the debilitating effects of AIDS, early care and treatment is imperative to reduce the physical, psychological and economic tolls of this disease. Early detection of HIV can prolong the duration and quality of life of these individuals with promising new treatment options.

I would like to take this opportunity to acknowledge the MOHP staff and all of the individuals who have contributed to the development of the National HIV/AIDS Clinical Care.

Special gratitude is due to:

• The National AIDS Program (NAP) for their on-going supportive efforts and valuable insight.
• The reviewers and editors for their technical cooperation in developing and refining the guidelines.

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• The United Stated Agency for International Development (USAID)
• Family Health International’s Implementing AIDS Prevention and Care (IMPACT) Project in Egypt.

I look forward to the success of these services in maintaining the good health of all Egyptians.

Sincerely,

Dr. Nasr El Sayed
First Undersecretary
Ministry of Health and Population
# Acronyms

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<th>Definition</th>
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<tbody>
<tr>
<td>ABC</td>
<td>Abacavir</td>
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<tr>
<td>ADC</td>
<td>AIDS Dementia Complex</td>
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<td>AFB</td>
<td>Acid-Fast Bacilli</td>
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<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
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<tr>
<td>Anti- HAV</td>
<td>Hepatitis A Antibody</td>
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<td>Anti- HBC</td>
<td>Hepatitis B Core Antibody</td>
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<tr>
<td>Anti- HBs</td>
<td>Hepatitis B Surface Antibody</td>
</tr>
<tr>
<td>Anti- HCV</td>
<td>Hepatitis C Antibody</td>
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<tr>
<td>ART</td>
<td>Antiretroviral Therapy</td>
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<tr>
<td>ARV</td>
<td>Antiretroviral</td>
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<tr>
<td>AZT</td>
<td>Zidovudine</td>
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<tr>
<td>CBC</td>
<td>Complete Blood Count</td>
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<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
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<tr>
<td>CNS</td>
<td>Central Nervous System</td>
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<td>CSF</td>
<td>Cerebrospinal fluid</td>
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<td>C&amp;S</td>
<td>Culture and Sensitivity</td>
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<td>CSWs</td>
<td>Commercial Sex Workers</td>
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<td>CT</td>
<td>Computerized Tomography</td>
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<tr>
<td>d4T</td>
<td>Stavudine</td>
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<tr>
<td>ddI</td>
<td>Didanosine</td>
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<td>DNA</td>
<td>Deoxyribonucleic Acid</td>
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<td>DS</td>
<td>Double Strength</td>
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<td>Efavirenz</td>
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<td>ELISA</td>
<td>Enzyme linked Immunosorbent Assay</td>
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<tr>
<td>GI</td>
<td>Gastrointestinal</td>
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<tr>
<td>HAART</td>
<td>Highly Active Antiretroviral Therapy</td>
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<tr>
<td>Hb</td>
<td>Hemoglobin</td>
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<td>HBsAg</td>
<td>Hepatitis B Surface Antigen</td>
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<td>HBV</td>
<td>Hepatitis B Virus</td>
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<td>HCV</td>
<td>Hepatitis C virus</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>HCW</td>
<td>Health Care Worker</td>
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<tr>
<td>HIV</td>
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<td>Herpes Simplex Virus</td>
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<td>IDUs</td>
<td>Injecting Drug Users</td>
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<td>IM</td>
<td>Intramuscular</td>
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<td>IMPACT</td>
<td>Implementing AIDS Prevention and Care Project</td>
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<td>INH</td>
<td>Isoniazid</td>
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<td>IV</td>
<td>Intravenous</td>
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<td>KOH</td>
<td>Potassium Hydroxide</td>
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<tr>
<td>KS</td>
<td>Kaposi’s sarcoma</td>
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<td>LGV</td>
<td>Lymphogranuloma venereum</td>
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<td>LPV/r</td>
<td>Lopinavir/Ritonavir</td>
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<td>MAC</td>
<td>Mycobacterium Avium Complex</td>
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<tr>
<td>MOHP</td>
<td>Ministry of Health and Population</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>MSM</td>
<td>Men Who Have Sex with Men</td>
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<td>MTCT</td>
<td>Mother-to-Child Transmission</td>
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<td>NAP</td>
<td>National AIDS Program</td>
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<td>NFV</td>
<td>Nelfinavir</td>
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<td>NGU</td>
<td>Non-gonococcal Urethritis</td>
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<tr>
<td>NNRTIs</td>
<td>Non Nucleoside Reverse Transcriptase Inhibitors</td>
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<td>Nucleoside Reverse Transcriptase Inhibitors</td>
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<tr>
<td>NtRTIs</td>
<td>Nucleotide Reverse Transcriptase Inhibitors</td>
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<td>Non-steroidal Anti-inflammatory Drug</td>
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<td>NVP</td>
<td>Nevirapine</td>
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<tr>
<td>OIs</td>
<td>Opportunistic Infections</td>
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<tr>
<td>ORS</td>
<td>Oral Rehydration Salts</td>
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<td>PAP</td>
<td>Papanicolaou Smear</td>
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<td>PCP</td>
<td>Pneumocystis Carinii Pneumonia</td>
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<tr>
<td>PCR</td>
<td>Polymerase Chain Reaction</td>
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<tr>
<td>PEP</td>
<td>Post-Exposure Prophylaxis</td>
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</table>
PGL: Persistent Generalized Lymphadenopathy
PID: Pelvic Inflammatory Disease
PIs: Protease inhibitors
PLHA: People Living with HIV/AIDS
PML: Progressive Multifocal Leukoencephalopathy
PMTCT: Prevention of Mother-to-Child Transmission
PO$_2$: Partial Pressure of Oxygen
PPD: Purified Protein Derivative of Tuberculin Testing
PZA: Pyrazinamide
RBT: Rifabutin
RIBA: Recombinant Immunoblot Assay
RIF: Rifampin
RNA: Ribonucleic Acid
RPR: Rapid Plasma Reagin
RTV: Ritonavir
SIV: Simian Immunodeficiency Virus
SQV: Saquinavir
STIs: Sexually Transmitted Infections
TB: Tuberculosis
TDF: Tenofovir
TENS: Transcutaneous Electrical Nerve Stimulation
TLC: Total Lymphocytic Count
TMP/SMX: Trimethoprim/Sulfamethoxazole
TPHA: Treponema Pallidum Hemagglutination Assay
3TC: Lamivudine
UGI: Upper Gastrointestinal
USAID: United States Agency for International Development
VCT: Voluntary Counseling and Testing
VDRL: Venereal Disease Research Laboratory
VZIG: Varicella Zoster Immune Globulin
VZV: Varicella Zoster Virus
WBCs: White Blood Cells
WHO: World Health Organization
ZDV, AZT: Zidovudine
ZN: Ziehl Neelsen Stain
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Introduction

Despite dramatic improvements in understanding the epidemiology of HIV/AIDS, the natural history of the disease and increased production of effective antiretroviral therapies, the number of individuals infected with HIV/AIDS continues to grow, initiating severe economic and social repercussions as it strikes at the most economically productive age groups and cuts across all income levels.

More than 40 million people worldwide are infected with HIV/AIDS. This number is expected to increase with the advent of Voluntary Counseling and Testing (VCT) services and increased national surveillance. People requiring care and support are thus on the rise. Accordingly, HIV/AIDS may soon become a public health problem of primary importance.

These guidelines have been developed to share collective expertise, to reassure, inform and support physicians to face this epidemic. With accurate information, appropriate management can be designed to safely and competently care and treat persons suffering from Acquired Immunodeficiency Syndrome (AIDS).

The purpose of this guide is to highlight strategies for managing the health problems of AIDS patients at the different levels of care provision, in order to ensure a continuum of comprehensive care. A strategy is proposed for each level of care, as well as the necessary equipment and drugs for responding to the health needs of people living with HIV/AIDS (PLHA).
Background

Acquired Immunodeficiency Syndrome (AIDS) is a severe immunological disorder caused by the retrovirus Human Immunodeficiency Virus (HIV), resulting in a defect in cell-mediated immune response that is manifested by increased susceptibility to opportunistic infections and to certain rare cancers. It came to wide public attention in mid-1981, after clusters of deaths from Pneumocystis carinii pneumonia (PCP) and Kaposi’s sarcoma (KS) had been reported in young, previously healthy homosexual men in New York City, Los Angeles, and San Francisco. Previously, PCP and a very mild form of KS had only been reported in people who were immuno-compromised and in older men of European or Mediterranean descent respectively. In addition, KS affecting these young homosexual men was a very different form. In the early 1980’s, PCP incidence in the United States was so low that the drug used to treat it, Pentamidine, was only available through the Centers for Disease Control and Prevention (CDC) in Atlanta. The sudden rise in orders for Pentamidine alerted officials to the problem. Reports of similar findings came quickly from France, the Caribbean, and Central America.

In the United States, the disease was first called gay cancer, and then gay-related immune deficiency, because it was homosexual men who first exhibited the characteristic symptoms. In some areas in Africa, the disease was called “Slim” or “Slim Disease” because of the profound wasting and the association of death with progressive weight loss and diarrhea.

Etiology

Two types of HIV are recognized, HIV-1 and HIV-2. Worldwide, the predominant virus is HIV-1. Transmission of both types appears to cause clinically indistinguishable AIDS. However, HIV-2 is transmitted less easily, and the period between initial infection and illness is longer in the case of HIV-2. It is widely believed that the HIV infection resulted from an animal to human (zoonotic) transmission of HIV-1 that is closely related to the simian immunodeficiency virus (SIV), which infects chimpanzees. HIV-2, which is prevalent in West Africa and has spread to Europe and India, is almost indistinguishable from the SIV that infects sooty mangabey monkeys.

HIV-1

Three groups of HIV-1 have been identified: M, N and O. Because of its high rate of replication, HIV-1 mutates rapidly into subtypes. There are many genetically distinct subtypes of HIV-1 within the major group (group M), containing subtypes A to K. In addition, group O (Outliers) contains a distinct group of very heterogeneous viruses. These subtypes are unevenly distributed throughout the world. A person can be co-infected with different subtypes. Currently subtype C accounts for more than half of all new HIV infections worldwide.
HIV-2

HIV-2 has four subtypes (A, B, C and D) and is confined primarily to West Africa. Compared to HIV-1, HIV-2 is less transmissible, is associated with a lower viral burden, and has a slower rate of both CD4 cell decline and clinical progression.

Structural Composition and Genomic Organization of the HIV Virus

HIV consists of an inner nucleoprotein core surrounded by an outer envelope. The envelope is composed of a lipid bilayer (gp 120 and gp 41). The outer membrane proteins are primarily responsible for mediating binding to the CD4 cells and chemokine receptors, which is an essential step to membrane fusion and resultant infectivity.

The viral core is comprised of two copies of single-stranded genomic ribonucleic acid (RNA) and several proteins involved in the process of viral replication. These proteins include the p24 capsid protein, the p17 matrix protein, and the p6 and p7 nucleocapsid proteins. The matrix protein probably plays an important role in maintaining structural integrity of the virus. The capsid protein forms a shell around the genomic material. Within this shell, the nucleocapsid proteins are found, along with several enzymes that participate in the replication of the virus, including reverse transcriptase, integrase, and protease.

Figure 1: The Human Immunodeficiency Virus
HIV Lifecycle

HIV uses infected host cells to produce multiple copies of new HIV and is continuously using new host cells to replicate itself. As many as ten million viruses are produced daily. HIV can infect a variety of cells such as CD4 helper T-cells, macrophages and dendritic cells. After exposure and within the first 24 hours, HIV first attacks dendritic cells in the mucous membranes and skin. These infected cells then make their way to the lymph nodes and eventually to the peripheral blood within five days after exposure, where viral replication becomes very rapid. The HIV lifecycle can be divided into the following phases:

**Binding and entry:** The envelope proteins gp 120 and gp 41 bind to CD4 cell receptors and co-receptors. This binding results in the fusion of the HIV membrane with the CD4 cell membrane. The HIV membrane and the envelope proteins stay on the outside of the CD4 cell while the core of the HIV enters inside it. CD4 cell enzymes interact with the core of the HIV and stimulate the release of viral RNA and the viral enzymes: reverse transcriptase, integrase, and protease.

**Reverse transcription:** The HIV RNA must be converted to deoxyribonucleic acid (DNA) before it can be incorporated into the DNA of the CD4 cell. This incorporation is required for the virus to multiply. The conversion of HIV RNA to DNA is known as the process of reverse transcription and is mediated by the HIV enzyme, reverse transcriptase. The result is the production of a single strand of DNA from the viral RNA. The single strand of this new DNA then undergoes replication into double-stranded HIV DNA.

**Integration:** Once reverse transcription has occurred, the viral DNA can now enter the nucleus of the CD4 cell. The viral enzyme, integrase, then inserts the viral DNA into the CD4 cell’s DNA. This process is known as integration. The CD4 cell has now been changed into a “machine” used to produce more HIV.

**Replication:** The new DNA, which has been formed by the integration of the viral DNA into the CD4 cell, causes the production of messenger DNA that initiates the synthesis of HIV proteins.

**Budding:** The HIV proteins and viral RNA, all the components needed to make a new virus, gather at the CD4 cell membrane to form new viruses. These new viruses push through the different parts of the cell wall by budding. Many viruses can push through the wall of one CD4 cell. These new viruses leave the CD4 cell and contain all the components necessary to infect other CD4 cells.

**Maturation:** The new virus has all the components necessary to infect other CD4 cells but cannot do so until it undergoes a maturation process. During this process, the HIV protease enzyme cuts the long HIV proteins of the virus into smaller functional units that then reassemble to form a mature virus. The virus is now ready to infect other cells.
Background

Figure 2: The HIV Lifecycle

Modes of HIV Transmission

HIV has been isolated from all body fluids yet only blood, semen, vaginal fluid and breast milk play a role in infection. Tears, saliva, sweat, stool and urine are considered non-infectious.

There are only three modes of HIV transmission:

Sexual transmission: This is the predominant mode of HIV transmission worldwide. Unprotected sexual contact (i.e., without condoms) with an infected person can transmit HIV. Risk of infection increases in the following circumstances:

- Multiple partners
- Presence of other sexually transmitted infections (STIs)
- Penetrative anal sex

Parenteral transmission: Transmission through infected blood as in:

- Subcutaneous, intravenous, intramuscular, and intrasternal injections using needles contaminated with HIV infected blood (e.g., intravenous drug use and needle stick injuries)
- Tattooing, ear piercing and/or circumcision, using HIV contaminated equipment
- Invasive procedures using HIV contaminated instruments
- Transfusions with infected blood and blood products
**Perinatal transmission:** From an HIV positive mother to her baby inutero, during delivery and/or postpartum through breastfeeding.

HIV is not transmitted by casual contact with an infected person such as:

- Kissing, hugging, touching and shaking hands
- Sharing plates, spoons or other utensils
- Coughing and sneezing
- Contact with toilet seats
- Insect or animal bites
- Casual contact at work, school or on the street

**Factors Affecting Risk of Transmission**

There are several factors that impact the likelihood of viral transmission. These factors include:

**Factors that increase risk of transmission**

- Infectiousness of the host: carriers of HIV have a high viral load during the initial stages of infection and at the more advanced stages
- Inflammation or disruption of genital or rectal mucosa
- Lack of circumcision in heterosexual men
- Sex during menstruation
- Presence of an ulcerative or non-ulcerative STI
- Viral properties: based on the different types of HIV
- Socioeconomic factors may facilitate the transmission of HIV, such as social mobility, stigma and denial, war, drug use, alcohol consumption, poverty, etc.

**Factors that decrease risk of transmission**

- Correct and consistent use of latex condoms
- Antiretroviral therapy (ART) may decrease, but not eliminate, the risk of HIV transmission; ART has been shown to reduce vertical transmission from a mother-to-child by more than 50% when administered late in pregnancy or during labor
The Natural Course of HIV Disease in Adults

The following three phases are distinguishable during the natural course of HIV infection:

1. Early infection and sero-conversion (1-3 months): At this stage, the viral load peaks. The number of CD4 cells drops. Antibodies are not yet present. The person might, therefore, be highly infective, while the HIV antibody test is negative.

2. Chronic phase of about 8-10 years: During this period most patients have no symptoms. Some curable infections may occur during this stage. Some of these illnesses may be life-threatening if they are not adequately treated.

3. Severe immunodeficiency and AIDS: The virus gains the upper hand when the CD4 cell level drops below 200 cells/mm$^3$ of blood. Severe opportunistic infections and other complications usually occur. The clinical diagnosis of AIDS is usually made at this final stage.
Diagnosis of HIV/AIDS

Clinical and Laboratory Staging of HIV/AIDS

In countries with limited laboratory facilities, patients are diagnosed clinically based on the World Health Organization (WHO) case definitions for HIV/AIDS that include major and minor signs and symptoms. The disease is suspected in the presence of at least two major signs and one minor sign.

**Major signs include:**
- Weight loss of 10% or more of body weight
- Prolonged fever for one month or more
- Chronic persistent diarrhea for more than one month

**Minor signs include:**
- Oro-pharyngeal candidiasis
- Persistent cough for more than one month
- Generalized pruritic skin infection
- Generalized lymphadenopathy
- History of herpes zoster
- Chronic progressive disseminated herpes simplex infection

The presence of either generalized KS or cryptoccocal meningitis is enough for the diagnosis of AIDS.

WHO has developed a clinical staging system (Table 1) and an improved clinical classification system which combines clinical and laboratory data, including CD4 count and total lymphocytic count (Table 2). There is a correlation between CD4 cell counts and the different infectious and non-infectious complications. Based on this correlation, the clinical staging system may be useful to assess the progress of the disease in the absence of facilities for CD4 testing.
### Table 1: Clinical Staging System

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<tr>
<td>• Asymptomatic infection</td>
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<tr>
<td>• Persistent generalized lymphadenopathy</td>
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<tr>
<td>• Acute retroviral infection</td>
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<td>• Performance scale 1: asymptomatic, normal activity</td>
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<tr>
<th>Clinical Stage 2</th>
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<tr>
<td>• Unintentional weight loss, &lt; 10% of body weight</td>
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<tr>
<td>• Minor mucocutaneous manifestations (e.g., seborrheic dermatitis, prurigo, fungal nail infections, oropharyngeal ulcerations, angular cheilitis)</td>
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<tr>
<td>• Herpes zoster within the previous 5 years</td>
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<tr>
<td>• Recurrent upper respiratory tract infections (e.g., bacterial sinusitis) and/or</td>
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<tr>
<td>• Performance scale 2: symptoms, but nearly fully ambulatory</td>
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<th>Clinical Stage 3</th>
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<tr>
<td>• Unintentional weight loss, &gt; 10% of body weight</td>
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<tr>
<td>• Chronic diarrhea &gt; 1 month</td>
</tr>
<tr>
<td>• Prolonged fever (intermittent or constant) &gt; 1 month</td>
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<tr>
<td>• Oral candidiasis (erythematous or pseudomembranous)</td>
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<tr>
<td>• Oral hairy leukoplakia</td>
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<tr>
<td>• Pulmonary tuberculosis (typical or atypical), within the previous year</td>
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<tr>
<td>• Severe bacterial infections (e.g., pneumonia, pyomyositis)</td>
</tr>
<tr>
<td>• Vulvovaginal candidiasis, chronic (&gt; 1 month) or poorly responsive to therapy and/or</td>
</tr>
<tr>
<td>• Performance scale 3: in bed &lt; 50% of normal daytime, during previous month</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Stage 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>• HIV wasting syndrome</td>
</tr>
<tr>
<td>• PCP</td>
</tr>
<tr>
<td>• Toxoplasmosis of the brain</td>
</tr>
<tr>
<td>• Cryptosporidiosis with diarrhea &gt; 1 month</td>
</tr>
<tr>
<td>• Isosporiasis with diarrhea &gt; 1 month</td>
</tr>
<tr>
<td>• Cryptococcosis, extrapulmonary</td>
</tr>
<tr>
<td>• Cytomegalovirus (CMV) disease of an organ other than liver, spleen or lymph node</td>
</tr>
<tr>
<td>• Herpes simplex virus (HSV) infection, mucocutaneous (&gt; 1 month) or visceral (any duration)</td>
</tr>
</tbody>
</table>
Clinical Stage 4 (cont.)

