



Clinical Management of Opportunistic Infections

Participant's Handbook

September 2005



Acknowledgments

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Course Evaluation

Placeholder for Faculty List

(To be created by facilitator from template in Facilitator Guide)

Clinical Management of Opportunistic Infections
Government Hospital of Thoracic Medicine
Tambaram Sanatorium, Chennai

NOTE: This schedule is approximate and reflects all 7 sessions of this course. The length of sessions will be determined by participant knowledge of OIs, number of questions, and amount of discussion. These sessions do not have to be taught over 6 days in 1 week but may be covered across several days within 3 to 4 weeks.

Day 1	Day 2	Day 3
Registration/Lunch 30 minutes Pre Assessment 20 minutes Session 1: Overview of Opportunistic Infections 1 ½ hours Tea Break 15 minutes Session 1: Overview of Opportunistic Infections 1 ½ hours	Lunch 30 minutes Session 2: Fungal and Parasitic Infections 1 ¾ hours Tea Break 15 minutes Session 2: Fungal and Parasitic Infections 1 ¾ hours	Lunch 30 minutes Session 3: Viral Infections 1 ½ hours Tea Break 15 minutes Session 3: Viral Infections 1 ½ hours
Day 4	Day 5	Day 6
Lunch 30 minutes Session 4: TB and Other Bacterial Infections 1 ½ hours Tea Break 15 minutes Session 4: TB and Other Bacterial Infections 1 ½ hours	Lunch 30 minutes Session 5: Malignancies Associated with Immunosuppression 2 hours Tea Break 15 minutes Session 6: Prevention of Opportunistic Infections 1 ½ hours	Lunch 30 minutes Session 7: Clinical Management of Common Medical Problems 1 ½ hours Tea Break 15 minutes Session 7: Clinical Management of Common Medical Problems 1 ½ hours Post Assessment 20 minutes Course Evaluation 15 minutes

Glossary of Terms

The definitions in this glossary were taken from the “Glossary of HIV/AIDS-related Terms” compiled by UNAIDS and available at:

http://www.unaids.org/Unaid/EN/Resources/Terminology/glossary+of+hiv_aids-related+terms.asp. Terms not found in this UNAIDS database were defined by I-TECH trainers for a training session held in Namibia. These are indicated with an asterisk (*).

Abacavir (ABC)	A nucleoside reverse transcriptase inhibitor antiretroviral medicine used in HIV infection with at least 2 other antiretroviral medicines.
Aciclovir	Antiviral medicine used to treat the symptoms of herpes simplex virus infection, herpes zoster virus (shingles), and disseminated varicella zoster virus (chicken pox) in immunocompromised patients.
Adherence	The extent to which a patient takes his or her medication according to the prescribed schedule (also referred to as “compliance”).
AIDS	Acquired Immune Deficiency Syndrome. The most severe manifestation of infection with the human immunodeficiency virus (HIV).
AIDS Defining Conditions	Numerous opportunistic infections and neoplasms (cancers) that, in the presence of HIV infection, constitute an AIDS diagnosis. Persons living with AIDS often have infections of the lungs, brain, eyes and other organs, and frequently suffer debilitating weight loss, diarrhoea, and a type of cancer called Kaposi's sarcoma.
ARV	Antiretroviral. Drug used to fight infection by retroviruses, such as HIV infection.
ART or ARVT	Antiretroviral Therapy. A treatment that uses antiretroviral medicines to suppress viral replication and improve symptoms.
Asymptomatic	Without symptoms. Usually used in the HIV/AIDS literature to describe a person who has a positive reaction to one of several tests for HIV antibodies but who shows no clinical symptoms of the disease.
CD4 Cells	<ol style="list-style-type: none">1. A type of T cell involved in protecting against viral, fungal, and protozoal infections. These cells normally orchestrate the immune response, signalling other cells in the immune system to perform their special functions. Also known as T helper cells.2. HIV's preferred targets are cells with a docking molecule called “cluster designation 4” (CD4) on their surfaces. Cells with this molecule are known as CD4-positive (or

CD4+) cells. Destruction of CD4+ lymphocytes is the major cause of the immunodeficiency observed in AIDS, and decreasing CD4+ lymphocyte levels appear to be the best indicator for developing OIs.

CD4 Receptors	The chemical on the surface of a CD4 lymphocyte to which HIV attaches.*
CD4 Count	A way of measuring immunocompetency by counting the lymphocytes that carry the CD4 molecule. Normal is well over 1000/ml of blood. A count lower than 200/ml is an indicator of AIDS.*
Combination Therapy	(For HIV infection or AIDS.) Two or more drugs or treatments used together to achieve optimum results against infection or disease. For treatment of HIV, a minimum of 3 antiretrovirals is recommended. Combination therapy may offer advantages over single-drug therapies by being more effective in decreasing viral load. An example of combination therapy would be the use of 2 nucleoside analogue drugs (such as lamivudine and zidovudine) plus either a protease inhibitor or a non-nucleoside reverse transcription inhibitor.
Combivir	A combined pill containing zidovudine and lamivudine that was USFDA-approved in 1997 for the treatment of HIV infection in adults and adolescents 12 years of age or older.
Didanosine (ddl)	A nucleoside reverse transcriptase inhibitor antiretroviral medicine used in HIV infection with at least 2 other antiretroviral medicines.
DNA	Deoxyribonucleic acid. Except for a few viruses, all living cells carry genetic information as DNA.*
Efavirenz (EFV or EFZ)	A non-nucleoside reverse transcriptase inhibitor for combination use with at least 2 other antiretroviral drugs for adults and children with HIV. Contraindicated in pregnancy; substitute nevirapine for efavirenz in pregnant women or women for whom effective contraception cannot be assured.
Efficacy	(Of a drug or treatment). The maximum ability to produce a result, regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed.
ELISA Test	Acronym for enzyme-linked immunosorbent assay. A type of enzyme immunoassay (EIA) to determine the presence of antibodies to HIV in the blood or oral fluids. Repeatedly reactive (i.e. 2 or more), ELISA test results should be validated with an independent supplemental test of high specificity, such as the Western blot test.
Epidemiology	The branch of medical science that deals with the study of incidence, distribution, and control of a disease in a population.

Fusion	The stage of the HIV life cycle in which the virus binds to the CD4 receptor, activates other proteins on the surface of the cell, then fuses with the T helper or macrophage cell.*
Fusion Inhibitor (FI)	A category of ARV drugs that are designed to attack the fusion stage of the HIV life cycle. Drugs in this category are not available in India.*
Generics	All drugs carry a generic name—an INN (International Non-proprietary Name)—which is the official name given to the molecule/medicine.
HAART	Highly Active AntiRetroviral Therapy. The name given to treatment regimens recommended by leading HIV experts to aggressively suppress viral replication and progress of HIV disease. The usual HAART regimen combines 3 or more different drugs such as 2 nucleoside reverse transcriptase inhibitors and a protease inhibitor, 2 NRTIs and a non-nucleoside reverse transcriptase inhibitor or other combinations.
HIV	Human Immunodeficiency Virus. The virus that weakens the immune system, ultimately leading to AIDS.
HIV-1	Human Immunodeficiency Virus Type 1. The retrovirus isolated and recognised as the aetiologic (i.e., causing or contributing to the cause of a disease) agent of AIDS. HIV-1 is classified as a lentivirus in a subgroup of retroviruses. Most viruses and all bacteria, plants, and animals have genetic codes made up of DNA, which uses RNA to build specific proteins. The genetic material of a retrovirus such as HIV is the RNA itself. HIV inserts its own RNA into the host cell's DNA, preventing the host cell from carrying out its natural functions and turning it into an HIV factory.
HIV-2	Human Immunodeficiency Virus Type 2. A virus closely related to HIV-1 that has also been found to cause AIDS. It was first isolated in West Africa. Although HIV-1 and HIV-2 are similar in their viral structure, modes of transmission, and resulting opportunistic infections, they have differed in their geographical patterns of infection.
HIV Antibody Test	If positive, the results of this test indicate that the person has been exposed to HIV and has developed antibodies to the virus after the window period of up to 12 weeks has passed.
Immunodeficiency	Breakdown in immunocompetence (i.e., the ability of the immune system to resist or fight off infections or tumours) when certain parts of the immune system no longer function. This condition makes a person more susceptible to certain diseases.

Immune Reconstitution Syndrome	As the number of CD4 cells increases in a patient on HAART, these cells recognise antigens to which the patient has been previously exposed, leading to symptoms of the diseases these antigens represent, e.g., TB. Actual infection may or may not be present.*
Immunology	The study of the immune system.*
Incidence	The number of new cases within a specific period of time.*
Integrase	An enzyme used to integrate HIV DNA into the host cell's own DNA.*
Interferon	A protein that can inhibit the development of a virus in a cell.
Lamivudine (3TC)	A nucleoside reverse transcriptase inhibitor antiretroviral medicine used in HIV infection with at least 2 other antiretroviral medicines.
Lopinavir	A protease inhibitor antiretroviral drug used in combination with 2 other antiretroviral medicines.
Maternal Antibodies	Antibodies passed from mother to foetus during pregnancy. Diagnosis of HIV through antibody testing for infants under 18 months is complicated by maternal antibodies.
Nelfinavir (NFV)	A protease inhibitor antiretroviral medicine used for the treatment of HIV infection in combination with 2 other antiretroviral medicines.
Nevirapine (NVP)	A non-nucleoside reverse transcriptase inhibitor used in HIV infection in combination with at least 2 other antiretroviral drugs; used in prevention of mother-to-child transmission in HIV-infected patients.
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitors. A class of drugs that inhibit an enzyme used by HIV called "reverse transcriptase." The non-nucleoside reverse transcriptase inhibitors include efavirenz and nevirapine. They interact with a number of drugs metabolised in the liver; the dose of protease inhibitors may need to be increased when they are given with efavirenz or nevirapine. Nevirapine is associated with a high incidence of rash and occasionally fatal hepatitis. Rash is also associated with efavirenz but is usually milder. Efavirenz treatment has also been associated with an increased plasma cholesterol concentration.
NRTI	Nucleoside Reverse Transcriptase Inhibitors. A category of ARV drugs that binds to the active site of the HIV reverse transcriptase, stopping the production of HIV DNA. Drugs in this category include zidovudine (AZT), didanosine (ddl), zalcitabine (ddC), stavudine (D4T), lamivudine (3TC), and abacavir, zalcitabine, and tenofovir.*

Opportunistic Infections (OIs)	Illnesses caused by various organisms, some of which usually do not cause disease in persons with healthy immune systems. Opportunistic infections common in persons diagnosed with AIDS include <i>Pneumocystis carinii</i> pneumonia; Kaposi's sarcoma; cryptosporidiosis; histoplasmosis; other parasitic, viral, and fungal infections; and some types of cancers.
PCR	Polymerase chain reaction. A laboratory method to find and measure very small amounts of RNA or DNA. It is used as the "viral load" test to diagnose HIV in infants and to measure the level of HIV RNA in the blood of infected persons.*
PEP	Post-Exposure Prophylaxis. The use of ARV therapy just after a possible exposure to HIV has occurred. Recommended after rape, an occupational exposure to HIV (e.g., needle-stick injury) or just after birth for infants who are born to HIV infected mothers.*
PLWHA	Acronym for "person/people living with HIV/AIDS."
PMTCT	Acronym for "prevention of mother-to-child transmission."
Prevalence	The number of cases at any time during the study period, divided by the population at risk.*
Protease	An enzyme used by HIV to process new copies of the virus after it has reproduced; drugs specifically aimed at this enzyme are called "protease inhibitors" (see below). Human cells also use protease enzymes, but they are different from the HIV protease.
Protease Inhibitor (PI)	Antiviral drugs that act by inhibiting the virus protease enzyme, thereby preventing viral replication. Specifically, these drugs block the protease enzyme from breaking apart long strands of viral proteins to make the smaller, active HIV proteins that comprise the virion. If the larger HIV proteins are not broken apart, they cannot assemble themselves into new functional HIV particles. The protease inhibitors include amprenavir, indinavir, lopinavir, nelfinavir, ritonavir, and saquinavir.
RNA	Ribonucleic acid*
Rapid Test	HIV blood, saliva, urine, or vaginal secretions test that yields same day results. Only rapid blood (finger stick) tests are currently available in India.*
Resistance	The ability of an organism, such as HIV, to overcome the inhibitory effect of a drug, such as AZT or a protease inhibitor.

Retrovirus	A type of virus that, when not infecting a cell, stores its genetic information on a single-stranded RNA molecule instead of the more usual double-stranded DNA. HIV is an example of a retrovirus. After a retrovirus penetrates a cell, it constructs a DNA version of its genes using a special enzyme called reverse transcriptase. This DNA then becomes part of the cell's genetic material.
Reverse Transcriptase	This enzyme of HIV (and other retroviruses) converts the single-stranded viral RNA into DNA, the form in which the cell carries its genes. Some antiviral drugs approved by the FDA for the treatment of HIV infection (e.g., AZT, ddI, 3TC, d4T, and ABC) work by interfering with this stage of the viral life cycle. They are also referred to as reverse transcriptase inhibitors (RTIs).
Ritonavir	A protease inhibitor antiretroviral medicine used in HIV-infection, as a booster to increase effect of indinavir, lopinavir, or saquinavir and in combination with 2 other antiretroviral medicines.
Saquinavir (SQV)	A protease inhibitor antiretroviral medicine used in HIV infection in combination with 2 other antiretroviral medicines and usually with low-dose ritonavir booster.
Sentinel Surveys	This form of surveillance relates to a particular group (such as men who have sex with men) or activity (such as sex work) that acts as an indicator of the presence of a disease.
Seroconversion	The development of antibodies to a particular antigen. When people develop antibodies to HIV, they “seroconvert” from antibody-negative to antibody-positive. It may take from as little as 1 week to several months or more after infection with HIV for antibodies to the virus to develop. After antibodies to HIV appear in the blood, a person should test positive on antibody tests. See “Window Period.”
Side Effects	Medical problems that result from ARV drug toxicities. Common side effects include: Peripheral neuropathy, lipodystrophy, hepatitis, pancreatitis, and lactic acidosis.*
STI	Also called venereal disease (VD), an older public health term, or sexually transmitted disease (STD). Sexually transmitted infections are spread by the transfer of organisms from person to person during sexual contact.
Surveillance	The ongoing and systematic collection, analysis, and interpretation of data about a disease or health condition. Collecting blood samples for the purpose of surveillance is called serosurveillance.

Symptomatic	Having evident signs of disease: Weight loss, fever, diarrhoea, enlarged glands, oral candida, herpes, skin problems.*
Transcription	The process of duplication or copying information from DNA.*
Translation	The synthesis of proteins under the direction of RNA.*
VCTC	Acronym for “voluntary counselling and testing centre.”
Viral Load	In relation to HIV: The quantity of HIV RNA in the blood. Research indicates that viral load is a better predictor of the risk of HIV disease progression than the CD4 count. The lower the viral load the longer the time to AIDS diagnosis and the longer the survival time.
WHO Staging System	A classification of the clinical stages of HIV disease developed by the World Health Organization.*
Window Period	Time from infection with HIV until detectable seroconversion. During this time HIV antibody tests will be negative, even though the person is infected. Ninety percent of infected individuals will test positive within 3 months of exposure and 10% will test positive within 3 to 6 months of exposure.*
Zidovudine (ZVD or AZT)	A nucleoside reverse transcriptase inhibitor antiretroviral medicine, zidovudine was the first antiretroviral drug to be introduced. Used in HIV infection in combination with at least 2 other antiretroviral drugs, and in monotherapy of maternal-foetal HIV transmission.

Clinical Management of Opportunistic Infections

Pre Assessment

Date: _____

1. A 35-year-old male comes to our OPD with a report from a VCTC of a rural hospital. The report was given to him 10 days ago and states that the patient is positive for HIV. He is asymptomatic except for mild fever of 3 days' duration. Until this hospital visit, he was able to attend to his work at full capacity. Examination revealed the presence of lymphadenopathy in cervical and axillary areas.

What is his WHO clinical staging?

- a. Stage 1
 - b. Stage 2
 - c. Stage 3
 - d. Stage 4
2. A 39-year-old HIV+ female patient comes to the outpatient department with loss of weight, difficulty in swallowing and painful swallowing. She is also suffering from coughing and breathlessness. The clinical examination and the laboratory tests revealed the diagnosis of PCP and oro-oesophageal candidiasis with wasting (BMI is 15).

What is her WHO clinical staging?

- a. Stage 1
 - b. Stage 2
 - c. Stage 3
 - d. Stage 4
3. The clinical data of 2 HIV+ patients are given below. Read the data and then answer the questions.

Mr. D-35 yrs: Suffering from tuberculous retro-peritoneal lymphadenopathy; his CD4 cell count is $126/\text{mm}^3$.

Mr. G-43 yrs: Suffering from herpes zoster; his CD4 cell count is $367/\text{mm}^3$.

True False

- | | | |
|---|--------------------------|--------------------------|
| A. The CD4 cell count gives a clear indication about the level of immunosuppression | <input type="checkbox"/> | <input type="checkbox"/> |
| B. Mr. D is more immunosuppressed than Mr. G. | <input type="checkbox"/> | <input type="checkbox"/> |

4. Mrs. Radha is a 35-year-old female HIV+ patient. She has been admitted to the hospital with sudden onset of breathlessness, non-productive cough, and fever. In addition she is suffering from watery, explosive and voluminous diarrhoea and is passing stools at least 20 to 25 times a day.

What opportunistic infections do you suspect in this patient?

- a. Pulmonary tuberculosis and amoebiasis
 - b. *Pneumocystis jiroveci* pneumonia (PCP) and cryptosporidial diarrhoea
 - c. Bacterial pneumonia and cholera
 - d. Kaposi's pneumonitis and HIV enteropathy
5. A 24-year-old female patient is hospitalised with pneumocystis jiroveci pneumonia (PCP). The drug of choice for the treatment and the duration of treatment are:
- a. Clindamycin for 10 days.
 - b. Cotrimoxazole for 21 days
 - c. Dapsone for 28 days
 - d. Atovaquone for 21 days
6. A 43 yr old female HIV+ patient is admitted for difficulty in swallowing and complains of retrosternal pain on swallowing. Angular cheilitis is present on clinical presentation. The most likely diagnosis is
- a. CMV oesophagitis
 - b. Tuberculous ulcer in the oesophagus
 - c. Oesophageal candidiasis
 - d. Aphthous ulcers in the oesophagus
7. A 26-year-old male HIV+ patient is hospitalised with severe headache and altered sensorium. His cerebrospinal fluid analysis showed cryptococcal organisms by staining and by culture. Choose 1 of the following drugs to treat this patient:
- a. Clindamycin
 - b. Itraconazole
 - c. Ketoconazole
 - d. Amphotericin-B
8. A 34-yr-old female HIV+ patient is admitted with flu-like symptoms, lymphadenopathy, headache, and convulsions. Her MRI scan of the brain shows ring-enhancing lesions. What is the most likely first diagnosis?
- a. Primary cerebral lymphoma
 - b. Cerebral toxoplasmosis
 - c. Cerebral cysticercosis
 - d. Tuberculoma of the brain

9. A 23-year-old female is admitted for recurrent episodes of red, painful, burning, itchy, sores on the mouth and genitalia. She was found to be HIV-positive 2 years ago. The most likely diagnosis is:
- Herpes simplex virus infection
 - Oral hairy leukoplakia
 - Herpes zoster infection
 - Candidal lesions
10. A 35-year-old HIV+ patient is admitted to the hospital for herpes zoster infection. Choose the correct treatment:
- Acyclovir, 800 mg, 2 times daily, for 7 to 10 days
 - Acyclovir, 800 mg, 3 times daily, for 7 to 10 days
 - Acyclovir, 800 mg, 4 times daily, for 7 to 10 days
 - Acyclovir, 800 mg, 5 times daily, for 7 to 10 days
11. A 55-yr-old HIV+ female patient is admitted to the hospital for CMV retinitis . She had a course of treatment for cryptococcal meningitis and she is now on fluconazole prophylaxis. Estimate her likely absolute CD4 cell count:
- <50
 - 50-200
 - 200-350
 - >350
12. This patient is started on ganciclovir therapy. Complications that can occur in this patient include:
- Anaemia
 - Neutropaenia
 - Thrombocytopaenia
 - Renal insufficiency
 - All of the above
13. A 32-year-old male patient presents with cough with expectoration, 5 days of fever, and 3 days of loose stools. The final diagnoses include tuberculous mediastinal lymphadenopathy, bibasilar pulmonary tuberculosis, and oro-oesophageal candidiasis. His sputum is negative for AFB.

This patient needs to be tested for HIV because of

- Presence of 5 days of fever
- Presence of 3 days of loose stools
- Oro-oesophageal candidiasis
- Sputum negative for AFB

14. The above patient is found to be HIV-positive and his CD4 cell count is 45 cells/mm³. Choose the most appropriate management:
- a. This patient should be started on anti-tuberculosis drugs, antifungal drugs, and antiretroviral drugs simultaneously.
 - b. This patient should be started on anti-tuberculosis drugs and antifungal drugs. Antiretroviral drugs can be started after the completion of antifungal and anti-tuberculous therapy.
 - c. This patient should be started on anti-tuberculosis drugs and antifungal drugs. Antiretroviral drugs can be started after the intensive phase of anti-TB therapy is completed.
 - d. This patient should be started on anti-tuberculosis drugs and antifungal drugs initially. Antiretroviral drugs can be started as soon as the patient is able to tolerate the anti-TB therapy.
15. The above patient is started on rifamycetin based anti-TB therapy. Choose the correct antiretroviral regimen for this patient.
- a. Zidovudine, lamivudine, and nevirapine
 - b. Stavudine, lamivudine, and nevirapine
 - c. Zidovudine, lamivudine, and nelfinavir
 - d. Zidovudine, lamivudine, and efavirenz

Clinical Management of Opportunistic Infections

Post-Assessment

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1. A 35-year-old male patient comes to our OPD with a report from a VCTC of a rural hospital. The report was given to him 10 days ago and states that he is positive for HIV. He is asymptomatic except for mild fever of 3 days' duration. Until this hospital visit, he was able to attend to his work at full capacity. Examination revealed the presence of lymphadenopathy in cervical and axillary areas.

What is his WHO clinical staging?

- a. Stage 1
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- Zidovudine, lamivudine, and nevirapine
 - Stavudine, lamivudine, and nevirapine
 - Zidovudine, lamivudine, and nelfinavir
 - Zidovudine, lamivudine, and efavirenz

Clinical Management of Opportunistic Infections Course Evaluation

1. Please complete the following by ticking the column of your choice.

<i>PLEASE RATE THE QUALITY OF THE FOLLOWING...</i>	POOR	FAIR	GOOD	VERY GOOD	EXCELLENT
Overall Content of Course					
PowerPoint Slides					
Participant's Handbook					
Presentation of Material by Trainers					
Participant/Group Activities					
Facilitation of Activities by Trainers					

2. Think about what you *already knew* and what you *learned during* this training about opportunistic infections. Then evaluate your knowledge in each of the following topic areas related to opportunistic infections **Before** and **After** this training.

1 = No knowledge or skills

3 = Some knowledge or skills

5 = A lot of knowledge or skills



BEFORE TRAINING					SELF-ASSESSMENT OF YOUR KNOWLEDGE AND SKILLS RELATED TO:	AFTER TRAINING				
1	2	3	4	5	Session 1: Overview of Opportunistic Infections	1	2	3	4	5
1	2	3	4	5	Session 2: Fungal and Parasitic Infections	1	2	3	4	5
1	2	3	4	5	Session 3: Viral Infections	1	2	3	4	5
1	2	3	4	5	Session 4: TB and Other Bacterial Infections	1	2	3	4	5
1	2	3	4	5	Session 5: Malignancies Associated with Immunosuppression	1	2	3	4	5
1	2	3	4	5	Session 6: Prevention of Opportunistic Infections	1	2	3	4	5
1	2	3	4	5	Session 7: Clinical Management of Common Medical Problems	1	2	3	4	5

3. To what extent do **you** feel prepared to perform tasks related to opportunistic infections care and treatment?

1	2	3
Not At All Prepared	Somewhat Prepared	Well Prepared

If you do NOT feel prepared to perform job tasks related to opportunistic infections, please explain briefly why you do not.

4. What topic areas related to opportunistic infections would you like **more information** on, if any?

5. What did you **like** about the course?

6. Please share any comments you have that would help us **strengthen** or **improve** this course. If you were asked to redesign the course, what would you **change**?



Clinical Management of Opportunistic Infections

Participant's Handbook

Section Two About This Course

I. What will you learn in this course?

The aim of this training course is to provide basic information on opportunistic infections to physicians in India so that they can care for and treat their patients.

At the end of the course, it is expected that participants will be able to:

- Identify opportunistic infections in individuals with HIV/AIDS.
- Describe common opportunistic infections (OIs) and their causes.
- Explain the various clinical presentations and relative frequencies of OIs.
- Identify the appropriate procedures and laboratory investigations required to make a diagnosis of opportunistic infections.
- Cite the preferred treatment regimen for opportunistic infections.
- Explain the recommended prophylactic regimens and cite the guidelines for initiation and discontinuation of prophylaxis for opportunistic infections.
- Describe environmental protection strategies that minimise the risk of acquiring specific opportunistic infections.
- Compare the advantages and disadvantages of using chemoprophylaxis.
- Explain which vaccinations and immunisations can be administered to HIV-positive patients.
- Advise HIV-infected patients on how they can care for symptoms of common opportunistic infections and support their bodies' immune systems.
- Provide appropriate clinical care for persons with HIV infection who present with some common medical problems related to HIV and opportunistic infections.

II. How is this course organised?

A variety of approaches to teaching and learning will be adopted, with the underlying assumption that participants are adult learners who will take considerable responsibility for their own learning. The focus will be on active learning and should emphasise the key knowledge and skills needed for physicians caring for individuals with opportunistic infections.

The course is a facilitator-led program and consists of 7 sessions. Sessions 3 to 4 hours long and include the following teaching/learning methods:

- Lecture
- Case studies
- Video case studies
- Role-plays
- Large- and small-group work and discussions
- Individual work

The sessions may be taught over the course of several days or over several weeks. Participants should receive a morning, lunch, and afternoon break if the training lasts all day. Be flexible in your timing. The amount of time for each session will vary depending on

participants' experience with opportunistic infections. Take advantage of more experienced participants who can help you train the physicians who have less knowledge of opportunistic infections.

The knowledge and skills participants bring to the course are important to the learning process and participants are encouraged to share their knowledge and skills and to raise issues that they find challenging in their practice.

III. What ground rules are used during the training course?

To help ensure that time spent at the training session is both productive and enjoyable, there are some rules and procedures that we ask participants to follow. The following information includes details on general procedures for the course and requirements for completion of the course. These ground rules are not meant to constrain participants but to contribute to a quality learning environment for everyone.

A. Identifying Expectations

At the beginning of the course, the facilitator will ask participants what they expect to learn from the course. Responses will be recorded and displayed throughout the duration of the course. The facilitator will identify which expectations are within the description of the course and which fall outside it. This will help participants understand what the course will and will not cover.

B. Determining Group Norms

It is important for course participants to establish and commit to their own group norms on the first morning of the course. The following are examples of group norms:

- Respect each other's confidentiality
- Respect each other's contributions, questions, and opinions
- Be on time
- Participate fully in discussions and exercises
- If you must leave early, please inform the Training Coordinator or facilitator before the session begins
- Turn off mobile phones

IV. How will this course be evaluated?

A. Pre- and Post-Assessments

An anonymous pre-assessment and post-assessment will enable course coordinators to evaluate the transfer of knowledge. Participants will be provided 20 minutes at the beginning of day 1 to complete the pre-assessment, and time at the end of day 4 to complete these instruments. Time permitting, answers to the assessment will be reviewed together as a group and/or distributed to participants as take-home materials.

B. End-of-Day Assessment

The facilitator will ask participants to write or discuss responses to the following 4 questions:

1. What did you enjoy the most about today?
2. What did you learn from today's sessions that you will use in your work?
3. What questions do you have about the material that was presented today?
4. What other comments do you have? Please be specific.

A Daily Evaluation Form is provided in your Participant's Handbook. The facilitator will review the feedback after the day's training, taking particular note of the questions participants provided. She or he will then prepare responses and use these to begin the next training unit.

C. Course Evaluation Form

Participants will be asked to complete an anonymous Course Evaluation Form to assess the content and delivery for each unit. Fifteen minutes will be provided at the end of the final day for participants to complete the form, and they will be collected at the close of that day.

V. How do I use this Participant's Handbook?

This *Participant's Handbook* was developed to help assist you as you participate in the course. The handbook contains the following information to help you be successful in the course:

- Information about This Course
- Training Schedule
- Glossary of Terms
- Session Outlines
- Worksheets
- Handouts
- Copies of PowerPoint slides
- References
- Notes pages
- Daily Evaluation Form
- Course Evaluation Form

Refer to this handbook frequently throughout the course. The facilitator will refer to it during each session.

VI. How can I learn most effectively in this course?

There are 5 important things that you can do as a participant to help create an effective learning atmosphere for yourself, the other course participants, and the facilitators.

A. Help to build an atmosphere of trust and support

One of the best ways to help build an atmosphere of trust and support is to listen thoughtfully to the ideas of other participants and provide constructive feedback that will help improve the learning for everyone. Let someone know if they've said or done something that you like. And help a fellow participant or facilitator if you see he or she is having a challenging moment. The best learning takes place in a humane environment; help us to build one!

B. Maintain a positive attitude

There will be times during the course when you might say to yourself, “I’m so tired!” That’s okay to say because you will be working hard and expending a lot of energy learning new things. But try to stay positive and productive as you participate in each session. Negativity does not support a quality learning environment

C. Contribute to the learning of others

Participants are the most valuable resource in a training course. They help each other learn through sharing relevant work experiences and providing different perspectives. If you see yourself and your fellow participants as resources, you will learn much more than if you rely solely on the course facilitators for learning the course content. Ask other participants questions, engage them in conversation, and consider sharing relevant examples from your own work experience.

D. Participate actively

A common assumption is that an active participant in a training course is someone who talks a lot. Not true! Participating actively actually requires more listening than talking. Looking at an individual as they are speaking, nodding your understanding, or using facial expressions that indicate “I’m listening” are active forms of listening.

Another way to actively participate in this training course is to contribute ideas during group exercises, answer questions posed by the facilitators, and ask your own questions of participants and facilitators. In short, participating actively means that it is apparent to others that your brain is on and attentive to each session’s activities.

E. Provide useful feedback at the end of the day

Because we believe that your perspective about how this course is progressing is crucial, we will ask you to give us feedback on each day’s session. Your enjoyment, learning, and understanding of the day’s content will be the focus of this feedback and should not take you long to complete. Please do provide us with this feedback so that we can monitor and evaluate the progress of the course. Thank you!



Clinical Management of Opportunistic Infections

Participant's Handbook

Section Three

Course Sessions 1-7



Clinical Management of Opportunistic Infections

Participant's Handbook

Session 1

Overview of Opportunistic Infections

Session 1: Overview of Opportunistic Infections

Aim: The aim of this unit is to introduce participants to common opportunistic infections in India.

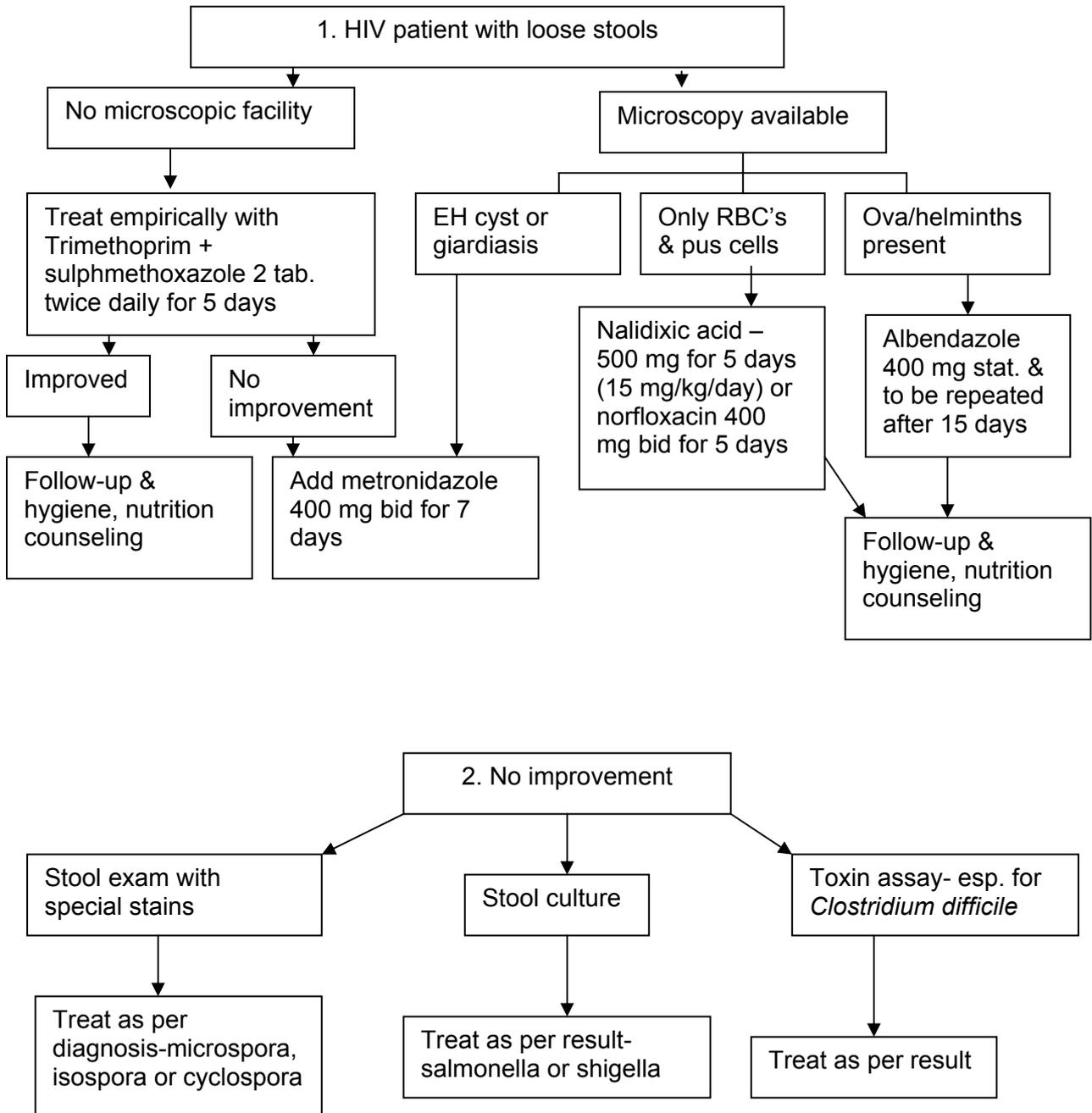
Learning Objectives: By the end of this session, participants will be able to:

- Define opportunistic infections in individuals with HIV/AIDS.
- Explain why opportunistic infections occur in persons with HIV.
- Describe common opportunistic infections and their causes.
- Use the WHO Staging System for HIV Infection and Disease.
- Explain the uses of primary and secondary prophylaxis.
- Identify resources at Tambaram Sanatorium that can help with diagnosis of opportunistic infections.

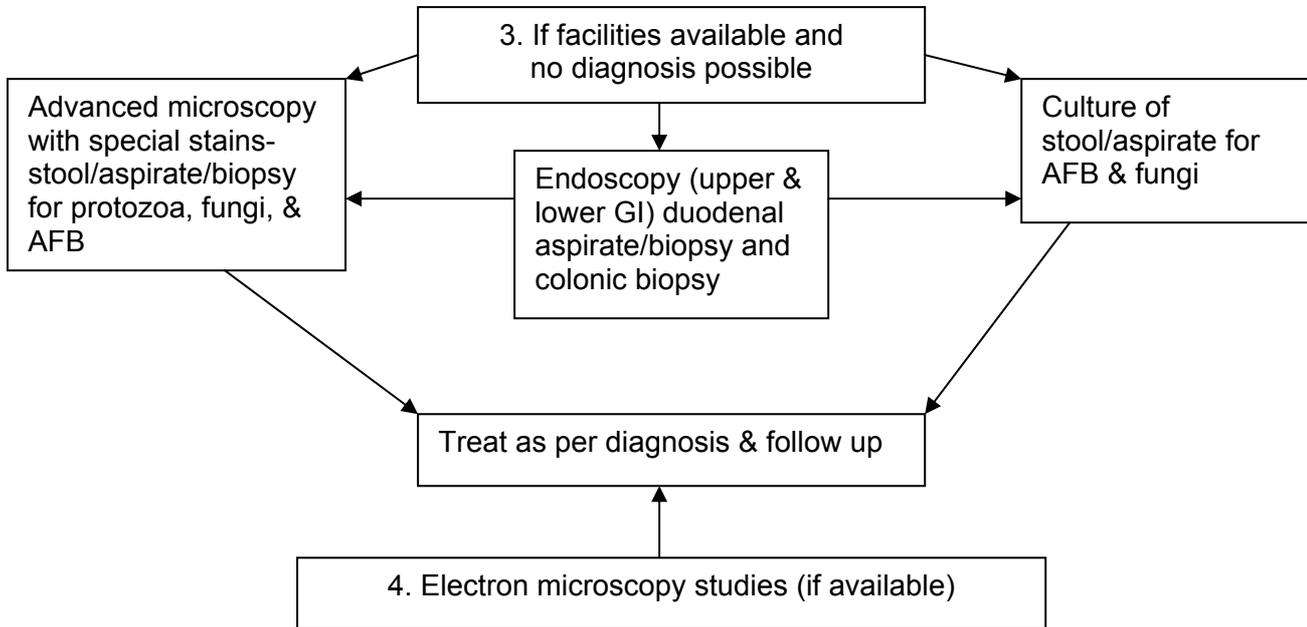
Key Points

1. An opportunistic infection is caused by organisms that would not produce significant disease in a person with a well-functioning immune system.
2. Individuals with HIV/AIDS are susceptible to opportunistic infections because their immune systems have been suppressed and are not capable of fighting disease.
3. There are several fungal, parasitic, viral, and bacterial opportunistic infections, and opportunistic malignancies most common to HIV-infected patients at GHTM.
4. Monitoring CD4+ white blood cells can help health-care providers know what opportunistic infections and other conditions to watch for and what treatment options to consider.
5. Primary prophylaxis or preventive treatment is used to prevent opportunistic infections in individuals with HIV/AIDS.
6. Secondary prophylaxis is used to prevent relapse of OI's in individuals already infected with an infection.

Diarrhoea Algorithm



Diarrhoea Algorithm (continued)





Handout 1.2

WHO Staging System for HIV Infection and Disease: Laboratory Classification

Lympho- cytes	CD4+/ mm³	Clinical Stage 1 Asymptomatic	Clinical Stage 2 Early	Clinical Stage 3 Intermediate	Clinical Stage 4 Late
>2000	>500	1A	2A	3A	4A
1000- 2000	200- 500	1B	2B	3B	4B
<1000	<200	1C	2C	3C	4C



WHO Staging System for HIV Infection and Disease: Clinical Classification

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

Introductory Case Study

Case-Study Instructions:

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
3. Discuss the case together and answer the related questions in the time you are given.

Introductory Case

Mr.R, is a 27-year-old unmarried construction worker. He has come to the hospital because he has been suffering from recurrent episodes of diarrhoea for 2 months. During your interview with him, he tells you that he does not drink boiled water and usually takes food from street vendors. He also shares with you that he had unprotected sex with a commercial sex worker 5 years ago. He does not know his HIV status.

Worksheet 1.1 (continued)

Introductory Case Study (continued)

Questions:

1. What are common causes of diarrhoea in the general population? What about in patients who are HIV+?
2. What will you specifically look for in the general and systemic examination?
3. What laboratory investigations will you perform?
4. What interventions would you recommend initially to treat his diarrhoea?
5. If the patient has *Cryptosporidium*, how will you treat him?
6. What will you advise the patient about food and drink in the future?

WHO Staging System Case Studies

Case-Study Instructions:

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
3. Discuss the case together and answer the related questions in the time you are given.

Case 1

A man has lost 9 kilograms in the last 3 months. Before that, he weighed 75 kilograms. He has complained of feeling feverish for the past month. For the past month, he has left work early every day and usually goes to bed in the late afternoon or early evening. He was treated for pulmonary tuberculosis 5 months ago.

Questions:

1. Does this man fit the WHO symptomatic criteria for HIV infection?

2. If so, what clinical stage is he in according to the WHO Staging System?

WHO Staging System Case Studies (continued)**Case-Study Instructions:**

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
3. Discuss the case together and answer the related questions in the time you are given.

Case 2

A woman has come in because she keeps having upper-respiratory problems, which you diagnose as bacterial sinusitis. She says she hasn't had any problem keeping up with her usual activities, despite the respiratory problems. Her weight has been stable as well. Her last visit to Tambaram was 4 years ago, when she was treated for herpes zoster. You notice that she appears to have a fungal infection on her toenails.

Questions:

1. Does this woman fit the WHO symptomatic criteria for HIV infection?

2. If so, what clinical stage is she in according to the WHO Staging System?



References

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Department of Health (2001). *HIV/AIDS Training Course*. Pretoria, South Africa: Department of Health.

HIV InSite (2004). Available online at: <http://hivinsite.ucsf.edu/>

Osmond, D (1998). Classification and Staging of HIV Infection, HIV InSite Knowledge Base Chapter, UCSF.

 **Notes**



Overview of Opportunistic Infections

Session One



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CENTER ON HIV





Learning Objectives (1)

- By the end of this session, participants should be able to:
 - Define opportunistic infections in individuals with HIV/AIDS
 - Explain why opportunistic infections occur in persons with HIV
 - Describe common opportunistic infections and their causes

Overview of OIs

Slide 2

- The aim of this session is to introduce participants to common opportunistic infections in India.