- Progressive multifocal leukoencephalopathy
- Any disseminated endemic mycosis (e.g., 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

and/or

- Performance scale 4: in bed > 50% of normal daytime during previous month

Any of the infections or clinical manifestations listed in Table 1 may be an indication for HIV testing. Although symptomatic HIV infections may sometimes be recognized clinically (in particular when the presence of opportunistic infections has been confirmed), HIV testing should be done whenever possible to confirm the clinical suspicion.

Table 2: Improved Classification Combining Clinical, CD4 Count and Total Lymphocytic Count

<table>
<thead>
<tr>
<th>Laboratory Component</th>
<th>Clinical Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD4 Cell Count (%)</td>
</tr>
<tr>
<td>A</td>
<td>≥500 (&gt;29%)</td>
</tr>
<tr>
<td>B</td>
<td>200-499 (14-28%)</td>
</tr>
<tr>
<td>C</td>
<td>&lt;200 (14%)</td>
</tr>
</tbody>
</table>

*Highlighted areas refer to progression to AIDS and should be treated with antiretroviral (ARV) drugs
Clinical and laboratory staging are important determinants for initiation of antiretroviral treatment; Table 2 is used to decide the initiation of ARV treatment. A combination of clinical stages and CD4 count and/or total lymphocytic count (TLC) is the decisive factor in starting ART. According to the WHO clinical HIV staging system, the initiation of ART depends on the clinical stage and the laboratory investigation, thus any patient suffering from clinical manifestations of the 4th stage should start ART regardless of CD4 count and TLC. On the other hand if the patient is asymptomatic, but the CD4 count is < 200/mm$^3$ he should also start ART.

**Laboratory Diagnosis of HIV**

HIV infection is usually diagnosed by serological tests that detect viral antibodies. Infection may also be detected by nucleic-acid based assays that either measure the number of copies of the virus in plasma by RNA PCR (Polymerase Chain Reaction) or detect the virus in the cells by DNA PCR.

Informed consent together with pre and post test counseling are essential for performing HIV serologic tests and should be obtained each time the test is offered.

**ELISA (enzyme-linked immunosorbsent assay)**

This is the most common test for HIV antibody detection. It is performed on a patient’s serum to identify HIV antibodies. Samples yielding a negative result are reported as negative provided that they are taken after the window period; the time between initial infection with HIV and when the body builds a measurable antibody response to it. ELISA tests are very sensitive but not always specific. In other words, other illnesses besides HIV can produce a positive test result, such as autoimmune diseases, certain viral infections, syphilis or hematological malignancies. Pregnancy is also thought to cause a false positive ELISA. Usually another test is used to confirm positive results yielded by ELISA.

**Western blot test**

Western blot test is used as a confirmatory test for a positive (reactive) ELISA. It detects antibodies to a number of specific HIV proteins and is considered to be very specific for HIV. Samples yielding a negative result are reported as negative provided that samples are taken after the window period. Alternatively, two different types of ELISA should be used for confirmation.

**Rapid tests**

There are various tests available that provide results in about 10 minutes. Their sensitivity approaches 100%; specificity is > 99% — analogous to ELISA screening tests. Reported negative tests are considered definitely negative; positive results should be confirmed with standard serology. Rapid tests are useful in situations where immediate results are recommended for management decisions, such as cases of occupational exposure and when there is doubt that clients may not return to receive their test results at testing sites, including VCT.
DNA PCR
This is a qualitative test for detection of an intracellular virus used primarily for early viral infection, neonatal infection and indeterminate serology.

RNA PCR (viral load)
Plasma RNA is routinely used to monitor the course and treatment of HIV infection. These tests report the number of copies of virus per milliliter of plasma.

Viral isolation
Qualitative or quantitative cultures are used for diagnosis of neonatal HIV infection, and for more in-depth viral analysis. The procedure is expensive and labor intensive.

HIV Testing in Egypt

HIV testing in Egypt takes place as follows:

- Voluntary Counseling and Testing (VCT) for clients who wish to know their own serostatus and do so voluntarily and with informed consent
- Diagnosis of individuals who present to care facilities with clinical indications of AIDS
- Screening of all donated blood
- Testing of anonymous sera for surveillance purposes amongst subpopulations (e.g., pregnant women)
- Mandatory testing of individuals who require certification for:
  - Work/study abroad programs in countries requiring certification of HIV serostatus
  - Work/study in Egypt (foreigners)

Mandatory testing is not performed in Egypt under any circumstances other than those listed above. It should also be noted that any individual has the freedom to refuse being tested under these categories whilst being aware of the implications (e.g., denial of access to work/study abroad). Test results are provided face to face during post-test counseling sessions.

Issuing of HIV test results

- Test results are provided by a counselor during a post-test counseling session. As much as possible, this is done by the same counselor who provided the pre-test counseling
- Results must be issued face-to-face, and not over the phone or through other persons
- All clients are given the opportunity to view their test result documents
- To avoid misuse of the test results, the documents should remain the property of the testing site
Target group for VCT services
Clients who are most likely to benefit from VCT services, and who should be actively targeted through service promotion and outreach include:

- Clients with known sexual exposure or needle sharing with an HIV infected person
- Clients known to be at risk of HIV infection through past or present practices or potential exposure, e.g., injecting drug users (IDUs), commercial sex workers (CSWs) and men who have sex with men (MSM)
- Clients who have clinical symptoms suggesting HIV infection (e.g., fever, illness of unknown origin, opportunistic infections including active tuberculosis without known reason for immune suppression)
- Clients with increased risk of HIV infection (e.g., having another STI or blood borne infection)
- Clients exposed to contaminated equipment

HIV testing for certification purposes
All clients requiring official certification of their HIV status should report to the Ministry of Health and Population (MOHP) Central Laboratory located at 19 El Sheikh Rehan Street, in front of the American University, Bab El Louk, Cairo, Egypt.

MOHP Protocol for HIV Testing
For diagnosis of HIV infection in Egypt, the following steps should be followed:

**Step (1):** ELISA is performed and the test result may be positive or negative:
- If test result is negative: declare as negative
- If test result is positive: refer to next step

**Step (2):** ELISA is performed (using another type of kit) if the first ELISA is reactive:
- If test result is negative: declare as negative
- If test result is positive: report as suspected case and refer to step three

**Step (3):** Western blot is performed as a confirmatory test if the 2nd ELISA is reactive:
- If Western blot is negative: report as negative case
- If Western blot is positive: report as confirmed positive case
- If the test result of Western blot is indeterminate, another blood sample is withdrawn one month later and tested for confirmation using Western blot

If a rapid test is used and is positive, then follow the above steps starting with the first ELISA screening.
Figure 3: MOHP Protocol for HIV Testing

* If still indeterminate, repeat after 6 months then after 12 months. If still indeterminate report as negative
HIV Prevention and Control

Addressing Modes of Infection

Prevention of sexual transmission of HIV

The key factors that affect the transmission of HIV are:

- Multiple sexual partners
- Unprotected sexual intercourse
- Presence of STIs and poor access to STI treatment
- Social vulnerability of women and young people
- Social, economic and political instability of the community
- Lack of knowledge and unknown serostatus

Accordingly, ways to reduce transmission of HIV include:

- Sexual abstinence
- Reliance on one sexual partner
- Delayed onset of sex, especially of adolescents
- Recognition of the symptoms of STIs
- Management of STIs
- Promotion of VCT services
- Sex education: safer sex practices, including consistent, proper use of condoms

Proper use of condoms

- Use a new condom for each act of vaginal, anal or oral intercourse.
- Put on the condom as soon as erection occurs and before any vaginal, anal or oral contact with penis.
- Hold the tip of the condom and unroll it on the erect penis, leaving space at the tip of the condom, yet ensuring that no air is trapped in the tip of the condom.
- Withdraw from the partner immediately after ejaculation, holding the condom firmly at the base of the penis to keep it from slipping off.
**Prevention of parenteral HIV infection**

Various precautionary measures should be taken to reduce the risk of HIV transmission via contaminated needles, blood and blood products. These precautions include:

- Enhanced blood safety through routine testing of all blood units, under the supervision of the MOHP
- Prohibit the importing of blood
- Avoid blood transfusions except in cases of emergency
- Provide health education for people with risk behaviors and advise them to abstain from donating blood
- Strictly avoid professional blood donation, as this increases the likelihood of individuals not disclosing essential health information
- Encourage auto transfusion
- Implement infection control programs in all health settings
- Use disposable syringes only once
- Provide full clinical examinations for all blood donors and exclude any individual suspected of being an unsafe blood donor
- Exclusion of those blood donors who are undergoing treatment for an STI

**Prevention of mother-to-child transmission**

Before the use of ART, mother-to-child transmission ranged between 17-35%. At the present time, this rate has fallen to less than 8% with the use of ART and proper precautions.

The risk of vertical transmission increases with:

- High maternal HIV viral load
- Older mothers
- Having unprotected sex during pregnancy
- Use of illegal drugs
- Premature delivery
- Premature rupture of membranes
- Natural delivery versus a cesarean delivery
- Prolonged labor
- Presence of cervical or vaginal infections
- Breast-feeding
Promoting the prevention of mother-to-child transmission (PMTCT) includes:

- Encouraging VCT of all couples before marriage
- Encouraging HIV infected mothers to use a contraceptive method to avoid pregnancy
- Providing health education for HIV infected pregnant women, to avoid HIV transmission through breast-feeding
- Preventing HIV perinatal transmission with the provision of ARVs

The following ARV therapy is recommended for the PMTCT:

**Nevirapine:**

- Single 200 mg oral dose at onset of labor for mother
- Single 2 mg/kg oral dose at age 48-72 hours for infant

**HIV Counseling and Testing**

HIV Counseling and Testing has been proven to play an essential role in HIV prevention.

**Benefits of HIV testing**

Various benefits to knowing one’s HIV status do exist. Knowledge of HIV serostatus is important in preventing the transmission of HIV onto others and in seeking medical care and treatment for HIV/AIDS. Furthermore, identifying women who are infected with HIV is essential in preventing the vertical transmission of HIV from mother-to-child. All testing for HIV should be accompanied with counseling, as this is an ideal time to educate individuals and couples on the facts of HIV/AIDS and to enable them to make informed decisions regarding their future.

**Goals of counseling**

- To educate people on how HIV is transmitted and how it can be prevented
- To provide risk reduction strategies for all persons
- To identify HIV infected individuals and provide them with proper clinical, psychological and social care and support
- To provide counseling for HIV positive persons on how to prevent potential transmission onto others and on how to live a productive and healthy life

**Components of HIV counseling**

Counseling for HIV is broken down into two components: pre-test counseling and post-test counseling.
Pre-test counseling
Pre-test counseling, which occurs before a client’s blood is tested for HIV antibodies, is conducted to:

- Determine a client’s understanding of HIV transmission, HIV prevention and the natural course of the disease
- Provide information on HIV/AIDS
- Discuss reasons for HIV testing and client’s risk of infection
- Discuss meaning of positive, negative and indeterminate test results and their implications
- Carry out a personalized risk assessment and personalized risk-reduction plan
- Discuss provisions made at the site for confidentiality
- Ensure that follow-up services are available
- Emphasize the importance of obtaining test results
- Evaluate support systems and possible reactions to stressors
- Obtain informed consent for HIV antibody testing
- Conduct condom demonstration

Post-test counseling
One aim of post-test counseling is to help clients understand and accept their test results. Post-test counseling is also a chance for counselors to help clients make choices based on their test results. Messages will differ for those who test positive and those who test negative. Below are the components of post-test counseling:

- Ensure that the client is ready to receive the result
- Disclose and interpret the test results:
  - For HIV-seronegative patients:
    - Readdress and reinforce the personalized risk-reduction plan
    - Discuss the need to repeat the test for those with recent exposure (< 3 months) or ongoing risk behavior
  - For persons with indeterminate Western Blot results:
    - Discuss prevalence and causes of indeterminate test results
    - For persons with high risk behavior, discuss the possibility of acute HIV infection and the need to repeat the test after the window period
  - For HIV-seropositive persons:
    - Differentiate between being HIV-infected and developing AIDS
    - Counsel patients that they are HIV-positive and discuss ways to avoid transmitting HIV onto others
    - Emphasize the importance of medical referrals, if necessary
    - Assess needs for psychological and social support and provide adequate referrals
    - Assess possibility of domestic violence and provide referrals
    - Encourage clients to return for follow-up services
Universal Precautions for the Prevention of HIV and Other Blood-borne Pathogens in Health Care Settings

“Universal precautions” are a simple, standard set of procedures to be used in the care of all patients at all times to minimize the risk of transmission of blood-borne viruses, including HIV.

Universal precautions used in health care settings include hand washing, use of protective clothing such as gloves, safe handling of sharp instruments, safe disposal of medical waste including sharps and decontamination of instruments and equipment.

The guiding principles for HIV infection control are that all blood, blood products and blood-contaminated materials should be assumed potentially infectious.

The main risks to health care workers (HCWs) are:

- Injury with a needle or sharp instrument which has been contaminated with infected blood
- Exposure of open wounds to infected blood (HIV is not transmitted through unbroken skin)
- Splashes of infected blood or body fluids onto the mucous membranes and/or eyes

The main risks to the patients are:

- Contaminated instruments (e.g. needles, syringes, scalpels etc.) that are reused without being adequately disinfected or sterilized
- Transfusions with contaminated blood
- Exposure of open wounds to infected blood

HCWs should be reassured that there is no risk of transmission through casual contact between people, such as sharing eating utensils or washing facilities.

Elements of Universal Precautions and Good Hygiene

**Hand washing** with soap and water. If hands are dried with a re-usable towel, the later should be washed regularly. Hand washing is particularly important after contact with body fluids or wounds.

**Gloves** should be worn for all procedures involving contact with blood or other potentially infected body fluids. If gloves are in short supply, priority should be given to procedures involving contact with blood. Gloves should be discarded after each patient. Heavy-duty gloves should be worn when materials and sharp objects are taken for disposal. Hands should be washed with soap and water routinely after the removal of gloves.
**Protective clothing** such as waterproof gowns or aprons, masks and eye shields should be worn only where exposure to large amounts of blood is likely to occur.

**Safe handling of sharps** with extreme caution. Sharps should never be passed directly from one person to another and their use should be kept to a minimum. Workers should never try to bend or break needles, nor attempt to recap needles in their sheaths, a manipulation associated with the majority of needle stick injuries. Puncture-resistant containers must be readily available for the disposal of all needles, and they should be kept close at hand and out of the reach of children. Sharps should never be thrown into ordinary waste bins or bags.

**Disposal of waste materials** All waste materials should be burnt and those that still pose a threat, such as sharps, should be buried in a deep pit (at least 30 feet from a water source).

**Cleaning and disinfection** of medical instruments between patients is essential. Special attention must be paid to instruments that are contaminated with body fluids. Disinfection and cleaning are recommended as HIV will be inactivated through boiling or using of chemical disinfectants. Non-reusable equipment such as disposable needles and syringes should not be reused. Reusable equipment should first be dismantled, cleaned, and then boiled for at least 20 minutes. For those instruments that are heat-sensitive, the following agents may be used:

- chlorine-based agents (e.g., household bleach)
- 2% glutaraldehyde
- 70% ethyl and isopropyl alcohol

**Accidents at Work**

- In case of injury with a sharp instrument, the wound should be washed thoroughly with soap and water and then covered with a waterproof dressing
- If a person receives splashes of blood or other body fluid into the mouth, the mouth should be rinsed out thoroughly with water and if the splash occurs to the eyes, they should be bathed either with saline or plain water
- Any accident should then be reported to the health officer in charge to ensure appropriate follow-up and possible treatment with post-exposure prophylaxis (see following section)

**Post-Exposure Prophylaxis**

Provision of antiretroviral drugs for post-exposure prophylaxis (PEP) for all phlebotomy staff is important in case of any potential exposure, such as needle stick injuries. The issuing of PEP should be considered after an exposure with the potential to transmit HIV, and hepatitis, based on the type of body fluid or substance involved, and the route and severity of exposure.

PEP should be started as soon as possible after potential exposure to HIV. The medications used in PEP depend on certain aspects of the exposure to HIV.
Treatment of exposure site
Immediately following exposure:

- Wash the exposed site (e.g., wound or intact skin) liberally with soap and water, but without scrubbing
- Flush exposed mucous membranes with water. If saline is available, flush eyes with saline
- Do not apply caustic agents, including antiseptics or disinfectants, to the exposed areas

Exposure report
Inform the medical officer of the exposure and complete the occupational exposure incident report form. Information to be reported includes:

- Date and time of exposure
- Exposure site(s)
- Where and how the exposure occurred
- If a sharp object was involved, include type and brand of device
- Type and amount of fluid
- Severity of exposure (e.g., depth of puncture wound)
- Exposure source:
  - Infectious status
  - If HIV infected, stage of disease, viral load, history of ART
- Counseling and post-exposure management
- Details on exposed HCW:
  - Existing medical status
  - Hepatitis B vaccine status

Evaluation of exposure
The physician will evaluate the exposure for potential transmission of HIV based upon:

Type and amount of body fluid/tissue:

- Blood
- Fluids containing blood
- Semen
- Vaginal secretions
- Cerebrospinal fluid (CSF)
- Synovial fluid
• Pleural fluid
• Peritoneal fluid
• Pericardial fluid
• Amniotic fluid

Type of exposure:
• Percutaneous injury
• Mucous membrane exposure
• Non-intact skin exposure
• Bites resulting in blood exposure

Infectious status of source:
• Presence of HIV antibody
• Presence of HBsAG
• Presence of Hepatitis C antibody (Anti-HCV)

Susceptibility of exposed person:
• Hepatitis B vaccine and response status
• HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) immune status

The exposed HCW will be offered an HIV test based on informed consent as well as pre-test and ongoing counseling as desired. The confidentiality of the exposed HCW will be maintained.

Evaluation of exposure source

If the HIV status of the source person is not known, the source person will be informed of the incident and consent obtained to perform HIV diagnostic testing.

Testing to determine HIV infection should be performed as soon as possible. A rapid HIV antibody test is recommended, accompanied by pre- and post-test counseling.

Confidentiality of the person that is the source of exposure will be maintained at all times. If the source person is negative for HIV, baseline testing or further follow-up of the exposed HCW is not necessary.

If the source person is not known, the exposure will be evaluated on the likelihood of high risk for infection and on where and under what circumstances the exposure occurred.
Management of exposure to HIV

Perform a baseline HIV test on the exposed HCW using a rapid antibody test. It is also recommended to perform a complete blood count (CBC) and liver and renal function tests.

Determine if the exposure is considered low-risk or high-risk for HIV infection.