Learning Objectives (2)

- By the end of this session, participants should be able to:
 - Use the “WHO Staging System for HIV Infection and Disease”
 - Explain the uses of primary and secondary prophylaxis
 - Identify resources at Tambaram Sanitorium that can help with diagnosis of opportunistic infections



Introductory Case Study



Mr.R, is a 27-year-old, unmarried, construction worker. He came to the hospital because he has been suffering from recurrent episodes of diarrhoea for 2 months

During your interview with him, he tells you that he does not drink boiled water and usually takes food from street vendors

He also shares with you that he had unprotected sex with a commercial sex worker 5 years ago. He does not know his HIV status

Overview of OIs

Slide 4

Step 2-Introductory Case (Slides 4-6)-15 minutes

- *Ask participants to read “Introductory Case Study” (Worksheet 1.1) and answer the questions that accompany it.*
- *Sample responses are provided in Worksheet 1.1 of this guide.*
- *As you discuss the case with participants, write their responses on the chalkboard or flipchart paper.*
- *Refer to the Diarrhoea Algorithm (Handout 1.1) in the Participant’s Handbook when discussing the answers.*



Questions for Discussion (1)

1. What are common causes of diarrhoea in the general population? What about in patients who are HIV+?
2. What will you specifically look for in the general and systemic examination?
3. What laboratory investigations will you perform?



Questions for Discussion (2)

4. What interventions would you recommend initially to treat his diarrhoea?
5. If the patient has cryptosporidium, how will you treat him?
6. What will you advise the patient about food and drink in the future?



Definition of Opportunistic Infections (OIs)

- Infections that the normal human body is capable of resisting but occur in persons with weakened immune mechanisms



Overview of OIs

Slide 7

- The human body is continuously exposed to pathogens that exist in the environment. The body comes into contact with pathogens through: 1. air that is breathed 2. ingestion of food and water 3. direct contact with skin and mucous surfaces.
- The body has a mechanism to resist and overcome most pathogens. The process of resistance to infection is known as immunity.
- The human body also carries normal commensals (bacteria, fungus and viruses) in their body, but they cannot produce disease in their host because of immunity. If the immunity goes down, these normal commensals can utilize this opportunity to produce disease in their host.
- The normal human immune system is able to detect substances that are foreign to the body and then to process and dispose of such substances.
- However, the body's defense mechanisms may be overcome if:
 - The size of the inoculum of invading pathogens is large
 - The body has not been previously primed to the invading pathogens
 - The immune system or immune mechanisms are weak, or
 - There is a breach in the epithelial barriers that protect against invasion.
- Persons with weakened immune responses become prone to developing infections that they would normally resist.
- Infections that the normal human body is capable of resisting but occur in persons with weakened immune mechanisms are known as opportunistic infections (OIs).
- The Acquired Immune Deficiency Syndrome (AIDS) is caused by the human immunodeficiency virus (HIV).
- In persons with HIV infection, the immune system is gradually destroyed, and the resulting immune suppression makes affected individuals prone to infections that may normally be overcome if the immune system was intact and functioning normally.



In Immunosuppressed Persons

- OIs occur more frequently, are more severe and less responsive to recommended treatment regimens
- Other “non-opportunistic” bacterial, viral, fungal and parasitic infections occur more frequently and often relapse after treatment

Overview of OIs

Slide 8

- Immunosuppressed individuals are also more prone to repeated attacks of bacterial and viral infections that may not be true opportunistic infections. In addition they are more likely to develop certain cancers.
- The occurrence of opportunistic infections in persons with HIV infection leads to considerable morbidity and significant mortality.
- HIV related immune deficiency differs from that due to other causes in its severity and inexorably progressive nature. It leads to multiple opportunistic infections in patients with advanced HIV infection, mostly with common endogenous and environmental organisms that usually pose little threat to human health.
- Opportunistic infections are the main cause of illness in people living with HIV infection and AIDS (PLHA). In immunosuppressed persons the following occur:
 - Opportunistic infections occur more frequently, are more severe and less responsive to recommended treatment regimens
 - Other “non-opportunistic” bacterial, viral, fungal and parasitic infections occur more frequently and often relapse after treatment
- Apart from the “true” opportunistic infections, a number of illnesses, termed opportunistic diseases, occur in immunosuppressed persons.
- Some of these illnesses may have a direct causal relationship with a pathogen, while in others a causal relationship has not been firmly established.
- Other conditions associated with immunosuppression caused by HIV infection include progressive multifocal leukoencephalopathy (PML), vacuolar myelopathy, cranial nerve palsies, peripheral neuropathy and Guillain Barré Syndrome.
- The onset of opportunistic infections and other opportunistic diseases is dependent on the level of immunosuppression and the prevalence of opportunistic pathogens in the environment. Hence the pattern of diseases encountered varies tremendously from place to place. (Zim, Module 1)



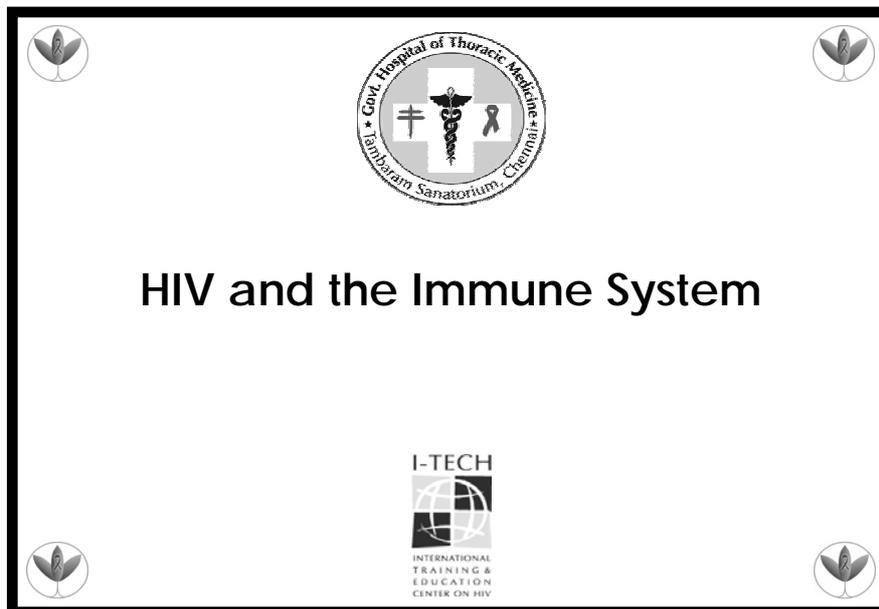
Discussion: OIs at Tambaram

1. What are some of the opportunistic infections you have seen at your facility?
2. How would you categorize them?

Overview of OIs

Slide 9

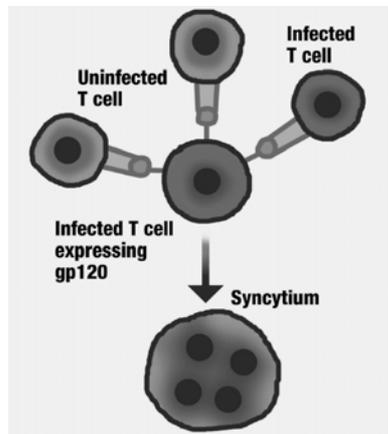
- The purpose of this discussion is to help participants relate the material to their experiences at Tambaram Sanatorium.
- What are some of the opportunistic infections you have seen at your facility? How would you categorize them?



- Within the body are a large number of different types of white blood cells.
- The cells responsible for providing immunity are the lymphocytes.
- There are two main types of lymphocytes in the circulation, the B cells and the T cells.
 - The B lymphocytes produce natural antibodies. The antibodies are proteins known as immunoglobulins.
 - The T lymphocytes are responsible for cell-mediated immunity. There are a large number of different types of T lymphocytes.
 - The majority of these T lymphocytes have a cluster of differentiation (CD) molecules on their surface. Each of these CD molecules reacts with an antigen or a chemical produced by other cells.
 - The T lymphocyte bearing the CD4 molecule is known as the CD4+ lymphocyte. This cell, also known as the helper cell, plays a crucial role in the immune response.
 - CD4+ cells are a type of white blood cells that send signals to other white blood cells to fight off infections in the body.
 - However, the CD4+ lymphocyte is the target for HIV.
 - Viruses cannot replicate by themselves the way other germs can. They need to get inside and infect cells of the body to be able to reproduce.
 - HIV enters CD4+ cells (as well as other cells in the body) in order to replicate, and eventually destroys them.



Destruction of CD4 Cell



1. HIV infected cell binds to other uninfected cell
2. Syncytium formation
3. Destruction of cell

Overview of OIs

Slide 11

- The destruction of CD4 cells can happen by two mechanisms:
 - Direct damage by the HIV virus.
 - Immune mechanisms triggered during the course of HIV infection.
- HIV can kill cells singly or after giant cell and syncytia formation.
 - Single cell killing occurs due to accumulation of unintegrated viral DNA and inhibition of cellular protein synthesis.
 - Syncytium formation is induced by virulent strains of HIV in a multistep mechanism.
 - CD4 cells expressing viral antigens on the surface attract CD4+ uninfected cells and the membranes of these fuse producing giant cells and syncytia.
 - One such HIV infected cell can eliminate hundreds of uninfected cells by syncytium formation.
 - Gp120 and other intracellular adhesion molecules bring about the cellular adhesion and subsequent damage.
 - Apoptosis of CD4 cells also add to depletion.
- The non-virologic mechanisms, which can destroy/damage CD4 cells, include: (1) autoimmune mechanisms (2) anergy (3) super antigens (4) apoptosis (programmed cell death), and (5) virus specific immune responses.
- A number of hypothesis and complex immune mechanisms have been postulated for CD4 cell depletion involving one or more of above-mentioned pathways.
- Killing these infection-fighting cells is why HIV is so damaging to the immune system.
- With the reduction in peripheral blood circulating CD4+ lymphocytes, immune suppression ensues and affected persons become prone to develop opportunistic infections. (Zim, Module 1)
- As the immune system becomes weakened by HIV, the CD4+ count begins to fall.
- The level of CD4+ cells is one of the important surrogate 'markers' –indications of how badly the immune system has been damaged or how quickly it is deteriorating (HIV/AIDS Training Course, South Africa, Module 10)



WHO Staging and Disease Correlation

WHO Stage	Some Typical Diseases*	CD4 Count	Viral Load**
I Asymptomatic	No symptoms or signs of any illness Persistent Generalized Lymphadenopathy	>500	10^3 to 10^6 ***
II Minor Symptoms	Cutaneous Manifestation Folliculitis, Dermatomal Herpes (Varicella) Zoster	500 to 350	10^3 to 10^4
III Moderate Symptoms	Oral Candidiasis, Oral Hairy Leukoplakia, Pulmonary Tuberculosis	350 to 200	10^4 to 10^5
IV AIDS-defining Illness	Kaposi's Sarcoma (KS), Oral KS MAC, Severe Chronic Herpes Ulcers, Toxoplasmosis, Cryptococcus	<200	10^5 to 10^6

*Staging of diseases is approximate and not the same for all individuals

**HIV RNA copies per ml of plasma

***Viral load spikes shortly after infection and then drops quickly when antibodies are formed

Overview of OIs

Slide 12

- This table depicts how the CD4 count and viral load are connected, and how as one goes up (viral load), the other will decrease (CD4). When CD4 counts begin to decrease, HIV disease progresses.
- The viral load is very high shortly after primary HIV infection. It falls steeply when the body develops antibodies and rises again after a number of years as the CD4 count drops.
- High viral load leads to higher transmission risk. Most often, after a number of years, high viral load is also a sign of more severe disease as people develop AIDS.
- Different HIV-related diseases (opportunistic infections) are related to declines in immune function. This is one way to assess (without the use of CD4 counts) the severity of immune suppression.
- It is rare to see esophageal candidiasis at CD4 counts greater than 200, therefore we know that person is quite sick and needs ART. The same is true for tuberculosis, although immune suppression is less severe the client is still eligible for ART.
- Herpes Zoster occurs while the CD4 count is still too high to be eligible for ART, however, this client should be watched closely because zoster indicates that the immune system is compromised.



Most Common OIs in India

- Tuberculosis
- Candidiasis
- Cryptosporidiosis
- Herpes zoster
- Toxoplasmosis
- Bacterial pneumonia
- Cryptococcal meningitis
- PCP
- Others

Overview of OIs

Slide 13

- The following slides briefly describe the fungal, parasitic, viral, bacterial and malignant opportunistic infections most commonly present in HIV-infected patients at Tambaram.
- Each of these, and several others within each category, will be discussed at length in subsequent sessions.



Fungal Opportunistic Infections





- *Pneumocystis jirovecii (carinii)* pneumonia (PCP) [1]: Although the *Pneumocystis jirovecii* organism does not cause illness in immunocompetent hosts, it can cause severe pneumonia in patients with HIV/AIDS.
- Another name for *Pneumocystis carinii* is *Pneumocystis jirovecii*.
- Patients usually present with
 - Cough
 - Shortness of breath, and
 - Fever
- Usually patients with PCP have a sudden onset of severe dyspnoea, but PCP may also present in persons with more chronic symptoms.
- Symptoms may be very severe, and an attack of PCP may lead to the death of the patient if not treated early and effectively.
- [1] From HIV Insite website: “Although *P. carinii* has long been considered a protozoan, recent studies of ribosomal RNA from the organism have shown greater homology with fungi, suggesting that it should be reclassified.”



What Is This Infection?



HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA

Overview of OIs

Slide 16

- The two main types of candidiasis are:
 - Localized disease (of the mouth and throat, and of the vagina)
 - Systemic disease (of the oesophagus, skin and nails and other viscera)
- It is commonly one of the presenting signs of HIV infection in individuals who do not have other reasons (e.g., recent antibiotic use, diabetes) to have fungal disease. (Baylor, p. 97)
- The symptoms of oesophageal candidiasis are difficulty in swallowing and pain in the chest that increases with swallowing.
- Disseminated candidiasis causes fever and symptoms in the organs affected by the disease.



Cryptococcosis



Overview of OIs

Slide 17

- Cryptococcosis most often appears as meningitis, and occasionally as pulmonary or disseminated disease.
- Cryptococcal meningitis is the most frequent systemic fungal infection in HIV-infected persons.
- The most common symptom patients present with is headache.
- The second most common is diplopia or double vision, and the third, indolent fever.



Parasitic Opportunistic Infections





Cryptosporidiosis

- Diarrhoeal disease caused by *Cryptosporidium parvum*
- Can live in the intestine of humans and animals
- Passed in the stool of an infected person or animal
- Symptoms
 - Diarrhoea
 - Abdominal pain with mild fever

Overview of OIs

Slide 19

- Cryptosporidiosis is a diarrhoeal disease caused by a *Cryptosporidium parvum*.
- It can live in the intestine of humans and animals and is passed in the stool of an infected person or animal.
- Symptoms include diarrhoea and abdominal pain with mild fever. (Zim, Specific OIs)
- If the biliary system is involved (gallbladder and biliary ducts), there may also be nausea and right upper quadrant abdominal pain. (Baylor, p. 97)



Microsporidiosis (1)

- Caused by microsporidia, intracellular protozoan parasites
- Infection occurs with the ingestion of spores
- Clinical manifestations vary according to the causal species, with diarrhoea being the most common manifestation

Overview of OIs

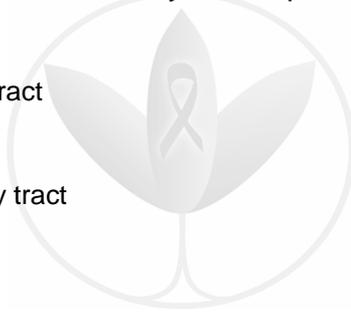
Slide 20

- Microsporidia are intracellular protozoan parasites.
- Infection occurs with the ingestion of spores.
- The clinical manifestations of microsporidiosis vary according to the causal species, with diarrhoea being the most common manifestation.



Microsporidiosis (2)

- Other infections caused by Microsporidiosis
 - Eyes
 - Respiratory tract
 - Gall bladder
 - Genitourinary tract
 - Muscles



Overview of OIs

Slide 21

- Infection of the eyes, respiratory tract, gall bladder, genitourinary tract, and muscles have also been described.



Viral Opportunistic Infections





Herpes Simplex Virus



HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA

Overview of OIs

Slide 23

- Herpes simplex virus infection (HSV) can be severe in patients with HIV/AIDS.
- Eruptions of HSV are red, painful, burning, itchy sores on the mouth and genitals.
- Dissemination may lead to infection of the lungs, the oesophagus, and the brain.



Herpes Zoster



HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA



HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA

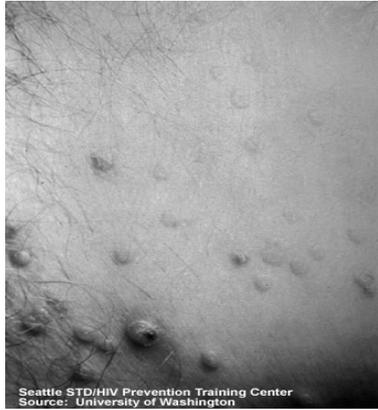
Overview of OIs

Slide 24

- Herpes zoster is the virus that causes chickenpox and shingles in children and adults, respectively, and is spread by aerosolized viral particles. (Baylor, p. 88)
- A person is contagious for 24 to 48 hours before a vesicular (raised, fluid-filled lesions) rash is observed, and until all of the lesions are crusted over. (Baylor, p. 88)
- In children initial infection results in the development of chicken pox, although most persons that become infected develop no symptoms and signs of infection.
- In immune suppressed persons, zoster is often multidermatomal in distribution and is persistent and extensive. It is associated with severe pain and debility. (Zim, Viral Infections)



Molluscum Contagiosum



Seattle STD/HIV Prevention Training Center
Source: University of Washington



Seattle STD/HIV
Prevention
Training
Center

Overview of OIs

Slide 25

- Molluscum contagiosum is a superficial skin infection caused by the molluscum contagiosum virus (MCV).
- The virus invades the skin causing the appearance of firm, flesh-coloured papules containing a white sebaceous material that can occur anywhere on the body and often remain unchanged for many months, after which they disappear.



**Bacterial/Mycobacterium
Opportunistic Infections**





Tuberculosis

- Most common opportunistic disease in people living with HIV
- Frequent first indication of HIV infection in developing countries
- Virus breaks the immune system down, making people living with HIV highly susceptible to TB
- TB in turn accelerates the progression of HIV to AIDS and shortens survival of patients with HIV infection

Overview of OIs

Slide 27

- TB is the most common opportunistic disease in people living with HIV and is a frequent first indication of HIV infection in developing countries.
- The virus breaks the immune system down, making people living with HIV highly susceptible to TB.
- TB in turn accelerates the progression of HIV to AIDS and shortens survival of patients with HIV infection. (TB India, p. 8)
- Immuno-suppressed persons may reactivate an old tuberculosis infection or may become infected de novo with *Mycobacterium tuberculosis*.



Pneumonia

- When caused by *Streptococcus pneumoniae*, may often be the first indication of HIV infection
- Other causes of pneumonia in persons with HIV infection
 - *Klebsiella pneumoniae*
 - *Pseudomonas aeruginosa*
 - *Staphylococcus aureus*
 - *Haemophilus influenzae* in children

Overview of OIs

Slide 28

- Pneumonia caused by *Streptococcus pneumoniae* may often be the first indication of HIV infection.
- Other causes of pneumonia in persons with HIV infection include:
 - *Klebsiella pneumoniae*
 - *Pseudomonas aeruginosa*
 - *Staphylococcus aureus*, and
 - *Haemophilus influenzae* in children



Bacterial Pneumonia Symptoms

- Cough
- Fever
- Systemic symptoms
 - Myalgia
 - Headache
 - Loss of appetite



Overview of OIs

Slide 29

- Patients with bacterial pneumonia present with:
 - Cough
 - Fever
 - Systemic symptoms of myalgia
 - Headache, and
 - Loss of appetite.
- They often have chest pain, difficulty in breathing, and tachypnoea, and they may also have haemoptysis.



Opportunistic Malignancies



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Lymphoma

- Disease in which cancer cells are found in the lymph system in patients who have AIDS
- Lymphomas are divided into two general types, Hodgkin's lymphomas and non-Hodgkin's lymphomas
 - The types of non-Hodgkin's lymphomas are classified by how quickly they spread
 - Low-grade
 - Intermediate-grade
 - High-grade

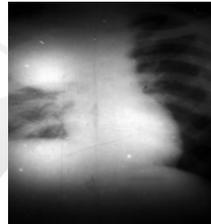
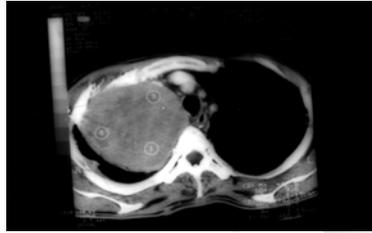
Overview of OIs

Slide 31

- AIDS-related lymphoma is a disease in which cancer cells are found in the lymph system in patients who have AIDS.
- Lymphomas are divided into two general types, Hodgkin's lymphomas and non-Hodgkin's lymphomas, which are classified by histology.
 - The types of non-Hodgkin's lymphomas are classified by how quickly they spread:
 - Low-grade
 - Intermediate-grade, or
 - High-grade



Squamous Cell Carcinoma



**Squamous cell carcinoma
of the lung**

← No metastasis in liver

Overview of OIs

Slide 32

- Chest X-ray (top right figure) showing a rounded, homogenous opacity in the right apical region of the lung.
- CT-scan (lower left figure) of the liver is normal with no metastasis.
- CT-scan (top left figure) of the lung showing involvement of lung parenchyma with tumor tissue.



WHO Staging System





WHO Staging System: Laboratory Classification

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

Overview of OIs

Slide 34

- For adults, the World Health Organization (WHO) has developed a system to categorize the immunosuppression of adults by their total lymphocyte counts (see Handout 1.2 “WHO Staging System for HIV Infection and Disease: Laboratory Classification”).
- In many parts of the world, CD4+ lymphocyte counts are not available.
- There is some evidence that the use of absolute (ALC) or total lymphocyte count (TLC) can be useful in the classification of HIV disease in resource-poor settings.



WHO Staging System: Clinical Classification-Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy
- Performance scale 1: asymptomatic, normal activity

Overview of OIs

Slide 35

- Patients can also be diagnosed clinically, based on the major and minor signs and symptoms listed on the Handout 1.3 “WHO Staging System for HIV Infection and Disease: Clinical Classification.”
- Two major signs or symptoms plus two minor signs or symptoms define symptomatic HIV infection.
- The WHO staging system applies to adults, and several studies have shown its reliability for predicting morbidity and mortality in infected individuals. (Zim, Module 1)
- More on diagnosing and treating the symptoms and infections shown on these handouts will be covered in the rest of this unit on opportunistic infections.
- *If anyone asks about the CDC Classification System, refer them to <http://www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm>. The CDC Classification System was not adopted by the WHO because it requires the capability to count CD4 lymphocytes, which is not possible in many resource-limited countries.*



WHO Staging System: Clinical Classification-Stage 2

- Weight loss, <10% body weight
- Minor mucocutaneous manifestation (seborrhoeic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, and angular cheilitis)
- Herpes zoster, within last 5 years
- Recurrent upper respiratory infections (i.e. bacterial sinusitis)
- And/or performance scale 2: symptomatic, normal activity

Overview of OIs

Slide 36

- A person in this stage may feel ill at times, but may still be able to do normal activities.
- The range of the CD4 lymphocyte count in this stage can be between 350 and 500 cells/mm³.



WHO Staging System: Clinical Classification-Stage 3 (1)

- Weight loss, >10% body weight
- Unexplained chronic diarrhoea, >1 month
- Unexplained prolonged fever (intermittent or constant), >1 month
- Oral candidiasis (thrush)

Overview of OIs

Slide 37

- A person in this stage often cannot do their normal activities but is in bed less than half the time.
- Typical CD4 lymphocyte count in this clinical stage will be between 200 and 350 cells/mm³.



WHO Staging System: Clinical Classification-Stage 3 (2)

- Oral hairy leukoplakia
- Pulmonary tuberculosis, within the past year
- Severe bacterial infections (i.e. pneumonia, pyomyositis)
- And / or performance scale 3: bed-ridden <50% of the day during the last month



WHO Staging System: Clinical Classification-Stage 4 (1)

- HIV wasting syndrome (weight loss of >10%, plus either unexplained chronic diarrhoea > 1 month, or chronic weakness and unexplained prolonged fever > 1 month)
- *Pneumocystis jiroveci* pneumonia
- Toxoplasmosis of the brain
- Cryptosporidiosis with diarrhoea, >1 month
- Cryptococcosis, extrapulmonary



WHO Staging System: Clinical Classification-Stage 4 (2)

- Cytomegalovirus (CMV) disease of an organ other than liver, spleen or lymph nodes
- Herpes simplex virus (HSV) infection, mucocutaneous >1 month, or visceral
- Progressive multifocal leukoencephalopathy (PML)
- Any disseminated endemic mycosis (i.e.) histoplasmosis, coccidioidmycosis



WHO Staging System: Clinical Classification-Stage 4 (3)

- Candidiasis of the oesophagus, trachea, bronchi or lungs
- Atypical mycobacteriosis, disseminated
- Non-typhoid Salmonella septicaemia
- Extrapulmonary tuberculosis
- Lymphoma
- Kaposi's Sarcoma (KS)
- HIV encephalopathy and/or performance scale 4: bed – ridden, >50% of the day during last month

Overview of OIs

Slide 41

- A person in this stage is often ill and may stay in bed more than 50% of the time.
- Typical CD4 lymphocyte count in this clinical stage is <200 cells/mm³.
- Involved organ systems: cutaneous and oral, respiratory, GI, neurological and ocular; generalized



Case Studies: Using the WHO Staging System

- Case Study Instructions:
- Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group
- Choose a recorder for your group. The recorder may write on note paper or flip chart paper
- Discuss the case together and answer the related questions in the time you are given

Overview of OIs

Slide 42

- The purpose of this exercise is to give participants practice in using the WHO Staging System for HIV Infection and Disease: Clinical Classification.
- Refer to the “WHO Staging System for HIV Infection and Disease: Clinical Classification” (Handout 1.2) and “WHO Staging System Case Studies” (Worksheet 1.1) in the Participant’s Handbook.



Using the WHO Staging System: Case 1

- Lost 9 kg in last 3 months
- Previously weighed 75 kg
- Feverish for past month
- Leaves work early, in bed by late afternoon, early evening
- Treated for pulmonary TB five months ago



Using the WHO Staging System: Case 1 Questions

1. Does this man fit the WHO symptomatic criteria for HIV infection?
2. If so, what clinical stage is he in according to the WHO Staging System?



Using the WHO Staging System: Case 1 Answers

1. Yes, because:
 - He lost more than 10% of his usual weight (9 kg out of 75 kg)
 - He has fever of 1 month duration (unexplained prolonged fever)
 - He had taken treatment for pulmonary tuberculosis
 - He is bed ridden for >50% of the day
2. Clinical Stage 3



Using the WHO Staging System: Case 2

- Bacterial sinusitis
- No problem keeping up with usual activities
- Weight stable
- Treated for herpes zoster four years ago
- Fungal infection on toenails



Using the WHO Staging System: Case 2 Questions

1. Does this woman fit the WHO symptomatic criteria for HIV infection?
2. If so, what clinical stage is she in according to the WHO Staging System?



Using the WHO Staging System: Case 2 Answers

- Yes, because:
 - Presence of mucocutaneous infection-fungal nail infection
 - Recurrent upper respiratory infection-bacterial sinusitis
 - History of herpes zoster infection four years ago
 - Performance scale-symptomatic normal activity
- Clinical Stage 2



Prophylaxis

- Primary prophylaxis: the use of medication to prevent OIs
- Secondary prophylaxis: long-term continuation of lower dose medication to prevent relapse of OIs
- Important to assess side effects of prophylaxis



Primary Prophylaxis

- Primary prophylaxis is when HIV infected people are given medicines to try to prevent them from developing an opportunistic infection
- The appropriate time to begin prophylaxis depends on:
 - The age of the patient
 - What infection is being prevented
 - What laboratory support and medications are available in a particular area

Overview of OIs

Slide 50

- Often times when people are known to be HIV-infected, they will be given medicines to try to prevent them from developing an opportunistic infection.
- This is known as primary prophylaxis.
- The appropriate time to begin prophylaxis depends on:
 - Age of the patient
 - What infection is being prevented
 - What laboratory support and medications are available in a particular area.
- Health care providers can monitor CD4+ lymphocyte counts, total lymphocyte counts, or use the WHO's Clinical Classification Staging System to help determine when to begin primary prophylaxis.
- When a person with AIDS dies, the cause of death is most often due to an opportunistic infection.
- Primary prophylaxis is a way to help patients lead longer, healthier lives.
- For example, when CD4+ lymphocyte counts are less than 200 cells/mm³, adults begin taking trimethoprim-sulfamethoxazole (TMP-SMZ) to prevent Pneumocystis jiroveci pneumonia.
- IF THERE IS NO FACILITY TO DO CD4 COUNTS, THEN PROPHYLAXIS CAN BE STARTED IN A SYMPTOMATIC PATIENT.
- TMP-SMZ is the first choice for PCP prophylaxis; Dapsone, a sulfone drug, is the second choice if patients exhibit a reaction to TMP-SMZ.
- Only about 30% of patients react to both drugs.



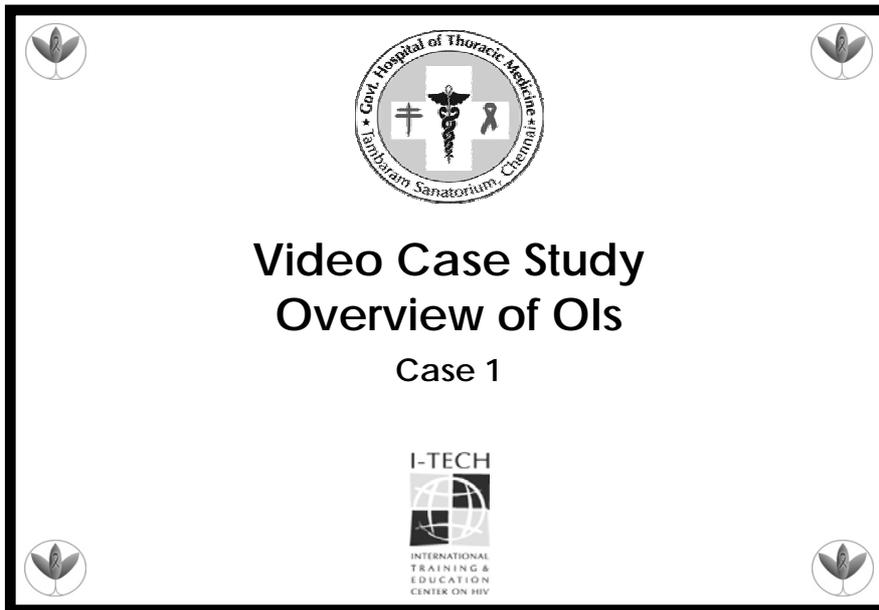
Secondary Prophylaxis

- Secondary prophylaxis is when an HIV-infected patient has been treated for a certain opportunistic illness and should stay on a lower dose of the medicine for the rest of his/her life in order to prevent a relapse

Overview of OIs

Slide 51

- After an HIV-infected patient has been treated for a certain opportunistic illness, s/he should stay on a lower dose of the medicine for the rest of his/her life in order to prevent a relapse.
- This is known as secondary prophylaxis.
- Many of the medicines used for prophylaxis have side effects.
- If a patient is going to be taking prophylactic medications for a long time, it is important to assess for side effects each time the patient is examined.
- This applies whether a patient is receiving primary or secondary prophylaxis. (Baylor, Opportunistic Infections, pp. 89-90)



- Refer to Overview of OIs Video Case Study Case 1 (Worksheet 1.3).
- Stop the video to discuss diagnosis and treatment of the patient before showing the corresponding video segments.



Key Points (1)

1. An OI is caused by organisms that would not produce significant disease in a person with a well-functioning immune system
2. Individuals with HIV/AIDS are susceptible to OIs because their immune systems have been suppressed and are not capable of fighting disease
3. There are several fungal, parasitic, viral, bacterial and malignant opportunistic infections most common to HIV-infected patients at GHTM in Tamil Nadu, India



Key Points (2)

4. Monitoring CD4+ white blood cells can help health care providers know what OIs to watch for and what treatment options to consider
5. Primary prophylaxis is used to prevent OIs in individuals with HIV/AIDS
6. Secondary prophylaxis is used to prevent relapse of an OI's in individuals already infected with an infection

Overview of OIs

Slide 54

- If time permits, tour wards within Tambaram to observe cases.
- Then reconvene to discuss what participants have seen.



Clinical Management of Opportunistic Infections

Participant's Handbook

Session 2

Fungal and Parasitic Infections

Session 2: Fungal and Parasitic Infections

Aim: The aim of this unit is to introduce participants to fungal and parasitic opportunistic infections.

Learning Objectives: By the end of this session, participants will be able to:

- Describe the various clinical presentations and relative frequencies of the following fungal and parasitic opportunistic infections:
 - *Pneumocystis carinii* pneumonia
 - Candidiasis
 - Fungal skin and nail infections
 - Seborrhoeic dermatitis
 - Cryptococcosis
 - Histoplasmosis
 - Cryptosporidiosis
 - Microsporidiosis
 - Scabies
- Identify the appropriate procedures and laboratory investigations required to make a diagnosis of each of the above opportunistic infections.
- Cite the preferred treatment regimen for each of the above opportunistic infections.
- Explain the recommended prophylactic regimens and cite the guidelines for initiation and discontinuation of prophylaxis for the above opportunistic infections.

Key Points

1. Candidial infections are probably the most common fungal infections seen in HIV-infected individuals.
2. *Pneumocystis carinii* pneumonia (PCP) and cryptococcal meningitis are life-threatening fungal infections. They may be treated adequately in most patients, but recurrences commonly occur if ARV therapy is not started.
3. PCP and cryptococcal meningitis are common causes of death in HIV-infected persons.

Handout 2.1

Treatment of Common Fungal and Parasitic Opportunistic Infections

PCP FIRST-LINE TREATMENT— FOR BOTH ADULT & PAEDIATRIC CASES:

Antimicrobial Agent	Dose	Frequency	Route	Duration
prim + sulpha-methoxazole (TMP-SMZ)	15-20 mg/kg/day	qid	PO	21 days

PCP FIRST-LINE TREATMENT— FOR SEVERE CASES

- For patients with respiratory failure, ARDS, cyanosis, or PaO₂ < 70.
- Also for patients who are vomiting and cannot take PO meds.

Antimicrobial Agent	Dose	Frequency	ute	Duration
Cotrimoxazole (CTZ)	15-20 mg of TMP/ kg	3-4 times per day	IV	Until patient can tolerate orally

ADJUNCTIVE TREATMENT FOR SEVERE PCP

Antimicrobial Agent	Dose	Frequency		Duration
Methyl Prednisolone OR	80 mg	qd	IM	1 week
Dexamethasone OR	8 mg	tid	IV/IM	1 week
Prednisolone	80 mg	qd	PO	5 days; then reduce dose to 40 mg for 5 days; then drop to 20 mg for 5 days again

PCP SECOND-LINE TREATMENT

Antimicrobial Agent	Dose	Frequency	Route	Duration
Dapsone	200 mg	qd AM only	PO	21 days
OR				
Clindamycin	600 mg	qid	PO	21 days
PLUS				
Primaquine	15 mg	qid	PO	21 days

Handout 2.1 (continued)

Treatment of Common Fungal and Parasitic Opportunistic Infections (continued)

PCP ALTERNATIVE TREATMENTS If the patient is allergic to Cotrimoxazole (usually to the sulphamethoxazole):

Antimicrobial Agent	Dose	Frequency	Route	Duration
	3-4 mg/kg/day	qd	IV	21 days
with Trimethoprim	100 mg AND 300 mg	bid		21 days
R				
Atovaquone	75 mg	tid	PO	21 days
PLUS				
Clindamycin with Primaquine	450 mg AND 15 mg	qid	PO	21 days

* Pentamidine should never be given rapidly or through intramuscular route because it may cause hypoglycaemia or dangerous hypotension.

ADULT PCP PROPHYLAXIS

Indications	1 st Choice	Alternative Choice
<u>Primary</u> *CD4 <200 or <14% *Oral thrush *History of AIDS-defining illness *PUO	Cotrimoxazole One double-strength daily	Aerosol pentamidine

Secondary prophylaxis: After an episode of PCP

PAEDIATRIC PCP PROPHYLAXIS

Drug	Paediatric dose	Frequency	Route	Duration
Cotrimoxazole Single strength: 80 TMP / 400 SMZ	<6 mths=1/4 tablet	qd	PO	For life
	6-12 mths=1/2 tablet	qd	PO	
	> 1year=1 tablet	qd	PO	

 **Handout 2.1 (continued)**

Treatment of Common Fungal and Parasitic Opportunistic Infections (continued)

ORAL CANDIDIASIS FIRST-LINE TREATMENT

Antifungal Agent	Dose	Frequency	Route	Duration
Clotrimazole lozenges to suck*	mg	5 times a day	PO	14 days
Clotrimazole Mouth Paint				
OR				
	1%	2-3 times per day	oral	14 days
Nystatin lozenges to suck*	100 mg	5 times a day	PO	14 days
OR				
Hamycin Mouth Paint*		2-3 times per day	Topical	
Miconazole Gel		3-4 times a day	Topical	
Clotrimazole Solution		3-4 times a day	Topical	

*Not available at Tambaram

ORAL CANDIDIASIS SECOND-LINE TREATMENT

Antifungal Agent	Dose	Frequency	Route	Duration
Fluconazole	200 mg	qd	PO	14 days
OR				
Fluconazole	200 mg	qd	PO	14 days

VAGINAL CANDIDIASIS FIRST-LINE TREATMENT

Antifungal Agent	Dose	Frequency	Route	Duration
Fluconazole	100 mg	Single dose	PO	Single dose
OR				
Fluconazole*	200 mg	Once a day	oral	3 days
OR				
Clotrimazole*	100 mg	Twice daily	Vaginal	3 days

VAGINAL CANDIDIASIS SECOND-LINE TREATMENT

Antifungal Agent	Dose	Frequency	Route	Duration
Ketoconazole	200 mg	bid	PO	3 days
OR				
Ketoconazole	200 mg	QD	PO	7 days

Handout 2.1 (continued)

Treatment of Common Fungal and Parasitic Opportunistic Infections (continued)

OESOPHAGEAL THRUSH FIRST-LINE TREATMENT

Antifungal Agent	Dose	Frequency	Route	Duration
Fluconazole	200 mg to 400 mg	qd	PO or IV	14-21 days

OESOPHAGEAL THRUSH SECOND-LINE TREATMENT

Antifungal Agent	Dose	Frequency	Route	Duration
Ketoconazole	400 mg	bid	PO	2-3 weeks
OR				
Itraconazole	200 mg	bid	PO	2-3 weeks
OR				
Amphotericin B (Not used much at GHTM due to side effects)		qd	IV	2-3 weeks

*Not available at Tambaram

PAEDIATRIC PROPHYLAXIS OF RECURRENT CANDIDIASIS

Antifungal Agent	Dose	Frequency	Route
Nystatin*			
Infants (1-12 months)	200 000 units	qd	PO
Children	000 units	qd	PO
Fluconazole			
Neonates (< 1month)	3-6 mg/kg	Every 72 hrs (<14 days old)	PO
Infants (1-12 months)	3-6 mg/kg	qd	PO
Children	3-6 mg/kg	qd	PO

DERMATOMYCOSIS, FIRST-LINE TREATMENT

ANTIFUNGAL Agent	Dose	Frequency	Duration
Clotrimazole	1%	bid	2-4 weeks
Econazole	1%	qd or bid	2-4 weeks
Ketoconazole	2%	qd	2-4 weeks
Miconazole	2%	bid	2-4 weeks
Butenafine	1%	bid	2-4 weeks
Terbinafine	1%	bid	2-4 weeks
Tolnaftate	1%	bid	2-4 weeks
Whitfield's Ointment			

 **Handout 2.1 (continued)**

Treatment of Common Fungal and Parasitic Opportunistic Infections (continued)

DERMATOMYCOSIS, SECOND-LINE TREATMENT

Antifungal Agent	Dose	Route of Administration	Fr	Duration
Griseofulvin	250-500 mg	PO	bid	1-3 months
Terbinafine	250 mg	PO	qd	2-4 weeks
Ketoconazole	200 mg	PO	qd	1-3 months
Fluconazole	50 mg 150 mg	PO PO	qd Weekly	1-3 months
Itraconazole	100-200 mg	PO	qd	1-3 months

ONYCHOMYCOSIS, FIRST-LINE TREATMENT

Antifungal Preparation	Dose	Frequency	Route	Duration
Terbinafine	250 mg	od		6 weeks for fingers OR 12 weeks for toes
OR				
Itraconazole	200 mg	b	PO	For 1 week each month for 2 months (fingers) and

CRYPTOCOCCAL MENINGITIS FIRST-LINE TREATMENT, SEVERE CASES

Antifungal Agent	Dose	Frequency	Route	Duration
Amphotericin B	0.7-1.0 mg/kg	q	IV	14 days
PLUS				
Flucytosine	100	qd	PO	2 weeks
Fluconazole	400 mg	qd	PO	10 weeks
THEN				
Voriconazole	200 mg		PO	For life
	6 mg/kg		PO	For life

CRYPTOCOCCAL MENINGITIS FIRST-LINE TREATMENT, MILD CASES

Antifungal Agent	Dose	Frequency	Route	Duration
Loading Dose: Fluconazole	800 mg	Single dose	PO	Single dose
THEN				
Fluconazole	400 mg	qd	PO	4-6 weeks
Maintenance Therapy: Fluconazole OR Itraconazole	200 mg/kg	qd	PO	For life

Handout 2.1 (continued)

Treatment of Common Fungal and Parasitic Opportunistic Infections (continued)

TOXOPLASMOSIS TREATMENT-PRIMARY THERAPY

Drug	Dose	Frequency	Route	Duration
Sulphadiazine	100 mg in doses up to 8 g	qid	PO or IV	3 months
Clindamycin	60 mg	qid	PO or IV	
PLUS				
	200 mg loading dose THEN 75 mg	See dose qd		3 months
PLUS				
Folinic acid	7.5 mg	q	PO	3 months

TOXOPLASMOSIS TREATMENT-MAINTENANCE THERAPY

Drug	Dose	Frequency	Route	Duration
Sulphadiazine OR Clindamycin	500 mg 600 mg	qid qd	PO PO	For life
PLUS				
Pyrimethamine	25	q	PO	For life
PLUS				
id	7.	q	PO	For life

HISTOPLASMOSIS FIRST-LINE TREATMENT

Antifungal Agent	Dose	Frequency	Route	Duration
Amphotericin B		qid	IV	3-14 days
THEN				
Itraconazole	mg	bid	PO	Long-term

CRYPTOSPORIDIOSIS RECOMMENDED TREATMENT

Antimicrobial Agent	Dose	Frequency	Route	Duration
Albendazole	400 mg	bid	PO	4 weeks
Azithromycin	500 mg	qid	PO	4 weeks
PLUS				
Paromomycin*	1g	bid	PO	4 weeks

*Not available at Tambaram

MICROSPORIDIOSIS RECOMMENDED TREATMENT

Antimicrobial Agent	Dose	Frequency	Route	Duration
Albendazole	400 mg	bid	PO	4 weeks

*Not available at Tambaram



Introductory Case Study

Case Study Instructions:

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
Discuss the case together and answer the related questions in the time you are given.