The following situations are considered high-risk exposure:

- Exposure to a large amount of blood
- Blood coming in contact with cuts and open sores on the skin
- Blood visible on a needle that caused a needle-stick injury
- Exposure to blood from someone who is HIV positive

Table 3: Post-Exposure Prophylaxis Regimens

<table>
<thead>
<tr>
<th>Regimen Category</th>
<th>Application</th>
<th>Drug Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic</td>
<td>Low risk exposure</td>
<td>• 4 weeks of both:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– Zidovudine 600 mg daily in divided doses (i.e.,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>300 mg twice daily) and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– Lamivudine (150 mg twice daily)</td>
</tr>
<tr>
<td>Expanded</td>
<td>High risk exposure</td>
<td>• Basic regimen and Nelfinavir 1250 mg twice daily</td>
</tr>
</tbody>
</table>

Note the following:

- Start ARV medications within 1-2 hours of exposure if possible. If a delay occurs, initiate PEP regardless of the interval. Currently, there is no defined interval after which PEP is not effective.
- Administer PEP regimen for 28 days.
- Perform recommended serology after exposure:
  - Two weeks: CBC, liver and renal function tests
  - Six weeks: HIV serology
  - Three months: HIV serology
  - Six months: HIV serology
- Offer counseling to the HCW exposed to HIV infection
• Assure maintenance of the HCW’s confidentiality
• Instruct on probability of infection from accidental exposure (CDC statistics):
  o 0.3% from percutaneous injury from an HIV infected source
  o 0.03% from mucocutaneous exposure from an HIV infected source
• Instruct on benefits and possible adverse effects of ARV prophylaxis
• Counsel on prevention of transmission, particularly among sexual partners, until HIV infection has been ruled out

* For more information about Prevention in Health Care settings refer to the National Guidelines for Infection Control.
Comprehensive Care for
People Living with HIV/AIDS (PLHA)

Introduction to Comprehensive Care for PLHA
The Basic Components of HIV Comprehensive Care are:

- Counseling and Testing for HIV infection
- Health care (including social, psychological, and medical care)
- Impact alleviation for HIV-affected families and friends (social support)

Care for PLHA should cover all stages of HIV infection, from asymptomatic infection to end-stage disease, death and care for family survivors.

Awareness of HIV serostatus allows for early access to HIV specific health care services. However, the stigma associated with HIV often discourages people from determining their HIV status. The longer it takes someone to find out that he/she is infected with HIV, the more chances there are for passing the infection onto others. Ideally, people should be informed of their serostatus through VCT in a confidential manner.

Comprehensive care for PLHA includes:

- Clinical care to manage HIV-related illnesses
- Emotional, psychological and spiritual care (to help PLHA, their families and friends to cope with the impact of HIV/AIDS)
- Social care to maintain a nutritional and economical balance when repeated health expenditures deplete the family's income, which in turn affects planning for the family’s future and securing basic support for survivors, particularly orphans
- Sexual education on managing sexual needs while protecting partners from infection is of paramount importance

The type of care and support to be emphasized within a comprehensive approach will vary as the disease progresses. Early-stage infection requires an emphasis on counseling and behavior change while late-stage disease requires an emphasis on palliative care (to alleviate symptoms) and social support. Medical interventions are needed at all stages to prevent and treat opportunistic infections (OIs) and HIV-related diseases.

HIV/AIDS Continuum of Care
The different elements of comprehensive care should complement and strengthen one another at all stages of the disease. For example: managing a clinical condition is easier and more effective if worries about infecting a partner and planning for the family’s future can be addressed through referral to counseling services that provide legal or social support.
The different elements of comprehensive care need not come from the same institution, but can be provided through networking with other services, institutions, and projects in the community (Figure 4).

![Figure 4: Comprehensive HIV/AIDS Care, Treatment and Support](image)

Continuum of care should include timely referrals between home, the community and a hospital (and vice versa), effective discharge planning, and follow-up at each level.

Functional and confidential referral systems must be in place to build on previous care efforts.

Important components of referral include:

- Medical referrals between a central hospital and community health center
- Psychosocial referrals between a counselor and a spiritual worker
- Referrals between a welfare officer and a home-based care program

Such coordination permits a continuum of care from the institutional level to the community and home-based care level.

A peer support group’s ability to make these linkages, exchange information, and offer emotional and moral support has been found to be essential all over the world. The HIV care continuum (figure 5) illustrates how linkages should function in a referral system.
Figure 5: The HIV Care Continuum

Please note that most people can be affected by HIV, either through their own or their partner’s risk behavior, or through infection of a family member. The HIV virus does not discriminate; it will affect and infect anyone. The human needs of HIV infected people will continue for as long as they live, just like everyone else. Those physical, social, emotional and sexual needs must be actively managed for those infected and affected by HIV. Table 4 depicts the most common standard care services that should be provided, based on infection status.
Table 4: Standard Care Services for HIV/AIDS by Infection Status and Phase of Infection

Stigma and HIV

To enter a care continuum, diagnosis must be made in a way that promotes and encourages further care-seeking behaviors and the provision of support. Stigma, where disapproval towards and prejudice against the person are expressed, discourages people from seeking care. This is especially true for sexual matters, where there is risk of infecting others. Encouraging and enabling a person who is infected with HIV to practice behaviors, which will protect others, is a crucial role of the caregiver.

Stigma is a trait or a quality that society defines as being shameful or unwanted. Stigma affects all aspects of caring for people with HIV. PLHA are stigmatized for many reasons:

- HIV is a slow, incurable disease that eventually results in illness and death
- Many people regard HIV as a death sentence
- The public often poorly understands how HIV is transmitted, and people are often irrationally afraid of acquiring HIV from people already infected with it
- HIV transmission is often associated with violations of social mores regarding proper sexual relations, so people infected with HIV are associated with behaviors others perceive as morally incorrect
Stigma prevents people from speaking about and acknowledging HIV as a major cause of illness and death. Stigma prevents PLHA from seeking medical and psychosocial care for themselves and from taking preventive measures to avoid infecting others. Prevention behaviors are also stigmatized and people are reluctant to practice behaviors that could associate them with the virus. A woman with HIV might want her partner to use a condom, but may be reluctant to ask because of the stigma associated with the possibility that she or her partner are at risk for HIV.

If one family member exhibits signs and symptoms of HIV, the entire family may face rejection and even violence from the community. Stigmatization prevents people from seeking testing and treatment for HIV. HCWs who help PLHA can also be stigmatized by being associated with the virus. Moreover, HCWs themselves may reject HIV persons and AIDS cases; accordingly, they will be unable to provide quality care.

**HIV and Discrimination**

People who do not understand how HIV is spread may discriminate against PLHA, for example, they may treat them unfairly because they are afraid of being infected with the virus. Discrimination occurs not only against PLHA but also against groups of people that may be more likely to have HIV, such as sex workers or other groups that are mistakenly thought to have a higher rate of HIV, such as foreigners.

Teaching people facts about HIV and means of transmission, protects everyone from unnecessary discrimination. Every HIV/AIDS persons should have access to high-quality care regardless of who they are and how they became infected.
Clinical Care of Patients with HIV/AIDS

Patient’s History

A comprehensive database is essential in assessing the patient’s current situation and formulating a plan of care. Always remember that the patient may be anxious and frightened. The physician should be able to empathize with the patient, gain his/her trust, have a non-patronizing attitude, show acceptance and provide reassurance.

In taking a patient’s history, the following information should be collected:

- History of HIV diagnosis: why the patient was tested, when did he/she test positive, possible mode of transmission, the presence of any classic symptoms
- History of HIV treatment: if the patient has been treated for any HIV disease and his/her response to treatment
- History of STIs: including a complete gynecological history
- Occurrence of other infections, such as tuberculosis (TB), Hepatitis A, B and/or C, Pneumococcal infections, etc.
- Complete medical history for other diseases such as malignancies, hypertension, etc.
- Sexual practices
- Mental health history: past and current problems
- Family history
- Social history including sources of social support

Physical Examination of HIV Infected Persons

A complete examination should be performed focusing on HIV/AIDS related clinical manifestations for early detection of any complications. Components of physical examination include:

General appearance: may denote problems related to HIV infection. Weight loss is a common manifestation in an HIV infected person due to many causes such as chronic diarrhea, loss of appetite, dysphagia and OIs.

Fever:

- Is the patient feverish? What is the presenting symptom?
- If fever is associated with respiratory symptoms, suspect TB or pneumonia
- If fever is associated with neurological symptoms, suspect cryptococcal meningitis.
Eyes: should be examined for anemia, jaundice, visual disturbances or edema.

Mouth: Any examination of an HIV infected person should include careful assessment of the oropharynx. There are many oral complications that may occur in an HIV infected person such as oral candidiasis, oral thrush, hairy leukoplakia, oral ulcers such as herpes simplex ulcers and even KS.

Lymph nodes: Lymphadenopathy may be the only presenting symptom in the acute stage of HIV infection. Persistent Generalized Lymphadenopathy (PGL) should be checked for.

Skin: Careful examination of the skin often yields early clues of HIV infection. Mucocutaneous manifestations can occur in the second clinical stage e.g., prurigo, angular stomatitis, oral ulcers, seborrheic dermatitis, Molluscum contagiosum, etc.

Chest: Chest manifestations, such as dyspnea, persistent cough (productive or dry), respiratory distress should be looked for. These might denote TB, bacterial pneumonia, and/or PCP. Chest problems may be an indication for starting TB or PCP prophylaxis.

Gastrointestinal (GI): Approximately half of AIDS patients suffer from diarrhea for numerous reasons such as: Salmonellosis, Shigellosis, Campylobacteriosis, Giardiasis, Amoebiasis and Cryptosporidiosis. Diarrhea may be the leading cause of death in AIDS patients.

Hepatosplenomegaly should be looked for as it may reflect disseminated infections such as Mycobacterium avium complex (MAC) or TB.

Central nervous system (CNS): The CNS should be examined carefully as HIV can affect the immune system and the nervous system. HIV can affect the CNS very early causing acute aseptic meningitis and in the terminal stage in the form of AIDS dementia. Neuropathy, numbness, loss of memory, diminished concentration and sensory motor retardation should be kept in mind while examining the patient.

Genital organs: Genital organs should be examined for STIs as they increase the vulnerability to and the transmission of HIV infection. Pelvic examination and Papanicolaou (PAP) smears are required for women.
Common HIV/AIDS Related General Manifestations

**Pain in HIV/AIDS Patients**

Pain associated with HIV is defined as persistent or recurrent pain localized in a part or in parts of the body, lasting more than 48 hours and not disappearing with simple comfort measures in a patient with symptomatic HIV infection. For most patients, physical pain is only one of several symptoms. Relief of pain should therefore be seen as part of a comprehensive pattern of care.

Physical aspects of pain cannot be treated in isolation from other aspects, nor can patients’ anxiety be effectively addressed when patients are suffering physically. Therefore, various factors affecting each patient must be addressed simultaneously.

The first principle of managing pain in HIV disease is an adequate and full assessment of the cause of pain, bearing in mind that most patients have more than one type of pain and different pains have different causes. While the cause of pain is often responsive to specific treatment, symptomatic treatment should not be delayed.

**Causes of pain in HIV/AIDS patients**

There are multiple causes of pain in HIV/AIDS patients, including:

- HIV/AIDS related pain, such as HIV neuropathy, myelopathy, myopathy, myositis, arthritis, vasculitis and KS
- Pain related to HIV/AIDS therapy, such as ARVs or other antivirals, drug therapy of TB or MAC and chemotherapy or radiotherapy

Women may suffer from pain more frequently than men because women also have pain syndromes of a gynecologic nature.

**Specific pain syndromes in patients with HIV/AIDS**

1) **Gastrointestinal pain syndromes**

**Oropharyngeal pain:**

- Candidiasis
- Necrotizing gingivitis
- Dental abscess
- Oral ulcers [caused by: HSV, CMV, Epstein-Barr Virus (EBV)]
- Mycobacterial infection
- Cryptococcal infection
- Histoplasmosis
- Aphthous ulcers
- KS
Common HIV/AIDS Related General Manifestations

**Esophageal pain** in the form of dysphagia or odynophagia caused by:
- Esophageal candidiasis
- Ulcerative esophagitis
- Infections: HIV itself, HSV, EBV, papovavirus, mycobacteria, cryptosporidium, or PCP
- KS and lymphoma
- Drug induced e.g., Zidovudine (AZT)

**Abdominal pain** due to:
- Infections
- Intestinal perforation caused by CMV infection
- Intestinal intussusception caused by campylobacteriosis
- Lymphoma
- Aseptic peritonitis (spontaneous)
- Toxic shock
- Herpes Zoster
- Tubal gonococcal or chlamydial infection
- ARV drugs (ddI and d4T causing pancreatitis, Indinavir causing nephrolithiasis)

**Biliary tract and pancreatic pain** due to:
- OIs leading to cholecystitis, hepatic biliary tract obstruction and hepatitis
- It may also be due to drug induced hepatic toxicity or pancreatitis

**Anorectal pain:**
- Perirectal abscess
- CMV proctitis, fissure
- Human Papilloma virus (HPV) and HSV

2) **Chest pain syndromes**

Syndromes involving chest pain are most often caused by:
- Infections
- Malignancies
- Pulmonary embolism
- Bacterial endocarditis
  and/or
- Coronary heart disease due to ARV drugs
3) Neurological pain syndromes

Neurological complications are mostly in the form of headache and neuropathy.

- Headache may be caused by HIV encephalitis, atypical aseptic meningitis, AIDS related malignancies (Lymphoma, KS and metastatic lymphoma), sinusitis, tension, migraine, ARVs and OIs
- Neuropathies may be caused by diseases such as Guillain-Barre syndrome and infections such as Herpes Zoster. They may also be drug induced or due to toxic or nutritional factors (e.g., alcohol, vitamin B₆ deficiency, vitamin B₁₂ deficiency)

4) Rheumatological pain syndromes

- Arthralgia and arthritis: Psoriatic arthritis, septic arthritis and HIV related arthritis
- Myopathy and Myositis: HIV related myopathy or polymyositis, drug induced myopathy due to AZT, pyomyositis and microsporidiosis myositis

5) Pain unrelated to AIDS: such as disc disease and diabetic neuropathy

Management of pain

The principles of pain management include:

- Identify the type of pain
  - Whether visceral, neuropathic or mixed
  - Distinguish between rest and movement pain
- Use multiple approaches:
  - Modify the disease with antivirals, antibiotics, chemotherapy, radiotherapy and surgery
  - Modify the perception of the pain, using medications, massage therapy, psychological support, relaxation therapy and therapeutic touch
  - Modify or interrupt pain transmission pathways, through transcutaneous electrical nerve stimulation (TENS), acupuncture, chiropractic, nerve blocks, and neurosurgery
  - Modify life style, by using occupational therapy assessments, physiotherapy and home making services
- Provide stepwise analgesia: analgesics are given in steps according to the degree of pain.
  - First line analgesics are used for mild pain and include Acetylsalicylic acid (600 mg/4 hours) or Paracetamol (1 g/4 hours).
  - Second line analgesics can be used for moderate pain not responding to first line analgesics and include weak opioid drugs in combination with first line treatments such as Codeine phosphate (60 mg/4 hours). Compound analgesics contain a sub-therapeutic dose of Codeine and should be used for this purpose
Common HIV/AIDS Related General Manifestations

- Third line analgesics, such as Morphine can be given in cases of severe pain, orally or by injection
- The dosage of morphine should be based on the response and often needs to be increased as the disease progresses (start with 5-20 mg/4 hours); for very severe pain there is no maximum dose.

Important factors that should be kept in mind when providing treatment for pain include the following:

- Never combine morphine with a weak opioid such as Codeine or Tramadol
- Minimize the number of different medications and the number of doses to be taken
- Use the least invasive route of administration
- Provide around the clock dosing for constant pain at rest
- Anticipate and educate about potential side effects and strategies for their control

Adjuvant drugs may be added at any stage according to the type of pain:

- Anticonvulsants such as Carbamazepine 200 mg three times daily given in case of neurological pain such as pain after Herpes Zoster
- Antidepressants, such as Amitriptyline 10–25 mg at bedtime given for the tingling and burning sensations of HIV peripheral neuropathy and nerve compression
- Non-steroidal anti-inflammatory drugs are used in case of bone pain, pain of inflammatory origin, such as rheumatic conditions and hepatomegaly
- Haloperidol 1.5 mg at bed time or twice daily reduces some of the side effects of Morphine such as nausea and agitation

Avoid peaking of pain by maintaining an appropriate level of analgesic therapy. Most patients in the final stages of AIDS will have severe pain and will benefit from adequate analgesic therapy. At this stage, oral morphine will be indicated often in combination with adjuvant drugs.

Some secondary effects of Codeine and Morphine are beneficial for persons with HIV disease, such as constipation, depression of cough reflex and mood alteration. Nausea occurs in most patients only during the initial two weeks of treatment with Morphine and may be reduced by adjuvant drugs such as Haloperidol, Chlopromazine or Hydroxyzine.
### Table 5: Analgesics and Adjuvant Drugs Recommended for Pain in HIV Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild pain:</strong></td>
<td></td>
</tr>
<tr>
<td>• Aspirin</td>
<td>600 mg/4 hours</td>
</tr>
<tr>
<td>• Paracetamol</td>
<td>1 g/4 hours</td>
</tr>
<tr>
<td><strong>Moderate pain:</strong></td>
<td></td>
</tr>
<tr>
<td>• Codeine</td>
<td>60 mg/4 hours</td>
</tr>
<tr>
<td><strong>Severe pain:</strong></td>
<td>Minimum 5 mg/4 hours. In more severe pain there is no maximum dosage (sometimes even more than 500 mg/4 hours is needed)</td>
</tr>
<tr>
<td>Injectable opioid drugs such as morphine</td>
<td></td>
</tr>
</tbody>
</table>

**Adjuvant Drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Anticonvulsants</td>
<td>Carbamazepine 200 mg three times daily</td>
</tr>
<tr>
<td>• Antidepressants</td>
<td>Amitriptyline 10–25 mg at bed time</td>
</tr>
<tr>
<td>• Non-steroidal anti-inflammatory drugs (NSAID)</td>
<td>Ibuprofen 200–400 mg three times daily</td>
</tr>
<tr>
<td></td>
<td>Indomethacin 25 mg three times daily</td>
</tr>
<tr>
<td>• Anxiolytics, hypnotics</td>
<td>Lorazepam 1 mg at bedtime.</td>
</tr>
<tr>
<td></td>
<td>Hydroxyzine 25 mg three times daily</td>
</tr>
<tr>
<td>• Antihistamines</td>
<td>Promethazine 10 mg at bed time</td>
</tr>
<tr>
<td>• Narcoleptics</td>
<td>Haloperidol 1.5 mg at bedtime or twice daily</td>
</tr>
</tbody>
</table>
Fatigue in HIV/AIDS Patients

Fatigue is a prevalent symptom in AIDS patients. It is associated with poor physical functioning and psychological distress. Fatigue is characterized by a spectrum of disturbances including, among others, muscle weakness, sleepiness, lethargy, depression (mood disturbances) and difficulty in concentration (cognitive disturbances).

Management of fatigue

In managing a person complaining of fatigue, use the following steps:

- Identify and treat the underlying cause
- Provide adequate rest balanced with appropriate exercise
- Help patient to assume the most comfortable position and when bed rest is required, help him/her to rest and turn from side to side to prevent bed sores
- Physical therapy
- Psychological and emotional support
- Drug therapy, including stimulants or corticosteroids

Management of fatigue with multiple causes includes providing:

- Psycho-stimulants:
  - Methylphenidate (Ritalin): 2.5–5 mg orally once or twice daily. Maximum 60 mg daily in 2 divided doses
    - Notes: Should not be given in the afternoon and should be avoided in case of anxiety and agitation
  - Dextroamphetamine (maxitron/metherdin): Same dose as Methylphenidate

- Corticosteroids:
  - Dexamethasone: 4-16 mg orally or IV daily in one dose or divided doses in patients with progressive disseminated MAC

Anemia in HIV/AIDS Patients

Anemia is a frequent clinical and laboratory finding in HIV positive patients. Anemia may also be the first clinical manifestation of HIV infection. Clinical signs, such as paleness of the conjunctiva, tachycardia and general weakness should raise suspicion about the presence of anemia. Clinical signs and symptoms are not sufficiently accurate to diagnose anemia or to assess its severity. Where possible, a laboratory test to assess the hemoglobin (Hb) level should be performed. Anemia may be moderate anemia (Hb values of 5-10 g/dl) or severe anemia (Hb values of less than 5 g/dl).
Management of anemia
Investigations for anemia in HIV positive patients should always include:

- CBC
- Liver Function Tests
- Urea, electrolyte status
- Stool analysis (microscopy, occult blood)
- Chest X-ray

Iron, vitamin B\(_12\) and folic acid concentrations should be determined as indicated, depending on results of the above-mentioned investigations and appropriate treatment should be given.