Case 1

Mr. AS, a 27-year-old agricultural worker, a known HIV-positive patient, presented with the complaints of fever, cough, and progressively worsening breathlessness over a period of 1 month.

The cough was associated with scanty sputum production. Sputum neither was yellowish-white and neither foul-smelling nor mixed with blood.

Two private practitioners treated him with amoxicillin and ciprofloxacin. On examination, he was dyspnoeic at rest; temperature was 37.66°C. The respiratory rate was 26/min. The respiratory system examination revealed intercostal indrawing, no change in vocal fremitus and vocal resonance, and on auscultation there were rales on both lungs and there was no bronchial breathing.

The other systems were clinically normal except tachycardia (pulse rate was 104/min.)



Role-Play: Common Opportunistic Infections

Role-Play Instructions—The Patient:

You will play the role of a patient with HIV at Tambaram Sanatorium. You will take on the characteristics in the scenario listed below. As much as possible, try to act like the patient described in the scenario. Your partner will play the part of a health-care provider. He or she will need to ask you questions to find out about your lifestyle, and will then need to advise you on how to avoid contracting *Cryptosporidium*.

HIV Patient Scenario:

You are a woman in her thirties who is infected with HIV. You have 3 children, ages 4 months, 3 years, and 5 years. You are responsible for the care of your children, including feeding, cleaning, and changing diapers. You grow some of your own food in your garden. Your home is near a river that is used by many people in the community for bathing and supplying water for animals to drink. About once a week, you and your family go to the river to bathe. This is something the children really love to do, especially when the weather is hot. You would strongly resist the idea of giving up bathing in the river.

You have been to Tambaram Hospital twice before with diarrhoea. You tell your doctor, “While I am here, I am ok. The diarrhoea goes away. When I go home, I get diarrhoea again.”

Role-Play Instructions—The Health-Care Provider:

You will role-play the part of a health-care provider to practise counselling and educating patients. Your partner will take on the role of a patient infected with HIV. He or she has been given specific characteristics as a patient. As a health-care provider, you will need to:

- Explain what cryptosporidiosis is, and how it can be contracted.
- Find out about the patient’s lifestyle and what may put him or her at risk of contracting cryptosporidiosis.
- Give specific advice to the patient to reduce their risk of contracting the disease.
- Answer any questions the patient may have.

Here are some tips you might give the patient to prevent diarrhoea:

- Use only boiled water for drinking.
- Do not eat hotel foods or eat outside the home. If you must do so, follow the advice below.
- Avoid spicy food.
- Eat only well-cooked food.
- Don’t eat curd or chutney.
- Don’t eat leftovers from the day before.
- Avoid eating coconut.
- Keep temperate (moderate) habits.



Case Study: Fungal and Parasitic Infections

Case Study Instructions:

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
Discuss the case together and answer the related questions in the time you are given.

Case 1

Mira is 22 years old. She is HIV-infected and lives on a farm with her family. Her responsibilities include taking care of the chickens and pigs and helping in the fields. She complains, sometimes in the middle of the day, of dizziness. Also, the only water available in the field is from a small stream. Currently she has no illnesses and is maintaining her weight.

Questions:

1. What interventions would you recommend for Mira?

2. What might be causing Mira to be dizzy?

3. What might help her symptoms?

Case Study: Fungal and Parasitic Infections (continued)**Case Study Instructions:**

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
3. Discuss the case together and answer the related questions in the time you are given.

Case 2

A 4-month-old infant presents to the clinic with low-grade fever, hypoxia, and a rapid respiratory rate. On auscultation the infant's lungs sound clear. When questioned, the mother states that last year, another of her babies died at 9 months of age from a severe diarrhoeal illness. That child had never grown well and always had thrush. This infant has had thrush once. The mother has never been tested for HIV.

Questions:

1. What might be a likely diagnosis for this infant? How could you confirm the diagnosis?
2. How would you treat this patient?
3. What would you advise the mother?
4. This mother will most likely need a lot of emotional support when faced with these issues. How might you provide this support? Practise how you might give advice to the mother.



Worksheet 2.4 (continued)

Fungal and Parasitic Infections Video Case Studies (continued)

Trigger Point: Treatment Questions

1. How do you treat PCP? What are the possible outcomes of treatment?
2. What are the outcomes or complications if PCP is not treated?
3. What are the possible complications of PCP drug therapy? What are some alternative treatments?

Session 2: Fungal and Parasitic Infections Case 3

Video Case Study Context

An adult male with the following symptoms: Oral ulcers, difficulty in mastication and swallowing, bleeding from the gum and oral cavity, white patches inside oral cavity, absence of taste, and loss of appetite.

Trigger Point: Diagnosis Questions

1. What is the clinical condition of this patient?
2. How do you collect a sample, and what tests would you do to confirm diagnosis?



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Notes



Session 2: Fungal and Parasitic Infections

Slide 1



Fungal and Parasitic Infections

Session Two





Learning Objectives

- By the end of this session, you will be able to:
 - Describe various clinical presentations and relative frequencies of several fungal and parasitic OIs
 - Identify appropriate procedures and laboratory investigations required to make a diagnosis
 - Cite the preferred treatment for these OIs
 - Explain recommended prophylactic regimens

Fungal and Parasitic Infections

Slide 2

- The aim of this session is to introduce participants to fungal and parasitic opportunistic infections.



Introductory Case Study (1)

- Mr. AS, 27 yrs old, agricultural worker, a known HIV positive patient, came with the complaints of fever, cough and progressively worsening breathlessness over a period of one month
- The cough was associated with scanty sputum production
- Sputum neither was yellowish white and neither foul smelling nor mixed with blood
- Two private practitioners treated him with amoxycillin and ciprofloxacin

Fungal and Parasitic Infections

Slide 3

- Read the case study and answer the questions that follow in “Introductory Case Study” (Worksheet 2.1) in the Participant’s Handbook.



Introductory Case Study (2)

- On examination, he was dyspnoeic at rest, temperature was 99.8°F. Respiratory rate was 26/mte
- Respiratory system examination revealed intercostal indrawing; no change in vocal fremitus & vocal resonance; on auscultation, rales on both lungs & no bronchial breathing
- Other systems were clinically normal except tachycardia (pulse rate was 104/mte)



Questions for Discussion

1. What opportunistic infections do you suspect in this patient?
2. What tests will you perform to arrive at a diagnosis?
3. Suggest the initial treatment at the time of admission
4. Do you change your treatment if there is clinical worsening?



Pneumocystis Jiroveci (Carinii) Pneumonia (PCP) (1)

- Patients usually present with:
 - Cough
 - Shortness of breath
 - Fever
 - Sudden onset of severe dyspnoea
- Can lead to death if not treated early.

Fungal and Parasitic Infections

Slide 6

- Pneumocystis jiroveci pneumonia (PCP) is a common HIV-associated opportunistic infection caused by Pneumocystis jiroveci.
- Although the Pneumocystis jiroveci organism does not cause illness in immunocompetent hosts, it can cause severe pneumonia in patients with HIV/AIDS.
- Early clinical symptoms can be subtle and include dry, nonproductive cough of extended duration.
- Patients usually present with cough, shortness of breath, and fever.
- Usually patients with PCP have a sudden onset of severe dyspnoea, but PCP may also present in persons with more chronic symptoms.
- Symptoms may be very severe, and an attack of PCP may lead to the death of the patient if not treated early and effectively.



Pneumocystis Jiroveci Pneumonia (PCP) (2)

Severity	Mild	Moderate	Severe
Symptoms	Cough, sweats, Grade 1 dyspnoea	Cough, fever, sweats, Grade 3 dyspnoea	Persistent fever, Grade 4 dyspnoea & tachypnoea
Blood Gas Analysis*	PaO ₂ normal	PaO ₂ 60-80 mm Hg SaO ₂ falls on exertion	PaO ₂ <60 mm Hg
Chest X-ray	Normal or minor perihilar markings	Diffuse bilateral interstitial shadowing	Extensive bilateral interstitial & alveolar markings

* Without O₂ Supplementation

Fungal and Parasitic Infections

Slide 7

- The clinical features vary depending upon the severity of the disease.



Diagnosis of PCP

- Shortness of breath, cough, extreme dyspnea
- Tachycardia
- Sweating
- Cyanosis
- Respiratory rate > 20/minute
- ABG: $\text{PaO}_2 < 60$ mm Hg without O_2
- $\text{SaO}_2 < 85$

Fungal and Parasitic Infections

Slide 8

- The diagnosis is often made on clinical grounds when a patient with HIV infection presents with shortness of breath.
- The patient may have a cough, but the main feature is extreme dyspnoea. (Zim, Specific OIs)
- The patient may be tachycardic, with sweating and cyanosis.
- The patient's respiratory rate can exceed 20 breaths per minute.
- The arterial blood gas may be less than 60, and the O_2 saturation less than 85.
- While diagnosis is often made on clinical grounds, it is better confirmed by chest X-ray, blood gas analysis, and sputum/respiratory secretions examination. If facilities are available, HRCT and gallium scanning can be done.
- However treatment should not be withheld for want of confirmed diagnosis.



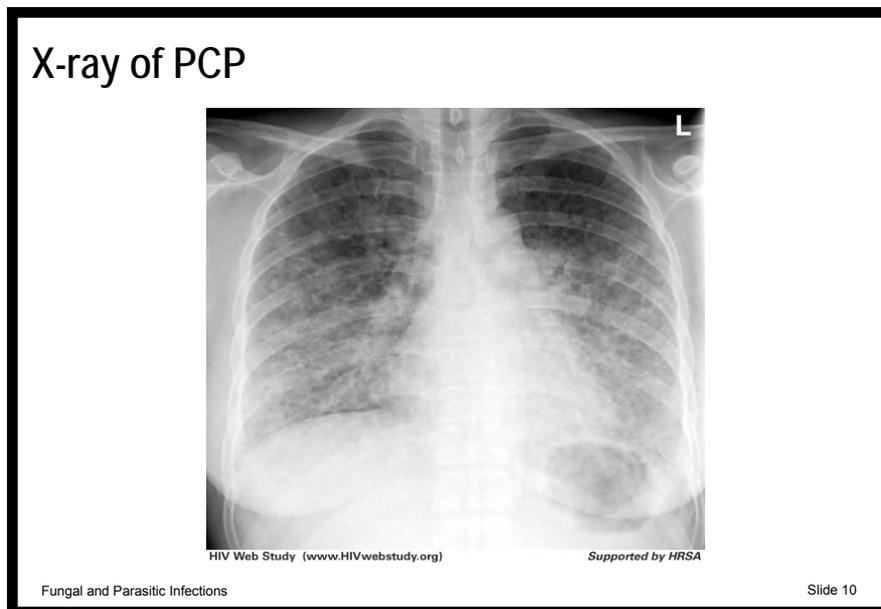
Diagnosis of PCP

- Lung sounds may be normal
- Chest X-ray may be normal or may show patchy infiltrates in both lung fields
- Confirmed when cysts of *Pneumocystis* are found in sputum or in bronchial lavage aspirate
- Classic chest X-ray: ground glass opacification in middle zones

Fungal and Parasitic Infections

Slide 9

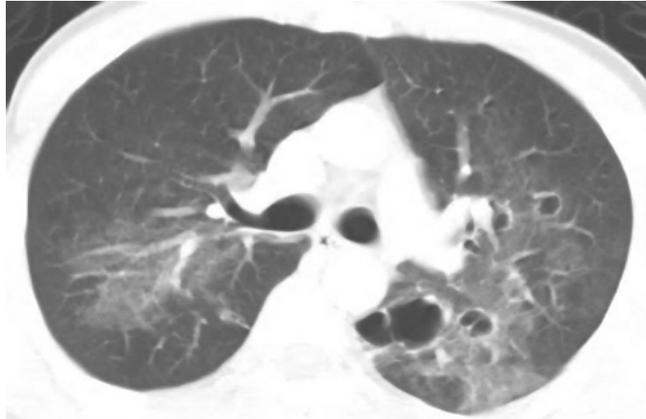
- Lung auscultation (sounds) may be normal, as rales and rhonchi may develop late in the clinical course. (Baylor, p. 96)
- Chest X-ray may be completely normal, or there may be evidence of patchy infiltrates in both lung fields.
- The classic chest X-ray appearance of a ground glass opacification in the middle zones of both lung fields may also be found.
- The diagnosis is confirmed by locating cysts of *Pneumocystis* in sputum or in bronchial lavage aspirate (a procedure that, if available, consists of washing that can retrieve cells or tissue from the lungs and the alveoli in them). (Zim, Specific OIs and Baylor, p. 96)
- Children can be very ill with this disease, and it is often the first AIDS-defining illness in a child. (Baylor, p. 96)
- The following clinical laboratory tests can be done for the diagnosis:
 1. Sputum/respiratory secretions demonstration of *Pneumocystis jiroveci*.
 2. The above specimens can be collected by ultrasonic nebulisation using hypertonic saline, or if facilities available, by bronchoalveolar lavage (BAL) or trans bronchial biopsy for demonstration of *Pneumocystis jiroveci*.
 - Very rarely open lung biopsy can be performed for histo-pathological examination.
 3. Partial pressure of Arterial oxygen (PaO_2) and Arterial oxygen saturation (SaO_2) at rest and after exertion.
 4. DTPA: (Technetium-99m- Diethylene Triamine Pentaacetic Acid) is administered as a radioaerosol. It is deposited in the alveoli and the rate of uptake into the blood stream is measured. DTPA clearance >4.5 is specific for PCP.



- This is an example of an X-ray consistent with pneumocystis jirovecii pneumonia:
 - § Diffuse bilateral lung parenchymal opacities and interstitial infiltrates
- § Typical radiographic findings of PCP are diffuse, bilateral, interstitial, or alveolar infiltrates.
- Other radiographic findings of PCP include:
 - Pneumothorax
 - Cystic changes
 - Lobar or segmental infiltrates
 - Nodules and/or
 - Pleural effusions.
- Apart from the findings in the previous table, PCP may present with:
 - Pneumothorax
 - Cystic changes
 - Lobar/segmental infiltrates
 - Nodules and/or
 - Pleural effusion
- HRCT (High resolution CT scan): Diffuse fine alveolar consolidation with bronchial wall thickening can be demonstrated, even when the chest x-ray is normal.



CT Scan



HIV Web Study (www.HIVwebstudy.org)

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Fungal and Parasitic Infections

Slide 11

- Slide showing contrast chest CT showing multiple cystic lesions and areas of ground-glass opacity
- Go over the treatment and prophylaxis specifications on “Treatment of Common Fungal and Parasitic OIs” (Handout 2.1).
- Patients with Pneumocystis Jirovecii Pneumonia usually are in respiratory failure and should ideally be admitted to hospital for management.
- Supportive therapy, including oxygen by mask and intravenous fluids may be necessary. (Zim, Specific OIs)
- Adult patients who have a CD4+ lymphocyte cell count below 200/mm³ or who have had oropharyngeal candidiasis (a fungal infection of the mouth and pharynx), should be started on preventative treatment. (Baylor, p. 96)
- PCP is best treated with trimethoprim sulfamethoxazole. Details of treatment are given in Handout 2.1, “Treatment of Common Opportunistic Infections”.
- The drug of choice is Cotrimoxazole which can be given orally in mild to moderate PCP and intravenously (if available) in moderate to severe cases.
- Dose : Trimethoprim 15-60 mg /kg/day and sulphamethoxazole 75-100 mg/kg/day (COTRIMOXAZOLE) in four divided doses.
- *NOTE: The first few days treatment is critical since the degradation of fungi exaggerates the pre-existing inflammatory process and causes hypoxia. The immediate mortality can be reduced if Corticosteroid is started within 48 hours if oxygen tension is less than 70mmHg. Short term course of steroid is usually helpful.*
- If a patient cannot tolerate the full prophylaxis dose of trimethoprim sulfamthoxazole, half the dose may be given everyday instead.



PCP First Line Treatment

PCP First Line Treatment				
Trimethoprim +	15-20 mg/kg/day	qid	PO	21 days
Sulpha- methoxazole (TMP-SMZ)	75-100 mg/kg/day			

Fungal and Parasitic Infections

Slide 12

- Refer to Handout 2.1 for PCP Treatment and Prophylaxis.
- Some patients are given the full dose everyday, as this will also protect them against toxoplasmosis. (Baylor, p. 96)
- After successfully treating the acute episode of PCP, it is necessary to continue secondary prophylaxis with trimethoprim 160mg/sulphamethoxazole 800mg on a long-term basis. (Zim, Specific OIs)
- If the patient is allergic to Cotrimoxazole (usually to the sulphamethoxazole) the following alternatives can be used:
 - Intravenous Pentamidine – 4 mg/kg/day. Pentamidine should never be given rapidly or through intra muscular route because it may cause hypoglycemia or dangerous hypotension.
- Other alternative treatments:
 - Dapsone 100 mg/day with Trimethoprim 300 mg /8th hourly
 - Atovaquone 750 mg/8th hourly
 - Clindamycin 450 mg/ 6th hourly with Primaquine 15 mg /day(Mild to moderate cases)



PCP First Line Treatment for Severe Cases

- For patients with respiratory failure, ARDS, cyanosis, or $\text{PaO}_2 < 70$
- Also for patients who are vomiting and cannot take PO meds

Cotrimoxazole (CTZ)	15-20mg of TMP/ kg	3-4 times per day	IV	Until patient can tolerate orally

Fungal and Parasitic Infections

Slide 13



PCP Prophylaxis in Adults

Primary		
*CD4 <200 or <14%	Cotrimoxazole	Aerosol Pentamidine
*Oral thrush	One double strength tablet daily	
*History of AIDS defining illness		
*PUO		

Secondary prophylaxis : After an episode of PCP



Paediatric PCP Prophylaxis

Cotrimoxazole (single strength 80 TMP/400 SMZ)	<6mths=1/4 tablet	qd	PO	For life
	6-12mths=1/2 tablet	qd	PO	
	>1yr=1 tablet	qd	PO	

Fungal and Parasitic Infections

Slide 15

- Children should also receive preventive treatment or prophylaxis if they:
 1. are an age specific CD4+ lymphocyte cell percentage less than 15
 2. have never had PCP, or
 3. have chronic oral candidiasis (thrush)
- Infants who are born to mothers known to be HIV-infected should begin PCP prophylaxis when they are 4-6 weeks of age and remain on prophylaxis until they are 12 months old, or until it can be determined definitively whether or not they are HIV-infected.
- If HIV-infected, their treatment should follow the guidelines for HIV-infected children.
- For children diagnosed as having HIV-related pneumonia, Cotrimoxazole prophylaxis should be commenced.



Complications of PCP

- Spontaneous pneumothorax
- Bronchopleural fistula refractory to closure
- Lung cavitation (solitary thin walled cavities)-chronic infection with PCP causes activation of pulmonary macrophages → release elastase → destroy lung tissue
- Respiratory failure
- Extrapulmonary pneumatosis (continued on next slide)

Fungal and Parasitic Infections

Slide 16

- Complications of PCP:
 - Spontaneous pneumothorax
 - Risk factors for the above complication are aerosol pentamidine therapy and prior PCP infection.
 - Management: Treatment of pneumothorax and PCP
 - Bronchopleural fistula refractory to closure.
 - Management: Treatment of pneumothorax by pleurodesis and PCP
 - Lung cavitation (solitary thin walled cavities)-chronic infection with PCP causes activation of pulmonary macrophages → release elastase → destroy lung tissue
 - Respiratory failure.
 - Management: Supportive care with continuous positive airway pressure (CPAP) by face mask
 - Mechanical ventilation and ICU care.
 - Salvage therapy with Trimetrexate and Eflornithine can be tried.
 - Extrapulmonary pneumatosis (continued on next page)



Pneumocystis Choroiditis



Image courtesy of The New York Eye and Ear Infirmary Digital Atlas of Ophthalmology - www.nyee.edu

Fungal and Parasitic Infections

Slide 17

- Extrapulmonary pneumatosis (continued)
 - External auditory polyps
 - Mastoiditis
 - Choroiditis
 - Cutaneous lesions
 - Digital necrosis secondary to vasculitis
 - Ascites with gross nodules in the stomach and duodenum
 - Hepatitis
 - Splenitis
 - Hilar and mediastinal lymphadenopathy
 - Thyroiditis
- Histopathological picture
 - Typical foci of eosinophilic frothy exudates and special staining reveal cysts of *Pneumocystis*.
 - Unlike in lung tissue, the lesions are often calcified (punctate or rim like)
 - Prognosis is poor with extensive extra pulmonary involvement and often results in multi organ failure and death.



Discussion: Experience Treating PCP at Tambaram

- How often do you see patients with PCP?
- What resources are there at Tambaram to diagnose and treat patients with PCP?
- Have you found any useful techniques or methods for caring for these patients?

Fungal and Parasitic Infections

Slide 18

- Share your experiences treating patients with PCP at Tambaram Sanatorium.



Candidiasis

- Oro-pharyngeal candidiasis (OPC): mouth and throat, commonly presents in HIV-infected persons
- Oesophageal candidiasis: difficulty swallowing, pain in chest
- Disseminated candidiasis: fever and symptoms in affected organs

Fungal and Parasitic Infections

Slide 19

- Candidiasis is one of the most common opportunistic infections associated with HIV.
- The two main types of candidiasis are *localized* disease (of the mouth and throat, and of the vagina) and *systemic* disease (of the oesophagus, skin and nails and other viscera).
- Vaginal candidiasis generally presents as a creamy white abnormal vaginal discharge.
 - Symptoms include: vaginal or vulvar pruritus, burning pain and dyspareunia.
- On examination the vagina may appear erythematous and pseudomembranous plaques are often seen.
- Disseminated candidiasis causes fever and symptoms in the organs affected by the disease (for example, blindness when it affects the eyes).
- Other organ involvement occurs rarely.
- A small number of patients develop broncho pulmonary candidiasis, presumably as an extension of oropharyngeal disease.
- Involvement of skin, brain, liver and kidneys are also described.
- Patients who are critically ill, have been treated with long-term systemic antibiotics, or have an indwelling catheter (e.g., central venous access device) may develop systemic candidiasis or candidemia. (Baylor, p. 97)
- Differential diagnosis:
 - Aphthous ulceration and herpes virus infections are the most common lesions confused with candidiasis. However, these lesions are usually more painful.
 - Hairy leukoplakia
 - Other fungal infections like histoplasmosis



Oro-pharyngeal Candidiasis



HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA

Fungal and Parasitic Infections

Slide 20

- Oral Candidiasis is classified into 4 categories:
 1. Pseudomembranous type: Characterized by the occurrence of painless white spots on the tongue, gums, buccal membrane, or throat.
 - Plaques are composed of necrotic materials, desquamated parakeratotic epithelia, and hyphae and yeast cells that do not penetrate beyond the stratum spinosum.
 - These plaques are easily removable.
 2. Acute atrophic (erythematous) type: occurs as red patches affecting the tongue, buccal membrane and gums.
 3. Chronic atrophic (angular cheilitic) type: occurs as painful red or white fissuring at the corners of the mouth.
 4. Chronic hyperplastic (leukoplactic) type: It is a chronic discrete lesion that vary in size and appearance and cannot be scrapped away.
- The mouth and throat variant (oropharyngeal candidiasis or OPC) is believed to occur at least once in the lifetime of all HIV-infected patients. (Zim, Specific OIs)
- It is commonly one of the presenting signs of HIV infection in individuals who do not have other reasons (e.g., recent antibiotic use, diabetes) to have fungal disease. (Baylor, p. 97)
- This does not lead to death, but can cause dysphagia and odynophagia.



Oro-pharyngeal Candidiasis (2)



Fungal and Parasitic Infections

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- The diagnosis of oropharyngeal candidiasis is made on clinical grounds. (Zim, Specific OIs)
- Patients have white or yellow plaques on the oropharyngeal mucosa and on the tongue.
- If oesophageal infection is also present, the patient may complain of inability to swallow or retrosternal chest pain when swallowing.
- Infants may begin to feed and then stop after the first few swallows, arching their backs and turning their heads because of difficulty in swallowing.
- The diagnosis may be confirmed by the microscopic examination of material obtained from lesions.
- The diagnosis of oesophageal candidiasis is made by direct visualization of oesophageal lesions by upper gastrointestinal endoscopic examination.
- In other sites, the diagnosis is made by histologic examination of tissue biopsies.
- The symptoms of oesophageal candidiasis are difficulty in swallowing and pain in the chest that increases with swallowing.



Candidiasis of the Finger Nails



Courtesy of Public Health Image Library/CDC/Sherry Brinkman

Fungal and Parasitic Infections

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- Candidiasis of the finger nails.



Candida Diaper Dermatitis



Courtesy of Public Health Image Library/CDC

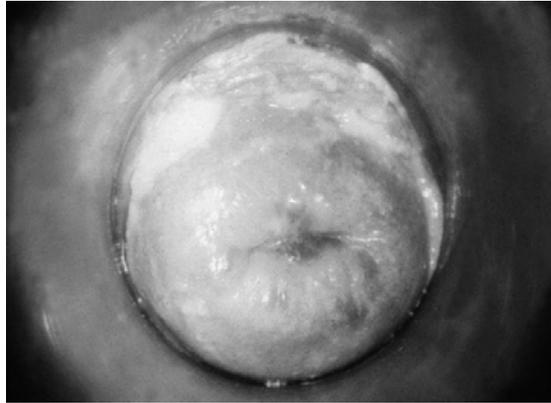
Fungal and Parasitic Infections

Slide 23

- Candidal dermatitis over the perineal region in a child.
- Similar Candida Dermatitis also found on other areas of skin and on adults.



Candidiasis of the Cervix



Courtesy of Public Health Image Library/CDC

Fungal and Parasitic Infections

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- Thick, white cheese like material over the cervical area, due to candidiasis.



Oral Candidiasis First Line Treatment (1)

Oral Candidiasis First Line Treatment (1)				
Clotrimazole mouth paint	10mg	5 times a day	PO	14 days
Clotrimazole lozenges to suck *				
OR				
Gentian Violet	1%	2-3 times per day	Topical	14 days
OR				

* Not available at Tambaram

Fungal and Parasitic Infections

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- Go over the first and second line treatment specifications on the Handout 2.1.
- Localized disease is treated first with topical drugs
- If there is a failure to respond to local treatment, systemic antifungal agents may be used.
- Oral candidiasis can be treated with gentian violet applied directly to the lesions, or nystatin liquid or tablets taken orally (or other topical antifungals).



Oral Candidiasis First Line Treatment (2)

Oral Candidiasis First Line Treatment (2)				
Nystatin lozenges to suck*	100 000 units	5 times a day	PO	14 days
OR				
Hamycin Mouth Paint*		2-3 times/day	Topical	
Miconazole Gel		3-4 times/day	Topical	
Clotrimazole solution		3-4 times/day	Topical	

* Not available at Tambaram

Fungal and Parasitic Infections

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- In patients with disseminated candidiasis and in those in whom topical therapy has failed, antifungal agents such as ketoconazole, itraconazole, or fluconazole may be given. (Zim, Specific OIs)



Vaginal Candidiasis First Line Treatment

Fluconazole	100 mg	Single dose	PO	Single dose
OR				
Miconazole*	200 mg	qd	Vaginal	3 days
OR				
Clotrimazole*	100 mg	tid	Vaginal	3 days

* Not available at Tambaram

Fungal and Parasitic Infections

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- Vaginal candidiasis should be treated with topical antifungal agents.



Oesophageal Thrush First Line Treatment

Fluconazole	200mg to 400mg	qd	PO or IV	14-21 days

Fungal and Parasitic Infections

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- If candidal oesophagitis is suspected, ketoconazole or fluconazole should be used for treatment.
- Systemic candidiasis that does not respond to other antifungal agents is treated with amphotericin B.
- The dose of amphotericin will depend on the severity of the illness.
- Patients who receive this drug should be carefully monitored when they are in the hospital.
- Administration of amphotericin B can be associated with shaking chills or rigors during infusion.
- Amphotericin B also causes:
 - Hypokalemia (decreased potassium in the serum),
 - Bone marrow suppression, and
 - Nephrotoxicity. (Baylor, p. 97)



Paediatric Prophylaxis of Recurrent Candidiasis (1)

Neonates (<1month)	100,000 units	qid	PO
Infants (1-12 months)	200,000 units	qid	PO
	400,000 units		
Children		qid	PO
OR			



Paediatric Prophylaxis of Recurrent Candidiasis (2)

Paediatric Prophylaxis of Recurrent Candidiasis (2)			
Neonates (< 1month)	3-6mg/kg	Every 72 hrs (<14 days old)	PO
Infants (1-12 months)	3-6mg/kg	qd	PO
Children	3-6mg/kg	qd	PO



Discussion: Candidiasis Treatment

- What forms of candidiasis are most common at this hospital?
- What resources are there at Tambaram to diagnose and treat patients with candidiasis?
- Have you found any useful techniques or methods for caring for these patients?



**Dermatological Manifestations of
Fungal and Parasitic Infections**





Fungal Skin and Nail Infections

- Dermatomycoses occur commonly in HIV infected and non-HIV-infected individuals
- Symptoms include:
 - Rash, usually itchy and dry, may include scales of dead skin
 - Lesions that may be found anywhere on the body
 - Fingernails and toenails that are distorted in color and shape (called onychomycosis)
- Topical applications of antifungal ointments and creams will usually clear lesions and rash

Fungal and Parasitic Infections

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- Causative Organisms:
 - T.rubrum
 - T.mentagrophytes
 - M.canis
 - E.floccosum
 - T.tonsurans,
 - T.verrucosum
 - T. soudanense (Candida causes typical nail and skin lesions)
 - Malassezia furfur causes taenia versicolor,
- Presentations:
 - T.pedis: Pruritic red lesions between toes, interdigital fissures, extension to adjacent skin and nails, scaling is present always.
 - Onychomycosis: starts with discolouration, usually at the distal nail end, at one side and then spreads to the other side and towards the cuticle.
 - It also can present as:
 - Onycholysis
 - Yellow nails
 - Subungual hyperkeratosis, distal and proximal nail plate) and
 - Superficial white onychomycosis (Proximal white onychomycosis is almost diagnostic of immunosuppression.)



Fungal Nail Infection



Courtesy of Public Health Image Library/CDC/Dr. Edwin P. Ewing, Jr.

Fungal and Parasitic Infections

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- Presentations (continued):
 - T.corporis: Circular, erythematous, scaly lesion with an irregular geographical border that spreads with central clearing (ringworm)
 - T.cruis: Red, scaly, patch, on the inner thigh with sharply demarcated borders. (jock itch)
 - T. capitis: (Ringworm of scalp)
 - T.pedis (Athlete's foot)
 - Fungal skin rashes (dermatomycoses) occur commonly in HIV infected and non-HIV-infected individuals.
 - The rash is usually itchy and dry, and on examination, scales of dead skin are visible.
 - The lesions may be found anywhere on the body.
 - On examination of skin scrapes, microscopically fungal elements may be found.
 - Nails may also become infected with fungi, and the infection results in distortion and destruction of the nails (onychomycosis).
- Diagnosis:
 - Scraping of the lesion or discoloured nail bed for KOH preparation. This may be supplemented with culture of scraping on Sabouraud's medium.



Tinea Infection-Foot



Courtesy of Public Health Image Library/CDC

Fungal and Parasitic Infections

Slide 35

- Taenia cruris



Tinea Corporis



Fungal and Parasitic Infections

Slide 36

- Common
- KOH preparation



Tinea-Nails

- Common
- >30% of patients
- Antifungal drugs



Fungal and Parasitic Infections

Slide 37

- Taenia infection of the finger nails and the dorsum of the hand and fingers.



Dermatomycosis First Line Treatment

Clotrimazole	1%	bid	2-4 weeks
Econazole	1%	qd or bid	2-4 weeks
Ketoconazole	2%	qd	2-4 weeks
Miconazole	2%	bid	2-4 weeks
Butenafine	1%	bid	2-4 weeks
Terbinafine	1%	bid	2-4 weeks
Tolnaftate	1%	bid	2-4 weeks
Whitfield's ointment			

Fungal and Parasitic Infections

Slide 38

- Treatment:
 - Topical applications of antifungal ointments and creams will usually clear the lesions.
 - Recommendations for treating dermatomycoses and onychomycosis appear in Handout 2.1, "Treatment of Common Fungal and Parasitic Opportunistic Infections." (Zim, Mgmt of Common Medical Problems)
 - First line treatment for Tinea corporis/T.cruis/T.pedis/T.capitis:
 - Topical agents for 2 weeks: 4 weeks for T.pedis
 - WHITFIELD'S OINTMENT
 - CLOTRIMAZOLE – 1% CREAM or LOTION - BID
 - ECONAZOLE – 1% CREAM QD or BID
 - KETOCONAZOLE (NIZRAL) 2% CREAM QD
 - MICONAZOLE 2% CREAM BID
 - BUTENAFINE 1% CREAM
 - TERBINAFINE 1% CREAM or GEL QD or BID
 - TOLNAFTATE 1% CREAM, GEL, SOLUTION, AEROSOL, BID
 - The relapse rate is reduced by ensuring strict adherence to general measures:
 - Keeping the skin dry and
 - Reducing maceration of flexural areas by the use of talcs
 - Different towels for body and feet
 - Avoiding sources of infection



Onychomycosis First Line Treatment

Onychomycosis First Line Treatment				
Terbinafine	250 mg	qd	PO	3 weeks

- Topical therapy is usually not effective
- Itraconazole pulse therapy also can be used
- Topical 5% amorolfine nail lacquer is a useful therapy for those taking multiple systemic drugs

Fungal and Parasitic Infections

Slide 39

- ONYCHOMYCOSIS: TOPICAL THERAPY IS USUALLY NOT EFFECTIVE
- TERBINAFINE 250 mg daily, for three months (This drug is hepatotoxic.)
- Itraconazole pulse therapy also can be used.
- Topical 5% amorolfine nail lacquer is a useful therapy for those taking multiple systemic drugs.



Seborrhoeic Dermatitis

Clinical Features and Treatment



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Seborrhoeic Dermatitis

- Common presenting feature in persons with HIV infection
- Probably caused by a fungus known as *Pityrosporum ovale* (also known as *Malassezia furfur*)
- Symptoms:
 - Erythematous, scaly rash, which may be extensive, persistent, and recurrent
 - Dandruff is seborrhoeic dermatitis of the scalp

Fungal and Parasitic Infections

Slide 41

- Rash appears on:
 - Face
 - Around nostrils
 - Nasolabial folds
 - Eyebrows
 - Scalp
 - Chest
 - Axillae
 - Upper trunk
 - Genital area
- Dandruff (also called *pityriasis capitis*) is seborrhoeic dermatitis of the scalp.
- Rash is erythematous and scaly and although harmless, may be extensive, persistent and recurrent in persons with HIV infection.
- Diagnosis:
 - The diagnosis is made on clinical grounds and may be confirmed by finding fungal elements on microscopic examination of skin scrapes.
 - Differential diagnosis: Psoriasis and T.capis



Seborrhoeic Dermatitis Treatment

- Frequent skin washing to remove scales is advised, and shampooing with selenium sulphide shampoo is effective
- Topical applications of 1% hydrocortisone are probably the most effective
- Ketoconazole 2% cream has also been shown to be effective

Fungal and Parasitic Infections

Slide 42

- Treatment:
 - Frequent skin washing to remove scales is advised, and shampooing with selenium sulphide shampoo is effective.
 - Zinc pyrithione or Ketoconazole shampoos also can be used.
 - Topical application of 1% hydrocortisone is probably the most effective.
 - Another steroid preparation used is Triamcinolone 0.1%
 - Ketoconazole 2% cream has also been shown to be effective.



Seborrheic Dermatitis



Fungal and Parasitic Infections

Slide 43

- Diffuse lesions
- Yellowish and scaly
- Over erythematous base
- Seen over scalp, face, anterior chest, back, and axillae



Cryptococcosis

- Cryptococcal meningitis: most frequent systemic fungal infection in HIV-infected persons
- Occasionally appears as pulmonary or disseminated disease
- Most common symptoms include headache, diplopia or double vision, and indolent fever

Fungal and Parasitic Infections

Slide 44

- Cryptococcosis is presumed to be a primary infection with *Cryptococcus neoformans* rather than reactivation of previously acquired disease.
- The organism is encapsulated yeast like fungus that is an important cause of infection and mortality in HIV/AIDS patients.
- The organism gains access to the human host via respiratory route and are controlled by intact cell mediated immunity.
- Sensitized T cells activate neutrophils and macrophages to ingest and kill cryptococcus.
- In the presence of immune deficiency, *cryptococcus neoformans* disseminates to the Central Nervous System. In 70 to 90% of patients it causes meningitis.
- Systemic mycoses such as cryptococcosis probably cause up to 10% of all HIV-associated deaths worldwide.
- Cryptococcosis most often appears as meningitis, and occasionally as pulmonary or disseminated disease.
- Cryptococcal meningitis is the most frequent systemic fungal infection in HIV-infected persons.
- Symptoms:
 - The most common symptom patients present with is headache. The second most common is diplopia or double vision. The third is indolent fever.
 - Other symptoms may include: neck stiffness, altered sensorium, and coma
 - Fever may be absent, however, in patients with cryptococcal meningitis (Zim, Specific OIs).
 - Patients may also have an altered mental status.
 - These symptoms usually evolve over weeks to months.



Cryptococcosis Organism

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

Fungal and Parasitic Infections

Slide 45

- Symptoms (continued):
 - Meningismus (irritation of the brain and spinal cord without inflammation) as well as signs and symptoms of increased intracranial pressure may be present. (Baylor, p. 98)
 - Without treatment, life expectancy is probably less than a month. (Zim, Specific OIs)
- Diagnosis:
 - Cryptococcosis is relatively easy to diagnose.
 - The centrifuged deposit of the cerebrospinal fluid is examined microscopically after a drop of India ink is added.
 - The yeasts are seen as organisms surrounded by a thick capsule. (Zim, Specific OIs)
Monocytes are present or elevated on CSF examination.
 - CSF findings: The opening pressure may be elevated reflecting concomitant increased intracranial pressure.
 - This pressure is higher than TB and other infections. CSF also may show numerous organisms and few lymphocytes.
- Prognostic Factors:
 - Mental status of the patient at the time of presentation. Altered mental status (confusion, lethargy or obtundation) indicate poor prognosis.
 - Other poor prognostic factors:
 - High CSF cryptococcal antigen titre
 - Low CSF leucocyte count (<20 cells/cu.mm)
 - Age less than 35 years
 - Positive extraneural cultures for cryptococcus and Hyponatremia



Cryptococcal Skin Lesions (1)



Fungal and Parasitic Infections

Slide 46

- In patients where cryptococcus manifests itself as subacute meningitis or meningoencephalitis, most present with:
 - Fever
 - Malaise, and
 - Headache
- Patients are generally symptomatic for 2 to 4 weeks prior to presentation.
- Overt meningeal symptoms and signs (neck rigidity and photophobia) are unusual.
- A minority of patients present with:
 - Lethargy
 - Altered mentation
 - Personality changes and
 - Memory loss.
- Focal neurological signs or seizures are unusual.



Cryptococcal Skin Lesions (2)



Fungal and Parasitic Infections

Slide 47

- Other system involvement:
 - Cutaneous involvement is common and the most common presentation is that resembling molluscum contagiosum.
 - Pulmonary involvement may be the initial manifestation with subacute onset of fever, cough, dyspnoea and hypoxia.
 - Myocarditis
 - Arthritis
 - The infection of prostate may serve as a nidus for relapse in patients who have been apparently successfully treated.



Cryptococcal Skin Lesions (3)



Fungal and Parasitic Infections

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Cryptococcal Skin Lesions (4)



Fungal and Parasitic Infections

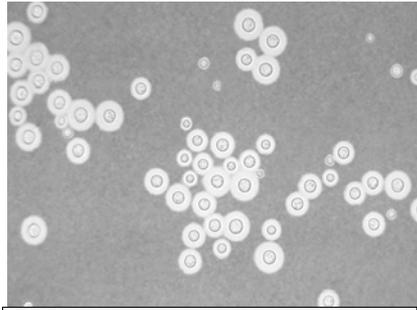
Slide 49

- Centrally umbilicated pearl like lesions of cryptococcal skin lesions resembling molluscum contagiosum.



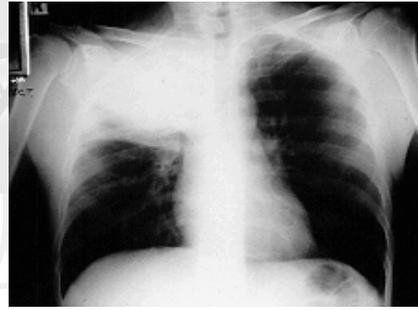
Cryptococcus (1)

Indian ink stain-showing encapsulated organisms



Courtesy of Public Health Image Library/CDC/Dr. Leonor Haley

X-ray showing pulmonary cryptococcal infection [right upper lobe].



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Fungal and Parasitic Infections

Slide 50

- Pulmonary lesions of Cryptococcus.



Cryptococcus (2)



Fungal and Parasitic Infections

Slide 51

- Demonstration of organism:
 - Staining of the specimen (CSF) with Indian ink or Mucicarmine OR Grams stain



Cryptococcal Meningitis 1st Line Treatment for Severe Cases

Amphotericin B	0.7-1.0 mg/kg	qd	IV	14 days
PLUS				
Flucytosine	100 mg/kg	qd	PO	2 weeks
THEN				
Fluconazole	400 mg	qd	PO	10 weeks
THEN	200 mg	qd	PO	For life
For children: Fluconazole	6 mg/kg	qd	PO	For life

Fungal and Parasitic Infections

Slide 52

- Go over the first line treatment specifications on Handout 2.1.



Cryptococcal Meningitis 1st Line Treatment for Mild Cases

Loading Dose: Fluconazole	800 mg	Single dose	PO	Single dose
THEN				
Fluconazole	400 mg	qd	PO	4-6 weeks
Maintenance Therapy: Fluconazole OR Itraconazole	200 mg/kg	qd	PO	For life

Fungal and Parasitic Infections

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Discussion: Cryptococcosis Treatment

- How often do you see patients with cryptococcosis?
- What resources are there at Tambaram to diagnose and treat patients with cryptococcosis?
- Have you found any useful techniques or methods for caring for these patients?



Toxoplasmosis (1)

- Protozoal infection caused by *Toxoplasma gondii*
- Usually occurs from ingestion of cysts excreted in faeces of infected cats, or from eating undercooked beef or lamb
- Commonly invades the brain, lymph nodes, spleen and central nervous system
- Less commonly invades the liver and myocardium

Fungal and Parasitic Infections

Slide 55

- Toxoplasmosis refers to the clinical and/or pathological evidence of disease caused by protozoa *Toxoplasma gondii*.
 - (To differentiate from *Toxoplasma* infection which is asymptomatic in 90% of children and adults.)
- Chronic infection refers to asymptomatic persistence of *Toxoplasma gondii* in the cyst form.
- In patients with HIV/AIDS, reactivation of chronic infection occurs.
- *Toxoplasma encephalitis* is the most common clinical entity and is the most frequent cause of focal intracerebral lesion in patients with AIDS.
- *Toxoplasma gondii* is an obligate intracellular protozoan.
 - Natural reservoirs include cat, birds and domestic animals.
 - The definitive hosts are members of the cat family; all other infected animals including humans are secondary hosts.
- Common route of infection:
 - Oral ingestion of undercooked/raw meat that contain the cysts
 - Food /water contaminated with oocysts
 - Transplacental transmission or puerperal transmission may occur in pregnant women.



Toxoplasmosis (2)

- Commonly invades:
 - Brain
 - Lymph nodes
 - Spleen
 - Central nervous system
- Less commonly invades:
 - Liver
 - Myocardium

Fungal and Parasitic Infections

Slide 56

- The organism commonly invades the:
 - Brain
 - Lymph nodes
 - Spleen and
 - Central nervous system.
- Although less common, it can also invade the liver and myocardium.



Toxoplasmosis (3)

- Flu-like symptoms
- Chronic infections may present with lymphadenopathy and atypical mononuclear cells similar to infectious mononucleosis
- In patients with AIDS, focal seizures, altered sensorium or coma → encephalitis and necrosis of the brain

Fungal and Parasitic Infections

Slide 57

- Clinical Features:
 - Toxoplasmosis is usually asymptomatic.
 - Flu-like symptoms are common:
 - Pneumonia with fever
 - Cough
 - Body ache
 - Malaise
 - Rash and,
 - Rarely, jaundice and myocarditis
 - Chronic infections may present with lymphadenopathy and atypical mononuclear cells similar to infectious mononucleosis.
 - Toxoplasmosis can also cause chorioretinitis and ureitis.
 - Most importantly in patients with AIDS who present with more severe symptoms, such as seizures, altered sensorium or coma, toxoplasmosis can cause encephalitis and necrosis of the brain.



Toxoplasmosis Diagnosis

- Serology
- PCR for detection of *T. gondii* DNA
- Mice inoculation and tissue culture
- Histology in which tachyzoites are demonstrated
- Radiology

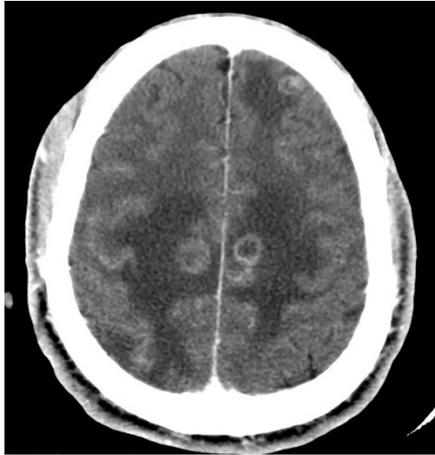
Fungal and Parasitic Infections

Slide 58

- Differential Diagnosis:
 - PCP, Pulmonary tuberculosis, histoplasmosis
- Laboratory Diagnosis:
 - Serology: Toxoplasma antibodies may be tested by a variety of methods including
 - Sabin-Feldman dye test
 - Agglutination tests
 - ELISA test
 - ISAGA (Immunosorbent agglutination assay)
 - PCR for detection of *T.gondii* DNA in body fluids and tissues
 - Mice inoculation and Tissue culture
 - Histology in which the tachyzoites are demonstrated with
 - Immuno peroxidase
 - Wright Giemsa
 - PAS
 - Eosin and methylene blue
 - Radiology: Abnormal, high density, multiple, round, nodular lesions in both the cerebral hemispheres with ring or nodular enhancement with GdDTPA is typically seen in CT scan.
- A CT scan of the brain may show lesions surrounded by cerebral edema.
- An MRI scan is a more sensitive and reliable test and toxoplasmosis may be found in the cerebrospinal fluid.
- A serological test, such as the Sabin-Feldman, may also be used. This method is not as useful as the CT scan or MRI, but may be helpful if used in conjunction with them.



Cerebral Toxoplasmosis



Fungal and Parasitic Infections

HIV Web Study (www.HIVwebstudy.org)

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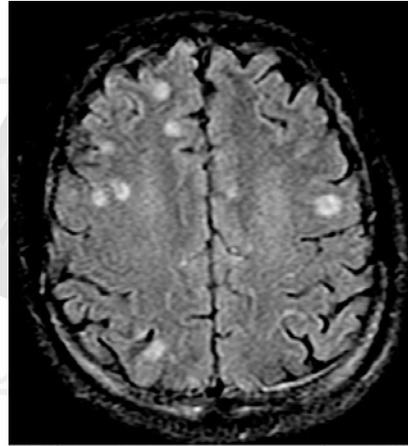
Slide 59

- Toxoplasmosis infection of the cerebral hemisphere: the scan shows multiple ring-enhancing lesions with surrounding vasogenic edema.
- Clinical Features:
 - Alteration of mental status
 - Seizures
 - Motor weakness and sensory deficit
 - Cranial nerve lesion
 - Cerebellar signs
 - Movement disorder
 - Neuro psychiatry manifestations
- Differential Diagnosis:
 - Aspergilosis, Cryptococcal meningitis, Candidiasis
 - Tuberculosis
 - CNS Lymphoma, PML,
 - Herpetic encephalitis, HIV encephalopathy
 - Lungs: prolonged febrile illness with cough and dyspnea



CNS Lesion

- 23 yrs, Mr. K came with headache and loss of weight
- Scan showing multiple enhancing lesions



HIV Web Study (www.HIVwebstudy.org)

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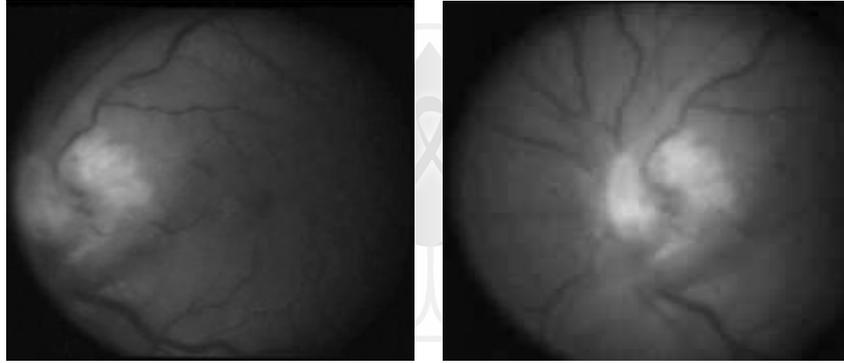
Fungal and Parasitic Infections

Slide 60

- CT scan with contrast of brain, showing ring enhancing lesion of toxoplasmosis.



Toxoplasmic Chorioretinitis (1)



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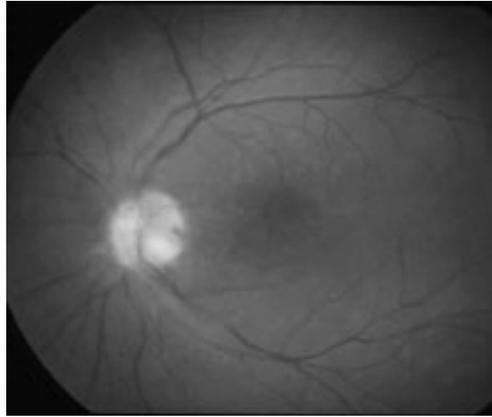
Fungal and Parasitic Infections

Slide 61

- Visual acuity was 20/20 in the right eye and counting fingers in the left.
- Ocular motility and intraocular pressures were normal.
- The ocular findings in the right eye were unremarkable.
- A relative afferent pupillary defect of the left eye was present. The anterior chamber had a 1+ cell and 1+ flare reaction. The lens was clear and the iris normal. The vitreous contained 2+ cells and absent vitreous haze allowing a clear view of the fundus.
- Peripheral retinal findings were normal however disc margins were blurred especially on the temporal side. There was a fluffy inflammatory extension from the disc to the superior papillomacular bundle area. A few cells were seen tracking off the disc into the vitreous. There was serous elevation of the papillomacular bundle with choroidal granularity
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Toxoplasmic Chorioretinitis (2)



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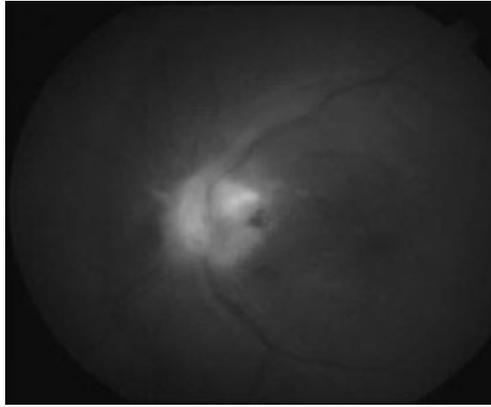
Fungal and Parasitic Infections

Slide 62

- The patient was started on per orem therapy of: pyrimethamine (Daraprim) 75 mg loading then 25 mg/day; sulfadiazine 1600 mg loading then 800 mg qid, clindamycin 300 mg/day; folinic acid 5 mg qod and prednisone 40 mg/day.
- After 1 week of therapy, visual acuity improved to 20/80; patient noted an inferior blind spot; anterior chamber reaction quieted down and vitreous cells decreased to 1+.
- After 2 weeks, vision was 20/60. There was a 60% reduction in disc and peripapillary swelling; a patch of nerve fiber layer hemorrhage in the temporal disc; and an incipient stellate pattern of lipid exudates in the macula giving the appearance of neuroretinitis.
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Toxoplasmic Chorioretinitis (3)



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Fungal and Parasitic Infections

Slide 63

- After 6 weeks of treatment, visual acuity improved to 20/25, anterior chamber and vitreous inflammatory reaction were absent, the hemorrhage was resolving and the disc had returned to near normal appearance. There was a strip of vitreous exudation from the disc into the posterior hyaloid. Steroids were tapered.
- After 7 weeks, vision was 20/20-3 and the only residual sign was that of minimal inactive vitreous exudation.
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Toxoplasmosis Treatment

- Pyrimethamine and sulfadoxine daily for at least six weeks
- Folic acid also added to this regimen to protect against hematologic toxicity of pyrimethamine
- High incidence of toxicity due in part to high prevalence (19–34%) of sulfonamide allergy in people co-infected with AIDS and toxoplasmosis

Fungal and Parasitic Infections

Slide 64

- Go over the primary and maintenance therapy specifications on the Handout 2.1 using slides in the PowerPoint presentation.
- The combination of pyrimethamine and sulfadiazine daily for at least six weeks is the standard approved treatment for toxoplasmosis.
- Folic acid, a B vitamin, is also added to this regimen to protect against the hematologic toxicity of pyrimethamine.
- The treatment is limited by a high incidence of toxicity, seen in up to 60% of people on the regimen. (Toxoplasmosis, 1987)
 - This high incidence of toxicity is due in part to a high prevalence (19–34%) of sulfonamide allergy in people with AIDS and toxoplasmosis (Haverkos, 1992).



NACO Guidelines for Toxoplasmosis Treatment- Primary Therapy

Sulphadiazine	100 mg/kg /day in 4 doses up to 8 g	qid	PO or IV	3 months
OR				
Clindamycin	60 mg	qid	PO or IV	
PLUS				
Pyrimethamine	200 mg loading dose THEN 75 mg	qd	PO	3 months
PLUS				
Folinic acid	7.5 mg	qd	PO	3 months

Fungal and Parasitic Infections

Slide 65

- When sulfa drugs cannot be tolerated, recent clinical practice has been to replace sulfadiazine with oral clindamycin.
- The most common side effect of clindamycin is diarrhoea.
- Clindamycin in combination with pyrimethamine has also shown to be effective maintenance therapy.
 - Clindamycin alone, however, does not appear to be effective in preventing relapse. (Toxoplasmosis, 1987)



Histoplasmosis (1)

- *Histoplasma capsulatum* or *Histoplasma duboisii* can cause acute or chronic illness
- Acute illness is influenza-like with fever, anorexia, arthralgia, myalgia, dry cough, and chest pain
- Very rarely reported in India



Histoplasmosis (2)

- Dissemination occurs soon after initial infection in immunosuppressed hosts, who develop:
 - Weight loss
 - Chest symptoms
 - Liver
 - Spleen and lymph node enlargement
 - Oral and skin lesions



Histoplasmosis Lesions

- Skin lesions may be:
 - Follicular
 - Maculopapular
 - Pustular
 - Erythematous
 - Nodular
 - Apulo-necrotic.
- Buccal lesions may be:
 - Ulcers
 - Nodules
 - Perforated palate



Histoplasmosis First Line Treatment

Amphotericin B	0.7-1mg/kg	qd	IV	3-14 days
THEN				
Itraconazole	200mg	bid	PO	Long term

Fungal and Parasitic Infections

Slide 69

- Go over the treatment specifications on Handout 2.1.



Cryptosporidiosis

- Diarrhoeal disease caused by a *Cryptosporidium parvum* that live in the intestine of humans and animals
- Parasite passed in the stool of infected person or animal
 - Forms cysts that can survive outside the body for long periods of time and are resistant to chlorine disinfection

Fungal and Parasitic Infections

Slide 70

- *Cryptosporidiosis* is a diarrhoeal disease caused by a *Cryptosporidium parvum*.
- It can live in the intestine of humans and animals and is passed in the stool of an infected person or animal. Cryptosporidiosis is a common cause of waterborne disease.
- The parasite can form cysts that allow it to survive outside the body for long periods of time and make it resistant to chlorine disinfection.
- Cryptosporidium infection is more common in countries that have increased crowding and poor sanitary conditions.
 - In endemic areas, the incidence increases during rainy periods.
 - It is also more frequent in children less than two years old, although outbreaks occur worldwide in all age groups.
- Transmission:
 - Transmission of cryptosporidiosis occurs via spread from an infected person or animal, or from a fecally contaminated environment such as a food or water source.
 - However, because autoinfection can occur, ingestion of only a few oocysts (10 to 50) can lead to severe disease and persistent infection, particularly in immunodeficient people.
 - A major source of infection is contaminated drinking or swimming water.
 - Foodborne outbreaks are uncommon.
 - Person-to-person transmission is common particularly among: (1) household members (2) sexual partners (3) children in daycare centers and their caretakers (4) healthcare workers
 - *C. parvum* by closely adhering to intestinal mucosa and invading the host cell membrane causes severe diarrhoea.
- Pathogenesis:
 - The pathogenesis of *Cryptosporidium* is not well understood.
 - The organisms cause a secretory diarrhoea that can be associated with malabsorption.
 - The organisms can spread via the intestinal lumen to involve the biliary system, where they can cause stricturing and cholangitis. Inflammatory changes may be present.



Cryptosporidiosis Symptoms

- Primary symptoms include diarrhoea and abdominal pain with mild fever
- If biliary system is involved (gallbladder and biliary ducts), may also be nauseous and right upper quadrant abdominal pain

Fungal and Parasitic Infections

Slide 71

- Clinical Picture: Cryptosporidium can cause an asymptomatic infection, a mild diarrhoeal illness, or severe enteritis with or without biliary tract involvement.
- Symptoms accompanying diarrhoea may include: (1) low-grade fever (39°C) (2) general malaise, weakness or fatigue (3) loss of appetite (4) nauseous and vomiting
- The incubation period is usually 7 to 10 days (range 5 to 28 days).
- The diarrhoea may be acute or chronic, transient, intermittent or continuous, and scant or voluminous with up to 25 L/day of watery stool. However, the infection may remain completely asymptomatic.
- Symptoms usually start 2 to 10 days after infection and may last about 2 weeks in immunocompetent hosts.
- Cholangitis, cholecystitis, hepatitis, pancreatitis, and respiratory tract infections may also occur.
- Infected persons pass millions of cysts in the faeces. HIV-infected persons who become infected develop repeated bouts of diarrhoea and severe chronic illness and wasting.
- Infection is easily transmitted to family members of infected patients. (Zim, Specific OIs)
- Fecal blood or leukocytes are rare unless there is coinfection with another enteric pathogen. Patients with chronic diarrhoea can develop profound weight loss.
- A number of other clinical manifestations of cryptosporidiosis have been described, including: (1) Cholecystitis (2) Cholangitis (3) Hepatitis (4) Pancreatitis (5) Respiratory tract involvement.
- Biliary tract involvement affects 10 to 30 percent of patients with AIDS and can result in acalculous cholecystitis or sclerosing cholangitis. Symptoms include right upper quadrant pain and fever.
- Infection may ascend from the intestine to the biliary tree, resulting in cholangitis.



Differential Diagnosis for Cryptosporidiosis

- The differential diagnosis for enteric cryptosporidiosis, particularly in HIV – infected patients, includes some pathogens relatively easy to identify, such as the bacteria:
 - Shigella
 - Salmonella
 - Campylobacter
 - Entamoeba histolytica
 - Isospora belli
- Other pathogens however are more difficult to exclude, particularly Cytomegalovirus, Mycobacterium avium and Microsporidia

Fungal and Parasitic Infections

Slide 72

- Diagnosis:
 - The diagnosis is made on finding the organisms in stool smears stained by the modified acid fast staining method.
 - The presence of laboratory abnormalities depends upon the severity and duration of infection.
 - Patients with severe, protracted disease can have evidence of malabsorption.
 - The serum alkaline phosphatase may be elevated in patients with biliary tract involvement. In such patients, ultrasound and CT imaging may show an enlarged gallbladder with a thickened wall and dilated intra- and extrahepatic biliary ducts.
 - Diagnosis of biliary involvement is confirmed by histology or by examination of bile for oocysts, since stool specimens may or may not be positive..
 - In patients with diarrhoea, the diagnosis is most commonly established by detecting the organisms in stool specimens. The organisms may also be present in duodenal aspirates, bile secretions, biopsy specimens from affected gastrointestinal tissue, or respiratory secretions.
 - Modified acid-fast stains are usually used, although the organisms also can be seen using hematoxylin and eosin, Giemsa, or malachite green staining.
 - With the modified acid-fast stain, the oocysts stain red or pink and are usually 4 to 6 μm in diameter.



Cryptosporidiosis Recommended Treatment

Cryptosporidiosis Recommended Treatment				
Albendazole	400 mg	bid	PO	4 weeks
OR				
Azithromycin	500mg	qd	PO	4 weeks
PLUS				
Paromomycin	1g	bid	PO	4 weeks

Fungal and Parasitic Infections

Slide 73

- Go over the treatment specifications on Handout 2.1.
- Treatment:
 - A recent study done by a post-graduate at the Institute of Basic Medical Sciences in Taramani showed Albendazole to be effective in treating cryptosporidiosis.
 - With effective antiretroviral therapy, the incidence of infection has been reduced.
 - Paromomycin and Azithromycin may be used in treating the infection, as shown in Handout 2.1, "Treatment of Common Opportunistic Infections."
 - There is no reliable therapy for cryptosporidiosis. Recovery from *Cryptosporidium* infection depends largely upon the immune status of the host.
 - Nonspecific therapies often given to immunodeficient patients include antidiarrhoeal agents and supportive care with enteral or parenteral nutrition.
 - A number of specific therapies have also been tried of which the largest experience has been with paromomycin.
 - Other therapies that have been tried have been associated with only temporary symptomatic benefits at best, without sustained parasitologic cure.
 - Nitazoxanide elixir was approved by the United States Food and Drug Administration (FDA) on November 22, 2002 for the treatment of cryptosporidiosis in children aged 1 to 11 years.
 - SPIRAMYCIN 1.5 to 2 gms. per day in 6 equal doses for 4-6 weeks is reported to give good response but currently not available in India.
 - Preferred regimens:
 - HAART with immune reconstitution is the only therapy that controls this infection.
 - Paromomycin 500 mg orally tid or 1000 mg orally bid with food for 14 to 28 days, then 500 mg orally bid.
 - Alternative therapy: 1. Nitazoxanide 500 mg orally bid. 2. Paromomycin 1000 mg bid + azithromycin 600 mg qd for 4 weeks, then Paromomycin alone 500 mg orally for 8 weeks.
- Refer also to the diagnosis and treatment of diarrhoea in Session 7, *Clinical Management of Common Medical Problems*.



Cryptosporidiosis Prevention

- Handwashing
- Proper disposal of contaminated material
- For immunosuppressed individuals: limiting oral exposure to water from lakes, streams, public swimming pools

Fungal and Parasitic Infections

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- HIV-infected persons should be educated and counseled about the ways that *Cryptosporidium* can be transmitted.
- Modes of transmission include:
 - Direct contact with infected adults and children, and infected animals;
 - Drinking contaminated water; and eating contaminated food.
- HIV-infected persons should avoid contact with human and animal faeces.
- They should be advised to wash their hands after contact with human faeces (e.g., diaper changing), after handling pets, and after gardening or other contact with soil.
- Good hygiene, such as handwashing and proper disposal of contaminated material, are the most important ways to prevent infection.
- Oocysts are resistant to most standard purification techniques, including filtration and chlorination.
- Spores can be eliminated with freezing, boiling, and by high concentrations of ammonia or formalin.
- Asymptomatic family or other contacts do not routinely require any specific investigation or therapy, but these individuals should be aware that they may be excreting cysts and therefore should take care with their personal hygiene.
- Boiling or filtering water may decrease the risk of infection in immunosuppressed patients.
 - However, the impact of low concentrations of oocysts in drinking water on human illness is not adequately understood. As a result, this approach is not universally recommended.
 - It is suggested that immunocompromised patients who are at high risk for severe infection limit their exposure to cryptosporidia by minimizing oral exposure to water from lakes, streams, and public swimming pools [86].



Discussion: Cryptosporidiosis Treatment

- How else could you treat the symptoms of cryptosporidiosis?
- How would you determine if the patient is dehydrated? How would you treat dehydration?



Role Play: Educating & Counseling Patients about Cryptosporidiosis

- Find a partner to role-play the scenario in which one person is a patient with HIV and the other is a health care provider
- You will take turns role-playing HIV-infected patients and health care providers to gain practice in educating and counselling patients about cryptosporidiosis
- After you finish the first scenario, switch roles, and follow the instructions on the worksheet

Fungal and Parasitic Infections

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- Participants should find a partner.
- Each pair will role-play the scenario in which one person is a patient with HIV and the other is a health care provider.
- Refer to Worksheet 2.2, “Role Play: Educating and Counseling Patients about Cryptosporidiosis.”
- Each person will take turns role-playing the HIV-infected patient and health care provider to gain practice in educating and counselling patients about cryptosporidiosis.
- The person who will role-play the patient will have specific instructions about the character s/he will play, and should try to make that character as real as possible.
- The health care provider will need to explain what cryptosporidiosis is and find out about the lifestyle of the patient so that the best advice can be given to reduce the patient’s risk of contracting the disease.
- After each pair has finished the first scenario, they will switch roles, following the instructions on the handouts.



Role Play Discussion Questions

- What was challenging about counselling and educating patients about cryptosporidiosis?
- What might encourage patients to make the changes you recommended?



Microsporidiosis

- Microsporidia are intracellular protozoan parasites that produce resistant spores
- At least three species that infect humans are found in domestic animals:
 - *Encephalitozoon cuniculi*
 - *Encephalitozoon intestinalis*
 - *Enterocytozoon bieneusi*
- Diarrhoea is most common manifestation but also infection of:
 - Eyes
 - Respiratory tract
 - Gall bladder
 - Genitourinary tract
 - Muscles

Fungal and Parasitic Infections

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- Microsporidia are intracellular protozoan parasites.
- There are over 1200 species of microsporidia, though human disease is caused by only about 14 species.
- The pathogens produce resistant spores, and at least three species that infect humans are found in domestic animals. These include:
 - *Encephalitozoon cuniculi*
 - *Encephalitozoon intestinalis*
 - *Enterocytozoon bieneusi*
- Infection occurs with the ingestion of spores.
- The infection is an opportunistic disease, occurring mainly in immunocompromised patients.
- The clinical manifestations of microsporidiosis vary according to the causal species, with diarrhoea being the most common manifestation.
- Other manifestations: infection of the eyes, respiratory tract, gall bladder, genitourinary tract, muscles
- Diagnosis:
 - The diagnosis is made on finding the spores in stool smears stained by the Chromotrope 2R method, if available.
 - When this method is not available, a Giemsa stain can be used.
 - A biopsy of the ileum can also be performed.



Microsporidiosis Recommended Treatment

Microsporidiosis Recommended Treatment				
Albendazole	400 mg	bid	PO	3 weeks

Fungal and Parasitic Infections

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- Go over the treatment specifications on Handout 2.1.
- Albendazole has been found to be effective in treating ocular and intestinal infections.
- In addition for ocular infection, topical fumagillin is recommended.
- Refer also to the diagnosis and treatment of diarrhoea in Session 7, *Clinical Management of Common Medical Problems*.



Scabies

- Caused by the mite *Sarcoptes scabiei*
- Female mite burrows into the skin and the burrows appear as raised lines up to several centimeters long
- The mite deposits eggs in the burrows and then migrates to other sites of the body
- The eggs hatch out and the develop into adult mites which mate and more eggs are deposited in new burrows



Scabies Examples



Courtesy of Public Health Image Library/CDC



Courtesy of the Cincinnati STD/HIV Prevention Training Center

Fungal and Parasitic Infections

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- Typical lesions of scabies involving the fingers and penis.



Symptoms (1)

- First Infestation: Usually little evidence for first month (range 2 to 6 weeks)
- Subsequent infestations: People usually become sensitized to mites with, symptoms generally occurring within 1 to 4 days
- Mites burrowing under the skin cause a rash most frequently found on the hands, particularly the web spaces between the fingers
 - Also found on folds of wrist, elbow or knee, ulna margins of forearms, penis, the breast, and shoulder blades

Fungal and Parasitic Infections

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- When a person is infested with scabies mites for the first time, there is usually little evidence of infestation for the first month (range 2 to 6 weeks).
 - After this time and in subsequent infestations, people usually become sensitized to mites, and symptoms generally occur within 1 to 4 days.
- Mites burrowing under the skin cause a rash.
- This rash is most frequently found on the hands, particularly the web spaces between the fingers.
- It is also found on:
 - Folds of the wrist
 - Elbow or knee
 - Ulna
 - Margins of the forearms
 - Penis
 - Breasts
 - Shoulder blades
- Burrows and mites may be few in number and difficult to find in some cases.
- Commonly there is severe itching, especially at night and frequently over much of the body, including areas where no mites are living.



Symptoms (2)

- Severe itching, especially at night, including areas where no mites are living
- Severe form of scabies more common among immunocompromised persons is Norwegian scabies
 - Characterized by vesicles and formation of thick crusts over skin, accompanied by abundant mites but only slight itching
 - Complications due to infestation are usually caused by secondary bacterial infections from scratching

Fungal and Parasitic Infections

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- Diagnosis:
 - The diagnosis is usually made on finding the rash and burrows.
 - Skin scrapes may reveal mites or ova on microscopic examination.



Treatment

- Treatment of choice is the topical use of 1% gamma benzene hexachloride
 - Permethrin or lindane application are also useful
 - Ivermectin in a single oral dose of 200 mg is an alternative drug that is effective for crusted scabies in immunocompromised persons
- Household precautions:
 - All clothes, bedding, and towels should be washed in hot water, and dried and ironed
 - All members of the household should also be treated

Fungal and Parasitic Infections

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- Several lotions are available to treat scabies.
- The treatment of choice is the topical use of 1% gamma benzene hexachloride.
 - Permethrin or lindane applications are also useful.
 - Ivermectin in a single oral dose of 200 mg is an alternative drug that is effective for crusted scabies in immunocompromised persons.
- All clothes, bedding, and towels should be washed in hot water, and dried and ironed.
- All members of the household should also be treated.



Case Study One

- Mira is 22 years old. She is HIV-infected and lives on a farm with her family
- Her responsibilities include taking care of the chickens and pigs and helping in the fields. She complains, sometimes in the middle of the day of dizziness
- Also, the only water available in the field is from a small stream. Currently she has no illnesses and is maintaining her weight

Fungal and Parasitic Infections

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- Read over the case studies and then respond to the questions on “Fungal and Parasitic Infections Case Studies” (Worksheet 2.3).



Case Study One Questions

1. What interventions would you recommend for Mira?
2. What might be causing Mira to be dizzy?
3. What might help her symptoms?



Case Study Two

- A four-month old infant presents to the clinic with low-grade fever, hypoxia, and a rapid respiratory rate
- On auscultation the infant's lungs sound clear
- When questioned, the mother states that last year, another of her babies died at 9 months of age from a severe diarrhoeal illness. That child had never grown well and always had thrush
- This infant has had thrush once. The mother has never been tested for HIV



Case Study Two Questions

1. What might be a likely diagnosis for this infant? How could you confirm the diagnosis?
2. How would you treat this patient?
3. What would you advise the mother?
4. This mother will most likely need lots of emotional support when faced with these issues. How might you provide this support? Practice how you might give advice to the mother



Session 2: Fungal and Parasitic Infections

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Govt. Hospital of Thoracic Medicine
Chennai
Jambaram Sanatorium

Video Case Studies

Fungal and Parasitic Infections
Cases 2-3

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- Refer to Fungal and Parasitic Video Case Studies Cases 2-3 (Worksheet 2.4).



Clinical Management of Opportunistic Infections

Participant's Handbook

Session 3

Viral Infections

Session 3: Viral Infections

Aim: The aim of this unit is to introduce participants to viral opportunistic infections.

Learning Objectives: By the end of this session, participants will be able to:

- Describe the various clinical presentations and relative frequencies of the following opportunistic infections:
 - Herpes simplex
 - Varicella zoster
 - Molluscum contagiosum
 - Cytomegalovirus
 - Human papilloma virus
 - Epstein Barr virus
 - Human herpes type 8
- Identify the appropriate procedures and laboratory investigations required to make a diagnosis of each of the above opportunistic infections.
- Cite the preferred treatment regimen for each of the above opportunistic infections.
- Explain the recommended prophylactic regimens and cite the guidelines for initiation and discontinuation of prophylaxis for the above opportunistic infections.

Key Points

1. Infection with the herpes viruses: Herpes simplex virus, varicella zoster virus, cytomegalovirus, and human herpes virus type 8 occur commonly in immunosuppressed persons with HIV infection.
2. Human papilloma virus infections are commonly seen in persons with HIV infection.
3. Antiviral agents are available for the treatment of some herpes virus infections.
4. Recurrences of viral infections are common, and they are commonly persistent.
5. A strong association exists between human papilloma virus infection and cervical and anogenital cancer.

Treatment of Viral Opportunistic Infections

HERPES SIMPLEX-MILD INFECTION, FIRST-LINE TREATMENT

Antiviral Agent	se	Frequency	Route	Duration
	200 mg	Five s dai	PO	7 days
OR				
Famciclovir*	250 mg	tid	PO	7-10 days
OR				
Valaciclovir*	1	bid	PO	7-10 days

HERPES SIMPLEX RECURRENCES

Antiviral Agent	se	Frequency	Route	Duration
	200 mg	Five s dai	PO	7 days
OR				
Famciclovir*	500 mg	bid	PO	7-10 days
OR				
Valaciclovir*	0 mg	bid	PO	7-10 days

HERPES SIMPLEX-SEVERE INFECTION, FIRST-LINE TREATMENT

Antiviral Agent	D		Route	Duration
Acyclovir	10 mg/kg	tid	IV	Until lesions heal
OR				
Valaciclovir*	1 g	bid	PO	7-10 days

HERPES SIMPLEX-VISCERAL INFECTION, FIRST-LINE TREATMENT

Antiviral Agent	se	Frequency	Route	Duration
	30 mg/kg	q	IV	14-21 days

HERPES SIMPLEX-SEVERE AND VISCERAL INFECTION, SECOND-LINE TREATMENT

Antiviral Agent	Dose	F uenc	Route	Duration
Foscarnet	60 mg/kg	bid		14 days
OR				
Valaciclovir*	1 g	tid	O	14 days

HERPES SIMPLEX PROPHYLACTIC TREATMENT

Antiviral Agent	Dose	Frequency	Route	Duration
Acyclovir (adults)	400 mg/kg	bid	PO	Twice daily, lifelong
Acyclovir (paediatric)	10/mg/kg	bid	PO	Twice daily

*Not available at Tambaram

 Handout 3.1 (continued)

Treatment of Viral Opportunistic Infections (continued)

DERMATOMAL ZOSTER, FIRST-LINE TREATMENT

Antiviral Agent	Dose	Frequency	Route	Duration
	800 mg	Five times daily		7 days
OR				
Famcyclovir*	500 mg	tid	PO	7-10 days

DISSEMINATED, VISCERAL, OPHTHALMIC ZOSTER, FIRST-LINE TREATMENT

Antiviral Agent	Dose	Frequency	Route	Duration
Acyclovir	30-35 mg/kg	qd	IV	7-10 days
OR				
Famcyclovir*	500 mg	tid	PO	7-10 days

DISSEMINATED, VISCERAL, OPHTHALMIC ZOSTER, SECOND-LINE TREATMENT

Antiviral Agent	Dose	Frequency	Route	Duration
Acyclovir	30-35 mg/kg		I	7-10 days
OR				
Foscarnet*	180 mg/kg		IV	10-14 days

VARICELLA ZOSTER, PEDIATRIC TREATMENT

Antiviral Agent	Dose	Frequency	Route	Duration
	20 mg/kg	Every 6 hours	orally	5 days

CMV GASTROINTESTINAL DISEASE, NEUROLOGIC DISEASE, AND RETINITIS, FIRST-LINE TREATMENT

Antiviral Agent	Dose	Frequency	Route	Duration
Ganciclovir*	5 mg/kg	bid	IV	2-3 weeks

Note: Long-term treatment with ganciclovir 5 mg/kg given IV daily may be needed after successful treatment.

CMV GASTROINTESTINAL DISEASE, NEUROLOGIC DISEASE, AND RETINITIS, FIRST-LINE TREATMENT

Antiviral Agent	Dose	Frequency	Route	Duration
Foscarnet*	90 mg/kg	bid	IV	3 weeks

Note: Long-term treatment with foscarnet 90 mg/kg given IV daily may be needed after successful treatment.

CMV RETINITIS, SECOND-LINE TREATMENT

Antiviral Agent	Dose	Frequency	Route	Duration
Ganciclovir intraocular implant				
PLUS				
Valganciclovir*	900 mg	bid	PO	21 days

*Not available at Tambaram



Worksheet 3.2

Role-Play: Counselling Patients about Genital Herpes

The purpose of this exercise is to give you practice in dealing with a sensitive health topic when interacting with patients. In this exercise, you will take turns role-playing a patient with HIV and a health-care provider. After you and your partner have completed the first scenario, switch roles and role-play the second scenario.

Scenario 1:

The patient is a 22-year-old married woman with HIV. She has also contracted genital herpes. The health-care provider must discuss this with her by explaining what the disease is, how she may have contracted it, and what her treatment options are. The health-care provider must make sure that the issue is dealt with sensitively and that the patient gets accurate information.

Scenario 2:

The patient is a 31-year-old single man with HIV. He does not have genital herpes, but he is sexually active and needs education about the risks of contracting genital herpes. The health-care provider must discuss genital herpes with him and provide information about how to prevent contracting the disease. The health-care provider must make sure that the issue is dealt with sensitively and that the patient gets accurate information.



Worksheet 3.3 (continued)

Video Case Studies: Viral Infections (continued)

Trigger Point: Treatment Questions

1. What is the drug of choice in treating herpes simplex?
2. What treatment regimen would you prescribe for this patient?
3. How will you prevent recurrence?

Session 3: Viral Infections Case 5

Video Case Study Context

An HIV+ adult female with the following symptoms: Low-grade fever for 1 week, pain in the left loin for 5 days, vesicles on the left side.

Trigger Point: Diagnosis Questions

1. What is your diagnosis for this patient? What is your diagnosis based on?
2. How might this presentation differ in immunocompetent (HIV-) patients?



Worksheet 3.3 (continued)

Video Case Studies: Viral Infections (continued)

Trigger Point: Treatment Questions

1. How do you treat herpes zoster?

2. What are possible post-treatment complications, and how do you treat them?

Session 3: Viral Infections Case 6

Video Case Study Context

An adult male with the following symptoms: Pain in the eye, watering; photophobia, and severe headache.

Trigger Point: Diagnosis Questions

1. What is the diagnosis for this patient?

2. What are potential complications of herpes zoster?

3. What are other ocular complications of HIV?

 **Worksheet 3.3 (continued)**

Video Case Studies: Viral Infections (continued)***Trigger Point: Treatment Questions***

1. How does the treatment for herpes zoster vary when the eyes are involved?
2. What are the recommended treatments for complications of herpes zoster?

Session 3: Viral Infections Case 7**Video Case Study Context**

An adult male with a history of typhoid and tuberculosis, presenting with the following symptoms: Papular lesions over face, papules of 5-10 mm with pearly white central umbilication.

Trigger Point: Diagnosis Questions

1. What are the differential diagnoses for this patient?
2. What investigations would you do in order to make the diagnosis?

Trigger Point: Treatment Questions

1. How would you treat this patient?
2. How do you prevent the further spread of infection?



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 **Notes**



Viral Infections

Session Three



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Learning Objectives

- By the end of this session, you will be able to:
 - Describe the various clinical presentations and relative frequencies of common opportunistic viral infections
 - Identify the appropriate procedures and laboratory investigations required to make a diagnosis of viral opportunistic infections
 - Cite the preferred treatment regimen for viral opportunistic infections; and
 - Explain the recommended prophylactic regimens and cite the guidelines for initiation and discontinuation of prophylaxis for viral opportunistic infections

Viral Infections

Slide 2

- *The aim of this session is to introduce participants to viral opportunistic infections.*



Introductory Case Study

- Ashok is a 35 year old salesman who tells you he has had multiple sex partners. He has been to Mumbai and Andhra Pradesh in the last few years and had possible repeated exposure to HIV
- He is presenting with pearly umbilicated papules on his face and genitalia. He also has a vesicular rash with erythematous base, which is intensely painful on the left side of the chest

Viral Infections

Slide 3

- *Read the case study and answer the questions that follow in “Introductory Case Study” (Worksheet 3.1) in the Participant’s Handbook.*



Questions for Discussion

1. What viral infections do you suspect in this patient?
2. How will you treat Ashok?
3. What atypical issues related to HIV should you consider when treating Ashok?



Herpes Simplex

- Herpes simplex virus infection (HSV) can be severe in patients with HIV/AIDS
- Eruptions of HSV are red, painful, burning, itchy sores on the mouth and genitals
- Dissemination may lead to infection of the lungs, the oesophagus, and the brain, and may also cause meningoencephalitis

Viral Infections

Slide 5

- Herpes simplex virus infection (HSV) can become disseminated in immunosuppressed subjects and can be severe in patients with HIV/AIDS. (Zim, Viral Infections, Baylor, p, 88)
- Patients with advanced HIV infection (CD4 count $<200/\text{mm}^3$) are at increased risk for recurrent and extensive HSV infections due to loss of cellular immunity. Furthermore, co-infection of macrophages and fibroblasts with HIV-1 and HSV-1 produces reciprocal increases in viral replication.
- These infections can occur anywhere on the skin or in the gastrointestinal tract, presenting as:
 - Extensive oral, genital, and/or perianal ulcers
 - Esophagitis with odynophagia
 - Chest pain
 - Esophageal ulceration with bleeding, and occasionally as colitis
- In these patients, HSV-1 can also cause: Tracheobronchitis, Pneumonia, Chorioretinitis, Neurologic disorders (meningoencephalitis). Acute necrotizing retinitis is rare.
- Differential diagnosis: Other diseases that present with oral lesions and/or severe pharyngitis include:
 - Aphthous stomatitis
 - Infections with streptococci
 - Enteroviruses (eg, herpangina),
 - Epstein Barr virus
 - Diphtheria, Stevens-Johnson syndrome or Candida Albicans.