Severe anemia, not responding to this therapy, should be further investigated by bone marrow aspirates or biopsy to identify possible bone marrow infiltration due to TB, metastatic carcinoma or fungal infections, for which specific management may be considered. Blood transfusion does not affect the result of bone marrow examination. In severely anemic patients blood transfusion should therefore not be delayed for this purpose.

Fever in HIV/AIDS Patients

In HIV/AIDS patients the causes of fever are varied and include infections, thrombosis, malignancy, transfusion related fevers, autoimmune disorders, granulomatous disorders and drug induced fevers. However, there are cases where the cause of fever may be unknown.

Management of fever
The main strategies for the treatment of fever include the following:

- History taking and physical examination
- Treatment of underlying cause
- Maintain hydration
- Local treatment (cold foments)
- Medications which include:
  - Antipyretics:
    - Acetaminophen (Paracetamol, tablets 500 mg and suppository 300 and 500 mg): 750–1000 mg orally or per-rectum every 6 hours
    - Ibuprofen (Brufen 200, 400 and 600 mg tab.): 200-600 mg orally every 6-8 hours
    - Indomethacin (Indocid capsules 25 mg and suppository 100 mg): 25-50 mg three times daily
Common HIV/AIDS Related General Manifestations

- Corticosteroids:
  - Dexamethasone 4-16 mg orally or intravenously (IV) daily in one dose or 2 divided doses in patients with progressive disseminated MAC
- In case of profuse sweating, ensure that the patient is dry and give the following drugs:
  - Anticholinergics: Hyoscyamine (Buscopan), but keep in mind this may cause dry mouth, constipation and confusion
  - H2-antagonists: Cimetidine (Tagamet, 200 and 400 mg tablets): 400-800 mg orally twice daily

Nausea and Vomiting in HIV/AIDS Patients

Nausea may be much more distressing than vomiting. Vomiting without nausea is probably due to a motility problem or mechanical obstruction. Causes of nausea and vomiting are usually multi-factorial and may include:

- Infections
- Irritation of GI mucosa
- Cerebral space occupying lesion
- Meningeal irritation
- Mental anxiety
- Mechanical obstruction
- Electrolyte imbalance
- Liver cell failure
- Uremia
- Drug induced (which may be caused by a wide range of drugs including ARVs and other drugs)

Management of nausea and/or vomiting

- Treat the underlying cause
- Restrict oral fluids and food intake if appropriate
- Intravenous fluid replacement and encourage electrolyte balanced fluid
- Position person upright
- Eat slowly and only small amounts
- Avoid greasy or spicy food
- Avoid alcohol or medications that may cause nausea
- In case of vomiting try liquid rather than solid food
• Give cold or iced water (sucking ice may help decrease nausea)
• Do not give food immediately after vomiting (ideally wait at least half an hour)
• Ask patient to use deep breathing exercises and relaxation techniques
• Provide antiemetics half an hour before meals
• Treatment of nausea and vomiting can include using one of the following drugs:
  o Chlorpromazine 25 mg or Metoclopramide three times daily each.

**Diarrhea in HIV/AIDS Patients**

Diarrhea in a patient with HIV is defined as liquid stools three or more times daily, continuously or intermittently for more than two weeks. Diarrhea occurs at some point in the clinical course of most HIV infections and the incidence and duration of diarrhea increases during the course of HIV disease. Chronic diarrhea is a very frequent and frustrating problem in PLHA, with at least 50% of them experiencing it sometime during the evolution of the disease.

**Diarrhea in PLHA is characterized by the following:**

• Nausea, weight loss, abdominal cramps and dehydration
• Intermittent watery diarrhea, without blood or mucous
• Bloody diarrhea can be due to Campylobacter infection
• In areas where prevalence of amoebiasis and bilharziasis is high, they should be considered
• No cause is identified in one-third to two-thirds of cases

**Differential diagnosis includes the following:**

• Bacterial infections: *Campylobacter*, *Shigella* and *Salmonella*
• Mycobacterial infections: *Mycobacterium tuberculosis*, *Mycobacterium avium complex*
• Protozoal infections: *Cryptosporidium species*, *Giardia lamblia*, *Isospora belli*, *Entamoeba histolytica*, *Microsporidium species*
• Toxin induced: *E. coli* and *Clostridium difficile*
• Helminthic infections: *Strongyloides stercoralis*
• Fungal infections: *Candida* species (seldom a cause of diarrhea)
• AIDS enteropathy: Direct cytopathic effect of HIV
• Non-infectious disorders: KS, lymphoma
Management of diarrhea

The key to good management is rehydration, reduction of sugar intake and provision of potassium supplements if potassium rich food (oranges, bananas) is not available. Management of acute diarrhea should follow the standard treatment guidelines. In case of persistent diarrhea, priority should be given to maintenance of adequate hydration and ensuring electrolyte balance preferably by means of oral fluids. Whenever possible, identify the cause and give specific treatment to alleviate it, otherwise management should be symptomatic by antidiarrheals (constipating agents). In alleviating the effects of diarrhea, it should be kept in mind that high energy food and protein intake reduces the degree of muscle wasting.

Constipating agents should never be used under the following circumstances:

- Patients with bloody diarrhea (due to the risk of toxic megacolon)
- Elderly patients
- Children

Prevention of diarrhea can be achieved through personal hygiene, hand washing, drinking boiled water and eating only thoroughly cooked meat and vegetables. An infectious agent can be identified in about 50% of patients with AIDS-associated diarrhea. Table 6 depicts the clinical features of dehydration according to their severity.

Table 6: Assessment of Dehydration

<table>
<thead>
<tr>
<th>Clinical Manifestations</th>
<th>Dehydration Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td>General appearance/condition</td>
<td>Restless, irritable</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td>Rapid</td>
</tr>
<tr>
<td>Respiration</td>
<td>Deep, may be rapid</td>
</tr>
<tr>
<td>Skin elasticity</td>
<td>Pinch retract slowly</td>
</tr>
<tr>
<td>Eyes</td>
<td>Sunken</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>Dry</td>
</tr>
<tr>
<td>Urine flow</td>
<td>Reduced amount and dark</td>
</tr>
</tbody>
</table>
Flow Chart 1: Management of Diarrhea

Persistent Diarrhea

History and physical examination

Dehydrated?

Yes

Correct with oral rehydration salts (oral or naso-gastric tube) or parenteral fluids

No

Hydration and general condition improved?

Yes

1. Maintain hydration
2. Consider supplemental feeding as tolerated

No

Refer to Level 1

Refer to Level 2
Flow Chart 2: Management of Diarrhea (Level 1)

- **Persistent diarrhea with blood**
  - No
    - Treat with Co-trimoxazole 2 tablets twice daily for 5 days
    - Continue supportive treatment (fluids, diet)
  - Yes
    - Treat with Nalidixic Acid, 1 g four times daily for 5 days
    - Continue supportive treatment (fluids, diet)

- **Diarrhea Improved?**
  - Yes
    - Maintain hydration and nutrition
    - Refer to level 2
  - No
    - Treat anemia if needed
    - Follow up
Referral patient with persistent diarrhea not responding to treatment prescribed at Level 1

Stool examination (3 times)

Are laboratory and/or clinical findings consistent with:
• Bacterial infection (fever, blood, or leukocytes in stool) or
• Protozoal infection (Amoebiasis, Giardiasis) or
• Helminthes

No

Give constipating agents as tolerated

No

Improved?

Yes

Follow up as needed

No

1. Stop all drugs
2. Maintain hydration
3. Maintain nutrition

Bacterial
Treat as indicated

Protozoal
Treat as indicated

Helminthes
Treat as indicated

Flow Chart 3: Management of Diarrhea (Level 2)
**Wasting in HIV/AIDS Patients**

Wasting is defined as involuntary loss of more than 10% of baseline body weight in conjunction with fever, weakness or diarrhea for more than 30 days. Serious weight loss is a problem for many people with AIDS and can be caused by HIV infection itself or other infections and malignancies. With AIDS, the body may lose its ability to absorb nutrients properly and diarrhea further reduces absorption. To keep functioning, the body must use its stored energy and the muscles start to break down.

Mechanisms of HIV wasting include:
- Diminished nutrient intake
- Excessive nutrient loss
- Metabolic dysregulation

**Management of weight loss**
- Treatment of underlying cause
- Proper intake of nutritious food
- Improvement of patient’s appetite through exercises and appetite stimulants
- Prevention and adequate management of diarrhea, nausea and vomiting
- Health education for patients
- Exercise is important for preventing weight loss and wasting because it stimulates the appetite, reduces nausea, improves functioning of the digestive system and strengthens muscles
- Drug treatment:
  - Appetite stimulants
  - Anabolic agents can be given

**Lymphadenopathy in HIV/AIDS Patients**

Swelling of lymph nodes is a symptom often encountered in PLHA. Lymphadenopathy may be localized or generalized. It is important to identify the possible underlying causes of localized lymphadenopathy in order to give appropriate treatment. It usually affects only one or two regions and is caused by local infection. Sometimes it may be due to TB or malignancy such as lymphoma.

Persistent generalized lymphadenopathy (PGL) is characterized by the following:
- More than two extrainguinal lymph node groups affected
- At least two nodes more than 1.5 cm in diameter at each site
- Duration of more than three months
- No underlying cause for the lymphadenopathy
Causes of lymphadenopathy:

- Infections including staphylococcal or streptococcal infections particularly associated with dermatological conditions, mycobacterial TB, syphilis, fungal, and viral
- Malignancies such as KS and lymphoma
- HIV infection itself; PGL in HIV patients is mostly due to normal immune reaction to HIV infection. Lymph nodes usually disappear as the immune suppression advances and OIs appear

**Management of lymphadenopathy**

- Treat the underlying condition
- No treatment is required if an underlying problem is not identified

**Dyspnea in HIV/AIDS Patients**

Dyspnea is defined as subjective shortness of breath at rest or on minimal exertion due to pulmonary, cardiac or other conditions such as anemia, fatigue, anxiety or depression.

**Management of dyspnea**

- Elevate the head of the bed
- Keep air moving
- Reduce environmental irritants
- Manage associated anxiety
- Educate and support patient and family on how to alleviate depression
- Treat the underlying cause
- Use oxygen

**Cough in HIV/AIDS Patients**

This may present with other signs and symptoms as hemoptysis, stridor, gagging, retching, crackles, etc. The causes may be pulmonary, cardiac, psychological, chemical and mechanical irritants and allergies.

**Management of cough**

- Distinguish between productive and non-productive cough
- Treat the underlying cause and manage associated symptoms
- Put the patient in a semi-sitting position
- Avoid irritants
- Provide abdominal splints for persistent coughing episodes
Flow Chart 4: Management of Respiratory Conditions (Part 1)

*Supportive treatment:* Fluid replacement, temperature management, supporting the patient, provision of enough fresh air, and symptomatic relief
Respiratory condition Level 1

Cough with fever

Yes

Co-trimoxazole 2 tabs twice daily for 5 days

No

Productive cough?

Yes

Treat with Co-trimoxazole 2 tabs twice daily for 5 days

Improved?

No

- Amoxicillin 250-500 mg orally three x daily for 5 days
  AND
  - Take sputum samples for Acid Fast Bacilli (AFB)

Yes

Improved?

No

Follow up as needed

Yes

- Level 2: Further investigations and treat accordingly

Flow Chart 5: Management of Respiratory Conditions (Part 2)

Note: Level 2 should include investigations for TB
Dry Itchy Skin in HIV/AIDS Patients

Itching and dry skin, in the absence of any other treatable cause are very common in persons with HIV. This can severely affect the patient’s well-being and requires appropriate attention and treatment.

Management of dry itchy skin

General recommendations for symptomatic relief of skin conditions include:

- Avoid exposure to dry wind
- Dry scaly lesions need a soothing lotion, such as calamine lotion, emulsifying ointment or Vaseline
- Dry skin after bath by patting with a soft towel then apply cream, body oil or lanolin
- Local corticosteroids as Hydrocortisone cream 1% may be useful if inflammation is present, in the absence of any bacterial, fungal or viral infection
- Oral antihistamines, such as Chlorpheniramine 4 mg orally every 8 hours and/or Promethazine 10 mg at bedtime, may be useful
- Hydroxyzine 25 mg at bedtime may be useful for severe itching
- Urea 10% cream

Dementia in HIV/AIDS Patients

Dementia is deterioration of intellectual faculties such as memory, concentration and judgment and is sometimes associated with emotional disturbances and personality changes. It may be related to HIV directly or it may result from other problems such as space occupying lesion, metabolic imbalance or infection. Patients with AIDS dementia complex (ADC) or HIV-associated dementia have the following clinical presentations:

- Early dementia is presented by dullness, diminished concentration, forgetfulness, mental slowing and short term memory loss.
- Late dementia is presented by indifference, disorientation, generalized weakness, fatigue, nighttime delusion, vacant stares, and withdrawal.
- Very late dementia is presented by confusion, dysarthria (difficulty in articulating words), mutism, seizures and incontinence.

Management of dementia

- Continue only essential medications
- Manage associated agitation
- Ensure protective safe environment
- Establish daily routines including regular activity and sleep times
- Reduce external stimuli, i.e., noise, conversations not directed to the person
- Make instructions clear and simple
- Provide occupational therapy
- Refer for psychiatric treatment
Depression in HIV/AIDS Patients

Depression is a psychiatric disorder characterized by an inability to concentrate, insomnia, loss of appetite, anhedonia (the absence of pleasure or the ability to experience it), a feeling of extreme sadness, guilt, helplessness and hopelessness, and thoughts of death. Depression is common in patients with HIV infection.

Management of depression

- Reducing doses of medications
- Eliminating unnecessary medications
- Supporting patients
- Treating depression with tricyclic anti-depressants and/or selective serotonin reuptake inhibitors
- Refer for psychiatric treatment

Anxiety in HIV/AIDS Patients

Anxiety is a state of apprehension, uncertainty, and fear resulting from the anticipation of a realistic or fantasized threatening event or situation, often impairing physical and psychological functioning. Anxiety in PLHA may be presented by insomnia, agitation, restlessness, irritability, sweating, palpitations, hyperventilation and worry. Anxiety may be related to HIV infection itself or be an effect of medications.

Management of anxiety

- Medications such as Lorazepam 0.25–2 mg/2 hours or Diazepam 2-10 mg three times daily
- Relaxation therapy
- Biofeedback (physical therapy)
- Refer for psychiatric treatment
HIV/AIDS Related Diseases

Respiratory Conditions

Pulmonary involvement is among the most common complaints of AIDS patients. At least one-third of them have cough lasting more than one month at sometime during the course of the disease. Other common complaints include dyspnea and/or chest pain. People with HIV often have symptomatic respiratory conditions not due to pyogenic infections. These may resolve without antibiotic treatment, however supportive treatment should be given. Pulmonary KS should be suspected in any patient with respiratory complaints and typical skin lesions and visceral lesions. Careful examination of the skin and oral cavity is the key of diagnosis. Referral for cytotoxic therapy should be considered.

Respiratory distress is defined as objective evidence of respiratory dysfunction, including wheezing, cyanosis, crackles, inability to clear secretions, stridor, intercostal indrawing and tachypnea (respiratory rate > 30/minute), hypoxemia, tachycardia and signs of ventilatory effort.

Overview

Respiratory symptoms may be due to a wide spectrum of pulmonary illnesses that includes both HIV and non-HIV-related conditions. The HIV-related conditions include both OIs and neoplasms. The OIs include bacterial, mycobacterial, fungal, viral, and parasitic pathogens.

- Bacterial pneumonia and TB can occur early in the course of HIV infection at CD4 > 500/mm³.
- PCP almost always occurs when the CD4 < 200/mm³.
- Toxoplasmosis, CMV and MAC usually occur at CD4 < 100/mm³.
- In the advanced stages of HIV/AIDS, there is often more than one pathogen causing respiratory infections

Etiology

Infections

- Pyogenic bacteria
- Mycobacterium TB and atypical mycobacteria
- PCP
- Fungal infections (candidiasis, cryptococcosis, histoplasmosis, coccidioidomycosis)
- Others: CMV, toxoplasmosis

Malignancies

- KS
- Lymphoma
HIV/AIDS Related Diseases

Other associated conditions

- Pleural effusion/empyema (associated with TB, bacterial infection or cancer)
- Pneumothorax (associated with TB, PCP or cancer)
- Pericardial effusion (often associated with TB)

Pneumonia

*Streptococcus pneumoniae* and *Haemophilus influenzae* are common bacterial causes of lung infection, as well as other bacteria in the streptococci family.

1) Pneumonia due to *Streptococcus pneumoniae*

*Streptococcus pneumoniae* is a common etiological agent that infects the upper respiratory tract and can cause pneumonia, as well as infections in other parts of the body such as in the bloodstream (bacteremia), lining of the brain and spinal cord (meningitis), bones (osteomyelitis), joints (arthritis), ears (otitis media) and sinuses (sinusitis).

**Clinical presentation:** Abrupt onset with fever, cough, production of purulent sputum, dyspnea and pleuritic chest pain (exacerbated by breathing)

**Recommended diagnostics**

- Chest X-ray
- blood culture and CBC
- Gram stain of sputum and sputum culture and sensitivity (C&S)

**Common findings**

- X-ray may show pneumonic consolidation, infiltrates or pleural effusions
- Leukocytosis and blood cultures may be positive

**Management and treatment**

- Cefotaxime 2 gm IV four times daily
- Ceftriaxone 2 gm/day IV
- Amoxicillin 750 mg orally three times daily
- Levofoxacin 500 mg orally/IV four times daily
- If *Streptococcus pneumoniae* is not resistant to penicillin, give 4 to 6 million units of Procaine Penicillin G in 2 to 4 IM injections
- Alternative treatment: Macrolide (Azithromycin, Clarithromycin, Erythromycin) and Vancomycin

**Notes:** If pneumonia fails to respond to standard antibiotics, consider other diseases, like TB.
2) Pneumonia due to Haemophilus influenzae

This is a gram-negative bacterium that occurs in the human respiratory tract and causes acute respiratory infections, acute conjunctivitis, and purulent meningitis.

Clinical presentation: Fever, cough, purulent sputum, dyspnea and signs of bronchopneumonia

Recommended diagnostics
- Chest X-ray
- CBC
- Gram stain of sputum

Common findings
- X-ray may show pneumonic consolidation, infiltrates or pleural effusions
- Leukocytosis
- Blood cultures may be positive

Management and treatment
- Cefuroxime
- Alternative regimens: TMP/SMX, Cephalosporins (2nd and 3rd generation) or Fluoroquinolones

Notes: Haemophilus influenzae vaccine is not indicated for adults

3) Pneumocystis Carinii Pneumonia (PCP)

A form of pneumonia that is relatively rare in normal, immunocompetent people but is the most frequently identified serious OI found in PLHA. Before the advent of effective treatment, it was a common immediate cause of death among PLHA, and can still be the first indication of AIDS, though it does not generally occur unless the CD4 count is < 200/mm³. PCP is the most frequently identified serious OI in HIV disease. Treatment is effective, but early recognition and treatment are important because of acute morbidity and mortality.