Herpes Simplex Lesions: Mouth



Courtesy of Public Health Image Library, CDC.
Dr. Thomas F. Sellers Emory University

Viral Infections

Slide 6

- Recurrent aphthous ulcers, which are most often confused with HSV infection, are never preceded by vesicles and occur exclusively on nonkeratinized mucosal surfaces, such as the inner surfaces of lips, buccal mucosa, ventral tongue, and mucobuccalfold.
- Primary HSV and HSV outbreaks in immunocompromised patients can also occur on nonkeratinized mucosa, but recurrent HSV always occurs on keratinized mucosa including the hard palate, dorsum of tongue, gingiva, and alveolar ridge.
- Diagnosis: Lesions that are suspicious for HSV infection can be tested for characteristic multinucleated giant cells or for the presence of HSV via viral culture.
 - Rapid diagnosis by Tzanck smear: Slides prepared from lesion scrapings are fixed with ethanol or methanol and stained with Giemsa or Wright stain preparations. The presence of multinucleated giant cells indicates infection with either HSV or varicella-zoster virus (VZV).
 - Papanicolaou cervicovaginal stains also can demonstrate intranuclear inclusions.
 - Viral culture: Viral medium and slides should be immediately transported to the appropriate laboratory, but may be stored at 4°C for up to nine hours.
 - Immunofluorescence staining: Slides prepared from lesion scrapings may be examined for herpes antigens via immunofluorescence microscopy. This analysis has been made possible by the generation of HSV type-specific monoclonal antibodies which are available in commercial antibody staining kits that permit identification and typing of isolates in tissue samples
 - Serology: Various serological assays have been used for diagnosis of HSV infection. They include virus neutralization, complement fixation, passive hemagglutination, ELISA, complement-mediated cytolysis, antibody-dependent cellular lysis, and radioimmunoassays
 - Polymerase chain reaction: Detection of HSV DNA levels by polymerase chain reaction has become an important diagnostic tool in cases of HSV-1 encephalitis.
 - The sensitivity of HSV PCR remains laboratory-dependent: it detects the presence of HSV DNA but does not determine if the virus is replicating.



Herpes Simplex Lesions: Penile



Courtesy of Public Health Image Library,
CDC, Dr. NJ Flumara, and Dr. Gavin Hart

Viral Infections



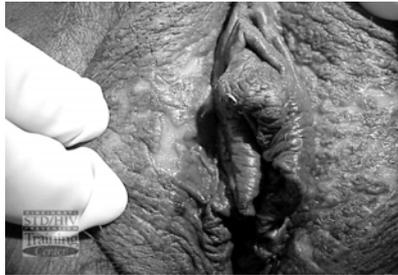
Seattle STD/HIV Prevention Training Center
Source: Connie Celum, Walter Stamm
Courtesy of STD/HIV Prevention Training Center,
Connie Celum and Walter Stamm

Slide 7

- Herpes simplex lesions over the penis.



Herpes Simplex Lesions: Vaginal



Courtesy of Cincinnati STD/HIV Prevention Training Center

Viral Infections

Slide 8

- Herpes simplex lesions over the vaginal mucosa.



Herpes Simplex Lesions: Skin



HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA



Courtesy of hivwebstudy.org. All rights reserved. © 2004

Viral Infections

Slide 9

- Herpes simplex lesions over the skin over the different parts of the body and face



Herpes Simplex-Mild Infection First-Line Treatment

First-Line Treatment				
Acyclovir	200mg	Five times daily	PO	7 days
OR				
Famciclovir	250mg	tid	PO	7-10 days
OR				
Valaciclovir	1g	bid	PO	7-10 days

Viral Infections

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- Go over the treatment and prophylaxis specifications on “Treatment of Viral Opportunistic Infections” (Handout 3.1),
- Acute disease usually resolves spontaneously, but treatment for the pain associated with the lesions may help the patient feel more comfortable.
- Genital herpes is a sexually transmitted infection (STI).
 - Using condoms can decrease a patient’s risk of contracting HSV. (Baylor, p. 88)
- The presence of HSV infection increases the risk of HIV acquisition”(Source: Wald A, Link K. Risk of human immunodeficiency virus infection in herpes simplex virus type 2–seropositive persons: a meta-analysis. J Infect Dis 2002; 185:45–52.)



Herpes Simplex Recurrences

Acyclovir	200mg	Five times daily	PO	5 days
OR				
Famciclovir	500mg	bid	PO	7-10 days
OR				
Valaciclovir	500mg	bid	PO	7-10 days



Herpes Simplex-Severe Infection First-Line Treatment

Acyclovir	10 mg/kg	tid	IV	Until lesions heal
OR				
Valaciclovir	1g	bid	PO	7-10 days



Herpes Simplex-Visceral Infection First-Line Treatment

Acyclovir	30mg/kg	qd	IV	14-21 days



Herpes Simplex Prophylactic Treatment

Acyclovir (Adults)	400mg/kg	bid	PO	Twice daily, lifelong
Acyclovir (Paediatric)	10 mg/kg	bid	PO	Twice daily



Pre-Role Play Discussion Questions (1)

1. Do you know other alternatives for treating herpes simplex?
2. Discussing the treatment and prevention of genital herpes could be uncomfortable for both health care providers and patients. What are some ways in which you can address this sensitively with patients?



Pre-Role Play Discussion Questions (2)

1. What concerns might the patient have?
2. What would make you more comfortable in discussing genital herpes with patients? Would this get in the way of delivering all the necessary information to the patient in a sensitive manner?

Viral Infections

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- *Refer to Worksheet 3.2, Role Play: Counseling Patients about Genital Herpes.*
- *Following the instructions, each partner should have a chance to role play a patient and a health care provider.*



Role Play Scenario One

- The patient is a 22 year-old, married woman with HIV. She has also contracted genital herpes
- The health care provider must discuss this with her by explaining what the disease is, how she may have contracted it, and what her treatment options are. The health care provider must make sure that the issue is dealt with sensitively and that the patient gets accurate information



Role Play Scenario Two

- The patient is a 31 year-old, single man with HIV. He does not have genital herpes, but he is sexually active and needs education about the risks of contracting genital herpes
- The health care provider must discuss genital herpes with him and provide information about how to prevent contracting the disease
- The health care provider must also make sure that the issue is dealt with sensitively and that the patient gets accurate information



Post-Role Play Discussion Questions

1. What was challenging about talking to patients about genital herpes?
2. How were you able to demonstrate sensitivity to the needs of the patient?
3. Can you offer additional suggestions for dealing with this kind of situation?



Role Play Teaching Points (1)

- Treatment options for genital herpes: Follow the options given in Handout 3.1
- Ways to make the discussion of treatment and prevention more comfortable:
 - Respect for the patient
 - Non-judgmental attitude
 - Non-threatening approach
 - Sensitivity to the needs and issues of the patients
 - Confidentiality assurance
 - Acknowledgement of alternate sexual behaviors

Viral Infections

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Role Play Teaching Points (2)

- Patient concerns:
 - Whether confidentiality is maintained
 - Pregnancy issues
 - Whether the disease is treatable and preventable
 - Consequences of the illness
 - Condom usage
 - Sexual practices
 - What precautions to take
 - Drug toxicities
 - Native treatment



Role Play Teaching Points (3)

- Ways to make you more comfortable:
 - Knowledge
 - Attitude
 - Confidentiality
 - Respect
 - Good communication skills
 - Experience
 - None of these should get in the way of delivering all the necessary information to the patient in a sensitive manner



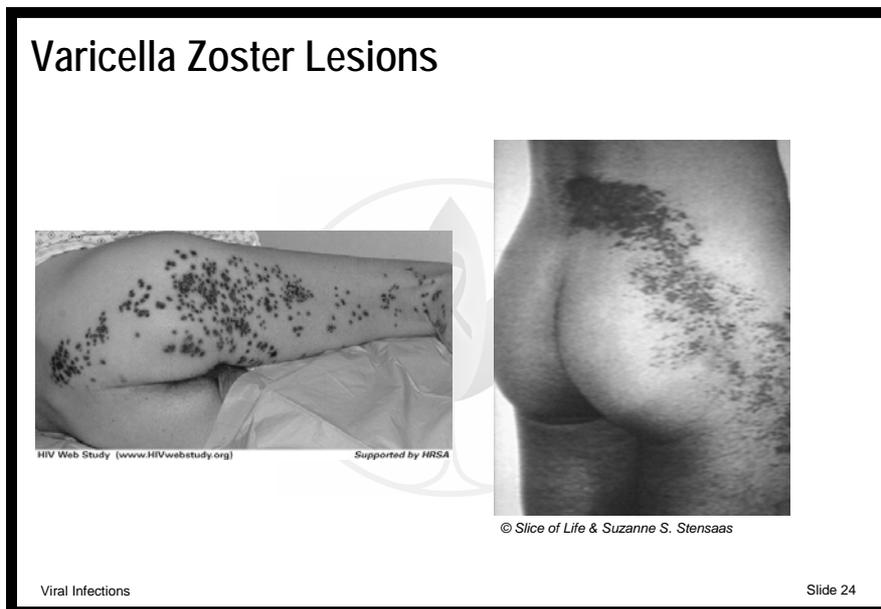
Herpes Zoster Virus

- Virus that causes chickenpox and shingles in children and adults; spread by aerosolized viral particles
- Contagious period is 24 to 48 hours before rash is observed and until all lesions are crusted over
- In immune suppressed persons, zoster is often multidermatomal and multi-segmental in distribution, persistent and extensive, and associated with severe pain and debility

Viral Infections

Slide 23

- Herpes zoster is the virus that causes chickenpox and shingles in children and adults.
 - Infection with this virus can be much more serious in a person with HIV/AIDS
- Varicella is transmitted by respiratory route and also spread by direct mucous membrane contact or by inhalation of infectious respiratory secretions.
- Varicella is spread by aerosolized viral particles. (Baylor, p. 88)
- Herpes virus varicella zoster often causes disseminated infection after initial exposure. (Zim, Viral Infections).



- A person is contagious for 24 to 48 hours before a vesicular (raised, fluid-filled lesions) rash is observed, and until all of the lesions are crusted over. (Baylor, p. 88)
 - In children initial infection results in the development of chicken pox, though most persons that become infected develop no symptoms and signs of infection.
- The virus lays dormant in the paraspinal ganglia for years and with immune suppression, from whatever cause, the virus replicates and produces lesions along the length of a cutaneous nerve in a dermatomal distribution.
- Dissemination can also occur at this time with involvement of:
 - Skin
 - Nervous system
 - Lungs
 - Mucous membranes
- In immune suppressed persons, zoster is often multidermatomal and multi-segmental in distribution and is persistent and extensive.
 - It is associated with severe pain and debility. (Zim, Viral Infections)
- Zoster varicellosis is a clinical entity where skin eruptions start like herpes zoster but progress relentlessly like varicella or chicken pox.



Healing Disseminated Herpes Zoster



Viral Infections

HIV Web Study (www.HIVwebstudy.org)

Supported by NRS&A

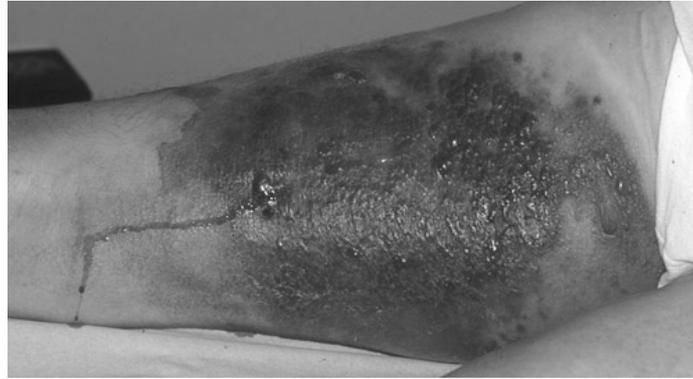
Slide 25

- Lesions on back that have started to crust and heal in this HIV-infected patient
- Herpes zoster infection is more frequent and serious in HIV infected persons.
- The course also may be more prolonged.
- There is an increased propensity to cutaneous dissemination and to recurrent zoster.



Herpes Zoster

Hemorrhagic Bullae, HZ



HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA

Viral Infections

Slide 26

- The lesions tend to become hyperkeratotic and necrotic.
- Atypical presentations, like ulcerative, excessively crusted, and verrucous lesions, also can occur.



Herpes Zoster Ophthalmicus



Viral Infections

Slide 27

- The right optic nerve is cupped with pallor.
- Two weeks after onset while on acyclovir therapy, the patient noted dimness of vision on the right eye.
- Herpes zoster ophthalmicus is more frequent in HIV patients.



Herpes Zoster: All Three Divisions of 5th Cranial Nerve



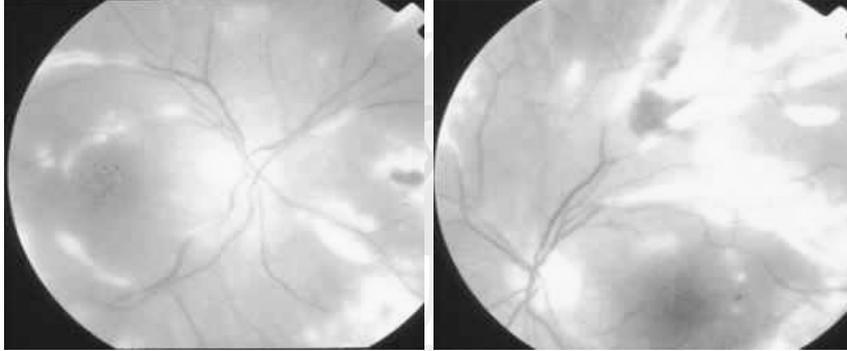
Viral Infections

Slide 28

- Healed herpes zoster lesions over one half of face involving all three divisions of the trigeminal nerve.



Acute Retinal Necrosis Syndrome



Courtesy of C. Stephen Foster M.D., Copyright © 1996-2005, All Rights Reserved

Viral Infections

Slide 29

- Acute retinal necrosis and herpes zoster optic neuritis can occur.
- Nervous system manifestations like myelitis, meningoencephalitis, and segmental motor paralysis also can occur.



Dermatomal Herpes Zoster



Viral Infections

Slide 30

- HZ is usually localized to one or two neuro dermatomes.
- The prodromal symptoms of tingling, burning, and shooting pain usually precede the onset of erythema and edema of the skin.
- Clusters of vesicles soon appear, which tend to coalesce and ulcerate.
- Superficial purulent crusts and scabs develop over the erosion.
- Residual scarring and hyperpigmentation occur after healing at the involved area.
- Diagnosis:
 - The diagnosis is usually made on clinical grounds.
 - If available, direct immuno-flourescent testing for antigen and ELISA for antibody are required mainly for extracutaneous herpes zoster.
 - Tzanck smear examination also can be done but this test cannot distinguish herpes zoster from herpes simplex.
 - Though viral culture is considered as gold standard, it is not available at our centers.



Dermatomal Zoster First-Line Treatment

Dermatomal Zoster First-Line Treatment				
Acyclovir	800mg	Five times daily	PO	7 days
OR				
Famcyclovir	500mg	tid	PO	7-10 days

Viral Infections

Slide 31

- Treatment:
 - Details about treatment appear on Handout 3.1, "Treatment of Viral Opportunistic Infections."
 - Although no treatment is necessary unless zoster is persistent, Acyclovir may be administered. (Zim, Viral Infections)
 - However, there is a vaccine available to protect patients against the virus.
 - In May 1999, the U. S. Centers for Disease Control and Prevention updated its varicella vaccine recommendations for HIV-infected children.
 - The new recommendations state that if an HIV-infected child has a CD4+ lymphocyte percentage greater than 25, the vaccine may be administered.
 - If an immunocompromised person comes into contact with someone with varicella, he or she can be protected with herpes-zoster globulin **taken as soon as possible**, if available.
 - Acyclovir, an antiviral medication, decreases the duration of the disease.
 - In children, acyclovir can be given intravenously or orally.
 - Acyclovir can cause pancytopenia (a decrease in all forms of blood cells), particularly when given in conjunction with ZDV.
 - It is important to increase the intake of fluids while receiving acyclovir to avoid crystalluria (the presence of crystals in the urine as a symptom of irritation) and possible acute renal failure. (Baylor, p. 88)
 - Acyclovir resistant cases require treatment with intravenous Foscarnet (180 mg/kg per day in two divided doses for) 10 to 14 days.



Herpes Zoster



Viral Infections

Slide 32

- Other general measures include local care with cold compresses and systemic or local antibiotics for secondary bacterial infections.
- Pain relieving agents also are helpful.



Disseminated, Visceral, Ophthalmic Zoster, First-Line Treatment

First-Line Treatment				
Acyclovir	30-35mg/kg	qd	IV	7-10 days
OR				
Famcyclovir	500mg	tid	PO	7-10 days

Viral Infections

Slide 33

- *Go over the treatment specifications on the Handout 3.1.*



Discussion: Herpes Zoster Treatment

- What can be done to increase the comfort of patients suffering from the symptoms of this infection?
- What resources are there at Tambaram to diagnose and treat patients with herpes zoster?



Molluscum Contagiosum

- Superficial skin infection occurring anywhere on the body that causes firm, flesh-coloured, papules containing a white sebaceous material
- Infection is spread through close body contact, sharing clothing and utensils, and is sexually transmissible
- Occurs more commonly, are more persistent, much larger, and more difficult to treat in persons in immunosuppressed individuals

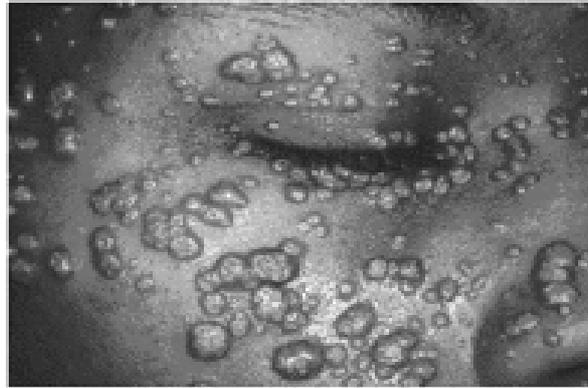
Viral Infections

Slide 35

- The DNA pox virus causes Molluscum Contagiosum.
- The infection in an HIV positive individual is characterized by a pearly white, yellowish, or flesh colored papules with central umbilication.
 - These lesions are widely disseminated, persistent, numerous and recur after treatment.
 - These lesions develop at any stage of the HIV illness but tend to be more numerous and severe when the CD4 cell count decreases to less than 250 cells/cu. mm.
 - Lesions can be spread by close contact, either sexual or nonsexual.
- Differential Diagnosis:
 - The skin lesions of:
 - Cryptococcosis
 - Histoplasmosis
 - Basal cell carcinoma
 - Benign sebaceous hyperplasia
 - Penicillium marneffi



Molluscum Lesion: Face



Molluscum Contagiosum in a Patient with the Acquired Immunodeficiency Syndrome, New England Journal of Medicine, Volume 338:888, March 26, 1998, Number 13, Copyright © 2005 Massachusetts Medical Society. All rights reserved

Viral Infections

Slide 36

- Molluscum lesions can also occur in the eyes.
- The lesions can occur in the eyelids, very large lesions may also irritate the eye mechanically.
- The recurrences are common.
- Secondary kerato conjunctivitis can occur.



Early Lesions of Molluscum



Viral Infections

Slide 37

- Early lesions of molluscum contagiosum over the neck.



Molluscum Contagiosum Lesions



Courtesy of Cincinnati STD/HIV Prevention Training Center

Viral Infections

Slide 38

- The typical appearance of the lesion
- Typical lesions of molluscum contagiosum-pearl like and centrally umbilicated.



Molluscum Contagiosum Treatment

- Simple ablation with a curette
- Cryotherapy
- Vesiculation and sloughing with Cantharidin

Viral Infections

Slide 39

- Treatment:
 - The lesions are thoroughly opened with a needle or scalpel.
 - The contents expressed and the inner wall treated with phenol solution, or tincture iodine, or 2.5% trichloro acetic acid or ferric subsulphate.
 - The lesions can be subjected to:
 1. Gentle cryotherapy (liquid nitrogen can be used)
 2. Electro dessication
 3. Electrosurgery for larger lesions
 4. The lesions also respond to antiretroviral therapy.
- Prevention:
 - Do not pick or shave the lesion because they tend to auto inoculate the virus and the virus will spread.



Discussion: Lesion Treatment

- For those of you with experience managing the symptoms of MCV, how have you treated these lesions?
- What seems to be the most effective method in your experience?



Cytomegalovirus (CMV) (1)

- Symptoms:
 - Fever and diarrhoea from CMV colitis
 - Dyspnoea from CMV pneumonitis
 - Blindness caused by CMV retinitis
- Many patients are completely asymptomatic
- A fetus exposed to CMV can suffer severe consequences such as mental retardation or even death

Viral Infections

Slide 41

- Cytomegalovirus (CMV) may affect multiple systems and organs in the body in immunosuppressed individuals.
- The incidence of CMV disease varies between geographical locations, but CMV causes significant suffering in HIV-infected persons worldwide.
- Symptoms include:
 - Fever and diarrhoea from CMV colitis
 - Dyspnoea from CMV pneumonitis
 - Blindness caused by CMV retinitis. (Zim, Viral Infections)
- However, many individuals with CMV have very few or no symptoms.
- A foetus exposed to CMV can suffer very severe consequences such as mental retardation or even death.
- In patients with HIV/AIDS, the most common complication of CMV is retinitis.
- This can lead to blindness if untreated.
- Patients should be advised to report to the clinic if they notice changes in their vision, including blurry vision, loss of peripheral vision, or “floaters.” (Baylor, p. 87)



Cytomegalovirus (CMV) (2)

- Cytomegalovirus (CMV) may affect multiple systems and organs in immunosuppressed individuals, especially the eyes (CMV retinitis)
- Mode of transmission:
 - Perinatal
 - Contact with urine and saliva
 - Kissing and sexual intercourse
 - Blood transfusion
 - Organ transplantation

Viral Infections

Slide 42

- CMV is a member of the herpes virus family.
- Intermittent virus shedding body fluids allows transmission via many routes, including:
 - Perinatal (via placenta and in the breast milk)
 - Contact with urine and saliva (especially in childhood)
 - Kissing and sexual intercourse
 - Blood transfusion and organ transplantation (The Foundation for Professional Development, p. 18)
- Retinitis due to CMV results from the hematogenous dissemination of CMV after activation of a latent CMV infection.
- Progression of the infection within the retina is generally to contiguous cells.
- Persons with lesions that first appear near the macula or optic nerve commonly complain of decreased visual acuity or defect in the visual field.
 - Retinal lesions at least 1500 milli microns from the edge of the optic nerve and at least 3000 milli microns from the center of the fovea or anterior to the equator of the eye may be asymptomatic or present with the complaints of “floaters” or loss of peripheral vision.
- CMV retinitis is not associated with pain or photophobia.
- Visual loss in CMV is due to:
 - Retinal necrosis due to direct infection of retinal cells with CMV. (This permanent, irreversible loss of vision is not amenable to therapy.)
 - Retinal involvement of the area near the macula may produce oedema in the macula and loss of central visual acuity. (This is reversible if recognized early and treated promptly.)
 - Retinal detachment after infection with CMV and retinal necrosis has occurred. Retina becomes thick, atrophic and is susceptible to breaks and detachments.



- Diagnosis for CMV retinitis:
 - CMV infection of the retina is the most common cause of blindness in HIV-infected individuals, and usually develops when the CD4+ cell count drops below 50 cells/mm³.
 - The symptoms of CMV retinitis include:
 - “Floaters,”
 - Reduced field of vision
 - Increased sensitivity to light (photophobia).
 - A large area of the retina can become infected before noticeable symptoms develop.
 - Diagnosis made by indirect ophthalmoscopy is preferable, as peripheral lesions may be missed in a direct dilated examination.
 - CMV appears as creamy granular areas around the retinal blood vessels with focal haemorrhages.
 - Sight threatening lesions include those within two disk diameters of the fovea and within one disk diameter of the optic disk.
 - Ideally, patients with CD4+ counts less than 50 cells/mm³ should be examined by indirect ophthalmoscopy every 3 months.

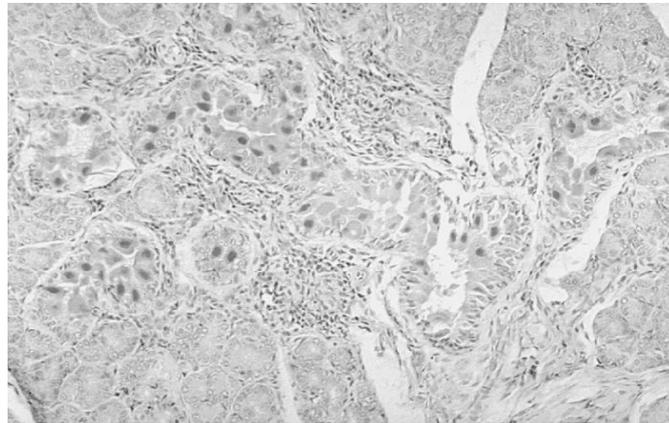


CMV Retinitis: Diagnosis Continued

- The portion of the vessel near the lesion may appear to be sheathed
- Occasionally, the lesion may present a more granular appearance
- Progression of retinitis is in a characteristic “brushfire” pattern, with a granular, white leading edge advancing before an atrophic gliotic scar
- CMV retinitis usually presents unilaterally, but untreated, becomes bilateral
- Differential diagnosis:
 1. Acute retinal necrosis secondary to herpes simplex or herpes zoster
 2. Intraocular lymphomas
 3. Toxoplasmic chorioretinitis
 4. Pneumocystic carinii retinitis
 5. Other infections like tuberculosis, syphilis, cryptococcus, candida, and histoplasmosis



Inclusion Bodies of CMV



Courtesy of Public Health Image Library, CDC. Dr.Haraszti

Viral Infections

Slide 45

- Slide showing inclusion bodies of CMV
- CMV at Other Sites:
 - In the gastrointestinal tract, CMV causes ulceration, typically in the oesophagus and the sigmoid colon. Diagnosis is by endoscopy and biopsy.
 - CMV pneumonitis often co-exists with other infections (especially *P. jiroveci*). Treatment of the other organism often results in resolution, and specific therapy for CMV in the lung is not always necessary.
 - In the central nervous system, CMV can produce painful radiculopathy with an associated CSF pleocytosis (surprisingly this typically shows a predominance of neutrophils)—diagnosis is by CMV PCR.
 - CMV encephalopathy is described, often as a terminal event. (The Foundation for Professional Development, p. 18)
- CMV Oesophagitis:
 - It is a common cause of oesophagitis in HIV patients second to candidal oesophagitis.
 - The presence of extensive, large, shallow ulcers of the distal oesophagus is the hallmark.
- Differential diagnosis:
 1. Candida
 2. Herpes simplex
 3. Histoplasmosis
 4. Kaposi sarcoma
 5. Lymphoma
 6. PCP
 7. M. tuberculosis etc.



CMV Colitis

- CMV Colitis can involve presence of:
 - Fever
 - Weight loss
 - Anorexia
 - Abdominal pain
 - Debilitating diarrhoea
 - Malaise
 - Extensive hemorrhage and perforation may be life threatening
- Differential Diagnosis:
 1. Cryptosporidium
 2. Microsporidium
 3. Giardiasis
 4. Entamoeba histolytica
 5. Salmonella
 6. Shigella, etc.



CMV Pneumonitis



Courtesy of medscape.com © 1994-2005

Viral Infections

Slide 47

- Present as an interstitial pneumonitis
- Dyspnoea on exertion, non-productive cough, and hypoxemia are the presenting signs and symptoms.
- CMV can also cause:
 - Hepatitis and biliary disease
 - Meningo encephalitis
 - Ventriculitis
 - Ascending poly radiculopathy



CMV Skin Lesions



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Viral Infections

Slide 48

- Disseminated CMV infection—two papular skin lesions documented to be caused by CMV



CMV First-Line Treatment

Ganciclovir*	5mg/kg	bid	IV	2-3 weeks
Foscarnet**	90mg/kg	bid	IV	3 weeks
<i>*Long term treatment with ganciclovir 5mg/kg given IV daily may be needed after successful treatment.</i>				
<i>**Long term treatment with foscarnet 90mg/kg given IV daily may be needed after successful treatment.</i>				

Viral Infections

Slide 49

- Go over the treatment specifications on Handout 3.1.
- Ganciclovir is the antiviral medication recommended for treating CMV.
- The main side effect of ganciclovir is neutropenia.
- Other side effects include:
 - Anaemia
 - Thrombocytopenia
 - Occasionally renal insufficiency. (Baylor, p.88)
- Relapsing disease can be prevented by initial high-dose induction therapy to bring the infection under control, followed by maintenance therapy.
 - Maintenance therapy is not always necessary in gastrointestinal CMV. (The Foundation for Professional Development, p. 19)



Discussion: CMV Treatment

- Since CMV is often asymptomatic, how have you been able to identify it in patients?
- What resources are there at Tambaram to diagnose and treat patients with CMV?



Human Papilloma Virus (HPV)

- HPV causes genital warts, flat warts and skin warts and is associated with cervical cancer and intraepithelial neoplasia of the cervix, vagina, vulva, penis and anus
- Genital and non-genital strains exist
- Over 75 different strains of HPV exist, with each viral strain appearing in a particular site and producing specific features
- Some strains cause oral lesions, others cause genital warts, while others cause cervical cancer

Viral Infections

Slide 51

- The human papilloma virus (HPV) causes genital warts, flat warts and skin warts.
- Both overt and subclinical infection occurs.
- HPV is also associated with:
 - Cervical cancer
 - Intraepithelial neoplasia of the:
 - Cervix
 - Vagina
 - Vulva
 - Penis
 - Anus (Zim, Viral Infections)
- Women who are immuno-compromised have a higher rate of cervical cancer, as well as a higher rate of recurrence of cervical cancer after treatment. (Baylor, p. 89)
- HPV is a ubiquitous virus and causes a broad spectrum of clinical presentations, from subclinical infections to warts and neoplasia.
- In HIV infected individuals HPV seems to be more likely to progress and the progression is more rapid.
 - HPV infections are extremely prevalent in HIV positive individuals.



HPV Strains and Associated Conditions

HPV-1, HPV-2, HPV-4	Common skin warts
HPV-13, HPV-32	Oral warts
HPV-6, HPV-11, HPV-16, HPV-18	Anogenital warts
HPV-16, HPV-18, HPV-31, HPV-33, HPV-35	Cervical cancer, anogenital cancer, other cancers

Viral Infections

Slide 52

- The strains of the human papilloma virus that cause genital warts are known as the "genital strains", while the strains that cause warts in sites other than the genital region are commonly referred to as the "non-genital" strains.
 - It is known that the "genital strains" can infect non-genital sites such as the anus and perianal areas.
 - They are commonly found in men and women who have genital warts.
 - Infants born to mothers with genital warts can develop warts.
- Over 75 different strains of the human papilloma virus are known to cause infection in humans.
 - Each viral strain appears to have an affinity for a particular anatomical site, and each produces a defined spectrum of pathological features.
 - Some strains cause oral lesions, others cause genital warts, while others cause cervical cancer.
 - The genital tract is the reservoir for all except two of the viral strains. The two exceptions being HPV 13 and HPV 32 which are restricted to the oral cavity.
- The large exophytic genital warts are caused by HPV types 6 and 11 and occasionally by type 16.
- HPV types 16 and 18 are associated with flat warts and types 16, 18, 31, 33 and 35 are associated with cancer of the cervix, cancer of the penis and anal and other cancers.
- The following table summarizes the virus strain types and the associated conditions. (Zim, Viral Infections)



Condyloma Acuminata

- Human Papilloma Virus infection
- Cryotherapy
- Electro-desiccation and curettage
- Frequently recur



Viral Infections

Slide 53

- Clinical Features:
 - Site of involvement: genital including anal and oral regions
 - Genital lesions in males seen over:
 - Penis
 - Urethra
 - Scrotum
 - Anal and perianal areas
 - In the rectum
 - The lesions are soft, sessile, with rough or smooth surface, and they are extensive, florid.
 - They relapse after treatment.
 - Exuberant cauliflower like growth may develop on the penile or perianal areas.



HPV Lesions (1)



Courtesy of Cincinnati STD/HIV Prevention Training Center



*Content Provided by the Division of
STD Prevention, CDC.*

Viral Infections

Slide 54

- In females, the lesions may be in the external genital areas or intragenital (intravaginal or cervical).
 - The lesions are soft, whitish, and sessile.
- Genital warts often enlarge and become friable during pregnancy and in some cases, may mechanically obstruct the vaginal canal during labour.



HPV Lesions (2)



Courtesy of Cincinnati STD/HIV Prevention Training Center

Viral Infections

Slide 55

- HPV lesions on the penis.



HPV: Oral Lesions



Courtesy of Public Health Image Library, CDC. Dr. Haraszi

Viral Infections

Slide 56

- Oral lesions may be of several kinds:
 - Efflorescent solitary lesion
 - Raised or pedunculated form
 - Faint or flattened variety over the lips
 - Large corrugated lesions over the buccal mucosa
- Other types:
 - Multiple plantar warts including mosaic warts
 - Common/flat plantar warts
 - Laryngeal lesions
 - Multiple, large, hyperkeratotic, verrucous lesions in peri ungula areas
 - Extensive flat or filiform warts on the bearded area of face



Exuberant, Cauliflower Like Anogenital Wart



Courtesy of Cincinnati STD/HIV Prevention Training Center

Viral Infections

Slide 57

- Cauliflower-like warty growth over the peri-anal area due to HPV.



Flat & Filiform Warts over Bearded Area



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Viral Infections

Slide 58

- Flat, filiform wart over the bearded area.
- Diagnosis is usually based on clinical pattern.
- HPV induced malignancies:
 - Bowenoid papulosis, which can lead to squamous cell carcinoma
 - Epidermo dysplasia verruciformis
 - Intra epithelial neoplasia of the anal and cervical mucosa.
- HPV infections of the skin in HIV positive individuals tend to occur in the same areas as in healthy individuals.
 - The possible reason is the HIV tat protein secreted from HIV infected cells exhibits a growth factor-like effect on HPV infected cells leading to:
 - Enhanced survival
 - Increased cell division
 - Abundant transcription of HPV DNA



Treatment of HPV

- Topical application of caustic chemical agents
 - 50% trichloroacetic acid,
 - 20 to 50% salicylic acid, and
 - 30% podophyllum
- Electrocauterization
- Laser therapy

Viral Infections

Slide 59

- Diagnosis and Prevention:
 - Women who are HIV-infected should have a Papanicolaou (PAP) smear every six months for the first year after diagnosis of HIV.
 - If these smears are negative, women with no other risk factors for cervical cancer should have a PAP smear done once a year.
 - Use of condoms can reduce the risk of transmission of STIs, and may reduce the risk of transmitting HPV. (Baylor, p.89)
 - *Note: Cervical cancer is covered in Session 5: Malignancies Associated with Immunosuppression.*



Epstein Barr Virus (EBV) (1)

- Patients with HIV have increased amounts of EBV in their oropharyngeal secretions and have higher EBV antibody titers than HIV-seronegative persons
- Minor symptoms similar to the common cold or “strep” throat; infection of the HIV-infected child with this virus can be associated with a pulmonary disease known as lymphoid interstitial pneumonia (LIP)

Viral Infections

Slide 60

- Infection with Epstein Barr Virus (EBV), a herpes virus, occurs commonly in persons with HIV infection, as well as in persons without HIV infection.
 - Patients with HIV have increased amounts of EBV in their oropharyngeal secretions and have higher EBV antibody titres than HIV-seronegative persons. (Zim, Viral Infections)
- EBV usually causes minor symptoms, very much like the common cold or “strep” throat.
- However, infection of the HIV-infected child with this virus can be associated with a pulmonary disease known as lymphoid interstitial pneumonia (LIP). (Baylor, p. 89)



Epstein Barr Virus (EBV) (2)

- EBV is also thought to cause a number of conditions including:
 - Oral hairy leukoplakia
 - Non-Hodgkin's lymphoma
 - Burkitt's lymphoma
 - Nasopharyngeal carcinoma



Oral Hairy Leukoplakia (1)

- Presents as raised, white, corrugated lesions of the oral mucosa, especially on the lateral aspect of the tongue
- Nonmalignant lesion of epithelial cells
- Can be diagnosed from biopsy and electron microscopy
- Treated with Acyclovir 800mg, five times a day for three weeks



Viral Infections

Slide 62

- Oral hairy leukoplakia occurs in HIV-infected patients as well as in some immunosuppressed transplant recipients.
- It presents as raised, white, corrugated lesions of the oral mucosa, especially on the lateral aspect of the tongue.
- It is a nonmalignant lesion of epithelial cells. (Zim, Viral Infections)
- It can be diagnosed from a biopsy and electron microscopy.
- Oral hairy leukoplakia can be treated with Acyclovir 800mg, five times a day for three weeks. (Tambaram slides)
 - However, most cases are not treated and those that are usually relapse after treatment. (Source: John Hopkins 2004 Medical Management of HIV Infection Bartlet and Gallant)
- Lesions clinically mimic candidiasis but are not readily scraped off.
 - Corrugations on the lateral margin continuous with flat areas of the ventral surface
 - Epithelial thickening with surface projections, acanthosis, vacuolations of group of cells in the stratum granulosum, no inflammatory cell infiltrations
- In situ hybridization for EBV—DNA infected nuclei show a purple signal.



Oral Hairy Leukoplakia (2)



Viral Infections

Slide 63

- Raised white lesions over the lateral border of the tongue.



Treatment of Oral Hairy Leukoplakia

- Acyclovir 200-400 mg five times daily orally
- Topical podophylline resin 20% in alcohol for 2 to 3 days
- Topical isotretinoin gel
- Lesions also regress with antiretroviral therapy



Lymphocytic Interstitial Pneumonitis (LIP)

- Occurs primarily in children, but can also occur in HIV+ adults
- Characterized by diffuse interstitial pulmonary infiltrates
- Patients with LIP may be initially asymptomatic but as disease progresses, may present with generalized lymphadenopathy hepatosplenomegaly and/or digital clubbing
- Antiretroviral treatment can decrease the complications associated with LIP

Viral Infections

Slide 65

- Continue with the lecture on LIP in the PowerPoint presentation.
- Lymphocytic interstitial pneumonitis (LIP) occurs primarily in children, but it also occurs in adults infected with HIV.
- It is characterized by diffuse interstitial pulmonary infiltrates. (Zim, Viral Infections)
- Patients with LIP may be initially asymptomatic.
- As the disease progresses, they may present with generalized lymphadenopathy hepatosplenomegaly and/or digital clubbing.
- Respiratory difficulties may become evident because of secondary bacterial infection.
- Antiretroviral treatment can decrease the complications associated with LIP.
- The most important clinical picture is hypoxemia.
- It is believed to be a lymphoproliferative disorder typically found in association with non-suppurative parotitis, extensive lymphadenopathy, and hyper gamma globulinemia.
- 4 years old boy (HIV POSITIVE) – with progressively increasing dyspnoea and failure to thrive over a period of 6 weeks.
- Parotid enlargement and clubbing were present.
- Chest X-ray- widespread nodular opacities.
- Lung biopsy- confirmed the diagnosis.
- Treatment:
 - Oral steroids-helpful in improving arterial oxygen saturation
 - Intravenous immunoglobulin therapy
 - Cotrimoxazole can also be added.



Non-Hodgkin's Lymphoma

- Oral NHL may present as ulcers or nodules
 - The oral lesions may be the first or only lesions of NHL
- Non-Hodgkin's lymphoma occurs fairly commonly in persons with immunosuppression from HIV
- It is thought that EBV plays a role in the causation of the tumor
 - EBV has been found in biopsy specimens of lymph nodes obtained from persons with non-Hodgkin's lymphoma

Viral Infections

Slide 66

- Burkitt-type lymphomas are associated with HIV infection and may occur before advanced immunosuppression sets in. This tumor is associated with EBV. The diagnosis of Burkitt-type lymphoma is made on careful examination of lymph node biopsies.
- It has been estimated that about 40% of patients who survive 36 months with an AIDS diagnosis will develop Non-Hodgkin's Lymphoma. (Source: Pluda JM, Yarchoan R, Jaffe ES, et al. Development of non-Hodgkin's lymphoma in a cohort of patients with severe human immunodeficiency virus (HIV) infection on long term antiretroviral therapy. *Ann Intern Med* 1990; 113: 276-282.)
- Neoplasia is a multistep process arising from several genotypic changes within the cells.
 - The changes may activate positive elements within the genome (proto oncogenes) or turn off inhibitory elements (tumour suppressor genes), together producing the malignant phenotype.
 - In HIV patients, it is thought that immunodeficiency, oncogenic viruses and cytokines all contribute to this process.
- Genetic aberrations occur as a normal consequence of cell division and differentiation.
- Many of the genetic changes are fatal for the cell, but some genetically altered cells will survive with the potential for further phenotypic change, leading to the development of malignancy and ultimately to a more aggressive tumour.



B-Cell Lymphoma

Widened Mediastinum



Courtesy of University of Florida. © 1996-2000

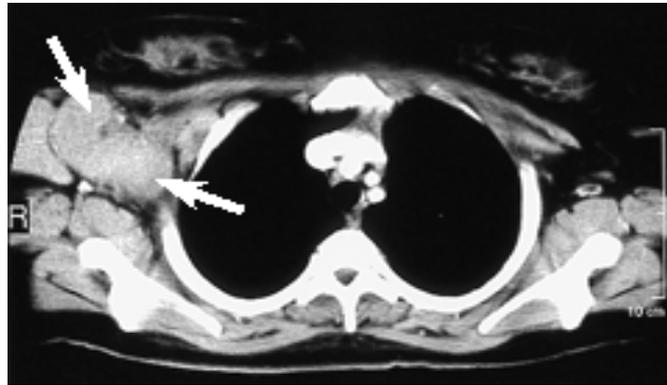
Viral Infections

Slide 67

- The immune response is vital in removing the premalignant cells, particularly those induced by oncogenic viruses.
 - It is also important for clearing foreign antigens which, when not removed, chronically stimulate the immune system, promoting excess cellular proliferation.
 - This increases the chance of malignant change. Immune deficiency also allows the activation of latent viruses, which add to the immune defect and may contribute to neoplasia.
- EBV is involved in the pathogenesis of Non-Hodgkin's Lymphoma



Right Axillary Lymphadenopathy



Courtesy of University of Florida. © 1996-2000

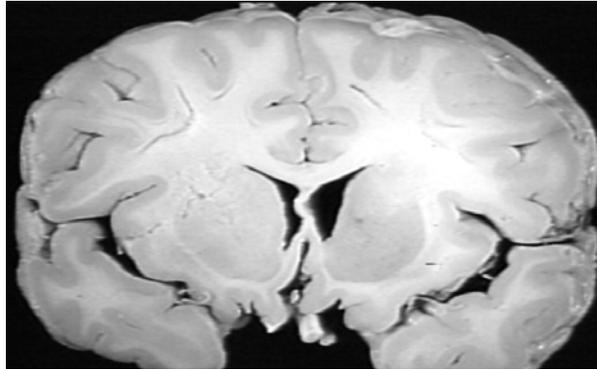
Viral Infections

Slide 68

- There is right axillary lymphadenopathy measuring approximately 7x5cm. Note the asymmetry between the right and the left (normal) axilla.



Primary CNS Lymphoma



© Slice of Life & Suzanne S. Stensaas

MRI

Gross Appearance

Viral Infections

Slide 69

- Brain MRI of lymphoma reveals a hyperdense lesion in the hypothalamic region
- Definitive diagnosis is made by stereotactic brain biopsy (DD from toxoplasmosis)



Discussion: EBV Treatment

- What diseases caused by EBV have you seen at Tambaram?
- Have you treated children with illnesses caused by EBV? What were their symptoms and what treatment did you prescribe?
- What resources are there at Tambaram to diagnose and treat patients with EBV?



Human Herpes Virus Type 8 (HHV8, KSHV)

- HHV8 or Kaposi sarcoma herpes virus (KSHV) has been shown to be the cause of Kaposi sarcoma
- Cancer of the lymphatic system that leads to generalized lymphadenopathy and lymphoedema of affected areas
- In HIV-infected persons, KSHV is more generalized and more rapidly progressive than in the endemic variety and often affects the viscera
- The lungs can be especially affected

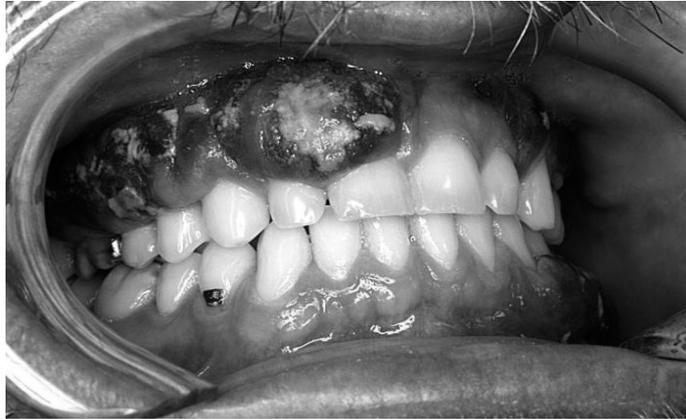
Viral Infections

Slide 71

- The human herpes virus type 8, also known as HHV8 or Kaposi sarcoma herpes virus (KSHV) has been shown to be the cause of Kaposi sarcoma. Kaposi sarcoma (KS) is a skin malignancy.
- This cancer of the lymphatic system leads to generalized lymphadenopathy and lymphoedema of affected areas.
- Kaposi sarcoma is the most common AIDS-related malignancy seen in certain parts of India.
- The cancer also occurs in persons without HIV infection (endemic Kaposi sarcoma).
- In HIV-infected persons, the cancer (epidemic Kaposi sarcoma) is more generalized and more rapidly progressive than in the endemic variety, and it often affects the viscera. Though any viscus in the body may be affected, the effects of the cancer are most severe on the lungs. (Zim, Viral Infections)
- KS that is associated with HIV/AIDS can present in two forms: mucocutaneous form and lymphadenopathic form.
- Cutaneous lesions can be flat, raised, or nodular, and usually have a purple or brown color. They can occur anywhere on the body, including the palms of the hands and inside the mouth.
- The most effective treatment for KS is antiretroviral therapy.
- Prognosis for KS seems to be related to the patient's overall immune status and the organ systems that are involved. (Baylor, p.89)
- *Note: Kaposi sarcoma is covered further in Session 5: Malignancies Associated with HIV/AIDS.*



Kaposi Sarcoma



Courtesy of Public Health Image Library, CDC. Sol Silverman, Jr., DDS

Viral Infections

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- Intraoral Kaposi sarcoma lesion with an overlying candidiasis infection.
- Multiple, extensive nodular purple lesions are apparent on the gingiva in this patient.
- The gingiva is the second common intraoral site and these lesions often become infected with dental plaque organisms.
- Kaposi Sarcoma in the Gastrointestinal Tract:
 - Patient can present with diarrhoea and GI bleeding



Kaposi Sarcoma: Nose



Courtesy of hivwebstudy.org. All rights reserved. © 2004

Viral Infections

Slide 73

- Plaque-like purple lesion on tip and left side of nose causing subtle edema of nose.



Kaposi Sarcoma Skin Lesions



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Viral Infections

Slide 74

- KS tumours are seen most often over the skin and mucous membrane as asymptomatic, pink to deep purple, or dark brown, round to oval shaped patches, which eventually becomes thickened plaques and nodular tumours.
- They may be single or multiple or in clusters, at the same site or at distant sites.
- Individual mucocutaneous KS lesions respond well to localized destructive treatments with:
 - Laser
 - Electrocauterization
 - Liquid nitrogen cryotherapy
- Vincristine, vinblastine, adriamycin, and interferon alpha can be used.



Kaposi Sarcoma Oral Lesions

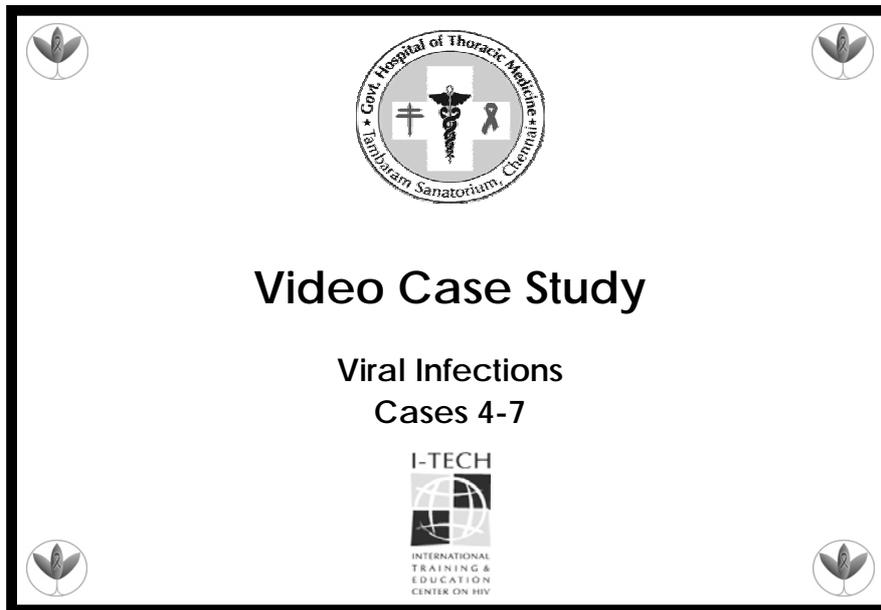


Courtesy of Public Health Image Library, CDC. Sol Silverman, Jr., DDS

Viral Infections

Slide 75

- Flat asymptomatic patches or plaques on the soft palate



- Refer to Viral Infections Video Case Studies Cases 4-7 (Worksheet 3.3).



Key Points (1)

1. Infection with the herpes viruses, herpes simplex virus, varicella-zoster virus, cytomegalovirus, and human herpes virus type 8 occur commonly in immunosuppressed persons with HIV infection
2. Human papilloma virus infection infections are commonly seen in persons with HIV infection



Key Points (2)

3. Antiviral agents are available for the treatment of some herpes virus infections
4. Recurrences of viral infections are common, and they are commonly persistent
5. A strong association exists between human papilloma virus infection and cervical and anogenital cancer

Viral Infections

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- If time permits and participants are willing, tour wards within Tambaram to observe cases.
- Then reconvene to discuss what participants have seen.



Clinical Management of Opportunistic Infections

Participant's Handbook

Session 4

TB and Other Bacterial Infections

Session 4: TB and Other Bacterial Infections

Aim: The aim of this unit is to introduce participants to TB and other bacterial opportunistic infections.

Learning Objectives: By the end of this session, participants will be able to:

- Describe the various clinical presentations and relative frequencies of the following opportunistic infections:
 - Tuberculosis
 - Atypical mycobacteriosis
 - Respiratory infections
 - Enteric infections
 - Other bacterial infections
- Identify the appropriate procedures and laboratory investigations required to make a diagnosis of each of the above bacterial opportunistic infections.
- Cite the preferred treatment regimen for each of the above bacterial opportunistic infections.
- Explain the recommended prophylactic regimens and cite the guidelines for initiation and discontinuation of prophylaxis for the above bacterial opportunistic infections.

Key Points

1. Tuberculosis is the most common opportunistic infection among HIV-infected persons.
2. Tuberculosis in HIV-infected persons can respond well to standard anti-TB regimens advocated in the DOTS regimen.
3. Bacterial pneumonias occur commonly in persons with HIV infection and are often the cause of death among people infected with HIV.
4. Bacterial infections can be treated using drug therapy.

RNTCP Guidelines for Treatment of Tuberculosis

Note: The prefix before the regimen is the number of months and the suffix is the number of doses in a week.

Treatment of Newly Diagnosed Cases

Intensive phase: 2(HRZE)₃, i.e., isoniazid, rifampicin, pyrazinamide, and ethambutol in a blister pack, administered 3 times a week for 2 months. The medication must be taken by the patient under the direct observation of the health staff.

When the patient has completed the initial intensive phase of 2 months and the sputum smear is negative for AFB, the continuation phase will start. If the sputum smear is positive at 2 months, the intensive phase of 4 drugs is continued for another month, after which the continuation phase is started, regardless of the results of sputum smear examinations.

The contents of the blister pack are:

Isoniazid 300 mg	Rimfampicin 450 mg	Pyrazinamide 500 mg	Ethambutol 400 mg
2 tablets	1 capsule	3 tablets	3 tablets

Continuation phase: In this phase, 4(HR)₃, i.e. isoniazid and rifampicin are given 3 times a week for 4 months. For patients with tuberculosis meningitis, disseminated TB or spinal disease with neurological complications, isoniazid and rifampicin should be given for 6 to 7 months (i.e., a total of 8 to 9 months of therapy).

The weekly blister pack for self-administration contains the following drugs to be taken 3 times a week with vitamins in the remaining days of the week:

Isoniazid 300 mg	Rifampicin 450 mg
2 tablets	1 capsule

Retreatment Regimen

Intensive phase: 2(HRZES)₃/1HRZE)₃, i.e., rifampicin combined with isoniazid, pyrazinamide, and ethambutol, supplemented with streptomycin for the first 2 months, followed by the same drugs without streptomycin for 1 month given 3 times a week.

The initial intensive phased should be given for 3 months. The tablets are given in the same type of blister pack as for the new smear-positive cases. If the sputum is smear-negative for AFB at 3 months, the continuation phase is started. If the sputum smear is positive at 3 months, the 4 oral drugs are continued for another month. If the sputum is still smear-positive at the end of the fourth month and facilities for culture are available, the sputum should be sent for culture and sensitivity after stoppage of the drugs for 3 days. Regardless of the availability of culture facilities, the patient should start the continuation phase after the fourth month.

Handout 4.1 (continued)

RNTCP Guidelines for Treatment of Tuberculosis (continued)

If the pretreatment studies showed resistance to both isoniazid and rifampicin or isoniazid and rifampicin resistance is found in a patient who remains smear-positive, the chances of achieving a cure are limited.

Continuation phase: 5(HRE)₃, i.e., 5 months of isoniazid, rifampicin and ethambutol 3 times a week. If the patient remains smear-positive after completion of the continuation phase he or she is no longer eligible for the retreatment regimen. The patient is managed as a chronic case.

The drugs are given in weekly blister packs. One weekly pack is given at a time. The blister pack contains vitamin tablets for the days when anti-tuberculosis drugs are not to be given.

The contents of the blister pack are:

Isoniazid 300 mg	Rifampicin 450 mg	Ethambutol 400 mg
2 tablets	1 capsule	3 tablets

Dosage for Children

Drugs	Daily Therapy	Thrice -Weekly Therapy
Isoniazid	5 mg/kg	10-15 mg/kg
Rifampicin	10 mg/kg	10 mg/kg
Pyrazinamide	25 mg/kg	35 mg/kg
Streptomycin	15 mg/kg	15 mg/kg
Ethambutol*	15 mg.kg	30 mg/kg

*Should not be given to children younger than 6 years of age.

From Central TB Division. (2003). *Technical Guidelines for Tuberculosis Control*. New Delhi, India: Directorate General of Health Services, Ministry of Health and Family Welfare. Available online at <http://www.tbcindia.org/documents.asp>

ART Recommendations for Individuals with TB-HIV Co-infection

Treatment in Special Situations

1. **Hospitalisation:** Generally, patients with PTB do not require hospitalisation. Those who are extremely ill can be hospitalized during the initial phase of treatment. If required, duration of therapy may be extended within the current RNTCP guidelines.
2. **Extrapulmonary TB:** The basic principles that support the treatment of extrapulmonary TB in HIV uninfected individuals also apply to HIV-infected patients. Most extrapulmonary forms of TB (including TB meningitis, TB lymphadenitis, pericardial TB, and disseminated or miliary TB) are more common among persons with advanced-stage HIV disease than among patients with asymptomatic HIV infection. The drug regimens and treatment durations that are recommended for treatment of extrapulmonary TB in HIV-negative persons are also recommended for treating HIV-positive patients. If the clinical or bacteriological response is slow, treatment may be prolonged, as mentioned previously. Also, in TB meningitis, a longer duration of treatment is recommended, as discussed next.
3. **Tuberculosis meningitis:** Tuberculosis meningitis is fatal if untreated. Patients should generally be referred to the hospital, and treatment should be started as soon as possible. The continuation phase should be given for 6 to 7 months (total treatment 8 to 9 months). Steroids should be given initially to reduce meningeal inflammation and reduced gradually.
4. **Pregnancy:** HIV-infected pregnant women who have tuberculosis or are suspected of having TB disease should be treated without delay. Streptomycin should not be given during pregnancy because of potential adverse effects on the foetus. Other drugs used in the RNTCP are safe during pregnancy. In patients on concomitant ARV, efavirenz should be avoided in view of its teratogenicity.

Anti-tuberculosis Therapy and Antiretroviral Therapy

To date no cure is available for HIV/AIDS. However, antiretroviral drugs are effective in reducing viral replication and prolonging life. These drugs fall into the following 3 groups: (i) Nucleoside reverse transcriptase inhibitors (NRTIs); (ii) Non-nucleoside reverse transcriptase inhibitors (NNRTIs); (iii) Protease inhibitors (PIs).

Some of the ARVs have adverse drug interactions with ATT, therefore, appropriate drug choices become imperative. Nucleoside reverse transcriptase inhibitors like zidovudine, didanosine, zalcitabine, stavudine, lamivudine, and abacavir can be safely co-administered with anti-tuberculosis drugs.

ART Recommendations for Individuals with TB-HIV Co-infection (continued)

Co-administration of rifampicin with protease inhibitors (ritonavir, indinavir, nelfinavir) or non-nucleoside reverse transcriptase inhibitors (nevirapine, delavirdine, thioben) is contraindicated. Protease inhibitors and non-nucleoside reverse transcriptase inhibitors may inhibit or induce cytochrome P-450 isoenzymes and thus these drugs may alter the serum concentration of rifamycins. Rifamycins induce cytochrome P-450 and may substantially decrease blood levels of the antiretroviral drugs resulting in the potential development of resistance. Rifabutin is a less potent cytochrome-450 inducer than rifampicin and thus can be used concurrently with the NNRTIs (e.g., nevirapine, efavirenz) or with certain protease inhibitors (e.g., indinavir, nelfinavir). Rifabutin is at present not available in India.

Isoniazid, ethambutol, pyrazinamide and streptomycin can be concurrently used with protease inhibitors or non-nucleoside reverse transcriptase inhibitors.

If a protease inhibitor or non-nucleoside reverse transcriptase inhibitor is to be started after giving rifampicin, then at least 2 weeks should elapse after the last dose of rifampicin. This time gap is necessary for reduction of the enzyme-inducing activity of rifampicin prior to commencement of antiretroviral drugs.

ATT for Patients on ART

If patients already on ART develop active TB then either the ART regimens should be suitably modified to be compatible with RNTCP regimens, or a non-rifampicin-based regimen should be used. However, ART should not be discontinued because of concerns of development of drug resistance.

Investigations for liver and renal functions together with blood sugar and serum lipid levels would have to be done at baseline and at periodic intervals to detect drug induced toxicity early. A pregnancy test would be done at baseline and at periodic intervals for women who are on efavirenz treatment and of child-bearing age. Baseline CD4/CD8 counts and if possible HIV viral load tests should be done at baseline and at 6 monthly intervals to monitor the response to antiretroviral therapy.

Immune Reconstitution Syndrome

For many opportunistic infections, including TB, there can be a transient worsening of symptoms 2 to 3 weeks after the initiation of ART. This is called immune reconstitution syndrome. For patients with TB, this syndrome has been reported to occur in as many as 30% of cases on ART in the developing world. The syndrome is characterised by fever, lymphadenopathy, worsening pulmonary lesions, and expanding lesions of the central nervous system (CNS). These reactions are typically self-limiting, although they may require the use of a brief course of corticosteroids in order to reduce CNS inflammation or severe respiratory symptoms. The initiation of ART can also unmask previously undiagnosed infections by augmenting the inflammatory response. In general, ART should not be interrupted if immune reconstitution occurs.

ART Recommendations for Individuals with TB-HIV Co-infection (continued)

WHO Recommendations

WHO recommends that people with TB/HIV complete their TB therapy prior to beginning antiretroviral treatment unless there is a high risk of HIV disease progression and death during the period of TB treatment (i.e., a CD4 count <200/mm³ or the presence of disseminated TB). In cases where a person needs TB and HIV treatment concurrently, first-line treatment options include ZDV/3TC (lamivudine) or d4T (stavudine)/3TC plus either an NNRTI or ABC (abacavir). If an NNRTI-based regimen is used, EFZ (efavirenz) would be the preferred drug as its potential to aggravate the hepatotoxicity of TB treatment appears less than with NVP (nevirapine). Except for SQV/r (saquinavir/low dose ritonavir). PIs are not recommended during TB treatment with rifampicin due to their interactions with the latter drug.

**Antiretroviral Therapy for Individuals with Tuberculosis
(WHO Recommendations-June 2002)**

Situation	Recommendations
Pulmonary TB and CD4 count <50/mm ³ or extrapulmonary TB	Start TB therapy. Start one of these regimens as soon as TB therapy is tolerated: <ul style="list-style-type: none"> • ZDV/3TC/EFZ** • ZDV/3TC/ABC • ZDV/3TC/SQV/r • ZDV/3TC/NVP*
Pulmonary TB and CD4 50-200/mm ³ or total lymphocyte count <1200/mm ³	Start TB therapy. Start one of these regimens after 2 months of therapy: <ul style="list-style-type: none"> • ZDV/3TC/EFZ** • ZDV/3TC/ABC • ZDV/3TC/SQV/r • ZDV/3TC/NVP*
Pulmonary TB and CD4>200/mm ³ or total lymphocyte count>1200/mm ³	Treat TB. Monitor CD4 counts if available. Start ART when indicated after ATT is completed.

* NVP is advised only in patients without other options because rifampicin reduces drug exposure to nevirapine by 31% and dose adjustments for NVP co-administered with rifampicin has not been established.

** In HIV-infected pregnant women who have tuberculosis, efavirenz is contraindicated due to its teratogenicity.

HIV and Tuberculosis in Paediatric Patients

The guidelines for management of TB in children are the same as those for adults except that ethambutol should not be given in young children, as they may not be able to report any diminution of visual acuity.

Active tuberculosis should generally be treated before ART is begun. CD4+ T cell measurements, when available, should be performed after resolution of acute infection. Tuberculosis is often presumptively diagnosed in children in resource-poor countries because of general difficulties of diagnosis in children. In HIV-infected children being treated for proven or presumptive tuberculosis, ART should generally be deferred until anti-tuberculosis therapy has been in progress for at least 2 months, and if deemed safe, until the completion of all anti-tuberculosis therapy. This is to avoid interactions with rifampicin and possible decreased adherence to ART and tuberculosis medications because of the number of drugs that have to be administered.

ART Recommendations for Individuals with TB-HIV Co-infection (continued)

If an HIV-infected child with tuberculosis has significant HIV symptoms and/or severe immunodeficiency and requires initiation of ART, the considerations about the choice of regimen are similar to those for adults, and include a triple-NRTI regimen (AZT+3TC+ABC) or a regimen of 2 NRTIs and efavirenz, and NNRTI, in children over 3 years. There are advantages in starting therapy using triple NRTI consisting of ABC, ZDV, and 3TC because of the frequency of suspected, empirically treated or proven tuberculosis in HIV- infected children in resource-limited settings and the lack of interactions of this combination of ARVs with anti-tuberculous medications. Efavirenz should be used only for those aged over 3 years because pharmacokinetic data for younger children is not available.

INH Chemoprophylaxis for TB and Other Issues

Preventive therapy for TB (i.e., treatment of latent TB) reduces the risk of development of active TB in HIV-infected individuals, although the durability of this effect may be limited by high rates of re-infection with TB in high TB burden countries like India.

WHO recommends TB preventive therapy if possible in areas where diagnostic testing, such as chest x-rays, is available to exclude active TB and where PPD skin testing is feasible. In such situations, isoniazid therapy (with pyridoxine supplementation) for 6 months in tuberculin skin test reactors could be given after exclusion of active disease.

In India, however, the issue of INH prophylaxis is complicated for the following reasons:

1. Difficulty in excluding active TB disease in those with HIV/TB co-infection
2. In a country like India, where the burden of TB is high, chemoprophylaxis may not prevent re-infection.
3. Widespread use of INH for chemoprophylaxis may contribute to an increase in INH resistance.
4. PPD skin test may not be feasible and is also not reliable in severely immunocompromised patients.

BCG Vaccination

Vaccination with BCG in HIV patients is effective in preventing the progression of infection with *M. tuberculosis* to TB disease provided it is given before infection. But complications from vaccinations have been reported as mycobacterial meningitis, cervical and axillary lymphadenopathy and disseminated BCG disease. WHO does not recommend BCG for children who show symptoms of HIV but recommends vaccination of healthy infants of HIV-infected mothers. If some complication does occur, it can be treated with anti-TB treatment.

Operational Research

Research should form an important part of the planning and implementation of collaborative HIV and TB programme activities. An operational research approach to the planning and management of HIV/TB programme collaboration and/or integration at central and district levels should be an integral part of the work plan for collaborative HIV and TB activities. Innovative approaches for HIV and TB are needed, and wherever possible HIV and TB programmes should work together with research institutes to encourage relevant basic science research and clinical trials to provide much needed new HIV/TB diagnostic tools and therapies.

Treatment of Bacterial Infections

Respiratory Bacterial Infections

Initial Empirical Therapy for Out-patients

ANTIBIOTICS	DOSE	FREQUENCY	ROUTE OF ADMINISTRATION
Macrolides- Clarithromycin	500 mg	bid	PO
Doxycycline	100 mg	bid	PO
Flurooquinolones- Levofloxacin	500 mg	qd	PO
Gatifloxacin	400 mg	qd	PO

Duration of Therapy

The decision is influenced by the severity of illness, the etiologic agent, response to therapy, other medical problems and complications. Therapy until the patient is afebrile for at least 72 hours is usually sufficient for *S. pneumoniae*. A minimum of 2 weeks of therapy is appropriate for *S. aureus* and *P. aeruginosa*, Klebsiella, etc.

Alternate Therapy for Out-Patients

ANTIBIOTICS	DOSE	FREQUENCY	ROUTE OF ADMINISTRATION
Erythromycin	250-500 mg	qid	PO
OR			
Amoxicillin+ Potassium Clavulanate	500 mg	tid	PO
OR			
Amoxicillin+ Potassium Clavulanate	875 mg	bid	PO
PLUS ONE OF THE FOLLOWING			
Cefuroxime Axetil	250-500 mg	bid	PO
Cefpodoxime Proxetil	100-200 mg	bid	PO
Cefprozil	250-500 mg	bid	PO

Duration of Therapy

The decision is influenced by the severity of illness, the etiologic agent, response to therapy, other medical problems and complications. Therapy until the patient is afebrile for a tleast 72 hours is usually sufficient for *S. pneumoniae*. A minimum of 2 weeks of therapy is appropriate for *S. aureus* and *P.aeruginosa*, Klebsiella, etc.

Treatment of Bacterial Infections (continued)

Treatment for Hospitalised Patients:

- General Medical Wards:
 - An extended spectrum beta-lactam (ceftriaxone or cefotaxime) with a macrolide (clarithromycin or azithromycin) is preferred if *H. influenzae* is suspected.
 - OR**
 - A fluoroquinolone (with enhanced activity against *S.pneumoniae*) such as gatifloxacin or levofloxacin.
- Alternatives:
 - A beta-lactam/beta-lactamase inhibitor (ampicillin-sulbactam or piperacillin-tazobactam) with a macrolide.
- Intensive-Care Wards:
 - A macrolide or a fluoroquinolone (with enhanced activity against *S.pneumoniae*) + An extended spectrum cephalosporin (ceftriaxone, cefotaxime)
 - OR**
 - A beta-lactam/beta-lactamase inhibitor (ampicillin-sulbactam, piperacillin-tazobactam).
 - Patients with penicillin allergies can be treated with a fluoroquinolone with or without clindamycin.

Enteric Bacterial Infections:

Gastrointestinal Pathogens in Persons with HIV Infection

	PATHOGEN	CLINICAL FEATURES	TREATMENT
BACTERIA	Non-typhoid salmonellosis	Fever, abdominal pain, diarrhoea, diarrhoea with blood, weight loss, anorexia, hepatosplenomegaly. Diagnosis on blood or stool culture	Ciprofloxacin 500 mg orally 4 times a day for 7 to 10 days
	Shigellosis	Fever, abdominal pain, bloody diarrhoea. Diagnosis on blood or stool culture	Ciprofloxacin 500 mg orally 2 times a day for 5 days
	<i>Campylobacter</i> infection	Fever, abdominal pain, diarrhoea, diarrhoea with blood. Diagnosis on stool microscopy	Mebendazole 100 mg orally twice daily for 3 days
	Clostridial infection	Diarrhoea, abdominal pain, blood in stool, pseudomembranous colitis	Metronidazole 200 mg orally 4 times a day for 10 days

	<i>Mycobacterium avium intracellulare</i>	Fever, night sweats, malaise, weight loss, abdominal pain, diarrhoea, haepatomegaly. Diagnosis on blood culture, bone marrow or lymph node or liver biopsy	Rifabutin PLUS ethambutol PLUS clarithromycin
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 Handout 4.3 (continued)

Treatment of Bacterial Infections (continued)

Atypical Mycobacteriosis, First-Line Treatment

Antibiotic	Dose	Frequency	Route	Duration
Clarithromycin	500 mg	bid	PO	12+ months
PLUS				
Ethambutol	15 mg/kg	o.d.	PO	12+ months

Atypical Mycobacteriosis, Second-Line Treatment

Antibiotic	Dose	Frequency	Route	Duration
Azithromycin	600 mg	o.d.	PO	12+ months
PLUS				
Ethambutol	15 mg/kg	o.d.	PO	12+ months
PLUS				
Rifabutin*	450 mg	o.d.	PO	12+ months

*Not available in India.

Atypical Mycobacteriosis, Prophylaxis

Age	Prophylaxis	Alternative Prophylaxis
Children (0-12 years)	Clarithromycin 7.5 mg/kg by mouth twice daily	Azithromycin 20 mg/kg by mouth weekly or rifabutin (>6 y/o) 300 mg by mouth daily
Adults (>12 years)	Clarithromycin 500 mg by mouth twice daily	Azithromycin 1.2 g by mouth weekly or rifabutin 300 mg by mouth daily

Staphylococcal Folliculitis Treatment

Antibiotic	Dose	Frequency	Route	Duration
Cephalexin	500 mg	qid	PO	7-21 days
OR				
Cloxacillin	500 mg	qid	PO	7-21 days



Video Case Study: TB and Other Bacterial Infections

Instructions for Participants

This video depicts 8 different cases during which a physician examines a patient with at least 1 opportunistic infection. After reviewing the symptoms of each patient, the video will reveal the diagnosis that the physician made for the patient and the treatment prescribed.

You will watch each case and then discuss the diagnosis and treatment of each patient before viewing the actions taken by the physician in the video. You may want to take notes as you watch each case and raise additional questions during the discussions.

Session 4: TB and Other Bacterial Infections Case 8

Video Case Study Context

A 44-year-old male with the following symptoms: Swelling in the neck, discharging pus, and breathlessness for past 3 months.

Trigger Point: Diagnosis Questions

1. What are the differential diagnoses for this patient?

2. What is the most probable diagnosis?

3. What is the stage of the disease?



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 **Notes**



Session 4: TB and Other Bacterial Infections

Slide 1



Tuberculosis and Other Bacterial Infections
Session Four



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Learning Objectives (1)

- By the end of this session, you will be able to:
 - Describe the various clinical presentations and relative frequencies of tuberculosis and other common bacterial opportunistic infections
 - Identify the appropriate procedures and laboratory investigations required to make a diagnosis of these opportunistic bacterial infections

TB and Other Bacterial Infections

Slide 2

- *The aim of this session is to introduce participants to TB and other bacterial opportunistic infections.*



Learning Objectives (2)

- By the end of this session, you will be able to:
 - Cite the preferred treatment regimen for these opportunistic bacterial infections
 - Explain the recommended prophylactic regimens and cite the guidelines for initiation and discontinuation of prophylaxis for these opportunistic bacterial infections



Introductory Case Study (1)

A 45 year old male labourer admitted with h/o cough with expectoration (6 months), fever (10 days), and loss of weight



TB and Other Bacterial Infections

Slide 4

- *Read the case study and answer the questions that follow in “Introductory Case Study” (Worksheet 4.1) in the Participant’s Handbook.*



Introductory Case Study (2)

- His past medical history revealed repeated history of cough with expectoration for which he was prescribed various antibiotics
- He gave history suggestive of exposure to sexually transmitted diseases
- He was a smoker
- On examination he was febrile, anemic and his body mass index was 16. Pulse 98/minute, regular. Respiratory rate 22/minute. No lymphadenopathy
- The respiratory system revealed coarse rales on both sides, more at the right apex with bronchial breath sound
- Other systems were normal

TB and Other Bacterial Infections

Slide 5



How Will You Proceed with the Investigations?

Sputum Tests:

- Gram stain
- Bacterial culture and sensitivity
- PCP
- AFB staining
- AFB culture (if available)

Other Tests:

- Chest X-ray PA view
- Mantoux test
- Urine for sugar
- Blood sugar
- WBC count
- Differential count



Test Results

<u>Sputum</u>	
AFB	Positive
Others	Negative
WBC Count	8700 cells/mm ³
Differential Count	P 74, L 23, E 03
Urine Sugar	Normal
Blood Sugar	98 mg%
Mantoux Test	No reaction

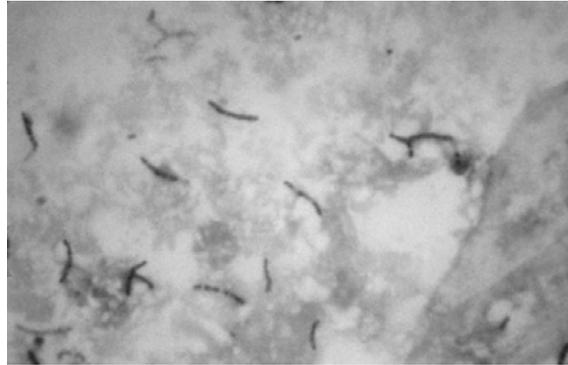
TB and Other Bacterial Infections

Slide 7

- Sputum tests:
 - Gram stain = NEGATIVE
 - Bacterial culture = NEGATIVE
 - PCP = NEGATIVE
 - Ziehl Neelson's staining-POSITIVE for AFB.



Mycobacterium Tuberculosis



Courtesy of Public Health Image Library/CDC/Dr. George P. Kubica

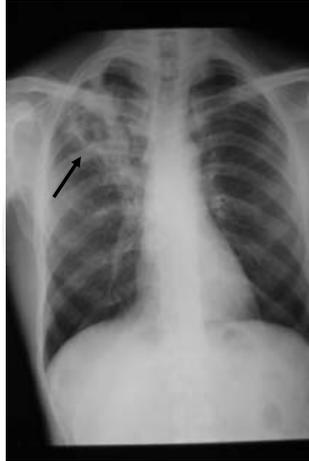
TB and Other Bacterial Infections

Slide 8

- Slender, long, curved, pinkish mycobacterium tuberculosis stained by Ziehl-Nielson's stain.
- Tuberculin skin test-negative
- Other tests were also within normal levels



Chest X-ray PA Before Treatment



TB and Other Bacterial Infections

Slide 9

- Right apical cavity with infiltrations



Case Study Discussion Questions

1. How do you manage this patient before the investigation results are ready?
2. What is your diagnosis?
3. How do you manage this patient?
4. What else is important in this patient in relation to HIV?



Chest X-ray PA After Treatment



TB and Other Bacterial Infections

Slide 11

- The X-ray of the patient showed fibrosis of the right apical lobe with pulling up of the transverse fissure.
- The tuberculous lung lesions heal with fibrosis.



Prevalence of TB (1)

- About one third of the world's population is infected with *Mycobacterium tuberculosis* (TB)
- India accounts for nearly one third of this global TB burden
- TB is the leading killer of patients with HIV/AIDS in developing countries, accounting for one-third of all AIDS deaths

TB and Other Bacterial Infections

Slide 12

- About one third of the world's population is infected with *Mycobacterium tuberculosis* (TB).
- Today, India accounts for nearly one third of the global TB burden. (TB India, p. 8)



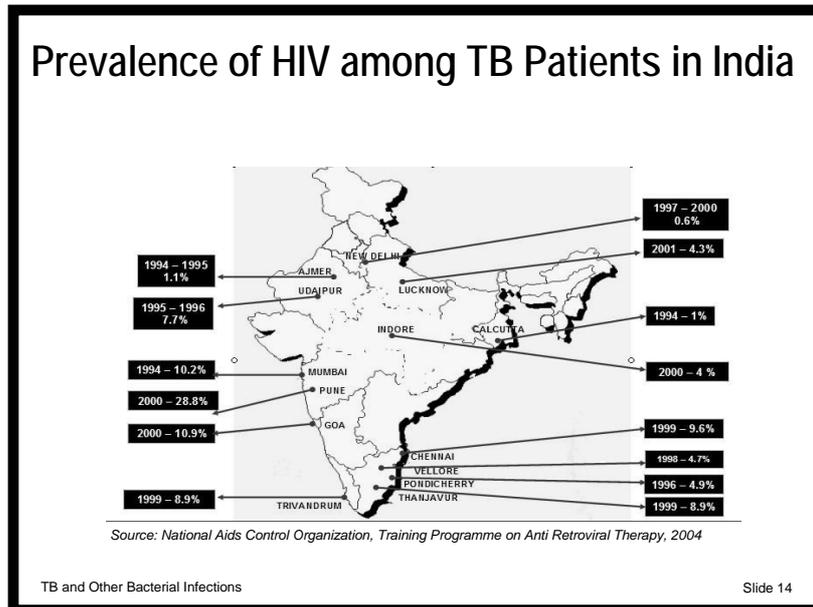
Prevalence of TB (2)

- Main reasons for the high incidence of TB
 - Increasing levels of poverty
 - Erosion of family support structure
 - Inadequate case detection, diagnosis and cure
 - HIV/AIDS pandemic

TB and Other Bacterial Infections

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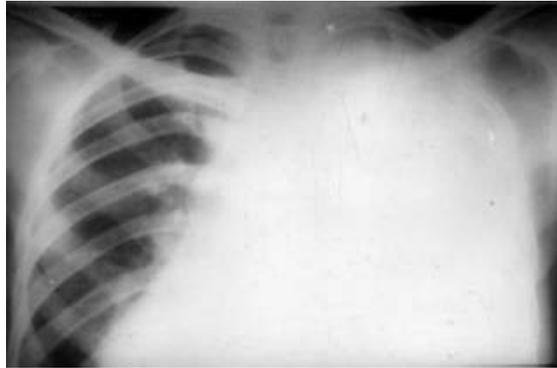
- The main reasons for the increase of TB cases are:
 - Increasing levels of poverty
 - Erosion of family support structure
 - Inadequate case detection, diagnosis and cure
 - HIV/AIDS pandemic. (Zim, TB)



- In persons with HIV infection, both pulmonary and extrapulmonary TB can occur.
- Among AIDS cases in India, an estimated 60% have TB. (TB India, p. 8)
- TB is the most common opportunistic disease in people living with HIV.
 - The virus breaks the immune system down, making people living with HIV highly susceptible to TB.
 - TB in turn accelerates the progression of HIV to AIDS and shortens survival of patients with HIV infection. (TB India, p. 8)
- Immuno-suppressed persons may reactivate an old tuberculosis infection or may become infected *de novo* with *Mycobacterium tuberculosis*.
- Patients may present with classic features of pulmonary disease as seen in non-HIV infected individuals or may have atypical pulmonary TB.
- Disseminated tuberculosis infection may manifest itself as:
 - Generalized lymphadenopathy
 - Meningitis
 - Pericarditis
 - Pleural effusion
 - Abdominal and peritoneal disease
 - Renal and osteal disease
- Although involvement of the adrenal and genital tract may occur, one disease related to the adrenal gland that HIV positive patients often present with is Addison's disease.
 - Addison's disease is quite frequently associated with HIV and TB co-infection in India.
- Lowered blood pressure and lowered cortisone level are often related to lower level functioning of adrenal glands



Pleural Effusion



Responds well to treatment

TB and Other Bacterial Infections

Slide 15

- TB is a frequent first indication of HIV infection in developing countries, and the diagnosis should always be considered in immunosuppressed persons.
- The implementation of the directly observed, short course treatment strategy (DOTS) recommended by WHO can be highly effective in treating TB patients.
- The internationally-recommended TB control strategy is DOTS.
- Once patients with infectious TB (bacilli visible in a sputum smear) have been identified using microscopy services, health and community workers and trained volunteers observe and record patients swallowing the full course of the correct dosage of anti-TB medicines.
- The most common anti-TB drugs are:
 - Isoniazid
 - Rifampicin
 - Pyrazinamide
 - Streptomycin
 - Ethambutol



DOTS (Directly Observed Treatment, Short-course) (1)

- Political commitment
- Case detection and diagnosis
- Standardized short-course chemotherapy with direct observation of drug intake

TB and Other Bacterial Infections

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- The WHO recommended DOTS regimen has five key components (WHO, What is DOTS?):
 1. Political commitment:
 - Government commitment to sustained TB control is **ESSENTIAL** for the mobilization of resources and the sustainability of TB programmes.
 2. Case detection and diagnosis:
 - Sputum smear microscopy is the most cost-effective method of screening pulmonary TB suspects referring to health services. It identifies sputum smear-positive, highly infectious TB cases.
 - TB is usually diagnosed using patient history, clinical examination and diagnostic tests. A sputum sample is submitted to the laboratory and the results of the microscopic exam are entered into the laboratory register. The goal of DOTS is for all patients to have a sputum smear microscopy exam and for all those diagnosed with TB to be registered and treated.
 3. Standardized short-course chemotherapy with direct observation of drug intake:
 - Short-course chemotherapy refers to a treatment regimen that lasts six to eight months and uses a combination of powerful anti-TB drugs. Directly observed therapy (DOT) is essential during the intensive phase of treatment (the first two months) to ensure that the drugs are taken in the right combinations and for the appropriate duration.
 - With direct observation of treatment, the patient doesn't bear the sole responsibility of adhering to treatment.
 - Health care workers, public health officials, governments, and communities must all share the responsibility and provide a range of support services patients need to continue and finish treatment.
 - One of the aims of effective TB control is to organize TB services that are an integral part of health systems so that the patient has flexibility in where he or she receives treatment, such as in the home.
 - Treatment observers can be anyone who is willing, trained, responsible, acceptable to the patient and accountable to the TB control services.



DOTS (Directly Observed Treatment, Short-course) (2)

- Drug supply
- Recording and reporting



TB and Other Bacterial Infections

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4. Drug supply

- Where DOTS is implemented, an accurate recording and reporting system provides the information needed to plan and maintain adequate drug stocks.

5. Recording and reporting

- The recording and reporting system is used to systematically evaluate patient progress and treatment outcome. The system consists of:
 - Laboratory register that contains a log of all patients who have had a smear test done;
 - Patient treatment cards that detail the regular intake of medication and follow-up sputum examinations;
 - TB register, which lists patients starting treatment and monitors their individual and collective progress towards cure;
 - Reporting forms from districts to the national level, which allow assessment of control efforts.
- A major problem with the DOTS system is that it has limitations in areas where HIV is epidemic because HIV changes the epidemiology of TB.
 - It increases the risk of reactivation, which in turn increases the available pool of infectious individuals.
 - This increase in turn increases TB incidence throughout the population, not just in those who are HIV infected.
- Thus a well-managed DOTS program by itself can control the emergence and spread of MDRTB and stabilize the rates of TB in an area where HIV is epidemic. But it cannot further reduce the rates of TB by itself. (Coberly, John Hopkins University)



DOTS and HIV

- Additional approaches are needed where HIV is epidemic:
 - Active case finding for people co-infected with HIV & TB
 - Preventive therapy for TB
 - Appropriate infection control programs in hospitals and other institutions

TB and Other Bacterial Infections

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- Thus, additional approaches will be needed where HIV is epidemic. These could include (Coberly, John Hopkins University):
 - Active case finding for people co-infected with HIV & TB, among contacts of new cases of TB, prisons, institutions, etc.
 - While active case finding is a suggested strategy, it is not proven to be of benefit.
 - Preventive therapy for TB needs to be considered for HIV(+), PPD positive people, or perhaps all HIV-infected, in the developing world;
 - Appropriate infection control programs are needed in hospitals and other institutions, e.g., ventilation and daylight in patient areas and segregation, if possible



Session 4: TB and Other Bacterial Infections

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TB Diagnosis



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Discussion: TB Diagnosis

- Have you noticed differences in diagnosing TB in patients who are not HIV-infected and those that are?
- What challenges have you encountered in diagnosing TB in HIV-infected patients?