Causative agent: Pneumocystis carinii (fungal) which is sometimes referred to as Pneumocystis Jiroveci

Clinical presentation
- Presentation is non specific and insidious
- Dry cough, progressive shortness of breath, fever and few chest signs
- The patient becomes increasingly ill as disease slowly progresses, with fever, severe dyspnea, and hypoxia, which may be accompanied by confusion and delirium
- Signs of pneumonitis on chest X-ray
**Recommended diagnostics**

- Induced sputum, broncho-alveolar lavage or biopsy
- When these investigations are unavailable, diagnosis depends on the clinical and chest X-ray findings

**Common findings**

- Definitive diagnosis rests in finding cysts in induced sputum, broncho-alveolar lavage or biopsy specimens
- Whenever possible, make attempts to identify the organisms
- Chest X-ray shows bilateral diffuse lace-like interstitial infiltrates extending from the perihilar region. In some cases, the X-ray may be completely normal

**Management and treatment**

- TMP/SMX 75 mg/kg/day orally or IV x 21 days + PO$_2$ < 70 mmHg or alveolar-arterial oxygen tension difference > 35 mmHg
- Prednisone 40 mg twice daily x 5 days, then 40 mg/day x 5 days, then 20 mg/day to completion of treatment

*Alternative treatment:*

- TMP 75 mg/kg/day orally + Dapsone 100 mg/day x 21 days
- Pentamidine 4 mg/kg/day IV x 21 days

**Tuberculosis: HIV-TB Interaction and Co-Infection**

**Overview**

Tuberculosis is the most common cause of death in people with HIV worldwide. This is due to the fact that HIV infection increases the likelihood that new infections with *Mycobacterium tuberculosis* (due to immune suppression) will progress rapidly to TB disease. Among HIV-infected individuals, the lifetime risk of developing active TB is 50%, compared to 5-10% in non-infected individuals. Additionally, in a person infected with HIV, the presence of other infections, including TB, allows HIV to multiply more quickly. This may result in more rapid progression of HIV infection.

HIV-related TB can present with typical or atypical clinical and/or radiological features. Atypical features are usually found in HIV infected individuals with severe immunosuppression. Initial signs of TB may become apparent at any time during the evolution of HIV-infection.

TB may be pulmonary or extra-pulmonary:

- **Pulmonary TB** is the most common form. Presentation depends on degree of immunosuppression:
  - With mild immunosuppression:
    - The chest X-ray typically shows upper lobe and/or bilateral infiltrates, cavitation, pulmonary fibrosis, and shrinkage
The clinical picture often resembles post-primary pulmonary TB, and a sputum smear is usually positive
  - With severe immunosuppression, the features are atypical, resembling that of primary pulmonary TB:
    - The sputum smear is often negative
    - The chest X-ray shows interstitial infiltrates, especially in lower zones, with no features of cavitation or fibrosis
    - The chest X-ray may look exactly like that in bacterial pneumonia
    - In the setting of an HIV epidemic, chest X-ray is not diagnostic for TB

- **Disseminated and extra-pulmonary TB** is more common in advanced HIV infection because the immune system is less able to prevent growth and local spread of Mycobacterium tuberculosis.
  - Unilateral or bilateral infiltrates in the lower lobes are seen more often than upper lesions and cavities
  - Most common forms are lymphadenitis, pleural effusion, pericarditis, miliary disease and meningitis

**Clinical presentation**
- History of contact with a chronically coughing person
- Cough lasting more than three weeks and not responding to ordinary antibiotic treatment
- Production of purulent, sometimes blood stained sputum
- Night fevers and sweats and weight loss
- Always ask a “new” patient if he or she has ever been treated for TB

**Recommended diagnostics**

1. Microscopic examination of specimen of sputum stained by the Ziehl Neelsen (ZN) method:
   - A person with suspected pulmonary TB should submit three sputum samples for microscopy:
     - **Sample 1**: On the first visit, the patient should provide an on-the-spot sputum sample
     - **Sample 2**: Give the patient a sputum container to take home for an early morning sample on the following day (that is, on day two)
     - **Sample 3**: On day two, when the patient brings in sample two, he or she provides another on-the-spot sample

An inpatient can provide three early morning sputum samples.
2. Radiology:

- If TB is still suspected despite negative smears, a chest X-ray should be done. The classical pattern is upper lobe infiltrates with cavitation
- Pulmonary TB patients with HIV infection rarely have typical chest X-rays; in severe immunosuppression, the appearance is often atypical, as described above

**Management and treatment**

HIV-infected patients should be treated according to the Egyptian National Guidelines in cooperation with the district TB supervisor.

**Neuropsychiatric Conditions**

**Overview**

The reported incidence of neurological abnormalities on clinical examination varies greatly, from 16% to 72%, among hospitalized patients. A wide range of neurological manifestations are reported, including cognitive defects, focal deficits such as hemiplegia and acute peripheral facial palsy, painful feet syndrome and encephalopathy. Some of these manifestations are caused directly by HIV itself, while others result from OIs caused by different pathogens or drugs.

The differential diagnosis of OIs involving the brain includes the following pathogens:

- Protozoal infection: *Toxoplasmosis gondii*
- Mycobacterial infection: *Mycobacterium tuberculosis*
- Fungal infection: *Cryptococcus neoformans, Candida* species (rare)
- Viral infection: CMV, *Herpes simplex* virus, *Varicella zoster* virus, JC virus which causes progressive multifocal leukoencephalopathy (PML)

**Bacterial meningitis**

Bacterial meningitis is often encountered during late stages of HIV disease, however prompt diagnosis and aggressive management and treatment ensure a quick recovery.

**Causative agents:** Commonly *Streptococcus pneumoniae* and *Neisseria meningitidis*

**Clinical presentation**

- Fever, headache, stiff neck and vomiting
- Malaise, irritability, drowsiness and coma
- May be preceded by respiratory illness or sore throat

**Recommended diagnostics**

- CSF examination
- CBC
- Blood C&S
Common findings

- Leukocytosis
- CSF shows increased pressure, cell count (100–10,000/mm³), protein (> 100 mg/dl) and decreased glucose (< 40 mg/dl or < 50% of the simultaneous glucose blood level)
- Gram-stained smear of the sediment of the CSF can reveal the etiologic agent.

Management and treatment

- Penicillin (24 million units daily in divided doses every 2-3 hours) or Ampicillin (12 g/daily in divided doses every 2-3 hours) or Chloramphenicol (4 to 6 g/IV daily). Continue treatment for 10 to 14 days.
- Crystalline penicillin (2-3 mega units) and Chloramphenicol (500-750 mg four times daily) for 10-14 days.

Cerebral toxoplasmosis

Cerebral toxoplasmosis is one of the most common HIV-related neurological complications. If the patient does not receive maintenance therapy, cerebral toxoplasmosis will recur.

Causative agent: *Toxoplasma gondii*

Clinical presentation

- Headache, fever
- Confusion and focal neurological signs (e.g., hemiplegia, seizures)

Recommended diagnostics

- Computerized Tomography (CT) scan or Magnetic Resonance Imaging (MRI)
- Toxoplasma IgG titers.
- In a resource-constrained setting, you can make a diagnosis based on clinical symptoms (HIV-infected individual presenting with headache, fever, focal neurological signs and normal CSF finding)

Common findings: CT scan or MRI will show lesions in the cerebral hemispheres.

Management and treatment

- Start anti-convulsants as: Epanutin 50-100 mg or Tegretol 100-200 mg 2-3 times daily only if the patient has convulsions.
- Treatment for acute phase:
  - Pyrimethamine 100-200 mg loading dose, then 50-100 mg/day orally + Folinic (or folic) acid 10 mg/day orally + Sulfadiazine 1-2 g four times daily for at least six weeks, or
  - TMP/SMX (10-50 mg/kg/daily) for four weeks
- Preferred regimen for suppressive therapy required after a patient has had toxoplasmosis:
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- Pyrimethamine 25-75 mg orally four times daily + Folinic acid 10 mg four times daily + Sulfadiazine 0.5-1.0 g orally four daily. If allergic to sulfa give Dapsone 100 mg orally once daily

- Provide physiotherapy as necessary

**Preventive measures**
- Avoid eating raw meat and exposure to cats, if possible.
- Diminish risk of transmission by cooking meat adequately and washing vegetables and fruits carefully before eating.

**Cryptococcal meningitis**

Cryptococcal meningitis is the most common life-threatening AIDS-related fungal infection (after PCP). Untreated, the disease runs a slowly progressive and ultimately fatal course. Patients who have completed initial therapy for cryptococcosis should receive lifelong suppressive treatment unless immune reconstitution occurs because of ART.

**Causative agent:** *Cryptococcus neoformans*

**Clinical presentation**
- Presentation is nonspecific at the beginning and possibly for more than one month in 87-90% of cases.
- Headache is secondary to fungal accumulation and has periods of exacerbation and remission until it becomes continuous.
- Fever, malaise and nuchal pain signify a worse prognosis.
- Nausea, vomiting and altered mental status occur in terminal stage.
- Extraneural symptoms include skin lesions, pneumonitis, pleural effusions and retinitis.

**Recommended diagnostics**
- India ink staining of spinal fluid and/or serum for cryptococcal antigen.
- CSF cryptococcal antigen test is positive in over 90% of cases.

**Management and treatment**

**Preferred regimen:**
- Amphotericin B 0.7 mg/kg/day IV + Flucytosine 100 mg/kg/day orally for 14 days, followed by Fluconazole 400 mg/day for 8-10 weeks.
- Finally, maintenance therapy with Fluconazole 200 mg/day for life, or after immune system recovery.

**Alternate regimen:**
- Amphotericin B 0.7 mg/kg/day IV + Flucytosine 100 mg/kg/day orally for 14 days, followed by Itraconazole 200 mg twice daily for 8 weeks
Fluconazole 400 mg/day orally for 8 weeks, followed by 200 mg once daily
Itraconazole 200 mg orally three times daily for 3 days, then 200 mg orally twice daily for 8 weeks, after initial treatment with Amphotericin B
Fluconazole 400 mg/day orally + Flucytosine 100 mg/kg/day orally
Secondary prophylaxis or chronic maintenance therapy: preferably Fluconazole 200 mg/day

Cytomegalovirus infection
Cytomegalovirus is a member of the herpes virus family that can cause serious complications in persons with weakened immune systems. It is a rare but devastating illness in resource-poor settings. CMV management needs special care; therefore early referral is essential

Causative agent: *Cytomegalovirus*

Clinical presentation
- Retinitis, characterized by creamy yellow white, hemorrhagic, full-thickness retinal opacification, which can cause visual loss and lead to blindness if untreated
- Patient may be asymptomatic or complain of floaters, diminished acuity or visual field defects
- Retinal detachment, if disease is extensive
- GI symptoms: diarrhea, colitis, esophageal ulceration appears in 12-15% of patients
- Neurological symptoms, such as encephalitis
- Respiratory symptoms and pneumonitis, present in 1% of patients

Recommended Diagnostics
- Fundoscopic exam to check for changes. Consult an ophthalmologist.
- Upper gastrointestinal (UGI) endoscopy, when indicated.

Common findings
- Although any part of the retina may be involved, there is a predilection for the posterior pole
- Involvement of the optic nerve head and macula region is common.
- Characteristically, this involves the retinal vessels, which are always abnormal in areas affected by retinitis.
- There is minimal or no accompanying uveitis.

Management and treatment
- Foscarnet 60 mg/kg IV three times daily or 90 mg/kg IV twice daily for 14-21 days; Ganciclovir 5 mg/kg IV twice daily for 14-21 days
- Patients without immune recovery will need to be on lifelong maintenance therapy for retinitis.
- Extraocular: Ganciclovir and/or Foscarnet
Progressive multifocal leukoencephalopathy (PML)
Progressive multifocal leukoencephalopathy is rare in the general community and relatively common in HIV infection (affecting 4% of all AIDS patients). It usually occurs when CD4 < 100/mm$^3$. PML is caused by the JC virus. Consider routine testing for HIV for any patient with PML.

Clinical presentation
- Afebrile, alert, no headache
- Progressively impaired speech, vision, motor function
- Cranial nerve deficit and cortical blindness
- Cognition affected relatively late

Recommended diagnostics
- CT brain scan may be normal or remarkable for areas of diminished density or demyelination (deterioration of the covering of the nerve).
- Polymerase chain reaction (PCR) of CSF for detection of the JC virus which is positive in about 60% of cases
- Differential diagnosis: toxoplasmosis and primary CNS lymphoma

Management and treatment
- There is no treatment for this illness.
- Highly active antiretroviral therapy (HAART) can improve symptoms and prolong life.

Gastrointestinal Conditions
Chronic diarrhea is a very frequent and frustrating problem in PLHA and is often accompanied by nausea, weight loss, abdominal cramps and dehydration. An infectious agent can be identified in about 50% of patients with AIDS-associated diarrhea. Differential diagnosis is based on the pathogens discussed below. It is clinically impossible to distinguish the different etiological agents of bacterial gastroenteritis without a stool culture.

Salmonellosis
Salmonellosis is a frequent cause of bacteremia in PLHA and is caused especially by eating improperly stored or undercooked foods.

Causative agent: *Salmonella*

Clinical presentation: Fever and general malaise, sometimes without GI symptoms

Recommended diagnostics
- Stool microscopy, multiple stool samples may be necessary
- Stool and blood cultures
- Serology: Widal test
**Common findings**

- Salmonella bacilli may be found in stool/blood cultures
- Positive Widal test with increased titers

**Management and treatment**

- TMP/SMX 1 double strength (DS) tab twice daily
- Chloramphenicol 250 mg four times daily for 3 weeks
- In case of signs of sepsis, IV therapy is necessary
- Shorter regimens are Ciprofloxacin 500 mg twice daily or Ofloxacin 400 mg twice daily or Ceftriaxone 2 g IV for 7-10 days
- Many patients often relapse after treatment, and chronic maintenance therapy (TMP/SMX DS daily) is sometimes necessary

### Shigellosis

Shigellosis is a very common disease suffered by PLHA. *Shigella* can be transmitted through food including raw vegetables, milk, dairy products and poultry. Transmission is usually through the feco-oral route. Water contaminated with feces and unsanitary handling of food by food handlers are the most common causes of contamination. In many developing countries, resistance of *Shigella* (and *Salmonella*) to TMP/SMX has increased.

**Causative agent:** *Shigella*

**Clinical presentation:** High fever, abdominal pain and bloody diarrhea

**Recommended diagnostics:** Stool microscopy (fresh examination and after concentration). Multiple stool samples may be necessary.

**Common findings:** *Shigella* bacilli found in stool

**Management and treatment**

- TMP/SMX 1 DS tab twice daily x 5 days or
- Amoxicillin 500 mg three times daily x 5 days
- If resistant to the above, give Ciprofloxacin 500 mg twice daily or Norfloxacin 400 mg twice daily x 5 days or Nalidixic acid 1 g four times daily x 10 days
- If the empiric therapy with TMP/SMX is not effective in patients with bacillary dysentery, you can try Fluoroquinolones, followed by a trial of Erythromycin, if symptoms of bloody diarrhea persist

### Campylobacter enteritis

Campylobacter enteritis is an acute bowel infection that is caused by bacteria multiplying in the small intestine. Common sources of infection include raw or undercooked poultry or meat, contaminated food or water, unpasteurized milk, contact with infected pets, farm animals, or infected infants and infected food handlers.
Causative agent: *Campylobacter*

Clinical presentation: Fever, bloody diarrhea, abdominal pain and weight loss

Recommended diagnostics: Stool culture

Common findings: *Campylobacter* bacilli found in stool culture

Management and treatment

- Erythromycin 500 mg twice daily x 5 days (1st choice)
- Fluoroquinolones are also effective, but resistance rates of 30-50% have been reported.

**Cryptosporidiosis**

Cryptosporidiosis may be the AIDS-defining presentation in patients who previously had few symptoms of HIV. Infection can cause permanent and life-threatening diarrhea. Infection is through contaminated materials such as water, uncooked or contaminated food that has been in contact with the feces of an infected individual or animal then transferred to the mouth and swallowed.

Causative agent: *Cryptosporidium*

Clinical presentation

- Recent and prolonged history of severe diarrhea, usually large volume, watery stools with abdominal pain, bowel noise and activity; no fecal white blood cells (WBCs)
- Severe weight loss/wasting in those with longer history

Recommended diagnostics: Three stool samples for staining/AFB smear

Common findings: oocysts present in stool

Management and treatment

- Rehydration (IV and/or ORS)
- Paromomycin 500 mg four times daily for 2-3 weeks; maintenance with 500 mg twice daily is often required

Antidiarrheal agents are often given until control of diarrhea:

- Codeine phosphate 30-60 mg three times daily
- Loperamide 2-4 mg three or four times daily (maximum of 32 mg in 24 hours)

Preventive measures: Cryptosporidia are highly infectious and can be transmitted through water, food, animal-to-human and human-to-human contact. Special precautions should be taken to prevent infection. People with HIV with CD4 < 200/mm³ should boil tap water for at least one minute to reduce risk of ingestion of oocysts in potentially contaminated drinking water. The use of ARV is protective against cryptosporidiosis
Isosporiasis
Isosporiasis is a parasitic infection of the epithelial cells of the small intestine.

**Causative agent:** *Isospora belli*

**Clinical presentation**
- Enteritis, watery diarrhea
- No fever
- Wasting, malabsorption

**Recommended diagnostics:** Three stool samples/unstained wet preparation

**Common findings**
- *Isospora belli* oocysts that can be easily identified in unstained wet stool preparations
- No fecal WBCs

**Management and treatment**
- Most cases are readily treated with TMP/SMX 1 DS tab four times daily for 10 days followed by one tab twice daily for 3 weeks, then chronic suppression with TMP/SMX (960 mg) daily.
- High dose of Pyrimethamine with Calcium Folinate to prevent myelosuppression
- Long-term maintenance therapy may be necessary to prevent relapse.

Amoebiasis
Amoebiasis is infection by a protozoan. This is usually contracted by ingesting water or food contaminated by amoebic cysts. It may be common in the general population in developing countries, but may be recurrent or more severe in HIV patients.

**Causative agent:** *Entamoeba histolytica*

**Clinical presentation:** can be asymptomatic or presenting with colitis, bloody stools, cramps

**Recommended diagnostics:** Stool exam

**Common findings**
- Ova or cysts in stool exam
- No fecal WBCs

**Management and treatment**
- Metronidazole 500-750 mg orally or IV three times daily x 5 to 10 days **or**
- Paromomycin 500 mg orally four times daily x 7 days
**Giardiasis**

Giardiasis is caused by an intestinal infection with protozoa that is transmitted via the feco-oral route through contaminated water and food. It is a common cause of diarrhea in the general population, but may be recurrent or more severe in HIV patients.

**Causative agent:** *Giardia lamblia*

**Clinical presentation:** Enteritis, watery diarrhea with possible malabsorption, bloating, flatulence

**Recommended diagnostics:** Stool examination

**Management and treatment:** Metronidazole 250 mg orally three times daily x 10 days.

**Strongyloidosis**

In immunocompromised patients, strongyloides can cause overwhelming infection, especially when cell-mediated immunity is impaired. This serious complication is called strongyloides hyper-infection syndrome and has a high case fatality rate. Hyper-infection strongyloidiasis is generally associated with other conditions of depressed host cellular immunity. Disseminated strongyloidiasis and heavy worm loads can occur in patients with HIV, but the full-blown hyper-infection syndrome is less common. The likelihood of developing the hyper-infection syndrome is also higher in patients taking high-dose steroids.

**Causative agent:** *Strongyloides stercoralis*

**Clinical presentation**

- Serpiginous erythematous skin lesions (larva currens), diarrhea, abdominal pain and cough
- Full-blown hyper-infection syndrome is characterized by a Gram-negative sepsis, with acute respiratory distress syndrome (respiratory rate of > 30/minute, hypoxemia, tachycardia and signs of ventilatory effort), disseminated intravascular coagulation and secondary peritonitis

**Recommended diagnostics**

- Stool microscopy (multiple stool samples may be necessary)
- Sputum sample
- Chest X-ray

**Common findings**

- In disseminated strongyloidiasis, filariform larvae can be found in stool, sputum, broncho-alveolar lavage fluid, pleural fluid, peritoneal fluid and surgical drainage fluid.
- The chest X-ray reveals diffuse pulmonary infiltrates

**Management and treatment**

- Ivermectin 12 mg daily x 3 days. This is also the drug of choice for the treatment of systemic strongyloidiasis.
- An alternative treatment is Albendazole 400 mg twice daily x 5 days.
- Maintenance therapy once a month is necessary to suppress symptomatic infection (Albendazole 400 mg or Ivermectin 6 mg once monthly).
Hepatitis

Hepatitis, an inflammation of the liver, is most often caused by a virus, but it can be the result of exposure to certain toxic agents, such as drugs or chemicals. Various types of hepatitis exist, causing both chronic and acute viral hepatitis.