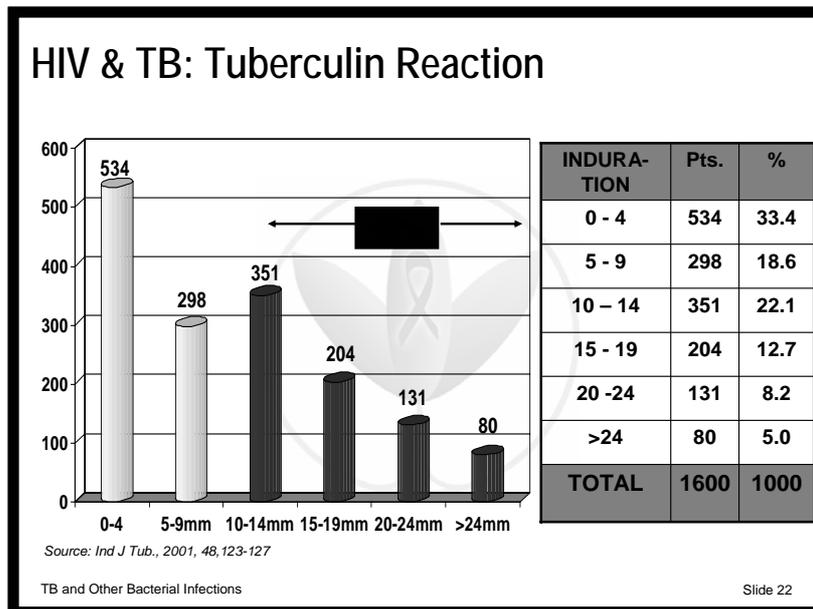
TB Diagnosis

- Clinical picture
- Sputum test
- Why aren't chest X-rays and tuberculin tests useful in diagnosing TB?

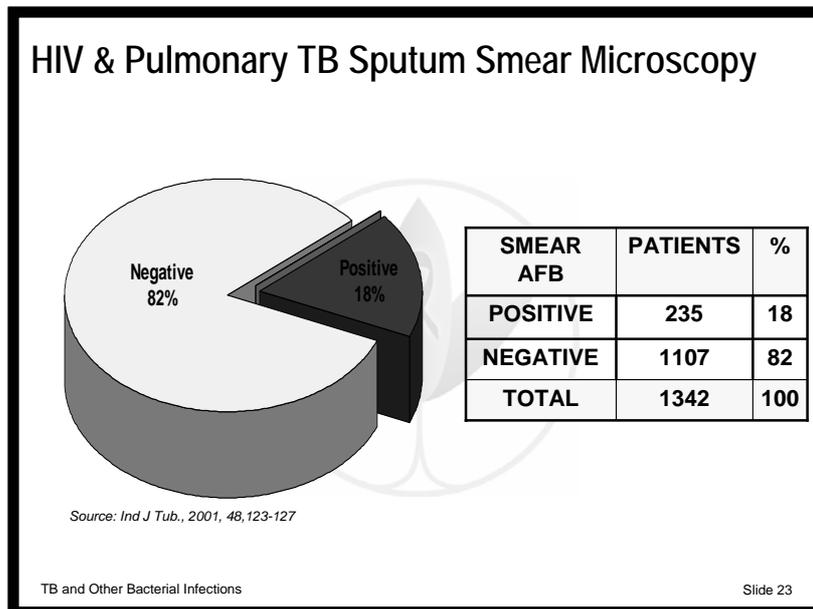
TB and Other Bacterial Infections

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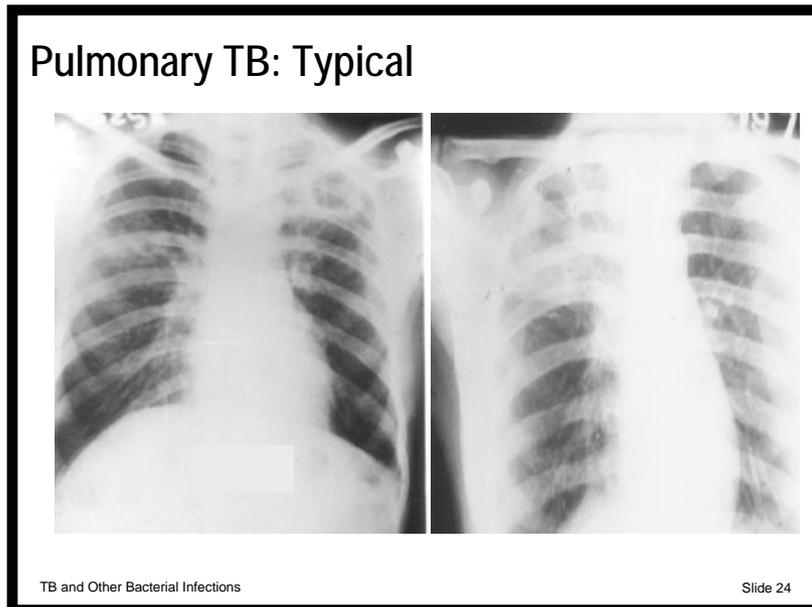
- There are two primary methods used to diagnosis TB: clinical picture and sputum test.
- The typical symptoms and signs of pulmonary TB are:
 - Cough with or without fever
 - Night sweats
 - Weight loss.
- Chest X-ray may show upper lobe infiltrates with or without cavitation.
- In immunosuppressed persons, the diagnosis may be difficult to make as TB in such hosts may present with:
 - Atypical symptoms
 - Lack of typical symptoms
 - Minimal changes on chest X-ray
- In addition, in persons with AIDS, the presence of other opportunistic infections and extrapulmonary TB may complicate the diagnosis. (Zim, TB) (Technical Guidelines for TB Control, p. 7)
- Chest X-ray can indicate a pulmonary abnormality but not the etiology.
- Diagnosis of TB is not aided by a tuberculin test, especially in the presence of HIV infection.
- Tuberculin tests can be negative during active TB infection



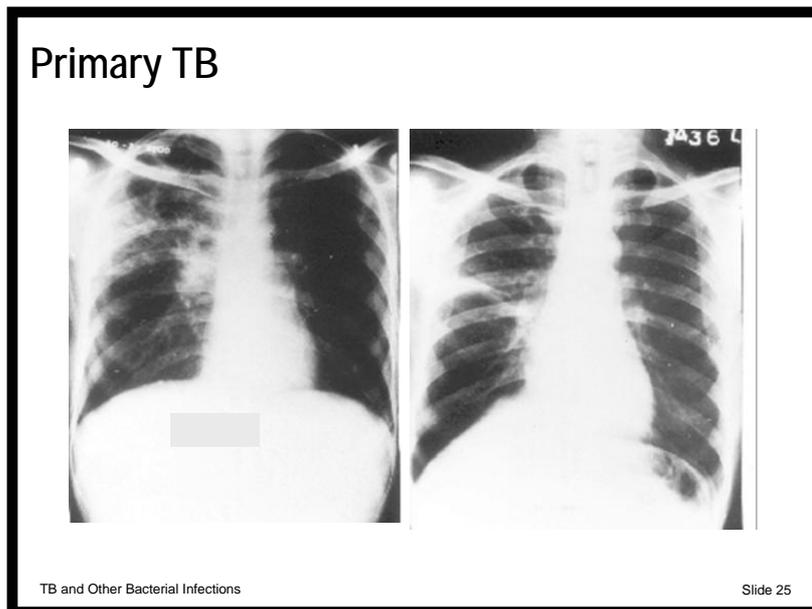
- Though useful for measuring the prevalence of tuberculosis infection in a community, it has limited value for the diagnosis of TB infection in adults in India; though it can be used as an adjunct to diagnose childhood TB.
- Furthermore, with progression of immunodeficiency and decrease in CD4 counts, cutaneous anergy to tuberculosis increases, compounding the issue further. (NACO, Guidelines for Management of TB in HIV Infected)
- Latent TB is diagnosed on the finding of positive tuberculin skin test in the absence of clinical or radiological evidence of TB. (Zim, TB)



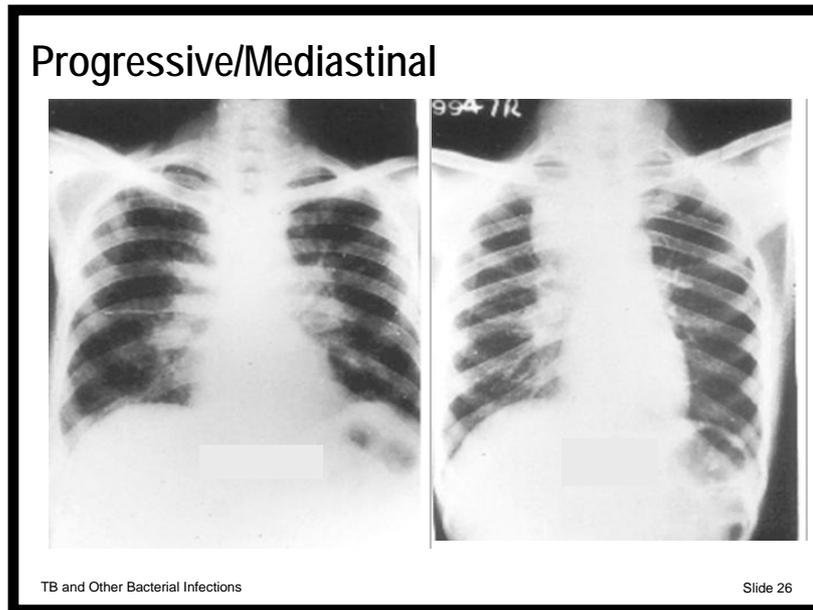
- Sputum microscopy is the cornerstone of diagnosis of TB even in high HIV-prevalence areas. (NACO, Guidelines for Management of TB in HIV Infected)
- Sputum microscopy is an effective tool for detection as it provides information on the infectiousness of the patient, aids in categorization of the patient for treatment and is an objective method to monitor the patient's progress.
- Other advantages of sputum microscopy are that it is relatively easy to perform and less expensive when compared to X-ray. (TB India, p. 12)
- Sputum may also be cultured for mycobacterium, and cultured colonies can be tested for antimicrobial resistance. (Zim, TB)
- Patients suspected of having TB should have three sputum specimens examined for acid-fast bacilli (AFB).
 - HIV-infected, smear positive patients tend to excrete significantly fewer organisms per ml of sputum than HIV- negative patients, which can lead to AFB being missed if the appropriate number of sputum samples, as well as high power fields, are not examined by microscopy. (NACO, Guidelines for Management of TB in HIV Infected)
- At the first visit to the microscopy centre, a spot specimen is collected. This is a specimen obtained on the spot after coughing and clearing the throat. Although ideally this specimen should be obtained under the supervision of a staff member, when extremely high patient loads are present (such as at government hospitals like Tambaram), this will likely not be possible.
- The patient is given a sputum container for collection of an early morning specimen and instructed to come with this sputum sample on the next working day. Upon returning with the early morning collection of sputum (the second specimen), a third spot specimen should be collected from the patient.
- All specimens should be examined at the nearest microscopy laboratory, as a rule, by the Ziehl-Neelson method. (Technical Guidelines for TB Control, p. 6-7)
 - However, in places where large numbers of sputum smears are examined everyday, smears can be examined using fluorescent microscopy.



- Sputum microscopy (continued): If the first spot specimen is positive by microscopy and the patient does not return for the second sputum test, an immediate search must be made to find the patient to prevent dissemination of infection in the community.
- In the interest of the patient, second and third specimens of sputum must be collected and examined.
 - It is therefore important to note down the complete address of all symptomatic patients who are being evaluated. (Technical Guidelines for TB Control, p. 7)
- Children often have difficulty producing sputum for laboratory studies. In this case, early morning gastric aspirates can be used. Culture can be used to identify *M. tuberculosis*. (Baylor, p. 86)
- Chest X-ray: Chest X-rays can play an important role in diagnosing HIV+ TB patients as these individuals can have different manifestations of TB because of their immunosuppressed status.
 - An HIV+ patient may have a chest X-ray with shadows indicative of TB but not respond to typical treatment.
 - The chest X-ray is indicated in persons suspected of having TB who are sputum smear-negative and who do not respond to 2 weeks of antibiotic therapy.
 - No radiographic pattern is pathognomonic of TB, although the classical hallmarks of the disease are:
 - Cavitation
 - Apical distribution
 - Pulmonary fibrosis
 - Shrinkage
 - Calcification



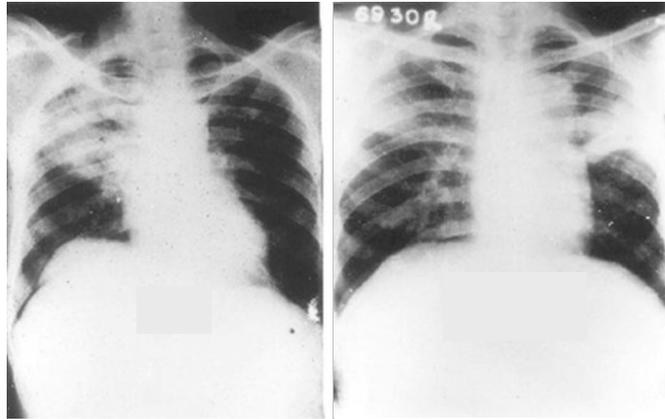
- HIV infected persons with a well preserved immune function will show these typical features.
 - However, as immune suppression worsens, chest X-rays more often show atypical findings such as:
 - Pulmonary infiltrates affecting the lower lobe
 - Intrathoracic lymphadenopathy
 - Miliary tuberculosis
 - Rarely a normal chest radiograph



- Hilar enlargement (right) and right superior mediastinal widening (left) due to tuberculous lymphadenopathy.



Pulmonary TB: Atypical



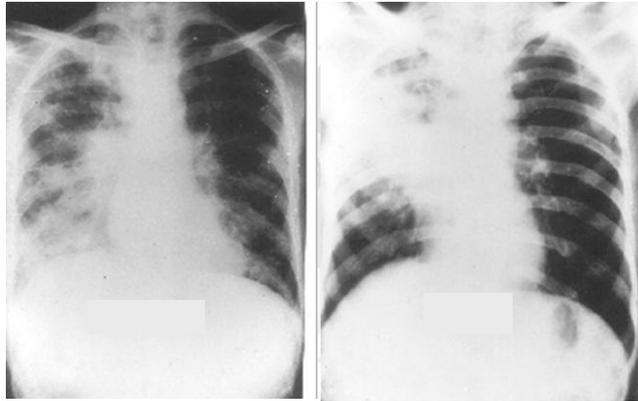
TB and Other Bacterial Infections

Slide 27

- Pneumonitis involving right upper lobe (left) and left upper lobe (right) due to tuberculosis.



Pulmonary TB: Progressive



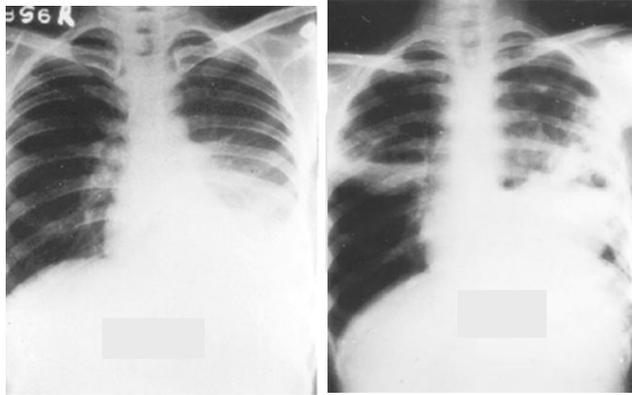
TB and Other Bacterial Infections

Slide 28

- Extensive lesion involving the lungs due to progressive tuberculosis.



Lower Lung-Field TB



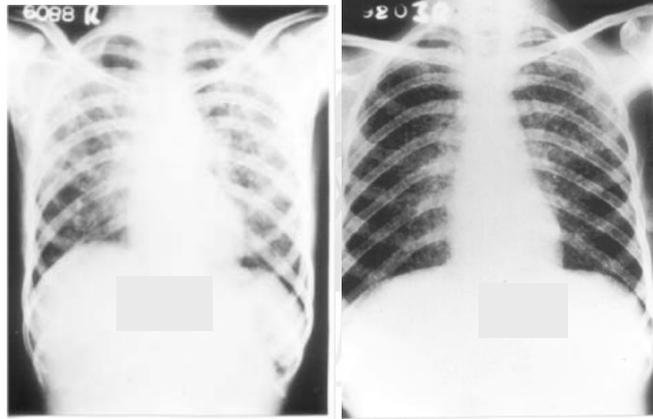
TB and Other Bacterial Infections

Slide 29

- Extensive pneumonitis involving the left lower lobe (left) and bilateral pneumonitis involving both lower lobes (right)



Miliary/Nodular



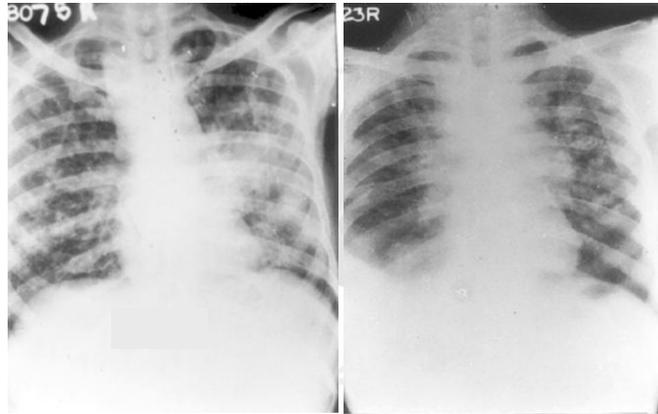
TB and Other Bacterial Infections

Slide 30

- Miliary mottling involving both the lungs.



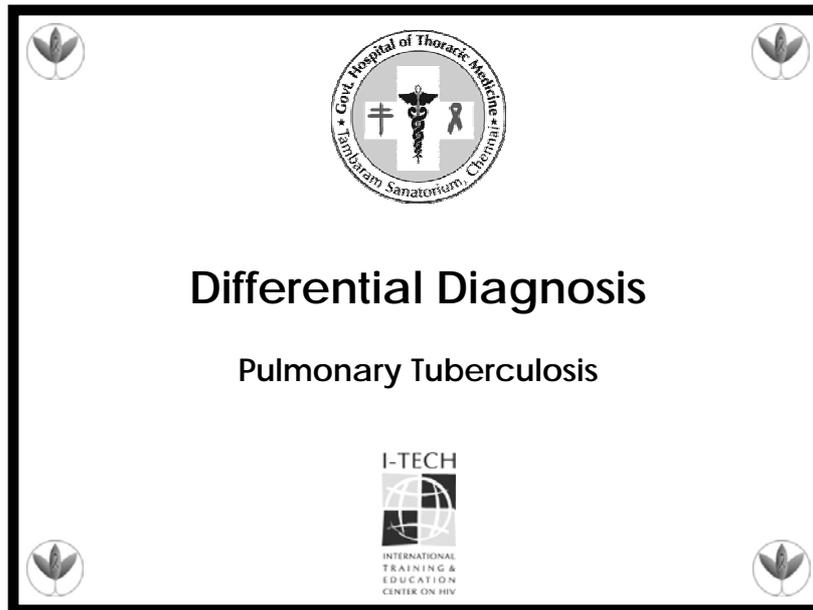
Disseminated



TB and Other Bacterial Infections

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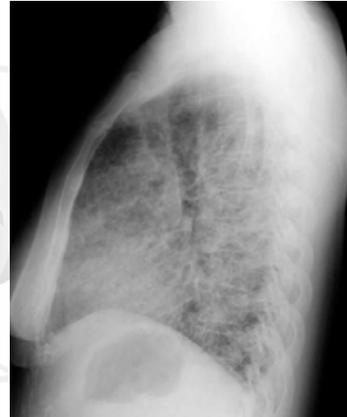
- Disseminated involvement of both the lungs.



- Disease other than TB can cause both the classical and atypical chest X-ray findings, and if sputum smears are negative, other conditions have to be considered in the differential diagnosis.
- Important HIV-related pulmonary diseases, which may be confused with pulmonary TB, are:
 - Bacterial pneumonias
 - Pneumocystis jiroveci pneumonia
 - Kaposi sarcoma
 - Fungal infections
 - Nocardiosis
 - Lymphoma
 - Others (CMV Pneumonitis)



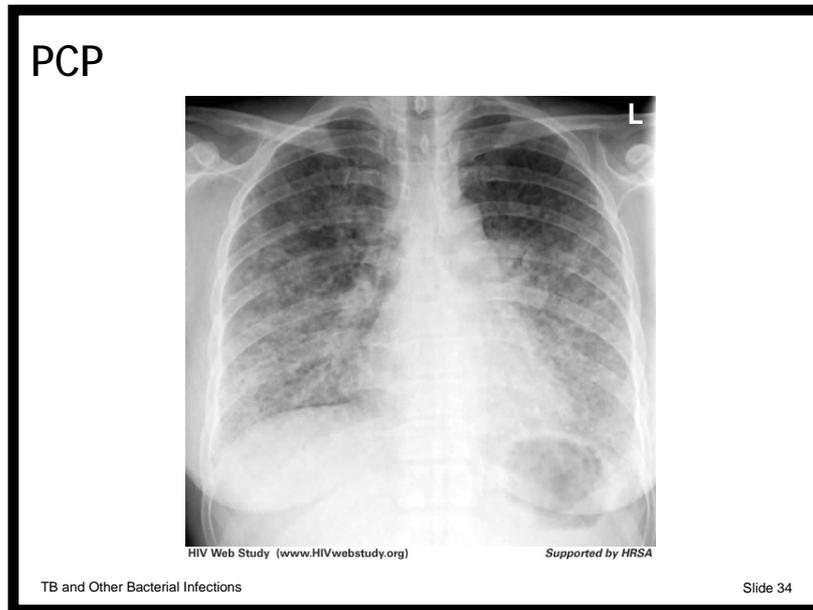
Pneumonia



TB and Other Bacterial Infections

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- 32 year old man presented with fever, chills, and dyspnoea
- Chest X-ray revealed pulmonary consolidation
- Gram stain-numerous polymorpho nuclear leucocytes and gram positive diplococci
- Blood culture-pneumococcus
- Four days later-bilateral diffuse infiltrations with pleural effusion



- Bilateral diffuse, infiltrates with a typical ground glass appearance of PCP



Differential Diagnosis

Kaposi Sarcoma	CMV Pneumonitis
	

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TB and Other Bacterial Infections

Slide 35

- Left slide-bilateral diffuse linear and nodular infiltrates
- Right slide-CMV pneumonitis confirmed by open lung biopsy and staining for inclusion body



B-Cell Lymphoma

Widened Mediastinum



Courtesy of University of Florida. © 1996-2000

TB and Other Bacterial Infections

Slide 36



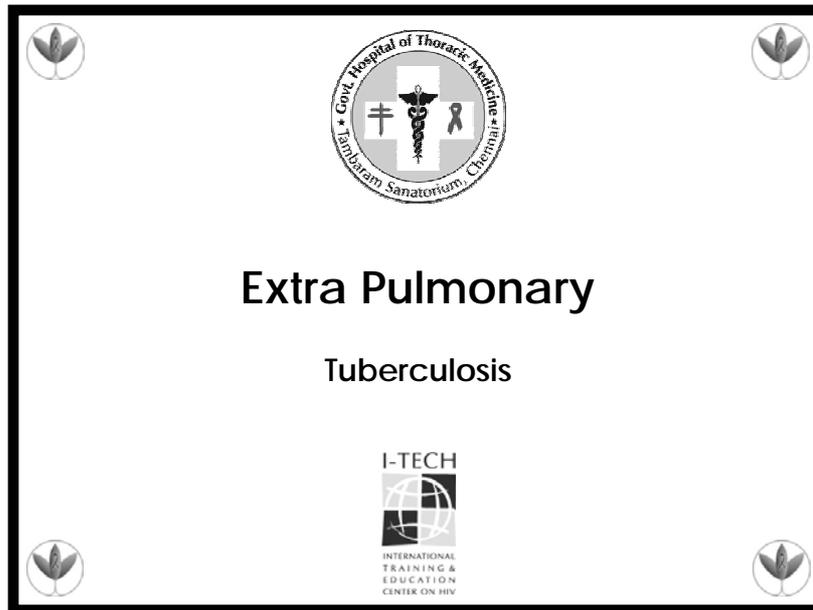
Early and Late Stages of HIV Infection

	Early Stage	Late Stage
Clinical Presentation	Often resembles Post-primary TB (Adult-type)	Often resembles Primary TB
Sputum Smear Result	Often positive	Often negative
Chest X-ray Appearance	Often shows cavities	Atypical presentation, often infiltrates Lower lung-field lesions, intra-thoracic lymph nodes & infrequent cavities

TB and Other Bacterial Infections

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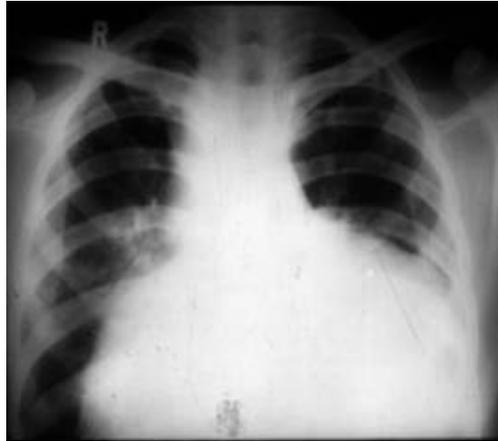
- This table highlights the differences between the PTB occurring in early and late stages of HIV infection. (NACO, Guidelines for Management of TB in HIV Infected)
- While sputum smears are more often negative in patients with HIV infection and TB, the Francis J. Curry National Tuberculosis Center in the US believes it is an overstatement to say that smears are often negative.



- HIV-infected patients very commonly develop extra-pulmonary tuberculosis.
- One common form appears as diffuse lymphadenopathy.
- If available, biopsy results will sometimes reveal granulomas, but most often, they are not seen.
 - Granulomas take place primarily in early immuno-suppressed patients.
 - Granulomas are areas in an organ where the tissue has been destroyed secondary to the body's reaction to the presence of disease.
- Both adult and paediatric patients may have tuberculosis in many different organs, including:
 - Lung
 - Spine, or
 - Central nervous system (Baylor, p. 86)



Pericardial Effusion



TB and Other Bacterial Infections

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- Chest X-ray showing typical appearance of pericardial effusion



Disseminated Tuberculosis



TB and Other Bacterial Infections

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- Ultrasound abdomen showing retro peritoneal and para-aortic lymphadenopathy



CNS & Tuberculosis



A case of tuberculous transverse myelitis responds to treatment with steroids and anti-tuberculous drugs

TB and Other Bacterial Infections

Slide 42

- A clinical picture of a patient with distended urinary bladder due to transverse myelitis



Tuberculosis Ascites



Abdominal ultrasound has to be done to identify retro-peritoneal lymph nodes.

TB and Other Bacterial Infections

Slide 40

- A patient with a typical clinical picture of ascites.



Lymph Node and Tuberculosis



Cervical Tuberculous Lymphadenitis:
FNAC is the test of choice

TB and Other Bacterial Infections

Slide 43

- An atypical feature of late-stage immunosuppression is TB lymphadenitis.
- Diagnosis in children can be made by a physician on the basis of:
 - Clinical symptoms
 - Positive Mantoux tuberculin skin test
 - Chest X-ray and
 - History of contact with a case of TB (Technical Guidelines for TB Control, p, 8)
- FNAC=fine needle aspiration cytology



Epitrochlear Lymph Node Abscess



AFB demonstrated in the pus

TB and Other Bacterial Infections

Slide 44

- Supra trochlear, axillary and bilateral cervical lymph node abscesses due to tuberculosis.



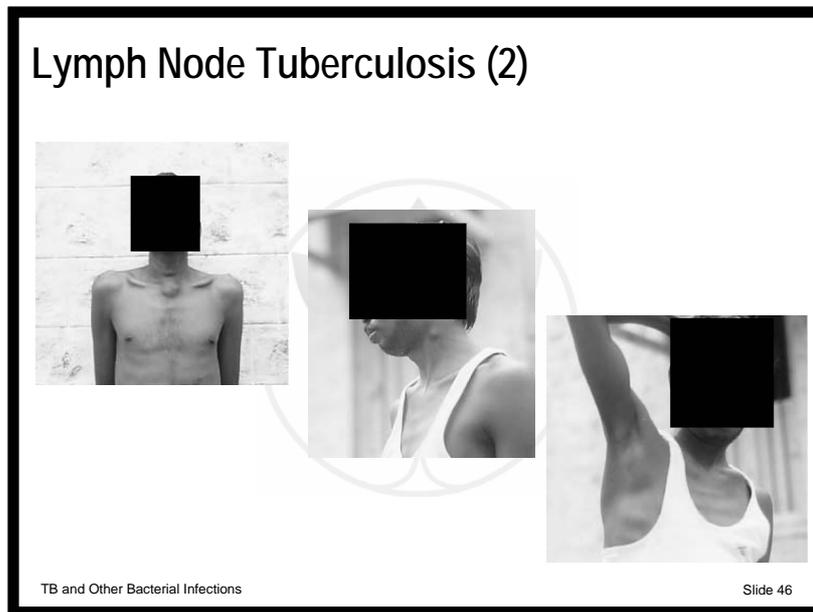
Lymph Node Tuberculosis (1)



TB and Other Bacterial Infections

Slide 45

- Tuberculous cervical and inguinal lymphadenopathy.



- Tuberculous cervical, axillary and supra sternal lymph node abscesses



Skin & Tuberculosis



Hyperkeratosis, hyperpigmentation of palm and sole



Skin Tuberculosis



TB and Other Bacterial Infections

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- Tuberculous ulcers involving skin-scrufuloderma



Healed Scrofuloderma

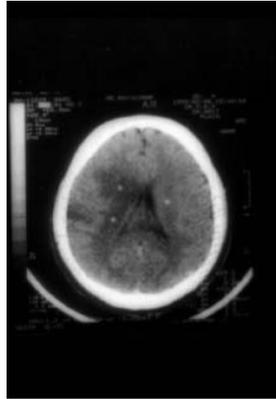


TB and Other Bacterial Infections

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Stroke in Young



- Mr.R. 25 Yrs. presented with stroke
- CT-scan showed ischemic infarct
- Probably tuberculous arteritis



Ruling out HIV (1)

- If any of the following conditions are present, HIV co-infection should be excluded:
 - Oral/oesophageal candidiasis
 - Chronic diarrhoea for more than one month
 - Herpes-zoster, especially multidermatomal
 - Recurrent pneumonia
 - Pneumocystis Jiroveci Pneumonia (PCP)
 - Oral hairy leukoplakia

TB and Other Bacterial Infections

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- In a patient with tuberculosis, if any of the following conditions are present, HIV co-infection should be considered (NACO, Guidelines for Management of TB in HIV Infected):
 - Oral/oesophageal candidiasis
 - Chronic diarrhoea for more than one month
 - Herpes-zoster, especially multidermatomal
 - Recurrent pneumonia
 - Pneumocystis jiroveci pneumonia (PCP)
 - Oral hairy leukoplakia



Ruling out HIV (2)

- If any of the following conditions are present, HIV co-infection should be excluded:
 - Present or past genital ulcerations
 - Kaposi sarcoma
 - Weight loss more than 10% within past 6 months
 - Generalized dermatitis
 - Fever of more than 1 month duration and pyrexia of unknown origin

TB and Other Bacterial Infections

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- In a patient with tuberculosis, if any of the following conditions are present, HIV co-infection should be considered (NACO, Guidelines for Management of TB in HIV Infected):
 - Present or past genital ulcerations
 - Kaposi sarcoma
 - Weight loss more than 10% within the past 6 months period
 - Generalized dermatitis
 - Fever of more than 1 month duration and pyrexia of unknown origin



Standard TB Treatment

- Recommended treatment by the Revised National Tuberculosis Control Programme guidelines (RNTCP):
 - Initial supervised phase of 2-3 months
 - Followed by a continuation phase of 4-5 months
 - Partially self-administered and checked by return of empty drug blister packs
- This treatment regimen must be modified when treating a patient co-infected with HIV and TB

TB and Other Bacterial Infections

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- Go over the “RNTCP Guidelines for Treatment of Tuberculosis” (Handout 4.1).
- Generally, treatment for TB includes:
 - An initial supervised phase of 2-3 months followed by
 - A continuation phase of 4-5 months, which is partially self-administered and checked by return of empty drug blister packs. (Technical Guidelines for TB Control, p. 12)
- This is the treatment recommended by the Revised National Tuberculosis Control Programme guidelines (RNTCP).



Acquired Drug Resistance and HIV

- Naturally occurring mutants resistant to one anti-tuberculosis drug exist in very small numbers
- Approximately 4-5% of HIV+ patients suffer from multiple drug-resistant TB
- Inappropriate anti-tuberculosis treatment or irregularity of medication:
 - Can cause a patient with drug-susceptible TB to develop drug-resistant TB
 - *Acquired drug resistance*
- Essential that correct drugs be given in the correct manner for the prescribed period

TB and Other Bacterial Infections

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- Every TB patient has millions of individual tubercle bacilli.
- Naturally occurring mutants resistant to one anti-tuberculosis drug exist in very small numbers and approximately 4-5% of HIV+ patients suffer from multiple drug-resistant TB.
- Inappropriate anti-tuberculosis treatment or irregularity of medication can cause a patient with drug-susceptible TB to develop drug-resistant TB.
 - This is called acquired drug resistance. To prevent this, it is essential that the correct drugs be given in the correct manner for the prescribed period. (Technical Guidelines for TB Control, p. 12)



Discussion: Drug Resistance

- What might happen if a patient with a drug-resistant strain of TB infects another person?



TB and Other Bacterial Infections

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- The tubercle bacilli which spread to the newly infected person are resistant to the same drug(s) as those of the source patient, even though the new patient has never taken these drugs in the past.
- This is called primary drug resistance. (Technical Guidelines for TB Control, p. 12)



Regimens for TB in HIV Patients: Treatment Category I

I	New smear positive pulmonary TB New smear negative, pulmonary TB, seriously ill New extra-pulmonary TB, seriously ill	2(EHRZ)3 (24 doses)	4(HR)3 (54 doses)
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TB and Other Bacterial Infections

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- Drug Regimens:
 - This table provides treatment regimens for the different categories of treatment and types of TB in an HIV Patient.
 - New cases of smear-positive pulmonary TB and clinically severely ill smear-negative pulmonary or extra-pulmonary TB cases should receive a six-month supervised short course chemotherapy (SCC).
 - The same applies for new, not-seriously-ill cases of smear-negative pulmonary and extra-pulmonary TB.
 - Retreatment of smear-positive relapses, previously-treated cases, and failures should receive an 8-month supervised SCC.
 - Patients with TB who refuse or are unable to take directly observed SCC or who cannot comply with SCC due to drug toxicity, should receive a 12-month self-administered standard regimen. (Technical Guidelines for TB Control, p. 17)
 - Although this regimen should be used in exceptional non-HIV cases, in HIV patients, such a protocol is advisable because of issues related to stigma and discrimination often associated with the disease.
 - The most important drugs used in the treatment of TB are:
 - Isoniazid (H)
 - Rifampicin (R)
 - Pyrazinamide (Z)
 - Streptomycin (S)
 - Ethambutol (E)



Regimens for TB in HIV Patients: Treatment Category II

II	Sputum smear positive relapses Sputum smear positive treatment failure cases Sputum smear positive cases, treatment after default	2(SEHRZ)3 + 1 (EHRZ)3 (24+12 doses)	5(HRE)3 (66 doses)
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TB and Other Bacterial Infections

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- Drugs and Regimens (continued)
 - The use of rifampicin or streptomycin for diseases other than mycobacterial diseases should be limited to very few indications and only be given after careful consideration.
 - Though these drugs are powerful antibiotics, their indiscriminate use in other diseases may lead to development of drug-resistant strains of *M. tuberculosis*. (Technical Guidelines for TB Control, p. 18)
 - Prefix = number of months
 - Suffix = number of doses in one week
 - H-Isoniazid
 - E-Ethambutol
 - R-Rifampicin
 - S-Streptomycin
 - Z-Pyrazinamide
 - For adults, drugs will be given in the recommended number of pills/capsules irrespective of body weight.
 - However, for patients weighing more than 60 kilograms, an additional capsule of rifampicin 150 mg will be added to the treatment regimen. (Technical Guidelines for TB Control, p. 18)
 - Duration of therapy: Treatment regimens recommended under RNTCP are the same irrespective of patient's HIV status. The duration of therapy will be as per treatment regimen and category. IF REQUIRED, DURATION OF THERAPY MAY BE EXTENDED WITHIN THE CURRENT RNTCP GUIDELINES.



Regimens for TB in HIV Patients: Treatment Category III

III	New smear negative, pulmonary TB, not seriously ill New smear negative, extra-pulmonary TB, not seriously ill	2(HRZ)3 (24 doses)	4(HR)3 (54 doses)
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Session 4: TB and Other Bacterial Infections

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Related Issues



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Treating New Cases and Children

- Newly diagnosed cases
 - Adults with new cases of AFB smear-positive pulmonary TB
 - Other newly diagnosed sputum-negative, seriously ill patients with severe forms of tuberculosis
- Dosage for children
 - Drugs are given in loose tablets according to body weight

TB and Other Bacterial Infections

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- Newly diagnosed cases should receive the regimen described on Handout 4.1, “Treatment of Tuberculosis”.
- Citation for dosage for children: Technical Guidelines for TB Control, p. 18
- The recommended dosages for children for daily and intermittent therapy are also shown in Handout 4.1, “Treatment of Tuberculosis.”



Retreatment

- For patients who have received anti-tuberculosis treatment for more than one month in the past
- Retreatment cases are at an increased risk of having multi-drug resistant disease. They include:
 - Smear-positive relapses
 - Smear-positive failure cases
 - Smear-positive patients being treated after default

TB and Other Bacterial Infections

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- *The retreatment regimen is described on Handout 4.1, "Treatment of Tuberculosis".*



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**TB and
ARV Therapy**



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TB and ARV Treatment

- Impact of ARVs on TB incidence
- Drug interactions
- Compatible TB and ARV regimens
- When to start ARVs
- Adverse reactions
- Paradoxical reactions

TB and Other Bacterial Infections

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- Patients with HIV and tuberculosis merit special consideration because of:
 - Drug interactions between NNRTIs/Pis and rifampicin.
 - Pill burden
 - Adherence and
 - Drug toxicity



Antiretroviral Therapy and TB

- Improved immune responses to TB with HAART
- Reduction in case rates of TB during HAART era
- HAART could reduce risk of primary infection, relapse and re-infection



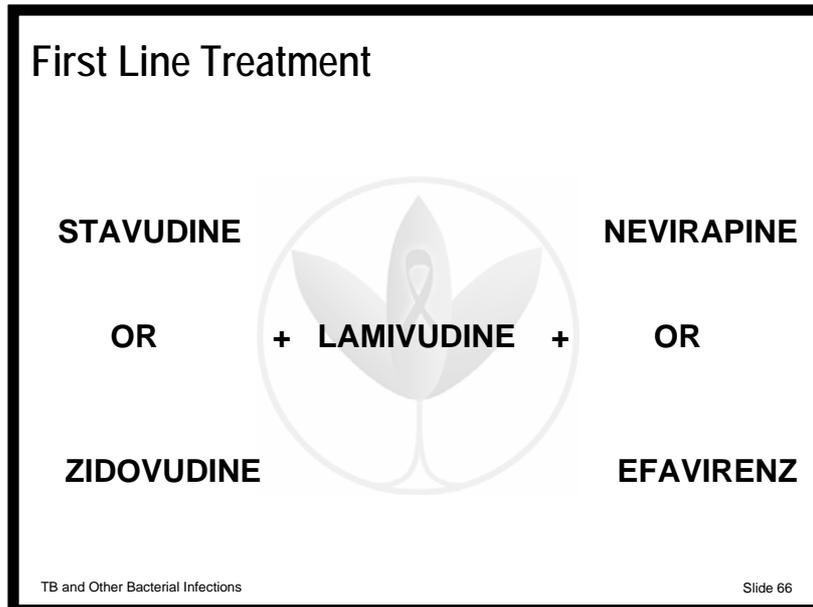
Initiation of ARV Therapy in TB Patients

- Start ARVs on all TB patients with a CD4 count <200
- Consider ARVs on all TB patients with a CD4 count < 350 (up to 200)
- In the absence of CD4 count, start ARVs on all TB patients

TB and Other Bacterial Infections

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- Optimal Time to Start ART in TB Patients:
 - Case fatality rate in many patients with TB during the first two months of TB treatment is high, PARTICULARLY when they present with advanced HIV disease, and ART in this setting may be life saving.
 - On the other hand, when deciding on the best time to begin treatment, keep in mind:
 - Pill burden
 - Drug-to-drug interaction
 - Potential toxicity
 - Immune reconstitution syndrome
 - The management of patients with HIV and TB poses many challenges, including that of achieving patient acceptance of both the diagnoses.
 - WHO recommends that ART in patients with CD4 cell counts below 200 cells mm^3 be started between two weeks and two months after the start of TB therapy, when the patient has stabilized on this therapy.
 - This provisional recommendation is meant to encourage rapid initiation of therapy in patients among whom there may be a high mortality rate.
 - However, deferring the start of ART may be reasonable in a variety of clinical scenarios.
 - For example, in patients with higher CD4 cell counts, the commencement of ART may be delayed until after the induction phase of therapy is completed in order to simplify the management of treatment.



- EFV: 600 or 800 mg
- The 800 mg dose of EFV achieves higher drug levels than those seen in the absence of Rifampicin and thus may reduce the chance of HIV drug resistance.
- However, it can also increase the toxicity risk.
- Other Combinations:
 - SOV/RTV 400/400 mg Bid,
 - SQV/r 1600/200 mg qd (in soft gel formulation-sgc) OR
 - LPV/r 400/400 mg bid
 - The current DHHS 4/7/05 guidelines suggest that this dosing of ritonavir with lopinavir is not well established.
 - In small pharmacokinetic studies, ritonavir 200 to 400 mg might be appropriate to boost LPV levels although there was a high incidence of hepatotoxicity (28%) suggesting that close monitoring is necessary
 - In combination with NRTI backbone are alternatives to EFV.
 - ABC is another alternative to EFV (concerns-hypersensitivity syndrome)
- Rifampin should not be used with boosted SQV since a higher incidence of hepatotoxicity was seen when 600 mg rifampin was used with RTV 100 + SQV 1000 mg BID in a pharmacokinetic study.
- Suggest LPV/r 400/400 mg



Discussion Question

- What are drug interactions between ATT and ARVs?