The primary mode of spread of hepatitis A virus is the feco-oral route through contaminated food and water. The virus can also be transmitted by close and intimate contact. It causes an acute form of hepatitis and does not have a chronic stage. Hepatitis B virus (HBV) can be transmitted through infected blood (including contaminated needles), sexual contact and from mother to baby at birth. HBV causes both acute and chronic hepatitis. Hepatitis C virus (HCV) is also transmitted through contact with infected blood and is probably not transmitted sexually. Hepatitis D affects only people with hepatitis B; those infected with both viruses tend to have more severe symptoms. Hepatitis E is spread by consuming feces-contaminated food or water.

Hepatitis can cause progressive liver damage, cirrhosis (scarring of the liver) and ultimately may result in liver failure or liver cancer and death. There are vaccines for hepatitis A and hepatitis B.

Approximately 30% of patients with HIV are also co-infected with HCV, which results in severe liver damage more often and more quickly in patients with HIV. Liver disease is currently the number one cause of death amongst HIV patients.

Causative agents: Hepatitis viruses A, B, C, D and E

Clinical presentation: Flu-like symptoms of lassitude, weakness, drowsiness, anorexia, nausea, abdominal discomfort, fever, headache, jaundice (including dark urine, gray stools, and mild pruritis) and hepatomegaly

Recommended diagnostics
- Serology for hepatitis A (anti-HAV IgM, anti-HAV IgG), B (HBsAg, anti-HBc, anti-HBs), and C (anti-HCV IgG [ELISA], anti-HCV IgG [RIBA], HCV RNA)
- Liver function tests (ALT, AST, alkaline phosphatase)

Management and treatment
- Symptomatic and supportive care. When available, interferon for treatment of hepatitis B and C
- Havrix vaccine as a preventive measure for patients at risk for hepatitis A. Epivir-HBV for hepatitis B
- Discourage alcohol consumption during convalescence

Prevention
- Frequent hand washing and good hygiene are important as hepatitis A spreads by the feco-oral route through contaminated food
- Hepatitis B and C are transmitted through contact with infected blood or sexual contact. Condoms can reduce risk of transmission. Discourage needle sharing

Notes
- Co-infection with HIV and hepatitis B and C signifies probable acceleration of HIV disease and hepatitis disease
- The hepatotoxic effect of some ARVs (for example, Nevirapine) and other drugs (for example, Ketoconazole) is significant
Mouth and Throat Conditions

Overview

Patients with AIDS have many conditions involving the oral cavity. An examination of the mouth needs to be part of the physical exam of every patient suspected of HIV infection; even in the absence of complaints. Oral lesions and difficult swallowing can develop rapidly. Patients often present with another complaint and it is the presence of oral thrush that raises the suspicion of HIV infection. Oral lesions may be debilitating because they interfere with correct feeding and increase the risk of weight loss. Painful eating and swallowing and decreased appetite decrease quality of life considerably.

Differential diagnosis includes the following pathogens:

- Bacterial infection: Anaerobic infections causing gingivitis
- Fungal infections: *Candida albicans*
- Viral infections: *Epstein-Barr* virus (hairy leukoplakia), HSV, CMV
- Oncologic conditions: KS

Oral and esophageal candidiasis

*Candida albicans* is the most common fungal infection diagnosed in HIV-infected patients. Candidiasis is usually limited to the skin and mucous membranes. Oral candidiasis (also called thrush) is a rare condition in a young healthy person, but is frequently the first indication of immune impairment in HIV-infected patients. It is commonly one of the presenting signs of HIV infection in individuals who do not have other reasons (e.g., recent antibiotic use) to have fungal disease.

Clinical presentation

- Pseudomembranous white/yellow colonies or clusters appearing anywhere in the oral cavity
- Angular cheilitis: fissuring at corners of mouth with or without visual colonization
- If esophageal infection is also present, the patient may complain of inability to swallow or retrosternal chest pain while swallowing

Management and treatment

Step 1: Topical antifungals:

- Nystatin (1 tablet of 500,000 IU four times daily), may be sucked or chewed
- Gentian violet: Local application of Gentian violet 1% aqueous solution twice daily x one week
- Miconazole gel (60 mg four times daily)
- Amphotericin B (10 mg lozenges four times daily) if available
Step 2: Systemic therapy (recommended when no improvement is seen after seven days with topical treatment and for all cases of esophageal candidiasis)

- 1st choice: Fluconazole (200 mg loading dose, then 100 mg/day until symptoms have resolved). If Fluconazole is not available (affordable), then use Ketaconazole (200-400 mg/day).
- 2nd choice: Itraconazole (100 mg twice daily, dose can be increased to a maximum of 400 mg daily x 10 to 14 days)
- 3rd choice: Amphotericin B (IV) (0.5-1.5 mg/kg/day)

Use intermittent therapy for as long as possible to delay the emergence of resistant candida.

Epstein-Barr virus infection

The Epstein-Barr virus is a virus of the herpes family that is the major cause of infectious mononucleosis and is associated with a number of cancers, particularly lymphomas in PLHA. You need to consider EBV when making a differential diagnosis for HIV. In an HIV infected child co-infection with EBV can be associated with lymphoid interstitial pneumonia. EBV is also associated with Burkitt’s lymphoma and often times the patient has oral hairy leukoplakia.

Clinical presentation
- Fever of unknown origin and other minor symptoms similar to the common cold, including malaise and pharyngitis
- Pharyngeal hyperplasia and lymphadenopathy

Recommended diagnostics
- CBC
- Endoscopic exam

Common findings
- Total white blood count can be normal or low
- Patient can be lymphopenic and/or have evidence of reactive lymphocytes on blood smear
- Ulcers are located in the mid-esophagus

Management and treatment: Primarily symptomatic

Oral hairy leukoplakia

This condition is caused by EBV. It is neither dangerous nor painful and does not require any treatment. It is a sign of immune suppression and is an indication of a poor prognosis.

Clinical presentation: include non-removable whitish plaques with vertical folds, mostly on the lateral surface of the tongue.
**Kaposi’s sarcoma**

Kaposi’s sarcoma (KS) is caused by a herpes virus infection in which cancerous cells, as well as abnormal growth of blood vessels, form solid lesions.

**Clinical presentation**

- Lesions appear as red or purple maculae or nodules. Sometimes they are painful and interfere with food intake and speech in case of oral involvement.
- When KS involves the oral cavity, it is considered to be an aggressive form; however, lesions can be stable for a long time.

**Cytomegalovirus esophagitis**

Even though the most frequent clinical manifestation of CMV disease is retinitis, GI symptoms do occur. Clinically it cannot be distinguished from candida esophagitis. Consider CMV infection in patients with esophageal symptoms that do not respond to empiric antifungal therapy. Most esophageal ulcers result from CMV infection (45%), the other main cause being aphthous ulcers (40%). In the presence of fever, CMV infection is more likely than aphthous lesions.

**Clinical presentation:** pain on swallowing

**Recommended diagnostics:** Endoscopic exam

**Common findings:** Esophageal ulcers are usually single or few in number, large, and deep and are located in the lower third of the esophagus.

**Skin Conditions**

**Overview**

Many patients with HIV infection (80-100%) develop dermatological conditions at some point in the course of the disease. Skin conditions may be very disabling, disfiguring and even life-threatening.

**Etiologies**

- Bacterial infections: *Staphylococcus aureus, Streptococcus* species, *Treponema pallidum, Bartonella* species
- Mycobacterial infections: *Mycobacterium tuberculosis, Mycobacterium avium complex*
- Viral infections: *Herpes simplex* and *Varicella zoster* viruses, molluscum contagiosum, condylomata accuminata
- Infestations: Scabies
- Fungal infections: Seborrhelic dermatitis, tinea corporis, pityriasis versicolor, *Penicillin marneffei, Cryptococcus neoformans, Histoplasma capsulatum, Candida* species
Classification by clinical presentation:

- Warm, inflamed, painful or fluctuating lesion: bacterial infection
- Discolored skin patches: fungal infection or KS
- Localized eruptions or localized pimple-like swellings: viral infection
- Prurigo, urticaria, macular, maculopapular or scaly lesions: classified as skin conditions including drug eruptions, seborrhoea, psoriasis and scabies

Bacterial infections of the skin

1) Skin abscess or Pyomyositis

**Causative agent:** most commonly by *Staphylococcus aureus*

**Clinical presentation:** abscess or affected area is fluctuant and warm

2) Furunculosis or Folliculitis

Careful management of furunculosis or folliculitis is needed in HIV patients because life-threatening disseminated infections may occur.

**Causative agent:** usually caused by *staphylococci*.

**Clinical presentation:** Skin sepsis around hair follicles

**Management and treatment for skin abscess, pyomyositis, furunculosis and folliculitis**

- Surgical drainage for abscess and myositis and local care of the lesion (topical antibiotic cream)
- Antibiotics such as:
  - Cephalexin or Dicloxacillin 500 mg orally four times daily x 7 to 21 days
  - Cloxacillin 500 mg orally four times daily x 10 days
  - Erythromycin 250-500 mg orally four times daily x five days
- Where facilities are available to determine the antibiotic sensitivity of the microorganisms responsible for abscesses, treat in accordance with the findings

**Notes**

- Although surgical drainage is all that is usually required in abscesses or pyomyositis, immunosuppressed patients receive antibiotics to prevent possible development of bacteremia or septicemia during the procedure and also to speed up recovery
- In severe cases, the patient may require IV treatment with penicillinase-resistant penicillin or cephalosporins because of the risk of systemic spread (pyomyositis)
- Careful management is needed in HIV patients because life-threatening disseminated infections may occur

3) Hydradenitis suppurative

Hydradenitis suppurative is a common, disabling dermatosis with a profound impact on a patients’ quality of life. The clinical presentation of the disease is characteristic and allows simple diagnosis. Patients are frequently bothered by pain, scarring, recurrent discharge and smell from the lesions.
HIV/AIDS Related Diseases

Clinical presentation: Recurrent multiple sores and boils in the arm pit or other wet areas

Management and treatment
- Local lesion care and/or surgical drainage
- Antibiotics:
  - Tetracycline 500 mg orally twice daily x 6 weeks
  - In case of treatment failure, use Cloxacillin or Erythromycin 250-500 mg orally four times daily x five days
  - Amoxicillin 250-500 mg orally four times daily x 5 days is also effective, and you can give it if none of the above-mentioned drugs are available
- Where facilities are available to determine the antibiotic sensitivity of the microorganisms responsible for abscesses, treat in accordance with the findings

4) Impetigo
Impetigo is a common infection of the surface of the skin that is usually caused by the bacteria Staphylococcus or Streptococcus.

Clinical presentation: multiple superficial skin sores

Management and treatment
- Gently keep the lesions clean with soap and water
- As impetigo is highly contagious, maintain good hygiene and hand washing techniques to prevent spreading to others
- In severe cases, give Cloxacillin or Erythromycin 50 mg/kg/day four times daily x 5 days

5) Syphilis
Syphilis is a chronic infectious disease caused by Treponema pallidum, either transmitted by direct contact, usually in sexual intercourse, or passed from mother-to-child inutero. It progresses through three stages characterized respectively by local formation of chancre, skin eruption, and systemic infection leading to general paresis. It is recommended that syphilis testing be offered to all clients presenting for VCT in high-prevalence areas because it is treatable in early stages, and has an accelerated course in HIV.

Causative agent: Treponema pallidum

Clinical presentation
- Primary syphilis:
  - A painless, indurated genital ulcer (chancre)
  - Inguinal lymphadenopathy
- Secondary syphilis:
  - Rash, usually involves the palms and soles and is maculopapular
  - Condyloma lata
  - Oral lesions
**Recommended diagnostics:** Venereal disease research laboratory (VDRL) or rapid plasma reagin (RPR) and confirmed by treponema pallidum hemagglutination assay (TPHA).

**Management and treatment:** Follow the *National Guidelines for the Management of Sexually Transmitted Infections*

**Notes**
- About 25% of untreated patients develop a systemic illness (weeks to months later) with fever, rash, condyloma lata, lymphadenopathy and oral lesions (mucous patch)
- VDRL or RPR is not positive until 7-10 days after appearance of chancre

**Fungal infections of the skin**

1) **Tinea (Dermatophytosis)**

Tinea is a fungal infection of the skin, hair or nails. Tinea corporis, tinea pedis, tinea cruris and onychomycosis all occur more frequently in HIV-infected patients. The most frequent is tinea pedis.

**Clinical presentation:** Hyper- or hypopigmented patches that are itchy, with or without a ring pattern and with scaling

**Management and treatment:**
- Use a topical broad-spectrum antifungal treatment, such as Clotrimazole cream 1%, daily up to three weeks
- Explain to the patient that local treatment may take a long time
- Widespread dermatophytosis may necessitate systemic treatment with Griseofulvin 500 mg once daily or Ketoconazole 200 mg daily x three weeks for skin lesions and up to six months for lesions of the nails

**Notes**
- Onychomycosis requires long-term therapy, and not all patients with dystrophic nails have a fungal infection; therefore, it is necessary to make the correct diagnosis
- Direct microscopy of potassium hydroxide (KOH) preparation is sufficient to confirm diagnosis
- Tinea cruris follows tinea pedis and onychomycosis in frequency. KOH preparation of skin scraping can distinguish it from seborrheic dermatitis

2) **Skin candidiasis**

This is an infection with a fungus of the genus Candida, especially *Candida albicans*. In immunocompromised patients, the candida infection can become systemic, causing much more serious disease.

**Clinical presentation:** Itchy, wet lesions, prominent in armpits, groin and under breast
Management and treatment

- Local application of 1% aqueous solution of Gentian Violet or Nystatin ointment twice daily, until lesions are cleared. A prolonged course of treatment may be required.
- If there is no response to therapy, try other topical antifungal drugs, such as Clotrimazole 1% cream.
- In severe cases, or if no response to therapy, Ketoconazole 200 mg orally twice daily x 10 days may be required.

Notes: Candida intertrigo is uncommon in PLHA, but severely immunocompromised patients may have balanitis (candidiasis of the penis), distal urethritis or paronychia (nail infection).

Viral infections of the skin

1) Herpes simplex
Herpes simplex, an acute viral infection, causes one of the most annoying skin conditions in AIDS patients. Chronic ulcers, lasting more than 3 weeks, are seen only with advanced immune suppression. If untreated, they can last for months and finally involve most of the genital and peri-anal skin and mucous membranes. Recurrences occur frequently (more than 6 times per year) in some patients.

Clinical presentation: Painful clusters of vesicles, ulcers or lesions on the mouth or anogenital area

Management and treatment: Follow the National Guidelines for the Management of Sexually Transmitted Infections

2) Varicella zoster (herpes zoster)
Herpes zoster is a viral infection commonly known as shingles. The pain associated with shingles can be intense and in a young person is highly predictive for HIV infection. Almost 25% of PLHA experience recurrences. If they involve the ophthalmic branch of the trigeminal nerve, they can involve the cornea and cause corneal scarring with loss of vision in that eye.

Clinical presentation: Painful clusters of vesicles on an erythematous patch of skin in a localized neurodermatomal distribution

Management and treatment

- Lesions may be self-limiting and may not need more than pain relief with aspirin or Paracetamol 500 mg four times daily and local lesion care with Gentian violet or antiseptics.
- Local application of Lidocaine gel 2% may help improve pain relief in some patients.
- Calamine lotion is cheap, soothes the skin, reduces intense pruritus and accelerates the drying up process.
- Stronger analgesics are sometimes needed, such as Paracetamol 1 g plus Codeine 60 mg every 4 hours.
• Acyclovir 800 mg orally four times daily x 7 days is indicated in patients with ophthalmic lesions or disseminated zoster
• Antibiotics for secondary infection recommendations as for impetigo
• Post-herpetic neuralgia is uncommon, but if present, should be treated with pain modifying agents: Phenytin 100 mg slowly increasing to 250-300 mg daily or Carbamazepine 100 mg daily increasing to 400 mg daily in 10 days

3) Molluscum contagiosum
Molluscum contagiosum is a skin disease that commonly spreads through direct contact including sexual.

Causative agent: a poxvirus

Clinical presentation
• Pearly white umbilicated papules (2-5 mm) that appear in the genital area. If transmission is non-sexual, they may also be found in any part of the body
• There can be very extensive multiple lesions, especially when on the face

Management and treatment
• Curettage (often followed by iodine)
• Unroof lesions with a needle and express the central materials
• Electro-cauterization
• Cryotherapy

Notes
• Differential diagnosis with disseminated cryptococcosis and histoplasmosis penicilliosis
• Those systemic mycoses are usually associated with fever, pulmonary or meningeal involvement
• Remission with ARVs is common

4) Condyloma acuminata (genital warts)
It is nearly always transmitted by sexual contact and can give rise to cervical and anal cancer. Patients with a small number of warts may be asymptomatic. Other patients may have pruritis, bleeding or pain. Incubation period: 1-6 months and recurrence rate is high. Women with genital warts should have an annual PAP smear (cervical cancer). This should be distinguished from Condyloma lata (secondary syphilis).

Causative agent: *Human papillomavirus* (HPV)

Clinical presentation: Soft fleshy growths with cauliflower appearance
**Management and treatment**

- Podophyllin resin (10-25% in Tincture of Benzoin):
  - Apply once or twice weekly until resolved
  - Should be washed off two hours after the first application
  - Contraindicated in pregnancy
- Electro-cauterization
- Cryotherapy with liquid nitrogen
- Surgical removal
- Laser surgery

**Other skin conditions**

**1) Drug eruptions**

**Clinical presentation:** Generalized skin eruption and/or inflamed mucous membranes

**Management and treatment**

- Withdraw drug(s)
- Local lesion care
- Give oral antihistamines

**Notes**

- Systemic corticosteroids are immune depressing and should be given only in life threatening situations
- Co-trimoxazole, Sulfadiazine, Acyclovir and anti-TB drugs are often associated with drug eruptions
- Drug eruptions are associated with certain ARVs: Nevirapine, Efavirenz (EFZ), AZT and d4T

**2) HIV-associated skin rash**

**Clinical presentation:** Itchy generalized maculopapular skin rash, erythroderma

**Management and treatment**

- Topical calamine lotion or antihistamines, such as Diphenhydramine 50 mg orally four times daily, Chlorpheniramine 4 mg orally three times daily, or Promethazine 10 mg twice daily
- Ultraviolet light and topical application of steroids may be helpful

**Notes**

- A generalized pruritic maculopapular skin rash resulting from eosinophilic folliculitis is typical of HIV
- Treatment is mainly symptomatic
3) Seborrheic dermatitis or generalized erythroderma

Clinical presentation: Generalized greasy scaling with excessive dandruff on the scalp, face and chest

Management and treatment
- Usually responds well to topical steroids (1% hydrocortisone), coal tar and soothing cream
- If response to therapy is poor, suspect secondary infection, which would require local antiseptics (Povidone iodine or Chlorhexidine) and may need systemic antibiotics (Cloxacillin or Ampicillin 250-500 mg three times daily x 5 days)
- May also be complicated by cutaneous fungal infection. In this case, combine topical steroids with Clotrimazole cream 1%
- With coexistent candidiasis, topical Ketoconazole is beneficial
- In severe cases, oral Ketoconazole 200 mg daily may be indicated
- Recurrence is frequent, and maintenance therapy may be necessary

4) Psoriasis

Clinical presentation: This condition presents as extensive plaques which have well demarcated borders and are covered with thick silvery white scales. It is often mistaken for a fungal skin infection. Lesions are often bilateral and favor the scalp, elbow, knees, hairline and intertriginous areas.

Management and treatment
- Coal tar in salicylate ointment applied twice daily
- Severe cases may respond to topical corticosteroids

5) Scabies

Clinical presentation: Parasitic skin infection characterized by superficial burrows, intense pruritis (most intense at night) and secondary inflammation

Management and treatment
- Permethrin 5%, Lindane 1%, Sulfur 5-10% (Topical)
- Ivermectin single oral dose (1 tab/30 kg)
- Change and launder clothes and bed linens

6) Kaposi's Sarcoma

Causative agent: The etiology of KS is associated with Human herpes virus-8

Clinical presentation: Dark patchy, painless swelling or nodules that are not itchy and do not have a ring pattern, with or without similar oral lesions
**HIV/AIDS Related Diseases**

**Management and treatment**

- Discrete solitary or few lesions are best left alone
- Treat lesions of the face or exposed parts of the body locally with cryotherapy (topical liquid nitrogen), intra-lesional therapy with either Vinblastine (0.2–0.4 mg at two-week intervals), or alpha interferon, and surgical excision
- In single lesions, results with any of the treatment choices mentioned are promising
- If lesions are disseminated or extensive, and if treatment is considered, biopsy should be done
- Radiotherapy for localized intraoral or pharyngeal KS, painful cutaneous KS and lymphedema of the face and extremities

**Notes**

- Remission reported with ARVs
- Visceral with lung involvement may mimic TB

**Sexually Transmitted Infections**

**Urethral discharge in men**

It is the most common STI in men and the characteristic manifestation of urethritis. Discharge is frequently accompanied by pain or burning when passing urine (*dysuria*) and sometimes by urethral itching. It can be associated with scrotal pain and swelling (*epididymitis*) which tends to be unilateral.

**Types of urethritis**

- Gonococcal urethritis caused by *Neisseria gonorrhoea*
- Non-gonococcal urethritis (NGU) caused by *Chlamydia trachomatis*, *Ureaplasma urealyticum* or *Trichomonas vaginalis*

**Management and treatment**

Follow the *National Guidelines for the Management of Sexually Transmitted Infections*

**Genital sores (ulcers or blisters)**

**Etiology**

- Syphilis
- Chancroid
- Lymphogranuloma venereum (LGV)
- Herpes simplex
Management and Treatment

Follow the *National Guidelines for the Management of Sexually Transmitted Infections*

Notes

- Skin conditions such as Molluscum contagiosum, Scabies, Condylomata acuminata and Syphilis also could be sexually transmitted
- For other STIs affecting women: refer to the section, 'Management of HIV Disease in Women'
Prevention of Opportunistic Infections

Overview

- Opportunistic infections (OIs) are infections caused by organisms that in a normal host would not cause disease
- Primary prophylaxis or preventive treatment is used to prevent OIs in individuals with HIV/AIDS
- CD4 lymphocyte count helps to determine when to begin primary prophylaxis. For example, when CD4 lymphocyte counts are < 200 cells/mm$^3$, adults begin taking TMP/SMX to prevent PCP as well as other diseases, such as toxoplasmosis and bacterial infections
- Secondary prophylaxis is the maintenance therapeutic dose that the patient receives to prevent relapse or disease recurrence
- When counseling patients with HIV, it is important to stress ways they can avoid OIs. Easy ways to avoid some of these infections are by good washing of food and hands and through general good hygiene
- Avoid unpasteurized dairy products, raw or undercooked eggs, meat, poultry or fish as sources of salmonella infection
- Avoid undercooked or raw meat as a source of toxoplasmosis. Risk of transmission can be reduced if meat is adequately cooked and vegetables and fruit are carefully washed before eating. Also avoid exposure to cats
- Advise patients and family to boil drinking water to avoid diarrheal diseases such as cryptosporidiosis

Prevention of Bacterial Infections

Streptococcus pneumonia

- One of the most common serious bacterial infections
- Can cause pneumonia, otitis media, septicemia, and other invasive illnesses
- The vaccine for pneumococcus should be given to all patients with HIV who are over two years old, if the vaccine is available
- There is now a new heptavalent conjugate vaccine for pneumococcus. This vaccine may be given to children as young as 2 months of age
Prevention of Opportunistic Infections

**Tuberculosis**

- Mycobacterium TB is now the most common cause of death in HIV-infected individuals worldwide
- Evidence shows that TB preventive therapy among HIV-infected people is effective
- Isoniazid (INH) may be given as a daily, self-administered therapy for six months at a dose of 5 mg/kg to a maximum of 300 mg. These individuals must be seen on a monthly basis and should be given a one-month supply of medication at each visit
- Prevention therapy is recommended for tuberculin-positive HIV-infected individuals who do not have active TB
- In some settings, tuberculin testing may not be feasible. Under these circumstances, the following individuals may still be considered for prevention therapy if they are infected with HIV:
  - Those living in populations with a high prevalence of TB infection (estimated to be > 30%)
  - HCWs
  - Household contacts of TB patients
  - Prisoners
  - Miners
  - Other selected groups at high risk of acquisition or transmission of TB
- Contraindication for TB prevention:
  - Preventive therapy is contraindicated in patients with active TB and in patients with active (chronic or acute) hepatitis
  - Active TB must be excluded before beginning preventive therapy
  - For individuals who consume alcohol daily, give INH with caution

**Mycobacterium avium complex (MAC)**

- MAC is found all over the world
- Symptoms of disseminated MAC are non-specific and include weight loss or failure to thrive (in children), fever, abdominal pain, diarrhea and lymphadenopathy
- The age of the individual is used as the indicator to start primary prophylaxis
- In adults, prophylaxis is recommended once the CD4 lymphocyte count is < 100 cells/mm$^3$
- Adults (> 12 years) Clarithromycin 500 mg orally twice daily
- For children, CD4 lymphocyte cell counts vary with age, but if they are below 15% for their age group, prophylaxis is recommended
- Children (0-12 years) Clarithromycin 7.5 mg/kg orally twice daily
- Recent studies suggest that once patients receive HAART therapy and the CD4 lymphocyte cell count increases to > 100 cells/mm$^3$ for three months, primary prophylaxis may be stopped. These recommendations apply only to adults and adolescents and not children
Prevention of Parasitic Infections

Cryptosporidiosis
- Cryptosporidiosis is spread by direct contact with infected adults, infected children, diapers and infected animals. Also, food or water contaminated with feces can spread infection
- There is no curative therapy currently available for cryptosporidiosis
- Prevention: through general good hygiene

Isosporiosis
- Isosporiosis spreads by the same routes of transmission as cryptosporidium and has the same symptoms as well
- TMP/SMX can be used to treat Isosporiosis, but there is a 50% relapse rate among adults
- Prophylaxis with TMP/SMX may be needed to prevent relapses
- The dose of TMP/SMX is the same as for PCP

Toxoplasmosis
- Toxoplasmosis is transmitted via raw meat particularly pork and lamb. It can be transmitted via cat feces. Thus meat should be thoroughly cooked
- Immunosuppressed individuals should avoid contact with stray cats or cat feces.
- Good hand washing can prevent infection
- Toxoplasmosis in the immunocompromised host usually causes CNS disease, specifically brain abscesses

Table 7: Toxoplasmosis Treatment and Prophylaxis

<table>
<thead>
<tr>
<th>Age</th>
<th>Secondary Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (0-12 years)</td>
<td>Pyrimethamine: 1 mg/kg/day orally (maximum 25 mg) and Sulfadiazine: 40 mg/kg/day orally three times daily and Folinic acid: 5 mg orally every 3 days</td>
</tr>
<tr>
<td>Adults (&gt; 12 years)</td>
<td>Pyrimethamine: 25 mg orally daily and Sulfadiazine: 1,000 mg orally three times daily and Folinic acid: 15 mg orally daily</td>
</tr>
</tbody>
</table>
Prevention of Fungal Infections

Adults:
The prophylactic dose of TMP/SMX is TMP 160 mg and SMX 800 mg once daily orally

Children:
- The prophylaxis dose for children is TMP 150 mg/m$^2$ and SMX 750 mg/m$^2$ in two divided doses for three consecutive days a week
- Like adults, this may be given everyday also to protect against toxoplasmosis
- If patients are unable to tolerate TMP/SMX, or have G6PD deficiency (an enzyme disorder affecting red blood cells), or are allergic to sulfa drugs or experience side effects Dapsone may be used. The dose of Dapsone for adults is 100 mg daily and for children, the recommended dose is 2 mg/kg/day, with a maximum dose of 100 mg/day
- Prophylaxis can be discontinued in adults and adolescents who have maintained a CD4 lymphocyte cell count > 200 cells/mm$^3$ for at least three months

Candidiasis
- *Candida albicans* is the most common fungal infection diagnosed in HIV-infected patients
- Oral candidiasis (also called thrush) is particularly common
- It is commonly one of the presenting signs of HIV infection in individuals who do not have other reasons (e.g., recent antibiotic use) to have fungal disease
- If esophageal infection is also present, the patient may complain of inability to swallow or retrosternal chest pain while swallowing
- An infant may begin to feed and then stop after the first few swallows, arching his back and turning his head because of difficulty in swallowing
- Daily Fluconazole is recommended for prophylaxis of frequent and severe recurrences of candidiasis. However, daily Fluconazole treatment can lead to the development of Fluconazole resistant candidiasis. Hence, an alternative is to use daily Nystatin for prophylaxis, particularly for oral thrush
- The prophylaxis dose of Fluconazole is the same as the treatment dose. For adults, Fluconazole 100-200 mg orally daily is recommended. For children, Fluconazole at 3-6 mg/kg/day orally is recommended
- The dose for Nystatin prophylaxis is the same as the treatment dose
Table 8: Fungal Infection Prophylaxis

<table>
<thead>
<tr>
<th>Age</th>
<th>Nystatin dose</th>
<th>Fluconazole dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates (&lt; 1 month)</td>
<td>100,000 units four times daily orally</td>
<td>3-6 mg/kg orally every 3 days (&lt; 14 days old)</td>
</tr>
<tr>
<td>Infants (1-12 months)</td>
<td>200,000 units four times daily orally</td>
<td>3-6 mg/kg orally daily</td>
</tr>
<tr>
<td>Children</td>
<td>400,000 units four times daily orally</td>
<td>3-6 mg/kg orally daily</td>
</tr>
<tr>
<td>Adults</td>
<td>400,000 -600,000 units four times daily orally</td>
<td>100-200 mg/kg orally daily</td>
</tr>
</tbody>
</table>

Cryptococciosis
- Cryptococciosis usually occurs in HIV-infected individuals with severe immune suppression and most commonly causes cryptococcal meningitis
- Treatment is usually Amphotericin B, plus Flucytosine for 2 weeks, followed by Fluconazole
- Secondary prophylaxis with Fluconazole is recommended for both adults and children for life. The doses are the same as the maximum doses listed above for candidiasis

Prevention of Viral Infections

Cytomegalovirus infection
- Recognition of the early manifestations of the disease is the most important method for preventing severe CMV
- Oral Ganciclovir is the only effective antiviral for CMV prophylaxis, but is not recommended for routine use due to its lack of cost-effectiveness
- Risk increases at CD4 T-lymphocyte counts of < 50 cells/mm³
- Individuals should be educated about the significance of increased floaters in the eye and should be advised to assess their visual acuity regularly by using simple techniques such as reading newsprint

Herpes simplex infection
- Primary infection can be prevented through safer sex (condom usage) at all times and specific avoidance of contact with herpetic lesions (genital or orolabial)
- Drug prophylaxis of initial episodes of HSV disease is not recommended
- Individuals with frequent or severe recurrences can be given daily suppressive therapy with oral Acyclovir or Famciclovir
Prevention of Opportunistic Infections

**Varicella zoster infection**
- Individuals who have no history of chickenpox or shingles should avoid exposure to persons who are infected with chickenpox or shingles
- Data are lacking on the effectiveness of Acyclovir for preventing chickenpox in susceptible individuals
- No preventive measures are currently available for shingles
- Pregnant women: VZIG (Varicella Zoster Immune Globulin) is recommended for VZV-susceptible, HIV-infected pregnant women within 96 hours after exposure to VZV

**Human papillomavirus (HPV) infection**
- Prevent exposure to HPV: safer sex practices (use of condom at all times) should be advised
- Prevention of HPV-associated genital epithelial cancers in HIV-infected women
- Pelvic examination and a PAP smear at first presentation and annually thereafter if normal
- Abnormal PAP smear results should be followed up in accordance with current accepted best practices

**Influenza**
- Influenza vaccine 0.5ml intramuscularly annually in all HIV infected individuals prior to the influenza season
- Amantadine 100 mg orally twice daily is an alternative for selected susceptible unimmunized individuals who are acutely exposed to influenza

**Hepatitis B**
- Hepatitis B Vaccine 0.5 ml IM injection x 3 doses (first then second after one month and third after 6 months) in all susceptible (Anti-HBc-negative) HIV-infected individuals
Table 9: Summary of Prevention of Opportunistic Infections in Adults

<table>
<thead>
<tr>
<th>Agent/Intervention</th>
<th>Dosage/Schedule</th>
<th>Indication</th>
<th>Disease Prevented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimethoprim-Sulfamethoxazole (TMP/SMX also known as Co-trimoxazole or Bactrim® or Septran®)</td>
<td>2 single strength (80/400 mg) or 1 double strength tablet (160/800 mg) orally daily for life</td>
<td>All symptomatic HIV infected individuals (WHO clinical stage 2, 3 or 4) or CD4 T-lymphocyte count &lt; 200/mm³ or if there has already been an active infection of PCP or toxoplasmosis</td>
<td>PCP, toxoplasmosis, bacterial pneumonia, diarrhea</td>
</tr>
<tr>
<td>PAP smear</td>
<td>At first presentation and annually thereafter</td>
<td>All HIV-infected women</td>
<td>To detect HPV-associated genital epithelial cancers, abnormal PAP smear results should be followed up in accordance with current accepted best practices.</td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>0.5ml IM injection x 3 doses according to manufacturer's instructions</td>
<td>All susceptible (anti-HBc-negative) HIV infected individuals</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Influenza vaccine</td>
<td>0.5ml IM injection annually prior to the influenza season</td>
<td>All HIV infected individuals</td>
<td>Influenza</td>
</tr>
</tbody>
</table>
Management of HIV Disease in Women

Gynecological Problems

Introduction
Gynecological problems are common among women living with HIV/AIDS and may be the presenting sign of immunosuppression in women.

HIV/AIDS contributes to the frequency and severity of many gynecological infections, including vaginal candidiasis, herpes simplex, pelvic inflammatory disease and genital warts. Treatment for many of these infections is relatively inexpensive, but women living with HIV/AIDS often require higher doses and longer courses of therapy; they may also suffer from more frequent recurrences.

1) Vaginal discharge

Etiology
- Gonococcal infection
- Chlamydia trachomatis
- Trichomonas vaginalis
- Bacterial vaginosis
- Candidiasis

Management and treatment
- Follow the National Guidelines for the Management of Sexually Transmitted Infections
- Ensure treatment of partners

2) Lower abdominal pain and fever/pelvic inflammatory disease (PID)

Etiology
- Gonococcal infection
- Chlamydia trachomatis
- Mixed bacterial infections (including anaerobes)
- TB

Management and treatment
- Counsel women to report these symptoms right away to ensure prompt diagnosis and treatment
- Treat bacterial infections aggressively with strong broad spectrum antibiotics, for example, Ciprofloxacin 500 mg twice daily x one week
• If STI is the cause, follow the National Guidelines for the Management of Sexually Transmitted Infections
• Exclude acute conditions (i.e., appendicitis, ectopic pregnancy)
• If the patient does not respond to treatment, refer her for a pregnancy test on blood to exclude ectopic pregnancy with a negative urine pregnancy test
• Exclude pelvic abscess or TB
• You may find huge pelvic abscesses in immunosuppressed patients following a pelvic infection or surgical procedures
• Drainage and appropriate antibiotic therapy to cover aerobic and anaerobic organisms is necessary

3) Malignancies

Etiology
• Cervical cancer
• KS

Management and treatment
Do not undertake extensive surgical intervention if equally effective treatments are available, such as radiotherapy. If HIV seropositive patients have a severely compromised immunological status, they often do not respond well to cancer surgery, radiotherapy or chemotherapy.

4) Amenorrhea and intermenstrual bleeding

Etiology
• Menstrual disturbances are often associated with chronic ill health and are frequent in women with HIV
• May be linked to general deterioration and weight loss due to HIV disease

Management and treatment
• Exclude other causes such as pregnancy, perimenopause, uterine fibrosis, genital tract infections, cervicitis, PID, TB and cancer
• Menses may return after treatment of other infections and weight gain
• Best management is to provide counseling and reassurance
• If the woman is sexually active and not using an effective method of contraception consistently, do a pregnancy test
HIV Infection and Pregnancy

Introduction

Each year, worldwide, two million women infected with HIV become pregnant, most of them in poor countries. Between one-quarter and one-third transmit the disease to their newborns in the perinatal period; during pregnancy, labor, or breast-feeding. That translates into about 2,000 new HIV-infected infants each day. Children born to HIV infected mothers who die are left orphaned and are harder to care for than the HIV-negative infants.

HIV presentation is the same in both sexes, but the disease has greater implications on a woman’s reproductive health; her ability to cope with pregnancy and the possibility of transmission of the virus to her unborn or newborn child. During the asymptomatic phase of HIV, most women are unaware of their infection until the disease is diagnosed in their infants. This may cause conflict within the family; relatives think she brought in the infection.

Effects of HIV on Pregnancy

Some studies in Africa suggest that HIV may have an adverse effect on fertility in both symptomatic and asymptomatic women. Pregnancy rates are lower and pregnancy loss is more common in those who are HIV infected. Others state that fertility is affected only in late HIV disease. When comparing changes in CD4 count/percentage over time, there is no difference between HIV-positive pregnant and non-pregnant women.

HIV does not seem to be a significant cause of congenital abnormalities or spontaneous abortion. Pregnancy does not accelerate disease progression in early HIV infection. Late HIV disease may affect the outcome of pregnancy, that is, poor fetal growth, preterm delivery, low birth weight and prenatal and neonatal death. Common HIV-related problems are not different in pregnant and non-pregnant women, and both groups should receive the same management (except for drugs that are contraindicated or used with caution, such as Streptomycin and Efavirenz).
Mother-to-Child Transmission (MTCT) of HIV

Introduction

HIV may be transmitted to the infant either during pregnancy, delivery or lactation; most transmission is thought to take place during delivery. For mothers known to be HIV-infected prenatally, the risk of transmitting HIV to infants through breast-feeding is 14% while for mothers who acquire HIV postnatally, the risk is as high as 29%.

Many studies indicate that the risk of breast milk transmission is higher in the first few months of life, with subsequent tapering off. However, the risk persists as long as the infant is breast-fed. HIV transmission is also higher if the mother has mastitis.

Factors that May Increase the Risk of Transmission

- High maternal viral load: > 5000-10,000 copies/ml (at time of seroconversion) and during late HIV disease, CD4 cell counts < 100 cells/mm³
- Recurrent STIs
- Malaria interferes with placental functions and eases viral transmission across the placenta
- Vitamin A deficiency
- Preterm delivery
- Firstborn twin
- Vaginal delivery
- Long duration of rupture of membranes (> four hours)
- Placental disruption
- Invasive procedures during delivery (for example, vacuum extraction, episiotomy, use of forceps, fetal scalp monitoring)
- Mechanical nasal suction after delivery
- Breast-feeding, and especially mixed feeding. One study suggested that mixed feeding might be a greater risk because the infant has a higher risk of contracting a viral or bacterial GI infection, which compromises the integrity of the intestinal wall making it easier for the HIV virus to pass into the infant’s bloodstream
**Measures to Reduce MTCT**

**During pregnancy**
- Provide voluntary counseling and HIV testing, plus psychosocial support.
- Diagnose and provide aggressive treatment of malaria, STIs and other infections as early as possible.
- Provide basic antenatal care including:
  - Iron supplementation
  - Discussion of MTCT and infant feeding options
  - Starting ART for MTCT
  - Information on practicing safer sex

**During labor and delivery**
- Delay rupturing of membranes
- Do only minimal digital examinations after rupture of membranes
- Reduce use of assisted delivery with forceps and the like and episiotomies
- Elective cesarean section has been demonstrated to have a more protective effect against MTCT than vaginal delivery. However, caesarean section has limited applications in resource-constrained settings where the procedure is associated with increased rates of maternal morbidity and mortality and transmission to HCWs can be an additional risk
- If not already on ART, give Nevirapine (NVP).

**After delivery**

The following recommendations proved to reduce the chances of MTCT after delivery:
- Avoid mechanical nasal suction
- Cleanse the newborn immediately of all maternal secretions and blood
- Support safer infant feeding
- Advise mother to avoid breast-feeding

**ARV Therapy and MTCT**

**Prevention of prenatal transmission**

The use of ARV therapy can reduce MTCT significantly. Women on treatment with ARVs for HIV infection have very low transmission if their viral load is < 1000 copies/mm³. Studies conducted in 1994 showed that administering AZT to women from the 14th week of pregnancy and to the newborn during labor decreased the risk of MTCT by nearly 70% in the absence of breast-feeding. A shorter regimen of AZT alone, starting
Mother-to-Child Transmission (MTCT) of HIV

from the 36th week of pregnancy, was shown to reduce the risk of transmission of HIV at six months by 50% in the non-breast-feeding populations and by 37% in those breast-feeding. A short course of NVP has been shown to reduce the risk of transmission and is the protocol most commonly used because clinical trials have demonstrated its efficacy in reducing MTCT. It has a low cost and is easy to use in MTCT programs.

The NVP regimen for the prevention of MTCT is:

- Intrapartum short course: 200 mg at the start of labor
- Postpartum for infant: 2 mg/kg, start within 48-72 hours

Other trials of short course ARV regimens using a combination of AZT and Lamivudine (3TC) also substantially decrease the risk of transmission.

**Women first diagnosed with HIV infection during pregnancy**

Women who are found to be HIV-infected during their first trimester of pregnancy may consider delaying initiation of ART. When determining treatment options, the severity of maternal HIV disease and potential benefits and risks of delaying ART until after the first trimester should be weighed. For women who are severely ill, the benefit of early initiation may outweigh the theoretical risk to the fetus. In these cases, recommend initiating with drugs such as AZT, 3TC and NVP or Nelfinavir (NFV).

**HIV-infected women on ART who become pregnant**

The various options available to HIV-infected women undergoing ART who become pregnant include:

- Suspend therapy temporarily during the first trimester
- Continue same therapy
- Change to a different regimen

When deciding which option will be the most beneficial, the following issues must be considered:

- Gestational stage of the pregnancy
- Severity of maternal disease
- Tolerance of regimen in pregnancy
- Potential for adverse fetal effects

The fetus is most susceptible to potential teratogenic effects of drugs during the first 10 weeks of gestation; the risks of ART to the fetus during this period are unknown.

**ART and breast-feeding**

Women who require ART and who are breast-feeding should continue their current ART regimen. The efficacy of potent ART taken by the mother solely to prevent postnatal transmission of HIV through breast milk is unknown, but is currently under study.
HIV-infected women who receive short-course ARV prophylaxis to reduce MTCT and require treatment postpartum

The following factors must be considered when offering short-course ARV prophylaxis to HIV-infected women:

- Short-course ARV regimens, which do not fully suppress viral replication, may be associated with development of ARV drug resistance
- Based on current information (until further research is done), prior administration of short-course AZT/3TC or single dose NVP for prevention of MTCT should not preclude use of these agents as part of a combination ARV drug regimen initiated for treatment of these women

Adherence to therapy in pregnancy and postpartum

Adherence may be more difficult in pregnant and postpartum women than non-pregnant women. Obstacles to adherence may include:

- Morning sickness and GI upset, which can be further compounded by ARV-associated nausea
- Fears that ARV drugs might harm the fetus

If for any reason there is a need to discontinue therapy temporarily during pregnancy, stop and restart all drugs together to reduce the potential for the emergence of resistance. Physical changes during the postpartum period, coupled with stresses and demands of caring for a newborn infant, may make adherence to treatment especially difficult after birth. Providing additional support for maintaining adherence to therapy during ante- and postnatal periods is important.

Prevention of OIs during Pregnancy

When determining the types of prophylaxis that should be offered to HIV-infected women during pregnancy, a gynecologist needs to be consulted. The various regimens used for the prevention of OIs during pregnancy are summarized in table 10.
Table 10: Prevention of Opportunistic Infections during Pregnancy

<table>
<thead>
<tr>
<th>OI</th>
<th>Prevention Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCP</strong></td>
<td>Use TMP/SMX, with Dapsone as the alternative. Because of theoretical concerns for teratogenicity, providers may choose to withhold prophylaxis in the first trimester or use aerosolized pentamidine.</td>
</tr>
</tbody>
</table>
| **Toxoplasmosis** | Primary prophylaxis: TMP/SMX, with theoretical concerns for teratogenicity in first trimester. Avoid pyrimethamine regimens.  
Secondary prophylaxis: This is a risk/benefit issue with concerns for teratogenicity of pyrimethamine vs. recurrent toxoplasmosis; most clinicians favor continued treatment  
A specialist should manage primary toxoplasmosis during pregnancy. |
| **TB** | INH + pyridoxine regimens are preferred for prophylaxis; some providers avoid INH in the first trimester because of theoretical concerns for teratogenicity.  
Be sure to perform a chest X-ray to rule out active TB using lead apron shields for the patient.  
RIF and RBT appear safe during pregnancy, but experience is limited.  
Avoid PZA, especially during the first trimester. |
| **S. pneumonia** | May give pneumovax. Because of HIV viral burst, some delay vaccination until after ART. |
| **Fungal infection** | General: avoid '-azoles' (fluconazole, ketoconazole and itraconazole) because of teratogenicity.  
Cryptococcosis, histoplasmosis and coccidioidomycosis: for secondary prophylaxis, Amphotericin B is preferred instead of -azoles, especially during first trimester |
| **CMV** | Standard recommendations apply |
| **HSV** | Oral Acyclovir during late pregnancy to prevent prenatal HSV transmission is controversial, but usually not used; Acyclovir prophylaxis to prevent severe recurrences may be indicated |
| **VZV, exposure**  
**Non-immune host** | VZIG within 96 hours of exposure is recommended |
| **HPV** | Avoid intravaginal 5-Fluorouracil. |
Terminal Illness and Palliative Care

A patient with terminal illness is often uncomfortable due to one or more of the conditions below. Good palliative and supportive care should address these conditions.

Psychological Support

In the terminal stages of HIV disease, one of the most important components of care is psychological support. This support is usually given by family, friends, relatives, members of the community and spiritual leaders, with the support of professional health staff, social workers and trained community counselors.

Pain Control

In the terminal stages, pain should be minimized by effective management. Strong analgesics in high dosage, such as oral or IM Morphine, might be indicated at this stage (see the section on pain in HIV/AIDS patients).

Anxiety and Insomnia

Good counseling and family support are essential to handle these conditions. Long acting anxiolytics, such as Diazepam, may further increase weakness. Short acting drugs, such as Lorazepam, are more appropriate for insomnia. Hydroxyzine can be used to treat anxiety and insomnia and does not increase weakness. This drug is also useful in combination with Morphine.

Dementia

Dementia is a progressively worsening condition of physical and mental incapacitation. It is usually caused by HIV infection itself and has no satisfactory medical treatment so it has to be handled palliatively. Again, counseling and family and psychosocial support are the best forms of management. Medicinal management will depend on the state of the patient. Sometimes there is excitement almost approximating psychosis. If this occurs, Haloperidol 2.5 mg two or three times daily may be indicated.

Anorexia, Nausea and Vomiting

There is no easy solution to loss of appetite in terminal illness. The family should be encouraged to continue providing frequent small amounts of food. Fluid meals may be tried, in particular if the patient has problems swallowing food. Oral rehydration may be necessary. Vitamin supplements should be given. Metoclopramide 10 mg three times daily may be beneficial particularly when nausea is present.
Hiccups

Hiccups are common in severe HIV disease and usually difficult to manage. Treat with Metoclopropamide 10 mg orally three times daily or Haloperidol 2.5 mg two or three times daily. Alternatively, Chlorpromazine, 100 mg two or three times daily may be beneficial. However these drugs are usually sedative and should be taken with caution.

Pressure Sores

The family should be taught to turn the patient at least once every two hours. If pressure sores develop, they should be kept clean and dry.

Mouth Care

Maintain oral hygiene and reduce symptoms of dry mouth by stimulating saliva (by sugar-free chewing gum or chewing palm leaves). The family should be taught to clean the mouth using a piece of wet cloth and salt water after every feeding.

Terminal Respiratory Distress

Many terminally ill patients develop dyspnea as they near death. This may be due to pneumonia or due to an untreatable chest condition like KS. Good ventilation and putting the patient in a comfortable sitting position should be done. Oxygen may give relief when available. This condition is very stressing for patients and families, which may require treatment with oral Morphine as needed every 4 hours plus Hydroxyzine 25 mg three times daily.

Caring for the Carers

People who look after terminally ill infected patients, for example family members, relatives and HCWs, need psychosocial support themselves. This can be provided in the form of counseling directed towards them by interdisciplinary team members and by mutual support by community members.
Antiretroviral Therapy (ART)

Many medicines are available for the treatment of HIV infection; however, none of these medications can cure HIV. Medications used to treat HIV are able to reduce the ability of the virus to replicate (or reproduce itself). When the virus is unable to replicate, symptoms experienced by a person infected with HIV are reduced. Individuals receiving ART are less susceptible to OIs, cancers and other illnesses. Many patients live longer as a consequence of ART.

The goals of ART include the following:
- Prolong and improve the quality of life for people living with HIV/AIDS
- To achieve a significant drop in viral load
- To achieve immune reconstitution that is quantitative (CD4 count in normal range) and qualitative (pathogen specific immune response)
- Provide an ARV regimen that not only achieves reduced viral loads, but also preserves future therapeutic options, is relatively free of side effects and is tailored to individual needs for adherence

Antiretroviral Groups

Each group of drugs affects a different point in the life of the virus within the cell.
- Nucleoside and Nucleotide reverse transcriptase inhibitors (NsRTIs and NtRTIs)
  - Lead to premature termination of the production of the HIV DNA chain
  - Are active against both HIV-1 and HIV-2
  - Resistance develops rapidly if given as single drugs alone (monotherapy)
  - Side effects include:
    - Nausea and vomiting
    - Anemia, neutropenia
    - Peripheral neuropathy
    - Pancreatitis
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
  - Are active only against HIV-1
  - Adverse effects include diffuse maculopapular rash, hepatitis, headache and nausea
- Protease Inhibitors (PIs)
  - The HIV protease enzyme is responsible for cleaving various polyproteins in the process of producing mature infectious virions
Interference with this enzyme by PIs leads to significant reduction of the virus in the body to undetectable levels

Rapid resistance will develop if PIs are used as single agents.

PIs are associated with multiple drug interactions because they inhibit cytochrome P450 enzymes.

For example: PIs increase the metabolism of Rifampicin and decrease its effectiveness in treating TB.

Side effects include GI problems, i.e., nausea and vomiting.

Indinavir should be taken with plenty of water to prevent kidney stones.

- **Entry Inhibitors**
  - This the most recent group of ARVs
  - It interferes with the virus’s ability to adhere and fuse to receptors at the surface of CD4 cells preventing viral invasion to these cells.
  - The well-known drug of this group is T-20

**Table 11: Antiretroviral Groups**

<table>
<thead>
<tr>
<th>Nucleoside reverse transcriptase inhibitors (NsRTIs)</th>
<th>Nucleotide reverse transcriptase inhibitors (NtRTIs)</th>
<th>Nonnucleoside reverse transcriptase inhibitors (NNRTIs)</th>
<th>Protease Inhibitors (PIs)</th>
<th>Entry Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (ZDV, AZT)</td>
<td>Tenofovir disoproxil fumarate (TDF)</td>
<td>Nevirapine (NVP)</td>
<td>Saquinavir (SQV)</td>
<td>T-20</td>
</tr>
<tr>
<td>Didanosine (ddI)</td>
<td></td>
<td>Efavirenz (EFZ)</td>
<td>Ritonavir (RTV)</td>
<td></td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td></td>
<td></td>
<td>(as Pharmacoenhancer)</td>
<td></td>
</tr>
<tr>
<td>Lamiduvine (3TC)</td>
<td></td>
<td></td>
<td>Indinavir (IDV)</td>
<td></td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
<td></td>
<td></td>
<td>Nelfinavir (NFV)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lopinavir/ritonavir</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(LPV/r)</td>
<td></td>
</tr>
</tbody>
</table>
WHO Recommendations for Initiating ARVs in Adults and Adolescents

WHO recommends that HIV-infected adolescents and adults start ART when they have:

- WHO stage IV disease (clinical AIDS), irrespective of CD4 cell count
- 2003 WHO guidelines: for stage III with CD4 < 350/mm$^3$ in the situation of rapid clinical decline
- WHO stages I and II disease, with CD4 cell count below 200/mm$^3$
- WHO stages II or III HIV disease, with a total lymphocyte count below 1200/mm$^3$
- In cases where CD4 count can not be assessed, total lymphocyte count of 1200/mm$^3$ or below can be used as a substitute indicator for treatment in the presence of symptomatic HIV disease
- An assessment of viral load is not considered essential for starting therapy

Treatment Guidelines for Egypt

Current treatment guidelines suggest that:

- Using a single drug is contraindicated
- Using at least 2 drugs is not recommended
- Use at least 3 drugs
- Combinations include:
  - Two nucleoside reverse transcriptase inhibitors plus one non-nucleoside reverse transcriptase inhibitor, or
  - Two nucleoside reverse transcriptase inhibitors plus one protease inhibitor, or
  - Three nucleoside reverse transcriptase inhibitors.

Before the initiation of therapy the following should be done:

- Confirm HIV test result
- Complete history and physical exam
- CBC
- CD4 count
- T-lymphocyte count
- Plasma HIV RNA viral load (if possible)
- VDRL for syphilis
- PPD
Antiretroviral Therapy (ART)

- PAP smear for early detection of cervical cancer
- Chest X-ray and sputum for TB
- Hepatitis A, B, and C serology
- Ophthalmology examination
- Toxoplasma titer
- CMV serology if indicated

Adherence

- Drug adherence is one of the key determinants of therapy success.
- Poor adherence can lead to virologic failure, evolution of drug resistance and subsequent immunologic and clinical failure
- Adherence is promoted by simplified, well-tolerated regimens involving as few pills as possible and administered no more than two times per day
- Counseling patients carefully before initiating therapy and involving physicians, nurses and other health care providers in the process is important
- Do not start ART at the first clinic visit—a period of education and preparation to try to maximize future adherence is important
- Once treatment has begun, continued monitoring of adherence is essential
- Physician assessment has repeatedly been shown to be the least reliable approach; pill counts are subject to error and manipulation
- Validated patient questionnaires have been shown to be one of the more reliable and easy-to-institute tools for monitoring adherence in the outpatient setting
- Each country and/or health center should develop its own brief, culturally appropriate questionnaire since one standardized tool may not applicable to all regions and cultures

When to Change ARV Therapy

Because of failure, defined in terms of:

Clinical failure: Clinical disease progression with development of an OI or malignancy when the drugs have been given sufficient time to induce a protective degree of immune restoration

Immunologic failure: A fall in the CD4 counts higher than 30% from the peak value or a return to a level at or below the pre-therapy baseline

Virologic failure: Failure to achieve undetectable viral load levels after 3-6 months; repeated, continual, detectable viremia indicative of incomplete viral suppression; the reappearance of a detectable viral load
Because of toxicity

Clearly defined toxicity to a single drug permits drug substitution without compromising the overall regimen. For example: you can substitute d4T for ZDV when ZDV-related symptoms or anemia appear or NVP for EFZ when EFZ-related CNS symptoms are unremitting.

When you cannot identify the drug causing the toxicity and/or low-grade, intolerable side effects compromise adherence, we recommend a complete regimen switch.

If an interruption in therapy is indicated to permit resolution of toxicity, suspend the entire regimen temporarily to prevent the emergence of drug resistance.

Most Common Side Effects of ARV Therapy

Fatigue

Symptoms of fatigue can be physical (it may be hard to get out of bed or to walk upstairs) or psychological (patient may find it hard to concentrate; suffer depression, anxiety, and/or stress).

Fatigue may result from sleep problems (having trouble falling asleep, staying asleep, and suffering sleep disturbances). Fatigue can also be a symptom of anemia.

Anemia

Anemia may be caused by HIV itself or be a side effect of drugs.

Headache

Headaches are generally treatable with nonprescription drugs and by stress reduction.

Nausea and vomiting

Persistent vomiting can lead to serious medical problems, such as dehydration, chemical imbalances or even tearing of the esophagus.

Diarrhea

Diarrhea can cause dehydration, weight loss and electrolyte imbalance.

Weight loss

Weight loss is a serious problem and may result from some of the other drug side effects such as vomiting, diarrhea, dry mouth, anemia or fatigue.

Dry mouth

Dry mouth can make chewing, swallowing and talking difficult; it can affect one’s sense of taste and can promote mouth problems, such as tooth decay and oral yeast infections.
Rash
Many people get a rash when starting ARVs, but most of the time it is mild and goes away after a couple of weeks.
Rash seems to be a slightly more common side effect among women taking certain ARV medications than among men. Nevirapine appears to be the main culprit, along with ABC, EFZ and amprenavir, as well as cotrimoxazole, INH and many antibiotics. Women also seem more prone to severe rash.
Sometimes the rash can be a sign of hypersensitivity that can include fever and flu-like symptoms, such as aches, pains, fatigue, headache, difficulty breathing, sore throat and cough.

Peripheral neuropathy
Peripheral neuropathy results from damage to the nerves, which may be caused by HIV itself or be a side effect of certain drugs. Signs of peripheral neuropathy include a sensation of burning, stinging, stiffness, tickling or numbness in the feet, toes or hands.

Menstrual problems
Women with weakened immune systems tend to have more problems with their periods, including irregular, heavier, lighter and/or painful periods, or no menstrual bleeding at all. These problems can also be a side effect of some medications: recently, excessive bleeding has been noted with the use of ritonavir.

Hair loss
Sudden or abnormal hair loss may result from taking certain medications.
Molluscum contagiosum

Oral candidiasis

Folliculitis

Molluscum contagiosum on the face

Hydradenitis suppurative

Impetigo

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Oral hairy leukoplakia

Varicella Zoster

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Infiltrative KS plaque of the palm

Elongated and oval KS lesions following the lines of cleavage

Nodular and papular KS lesions on the lower limb

Confluent KS lesions on the foot and toes
Colored Plates
provided by Dr Cherif Soliman

Extensive florid KS of the hard palate
KS lesions distributed allover the gingiva

KS of the bulbar conjunctiva
KS nodule on the gingiva

Chest X ray showing reticulo-nodular KS infiltrates
Large KS tumor on the foot
AIDS patient in terminal stage

Chest X-ray showing alveo-nodular KS infiltrates

CT head showing cerebral toxoplasmosis

Condyloma accuminata

CT head showing progressive multifocal leukoencephalopathy

Chest X-ray showing PCP mixed interstitial and alveolar infiltrates