TB and ARV Treatment Drug Interactions

- Rifampicins stimulate cytochrome P450 liver enzyme system that metabolizes PIs and NNRTIs
- Protease inhibitors and NNRTIs can enhance or inhibit this system leading to altered blood levels of RIF



Rifampicin Interactions for NNRTIs and PIs (1)

Antimycobacterials	NVP	EFV	IDV
Rifampin	Decreased 37% <i>Recommendation: Do not co-administer</i>	Decreased 25-33% <i>Recommendation: Consider EFV 800 mg daily</i>	Decreased 89% <i>Recommendation: Do not co-administer</i>

AMPRENAVIR : 81% ; RITONAVIR : 35%

TB and Other Bacterial Infections

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- NVP levels decrease 20-58% with rifampin.
- Also the potential for additive hepatotoxicity exists and this combination is not recommended



Rifampicin Interactions for NNRTIs and PIs (2)

Antimycobacterials	LPV AUC	NFV	SQV
Rifampin	Decreased 75% <i>Recommendation:</i> Do not co-administer	Decreased 82% <i>Recommendation:</i> Do not co-administer	Decreased 84% when given without RTV <i>Recommendation:</i> Do not co-administer

AMPRENAVIR : 81% ; RITONAVIR : 35%

TB and Other Bacterial Infections

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- Rifampin should not be used with boosted SQV since a higher incidence of hepatotoxicity was seen when 600 mg rifampin was used with RTV 100 + SQV 1000 mg BID in a pharmacokinetic study.



Efavirenz in HIV & TB

- In the absence of Rifampicin
 - EFV dose : 600 mg
- In the presence of Rifampicin
 - EFV dose : 800 mg
 - Reduce chance of Drug Resistance
 - Risk of Drug Toxicity

TB and Other Bacterial Infections

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- Increasing EFV to 800 mg daily is not always necessary and increases the risk of toxicity.



Alternatives to Efavirenz

SQV/r	400/400 mg 1600/200 mg	bid qd in SGC
LPV/RTV	400/400 mg	bid
ABC	300 mg	bid

TB and Other Bacterial Infections

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- Rifampin should not be used with boosted SQV since a higher incidence of hepatotoxicity was seen when 600 mg rifampin was used with RTV 100 + SQV 1000 mg BID in a pharmacokinetic study.



Nevirapine & Rifampicin

- Data limited and conflicting
- NVP are reduced in presence of Rifampicin
- Higher Rifampicin doses : some clinical reports
 - Adequate viral and immunological response
 - Acceptable toxicity
 - NVP should only be considered when no other options are available



Discussion Question

- What is the ART regimen for pregnant women?





ART in Pregnant Women

STAVUDINE
OR
ZIDOVUDINE



+ LAMIVUDINE +

NEVIRAPINE
SQV/r
OR
ABACAVIR



ART Recommendations for Individuals with TB & HIV (1)

ART Recommendations for Individuals with TB & HIV (1)		
CD4 < 200 mm³	Start TB treatment. Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months) EFV containing regimens	Recommended ART. EFV is contraindicated in pregnant women or women of childbearing potential without effective contraception

TB and Other Bacterial Infections

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- Go over the “ART Recommendations for Individuals with TB-HIV Co-infection” (Handout 4.2).



ART Recommendations for Individuals with TB & HIV (2)

CD4 between 200-350 mm³	Start TB treatment. Start one of the below regimens after initiation phase (if severely compromised start earlier): EFV containing regimens (2) or NVP containing regimens in case of rifampicin-free continuation phase TB treatment regimen	Consider ART
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Session 4: TB and Other Bacterial Infections

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ART Recommendations for Individuals with TB & HIV (3)

CD4 > 350 mm ³	Start TB Treatment	Defer ART
CD4 not available	Start TB Treatment	Consider ART

TB and Other Bacterial Infections

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HIV Infected Children

- For an HIV infected child with TB having significant HIV symptoms and/or severe immunodeficiency, the choice of regimen is similar to those for adults and include:
 - The triple NRTI regimen (AZT+3TC+ABC) or
 - A regimen of two NRTIs and efavirenz, an NNRTI, in children over 3 years

TB and Other Bacterial Infections

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- If an HIV infected child with tuberculosis has significant HIV symptoms and/or severe immunodeficiency and requires the initiation of ART, the considerations about the choice of regimen is similar to those for adults and include:
 - The triple NRTI regimen (AZT+3TC+ABC) or
 - A regimen of two NRTIs and efavirenz, an NNRTI, in children over 3 years.
- There are advantages in starting therapy using triple NRTI consisting of ABC, ZDV and 3TC because of:
 - The frequency of suspected, empirically treated or proven tuberculosis disease in HIV infected children in resource limited settings and
 - Lack of interactions of this combination of ARVs with anti-tuberculosis medications.



Discussion Question

- What are paradoxical reactions in tuberculosis?





Paradoxical Reactions in Tuberculosis

- Transient worsening of clinical signs and symptoms after initial response to anti-tuberculosis therapy

TB and Other Bacterial Infections

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- Paradoxical reactions are also called immune reconstitution inflammatory syndrome (IRIS) or simply immune reconstitution syndrome.



Paradoxical Reactions in Tuberculosis and HIV Co-infection

- Can happen with any antiretroviral regimen
- Mean onset of symptoms is 2 weeks
- Mean duration of symptoms is 3 weeks
- Most common symptoms include fever, cervical lymphadenopathy, intrathoracic lymphadenopathy
- Associated with restoration of tuberculosis reactivity

TB and Other Bacterial Infections

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- Examples of paradoxical reactions in tuberculosis and HIV co-infection:
 - The chest X-ray prior to ARV is clear whereas the chest X-ray after ART shows a cavitory lesion with surrounding pneumonitis.
 - The chest X-ray prior to ARV is clear whereas the chest X-ray after ART shows left basal pneumonitis



Managing TB and ARV Therapy

- Include experienced HCW in management
- Address adherence
- Help patient adjust to TB and HIV diagnoses
- Manage initial side effects from TB rx first
- Don't switch from 1st line TB drugs without evidence of significant side effect
- Discuss paradoxical reactions

Source: Burman and Jones, AJRCCM 2001

TB and Other Bacterial Infections

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Respiratory Infections



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Respiratory Infections

- Bacterial lower respiratory tract infections more frequent and severe in immunosuppressed persons with HIV
- Pneumonia caused by *Streptococcus pneumoniae* may be first indication of HIV infection
- Other causes of pneumonia in persons with HIV include *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*
 - *Haemophilus influenzae* in children.

TB and Other Bacterial Infections

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- Bacterial lower respiratory tract infections are common in the general population.
 - They are more frequent and more severe in immunosuppressed persons with HIV infection.
- Pneumonias are typically classified as either:
 - Community Acquired:
 - Occurs outside of the hospital or less than 48 hours after admission in a patient who is not hospitalized or residing in a long term care facility for more than 14 days before the onset of symptoms
 - Hospital Acquired (Nosocomial)
 - Occurs more than 48 hours after admission to the hospital and excludes any infection present at the time of admission.
 - Anaerobic pneumonias and lung abscesses can occur in both settings.
- Causative organisms:
 - The organisms are the same as those found in the HIV negative general population.
 - Pneumonia caused by *Streptococcus pneumoniae* may often be the first indication of HIV infection.
 - Other causes of pneumonia in persons with HIV infection include:
 - *Klebsiella pneumoniae*
 - *Pseudomonas aeruginosa* and *Staphylococcus aureus*
 - *Haemophilus influenzae* in children.
 - Opportunistic organisms like *Pneumocystis jirovecii* (carinii), MAC, Tuberculous bacilli and cytomegalo virus, can also occur.
 - Fungal, protozoal and helminthic infections also cause pneumonias.



Pneumonia and Lower Respiratory Tract Infections

- Opportunistic organisms like *Pneumocystis jiroveci*, MAC, tuberculous bacilli and cytomegalovirus, can also occur
- Fungal, viral, protozoal and helminthic infections can also cause pneumonias

TB and Other Bacterial Infections

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- Besides bacterial pneumonia and *Pneumocystis jiroveci* (*carinii*) pneumonia, lower respiratory tract infections in HIV-infected immunosuppressed persons may be the result of fungal and viral infections.
 - These are difficult to diagnose without sophisticated laboratory facilities and difficult to treat without effective agents.
- Viral pneumonias may be caused by:
 - Herpes simplex virus
 - Herpes zoster virus
 - Cytomegalovirus
- Fungal pneumonia may be due to:
 - *Histoplasma capsulatum* (not common in India)
 - *Cryptococcus neoformans*
 - *Aspergillus fumigatus*
- It should be remembered, however, that tuberculosis is probably the most common opportunistic infection encountered among immunosuppressed persons with HIV infection in the developing world. (Zim, TB and other Bacterial)
- Atypical infections and TB should always be suspected in persons with pneumonia that fail to respond to treatment with the standard recommended regimens.
- HOWEVER, making a specific diagnosis of fungal and other infections requires sophisticated laboratory tests.



Clinical Features

- Cough
- Chest pain
- Dyspnoea
- Tachypnoea
- Systemic signs-myalgia, headache and loss of appetite
- Purulent sputum
- Fever
- Tachycardia
- Cyanosis if severe
- Diminished air entry in the lungs
- Coarse crackles and pleural rub

TB and Other Bacterial Infections

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- Patients with bacterial pneumonia present with:
 - Cough
 - Fever
 - Systemic symptoms of:
 - Myalgia
 - Headache
 - Loss of appetite
- They often have chest pain, difficulty in breathing, and tachypnoea, and they may also have haemoptysis.
- Patients may present with:
 - Classic lobar pneumonia
 - Bronchopneumonia, or
 - Unresponsive and atypical pneumonia (Zim, TB and other Bacterial)



Diagnosis

- Diagnosis is usually made on clinical grounds
- Chest x-ray reveal lobar consolidation, diffuse lung infiltrates, or atypical changes including cavitary disease
- Causative agent may be identified by sputum tests and blood culture

TB and Other Bacterial Infections

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- The diagnosis of pneumonia is usually made on clinical grounds.
- An acute illness characterized by cough, purulent sputum, and fever.
- Other symptoms are:
 - Aches and pains
 - Vomiting
 - Anorexia
 - Pleuritic chest pain
 - Dyspnoea
- Physical signs:
 - Fever
 - Tachycardia
 - Cyanosis if severe
 - Diminished air entry in the lungs
 - Coarse crackles
 - Pleural rub
- Radiologic changes on chest X-ray may reveal:
 - Lobar consolidation
 - Patchy consolidation
 - Diffuse lung infiltrates, or
 - Atypical changes including cavitary disease



Haemophilus Influenzae

Note the patchy infiltrates and thickened interstitial markings throughout. The radiograph is non-specific.



Courtesy of Mary Johnson, Indiana State University. © 2003-2005.



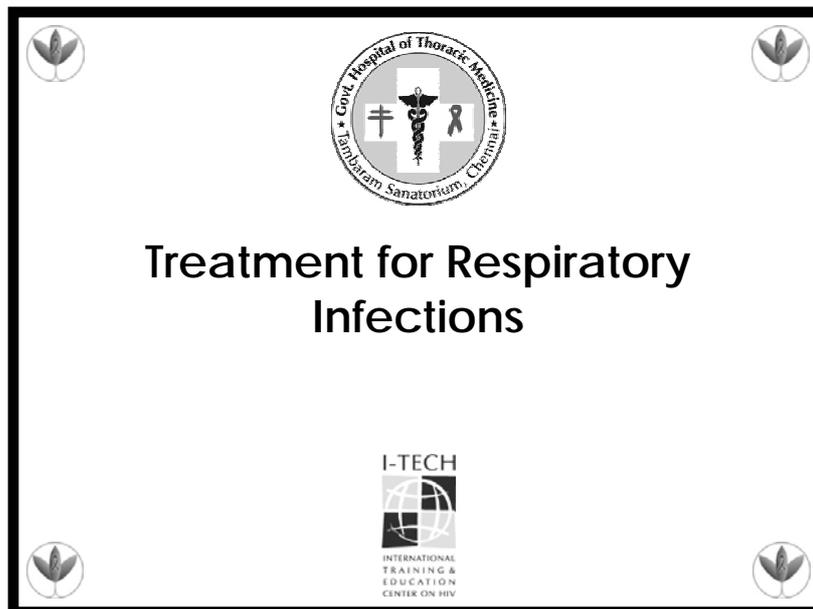
Other Tests

- Sputum for bacterial culture and sensitivity
- Blood for bacterial culture and sensitivity

TB and Other Bacterial Infections

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- The causative agent may be identified by sputum examination and by blood culture.
- The diagnosis of HIV infection should be suspected in any person presenting with pneumonia who is at risk for infection or has clinical features suggestive of HIV infection.
- Often bacterial pneumonias are the cause of death in persons with advanced immunosuppression and AIDS. (Zim, TB and other Bacterial)
- Atypical infections and TB should always be suspected in persons with pneumonia that fail to respond to treatment with the standard recommended regimens.
 - However, making a specific diagnosis of fungal and other infections requires sophisticated laboratory tests. (Zim, TB and other Bacterial)



- Treatment:
 - Rest
 - Fluids
 - Regular analgesics for pain
 - Paracetamol for fever
 - Antibiotics
- Hospital admission is required in following situations:
 - Poor social support
 - Present with confusion, shock, & dehydration, with suspected complications.



Treatment for Respiratory Infections

- Outpatient treatment
 - Initial empirical therapy
 - Alternate therapy
- Hospitalized patients
 - General medical wards
 - Intensive care wards

TB and Other Bacterial Infections

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- *Go over the Respiratory Infections section of “Treatment for Bacterial Infections” (Handout 4.3) using slides in the PowerPoint presentation.*
- *Ask participants if they have any questions.*
- Duration of therapy:
 - The decision is influenced by:
 - Severity of illness
 - Etiologic agent
 - Response to therapy
 - Other medical problems and complications
 - Therapy until the patient is afebrile for at least 72 hours is usually sufficient for *S. pneumoniae*.
 - A minimum of two weeks therapy is appropriate for *S. aureus* and *P. aeruginosa*, *Klebsiella*, etc.
 - Route of administration depends upon whether patients can take the drugs orally or not, absorption of oral drugs and other general factors.



Hospital Acquired Pneumonia (1)

- Occurs more than 48 hours after admission to the hospital and excludes any infection present at the time of admission
- At least two of the following signs and symptoms:
 - Fever
 - Cough
 - Leukocytosis
 - Purulent sputum

TB and Other Bacterial Infections

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- Common organisms for hospital acquired pneumonia
 - Pseudomonas aeruginosa
 - Staphylococcus aureus
 - Enterobacter
 - Klebsiella pneumoniae
 - Escherichia coli etc.
- Treatment:
 - Therapy should be started as soon as pneumonia is suspected
 - Initial therapy must be broad in spectrum and tailored to the specific clinical settings.
 - Since in patients with CD4 cell count less than $200/\text{mm}^3$, Pneumocystis jiroveci (carinii) also produce a similar appearance on X-ray, the patients may also be treated with Trimethoprim-sulphmethoxazole (Refer-session on PCP)



Hospital Acquired Pneumonia (2)

- New or progressive parenchymal infiltrate on chest radiograph
- Common in patients admitted in intensive care units



Considerations in HIV/AIDS and Pneumonias

- Any pathogen can cause pneumonia in HIV/AIDS patients
- Clinical tools to narrow the differential diagnosis:
 - Knowledge of underlying immunologic defects
 - Time course of infection
 - Fulminant course
 - Insidious course
 - Chest X-ray is rarely helpful in narrowing the differential diagnosis
 - Examination of expectorated sputum

TB and Other Bacterial Infections

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- Knowledge of underlying immunologic defects:
 - Defects in humoral immunity predispose to bacterial infections and the defect in cellular immunity leads to infections with viruses, fungi, mycobacteria, and protozoa.
- Time course of infection also provides clues to the etiology.
 - A fulminant course is often due to bacterial infection whereas an insidious course is more apt to be caused by viral, fungal, protozoal, and mycobacterial infections.
- Examination of expectorated sputum is important and may preclude the need for expensive, invasive diagnostic procedures.
 - Sputum induction is often necessary for diagnosis.
- Routine evaluation frequently fails to identify a causative organism.
- The clinician may begin empirical antimicrobial therapy and proceed to invasive procedures such as:
 - Bronchoscopy
 - Transthoracic needle aspiration or
 - Open lung biopsy
- The approach to management must be based on:
 - Severity of respiratory infection
 - Underlying disease
 - Risks of empirical therapy
 - Local expertise and experience with diagnostic procedures.



Enteric Infections



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Enteric Infections (1)

- Gastrointestinal infections commonly encountered in persons with HIV infection
 - May be:
 - Bacterial
 - Viral
 - Fungal
 - Protozoan
 - Helminthic
 - May involve:
 - Lips
 - Mouth
 - Oesophagus
 - Stomach
 - Small and large intestines
 - Rectum
 - Anus

TB and Other Bacterial Infections

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- Gastrointestinal infections are commonly encountered in persons with HIV infection. Infections may be:
 - Bacterial
 - Viral
 - Fungal
 - Protozoan
 - Helminthic.
- Infection of the gastrointestinal tract may involve:
 - Lips
 - Mouth
 - Oesophagus
 - Stomach
 - Small and large intestines
 - Rectum and anus (Zim, TB and other Bacterial)



Enteric Infections (2)

- HIV can cause enteropathy leading to:
 - Acute, acute-to-chronic, or chronic diarrhoea
 - Weight loss
 - Fever
 - Oro-pharyngeal candidiasis
- Malabsorption as a result of sub-total villous atrophy may also occur, though more common in children
- Perianal lesions such as bacterial skin infections may occur



Invasive Candida Oesophagitis

- The typical endoscopic appearance of candida oesophagitis presents as superficial white plaques on the mucosa
- Oesophageal candidiasis in patients with advanced HIV diseases can result in either superficially invasive disease or deep discrete ulcers

TB and Other Bacterial Infections

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- HIV can cause an enteropathy leading to acute, acute-on-chronic, or chronic diarrhoea.
- Patients with HIV enteropathy often also have:
 - Weight loss
 - Fever
 - Oro-pharyngeal candidiasis.
 - Weight loss can be quite severe.
 - Malabsorption as a result of sub-total villous atrophy may also occur, though this is more common in children.
- Perianal lesions such as bacterial skin infections, anal warts, and herpes may occur.
- Persons with HIV infection may have anorexia, nausea and vomiting, and are prone to gastrointestinal infection with a number of pathogens.
- These are shown in Handout 4.2, "Treatment of Bacterial Infections." (Zim, TB & Bacterial)
- *Go over treatment of Enteric Infections in "Treatment of Bacterial Infections" (Handout 4.3).*
- *Ask participants if they have any questions*



Discussion: Treating Enteric Infections

- Which of these infections do you commonly see at Tambaram?
- Have you found useful ways of distinguishing which infection a patient has?
- Do you know of other ways of treating the symptoms?



Other Bacterial Infections



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Atypical Mycobacteriosis (1)

- Mycobacterium avium complex disease (MAC) not commonly encountered in India
 - Prevalence in HIV-infected immunosuppressed persons in other parts of developing world not known
- Symptoms of disseminated MAC are non-specific and include:
 - Fever
 - Weight loss
 - Night sweats
 - Diarrhoea
 - Wasting

TB and Other Bacterial Infections

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- Atypical mycobacteria is a term coined to designate those organisms that stood apart from the Mycobacterium tuberculosis complex and the causative agent of Hansen's disease.
 - Among the earliest "atypicals" were organisms that belonged to the group known as Mycobacterium intracellulare of the "Battey bacillus," a group of acid fast staining respiratory pathogens causing a clinical picture indistinguishable from pulmonary tuberculosis.
 - Some more organisms were added to this list of atypical group.
 - Mycobacterium avium complex included M. avium and M. intracellulare.
- MAC organisms are ubiquitous in the environment, found in water, soil, and food.
- Transmission occurs via inhalation and ingestion.
- Both the respiratory tract and the gastro intestinal tract may be colonized before dissemination.
- However most patients have no evidence of colonization before developing disseminated disease.
- There is no evidence for person to person transmission. Current evidence points to newly acquired infection rather than activation of latent infection as the most likely precursor of the disseminated disease.
- Mycobacterium avium complex disease (MAC) is not commonly encountered in India, and its prevalence in HIV-infected immunosuppressed persons in other parts of the developing world is not known.



Atypical Mycobacteriosis (2)

- Organisms may be found in blood, secretions, and excreta of infected persons
- MAC can be grown in culture, but grows slowly. Acid-fast staining of bacilli will be positive, if available

TB and Other Bacterial Infections

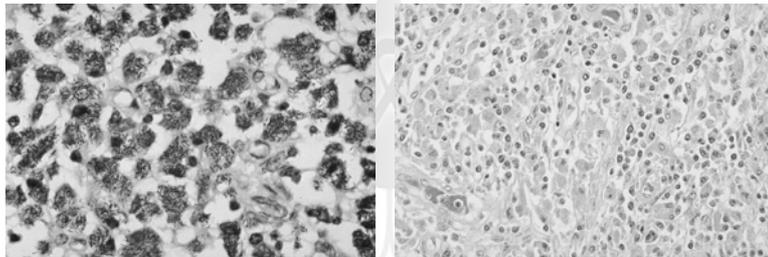
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- Symptoms of disseminated MAC are non-specific and include:
 - Fever
 - Weight loss
 - Night sweats
 - Diarrhoea
 - Wasting
- Organisms may be found in blood, secretions, and excreta of infected persons. (Zim, TB & Bacterial)
- MAC can be grown in culture, but it grows slowly.
- Acid-fast staining of bacilli will be positive, if available. (Baylor, p. 87)
- Clinical syndromes:
 - Asymptomatic colonisation of the respiratory or gastrointestinal tract
 - Found when investigating for other OIs
 - Transient MAC bacteremia has been described.
 - Colonisation may or may not progress to disseminated disease and the duration of colonization before dissemination can be quite variable and prolonged.



Mycobacterium Avium

Mycobacterium Avium shown in the Lymph Node



Courtesy of Public Health Image Library/CDC/Dr. Edwin P. Ewing, Jr.

TB and Other Bacterial Infections

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- It causes fever, weight loss and malabsorption.
- MAC is visible on histologic sections stained with acid fast stain. In this micrograph these organisms are present extensively in foamy macrophages. And often they do not form granulomas.
- Localized infection
 - Symptomatic localized infection is uncommon, but may occur in the gastrointestinal or upper respiratory tract.
 - Focal pneumonia may present as a chronic, dry cough.
 - Chest X-ray usually reveals either patchy or nodular infiltrates and there may be associated hilar or mediastinal lymphadenopathy.
 - Similar radiological findings occur in up to 5% of patients with disseminated disease MAC infection.
 - Localised disease of the gastro intestinal tract generally involves the small bowel and causes large volume, watery diarrhoea associated with cramping abdominal pain, malabsorption and severe weight loss.
 - At endoscopy the duodenal mucosa reveals a characteristic patchy, yellow/white pseudo membrane.
 - Localised lymphadenitis most commonly involves the anterior and posterior cervical chain and axillary nodes. Individuals often complain of fever and lethargy.



MAC: Disseminated Disease

- The most common presentation of MAC infection:
 - Patients complain of fever, night sweats, progressive weight loss
 - Up to half have watery diarrhoea, cramping abdominal pain, and nauseous and vomiting
 - Weakness and lethargy are also common
 - As tissue invasion occurs, primarily to the reticulo- endothelial system, lymphadenopathy (intra abdominal in particular) and hepato splenomegaly
 - Hepatic involvement is usually asymptomatic, but markedly elevated serum alkaline phosphatase levels may be used as an indicator of disseminated disease
 - Bone marrow involvement is often signaled by anaemia and increasing blood transfusion requirements. Symptoms due to other organ involvement are extremely rare

TB and Other Bacterial Infections

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- Diagnosis:
 - Clinical recognition
 - HIV-infected individuals with severe immuno deficiency and present with:
 - Persistent fever
 - Night sweats
 - Weight loss, and
 - Are found to be anaemic.
 - Laboratory diagnosis
 - Direct microscopic detection is appropriate for bone marrow, lymph node and liver biopsy specimens.
 - BACTEC culture system – detected in most blood cultures within two weeks.



Atypical Mycobacteriosis First-Line Treatment

First-Line Treatment				
Clarithromycin	500mg	bid	PO	12+ months
PLUS				
Ethambutol	15mg/kg	qd	PO	12+ months

TB and Other Bacterial Infections

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- Treatment:
 - Effective drug combination therapy can resolve or ameliorate the debilitating symptoms.
 - The drugs used are:
 - Azithromycin
 - Rifabutin
 - Ethambutol
 - Clarithromycin
 - Other drugs which can be used are:
 - Amikacin
 - Clofazimine
 - Ciprofloxacin
 - Rifampin
 - Sparfloxacin
 - Treatment for MAC requires at minimum a two-drug regimen including clarithromycin and ethambutol.
- *Details about the drug regimen are shown on Handout 4.3, "Treatment of Bacterial Infections."*
- *Go over the recommended dosages listed on the handout.*



Atypical Mycobacteriosis Prophylaxis

Children (0-12 years)	Clarithromycin 7.5 mg/kg by mouth twice daily	Azithromycin 20 mg/kg by mouth weekly or rifabutin (>6 y/o) 300 mg by mouth daily
Adults (>12 years)	Clarithromycin 500 mg by mouth twice daily	Azithromycin 1.2 g by mouth weekly or rifabutin 300 mg by mouth daily

TB and Other Bacterial Infections

Slide 107

- The CD4+ lymphocyte count is used as the indicator to start primary prophylaxis.
- In adults, prophylaxis is recommended once the CD4+ lymphocyte count is less than 100 cells/ul.
- For children, CD4+ lymphocyte counts vary with age, but if they are below 15 percent, prophylaxis is recommended. (Baylor, p. 87)



Staphylococcal Folliculitis (1)

- Skin infection localized to the hair follicle
- Lesions are small (less than 5mm in diameter), multiple, erythematous follicles that may have a centre of pus
 - Lesions are itchy and are often found in clusters
 - Usually the condition is caused by *Staphylococcus aureus*, although other organisms may also cause the infection
 - In HIV-infected persons, a pustular perifolliculitis occurs commonly

TB and Other Bacterial Infections

Slide 108

- Folliculitis is a skin infection localised to the hair follicle.
- Clinical Features and Diagnosis:
 - Folliculitis is often misdiagnosed as acne.
 - Folliculitis of other causes:
 - *Pityrosporum ovale* (intra follicular yeast)
 - *Demodex folliculorum* (intracellular mite)
 - Eosinophilic inflammation without a detectable infectious agent in eosinophilic folliculitis



Staphylococcal Folliculitis (2)

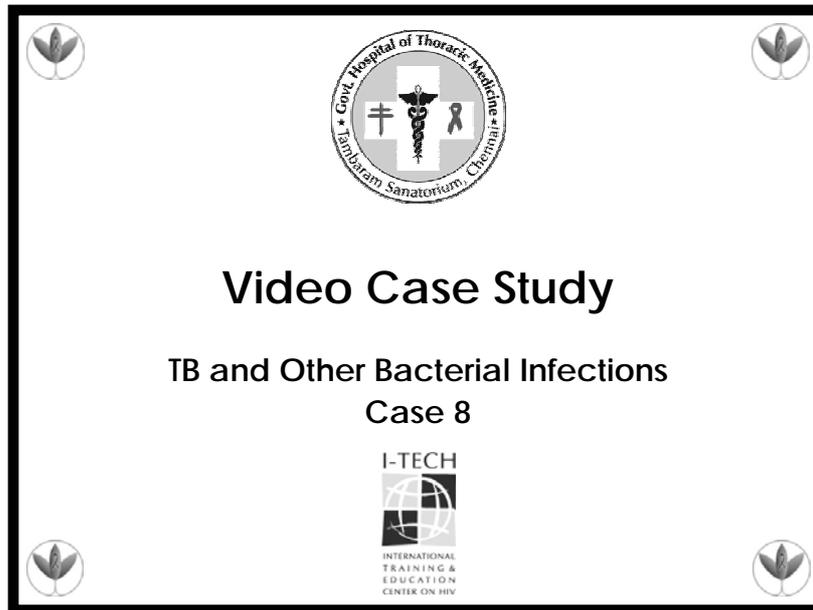
- Treatment is with antibiotics such as cephalexin or cloxacillin 500mg PO qid for 7-21 days



TB and Other Bacterial Infections

Slide 109

- Treatment:
 - P. ovale – Topical or systemic anti fungal agents
 - D. Folliculorum – Permethrin cream or metronidazole
 - Eosinophilic- Topical steroids , photo therapy with UVB, and/or PUVA
 - General measures: antihistamines



- Refer to TB and Other Bacterial Infections Video Case Study Case 8 (Worksheet 4.2).



Key Points

1. Tuberculosis is the most common opportunistic infection among HIV-infected persons
2. Tuberculosis in HIV-infected persons can respond well to standard anti-TB regimens advocated in the DOTS regimen
3. Bacterial pneumonias occur commonly in persons with HIV infection and are often the cause of death among people infected with HIV
4. Bacterial infections can be treated using drug therapy

TB and Other Bacterial Infections

Slide 111

- If time permits and participants are willing, tour wards within Tambaram to observe cases.
- Then reconvene to discuss what participants have seen.



Clinical Management of Opportunistic Infections

Participant's Handbook

Session 5

Malignancies Associated
with Immunosuppression

Session 5: Malignancies Associated with Immunosuppression

Aim: The aim of this unit is to introduce participants to malignancies associated with immunosuppression.

Learning Objectives: By the end of this session, participants will be able to:

- Describe the various clinical presentations and relative frequencies of the following opportunistic infections:
 - Kaposi sarcoma
 - Lymphoma
 - Cervical cancer
- Identify the appropriate procedures and laboratory investigations required to make a diagnosis of each of the above opportunistic infections.
- Cite the preferred treatment regimen for each of the above opportunistic infections.
- Explain the recommended prophylactic regimens and cite the guidelines for initiation and discontinuation of prophylaxis for the above opportunistic infections.

Key Points

1. Physicians must think in terms of not only the possibility of opportunistic infections but also malignancies when diagnosing and treating HIV-positive patients.
2. Kaposi sarcoma is a type of cancer that is more aggressive and common in HIV-infected persons than in the general populace. Kaposi sarcoma is very rare in South India.
3. AIDS-related lymphoma, a disease in which cancer cells are found in the lymph system in patients who have AIDS, can be difficult to treat because of patients' compromised immune systems.
4. The incidence of cervical dysplasia, a precursor to cervical cancer, is increased in HIV-infected women.
5. Kaposi sarcoma, lymphoma, and cervical cancer can be treated through radiation therapy, chemotherapy, and surgery.

Stages of Cervical Cancer

Stage	Test Results	Treatment Options
Stage 0	Cancer found only in the first layer of cells lining the cervix and has not invaded the deeper tissues of the cervix. Stage 0 is also called carcinoma in situ.	<ul style="list-style-type: none"> • Loop electrosurgical procedure (LEEP) • Laser surgery • Conisation • Cryosurgery • Hysterectomy (for women who cannot or no longer want to have children) • Internal radiation therapy (for women who cannot have surgery)
Stage I	In Stage I, cancer is found in the cervix only. Stage I is divided into Stages IA and IB, based on the amount of cancer that is found.	
Stage IA	A very small amount of cancer that can only be seen with a microscope is found in the tissues of the cervix. The cancer is not deeper than 5 millimeters and not wider than 7 millimeters.	<ul style="list-style-type: none"> • Hysterectomy with or without bilateral salpingo-oophorectomy • Conisation • Radical hysterectomy and removal of lymph nodes • Internal radiation therapy
Stage IB	In Stage IB, the tumour is still within the cervix and either: <ul style="list-style-type: none"> • Can only be seen with a microscope and is deeper than 5 millimeters (less than 1/4 inch) or wider than 7 millimeters (about 1/4 inch); or • Can be seen without a microscope and may be larger than 4 centimeters (about 1 1/2 inches). 	<ul style="list-style-type: none"> • Combination of internal radiation therapy and external radiation therapy • Radical hysterectomy and removal of lymph nodes • Radical hysterectomy and removal of lymph nodes followed by radiation therapy plus chemotherapy • Radiation therapy plus chemotherapy
Stage II	Cancer has spread beyond the cervix but not to the pelvic wall. Stage II is divided into Stages IIA and IIB, based on how far the cancer has spread from the cervix into nearby tissue.	



Handout 5.1 (continued)

Stage IIA	Cancer has spread beyond the cervix to the upper two thirds of the vagina but not to tissues around the uterus.	<ul style="list-style-type: none"> • Combination of internal radiation therapy and external radiation therapy • Radical hysterectomy and removal of lymph nodes • Radical hysterectomy and removal of lymph nodes followed by radiation therapy plus chemotherapy • Radiation therapy plus chemotherapy
Stage IIB	Cancer has spread beyond the cervix to the upper two thirds of the vagina and to the tissues around the uterus.	<ul style="list-style-type: none"> • Internal and external radiation therapy combined with chemotherapy
Stage III	Cancer has spread to the lower third of the vagina and may have spread to the pelvic wall and nearby lymph nodes. Stage III is divided into Stages IIIA and IIIB, based on how far the cancer has spread.	
Stage IIIA	Cancer cells have spread to the lower third of the vagina but not to the pelvic wall.	<ul style="list-style-type: none"> • Internal and external radiation therapy combined with chemotherapy
Stage IIIB	Cancer cells have spread to the pelvic wall and/or the tumour has become large enough to block the ureter. This blockage can cause the kidneys to enlarge or stop working. Cancer cells may also have spread to lymph nodes in the pelvis	<ul style="list-style-type: none"> • Internal and external radiation therapy combined with chemotherapy
Stage IV	Cancer has spread to the bladder, rectum, or other parts of the body. Stage IV is divided into stages IVA and IVB, based on where the cancer is found.	
Stage IVA	Cancer has spread to the bladder or rectal wall and may have spread to lymph nodes in the pelvis.	<ul style="list-style-type: none"> • Internal and external radiation therapy combined with chemotherapy
Stage IVB	Cancer has spread beyond the pelvis and pelvic lymph nodes to other places in the body, such as the abdomen, liver, intestinal tract, or lungs.	<ul style="list-style-type: none"> • Radiation therapy as palliative therapy to relieve symptoms caused by the cancer and improve quality of life • Chemotherapy



Introductory Case Study

Case Study Instructions:

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
3. Discuss the case together and answer the related questions in the time you are given.

Case 1- Part One

35-year-old male patient admitted for cough with expectoration, and chest pain of 1 month's duration. H/O loss of weight and loss of appetite were also present.

He gave history suggestive of treatment for pulmonary tuberculosis and he completed the treatment about 1 year ago. He was found to be HIV- positive about 3 years ago.

Question:

1. How will you proceed with this patient?

Introductory Case Study (continued)

Case 1- Part Two

His chest x-ray PA showed a homogenous rounded opacity in the right apex. The sputum was negative for AFB (3 specimens), *Pneumocystis carinii*, and for malignant cells. Gram stain and bacterial culture were negative.

2. What other investigations are needed for this patient?

Case 1- Part Three

The opacity was persistent even after a course of crystalline penicillin and cefotaxime.

CT scan of the chest was performed and it showed features suggestive of carcinoma right apical lobe. The scan of the liver and brain showed no secondaries in the above sites.

Transthoracic CT-guided biopsy revealed squamous cell carcinoma of the lung.



Worksheet 5.2

Role-Play: HIV and Cervical Cancer Education

In this exercise, you will have the chance to practise determining a patient's risk of having cervical cancer. Determining the risk will help you assess how frequently the patient should be screened for the disease. You and your partner will take turns role-playing a health-care provider and an HIV-infected patient.

When it is your turn to be the health-care provider: You will need to ask the patient about her lifestyle and state of health so that you can determine whether she is at greater risk of contracting cervical cancer. The following co-factors have been determined to increase risk of this disease:

- HIV infection
- Infection with herpes simplex virus
- Previous STIs
- Multiple sexual partners
- HPV infection
- Early age at first sexual intercourse
- High-risk sexual partner
- Lower socioeconomic status
- Cigarette smoking

What questions will you need to ask? At the same time, consider how it might feel to be the patient. What concerns might she have? How can you do this in a way that will encourage honest responses and decrease anxiety or discomfort for the patient?

When it is your turn to be the patient: As much as possible, try to take on the characteristics of one of these characters. Pick from the following characters to portray:

1. HIV-infected woman, 45 years old. Married, lower socioeconomic status. Although you are married, you are having an affair with a man other than your husband. You think that this man has had 4 or 5 other sexual partners, but you aren't sure. Aside from HIV, you have had no previous STIs. Your first sexual encounter was at age 24 when you were first married. You are a nonsmoker.
2. HIV-infected woman, age 33. Single, middle-class. Before you were diagnosed with HIV, you had many sexual partners, but you are currently in a monogamous relationship. Your first sexual encounter was at age 22. Aside from HIV, you have had no previous STIs. You are a nonsmoker.
3. HIV-infected female, age 16. Single, lower socioeconomic status. You have had many sexual partners since you worked in the sex industry until your recent diagnosis of HIV. Your first sexual encounter was at age 13. You don't know if you have had any previous STIs. You are a cigarette smoker.



References

Clinical Epidemiology Resource & Training Centre (2003), *Prevention of Opportunistic Infections: A Training Course for Doctors and Nurses*. Harare, Zimbabwe: University of Zimbabwe College of Medicine.

National Cancer Institute website provides information on specific AIDS-related cancers. <http://www.cancer.gov/cancerinfo/>.

Treatment Education Program (2002). *Kaposi's Sarcoma Fact Sheet*. New York, NY: Gay Men's Health Crisis. <http://www.gmhc.org/living/living.html>

 **Notes**



Session 5: Malignancies Associated with Immunosuppression

Slide 1



Malignancies Associated with Immunosuppression
Session Five





Session 5: Malignancies Associated with Immunosuppression

Slide 2

Learning Objectives (1)

- By the end of this session, you will be able to:
 - Describe the various clinical presentations and relative frequencies of Kaposi sarcoma, lymphoma, and cervical cancer
 - Identify the appropriate procedures and laboratory investigations required to make a diagnosis of each opportunistic infections

Malignancies

Slide 2

- *The aim of this session is to introduce participants to malignancies associated with immunosuppression.*



Session 5: Malignancies Associated with Immunosuppression

Slide 3

Learning Objectives (2)

- By the end of this session, you will be able to:
 - Cite the preferred treatment regimen for each opportunistic infections
 - Explain the recommended prophylactic regimens and cite the guidelines for initiation and discontinuation of prophylaxis for these opportunistic infections

Malignancies

Slide 3



Session 5: Malignancies Associated with Immunosuppression

Slide 4

Introductory Case Study-Part One

- 35 y.o. male patient admitted for cough with expectoration, and chest pain of one month duration
- H/O loss of weight and loss of appetite were also present. He gave history suggestive of treatment for pulmonary tuberculosis and he completed the treatment about one year ago. He was found to be HIV positive about 3 yrs. ago
- Question #1:
 - How will you proceed with this patient?

Malignancies

Slide 4

- *Read the case study and answer the questions that follow in “Introductory Case Study” (Worksheet 5.1) in the Participant’s Handbook.*



Session 5: Malignancies Associated with Immunosuppression

Slide 5

Case Study Question #1 Answer

- A complete clinical examination, followed by laboratory investigations
- The tests are as follows:
 - Chest X-ray
 - AFB staining of the sputum for *Mycobacterium tuberculosis* (three specimens)
 - Sputum tests for *Pneumocystis jiroveci*
 - Gram's staining of sputum
 - Sputum for malignant cells; sputum to be cultured for tuberculous and other bacterias

Malignancies

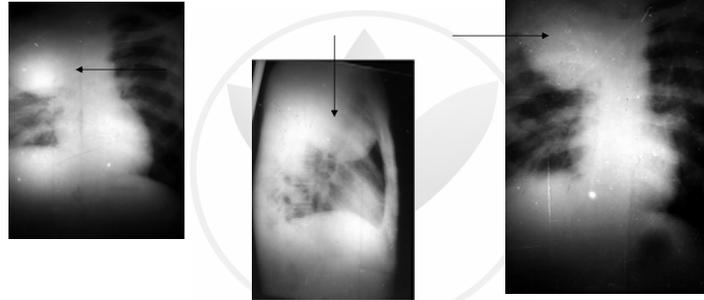
Slide 5



Session 5: Malignancies Associated with Immunosuppression

Slide 6

Part Two: Chest X-ray PA



Rounded opacity-right apex

Malignancies

Slide 6

- His chest X-ray PA showed a homogenous rounded opacity in the right apex.



Session 5: Malignancies Associated with Immunosuppression

Slide 7

Part Two: Other Test Results

- The sputum was negative for AFB (three specimens), *Pneumocystis jirovecii*, and for malignant cells
- Gram's stain and bacterial culture were negative
- Question #2:
 - What other investigations are needed for this patient?

Malignancies

Slide 7



Session 5: Malignancies Associated with Immunosuppression

Slide 8

Question #2 Answer

- CT scan of the chest
- CT scan of the abdomen
- CT scan of the brain

Malignancies

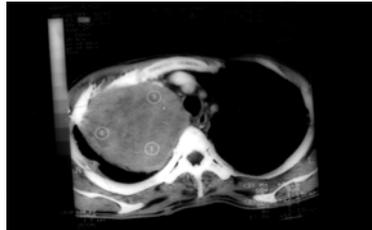
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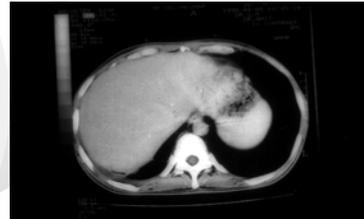
Session 5: Malignancies Associated with Immunosuppression

Slide 9

CT Scan Results



Lung showed a malignant lesion.



No metastasis in the liver

Malignancies

Slide 9

- CT scan is suggestive of a malignant lesion in the lungs. There are no metastatic lesions in the liver.



Case Study Further Investigation Results

- The opacity was persistent even after a course of crystalline penicillin and cefotaxime
- CT scan of the chest was performed and it showed features suggestive of carcinoma right apical lobe and the scan of the liver and brain showed no secondaries in the above sites
- Transthoracic CT guided biopsy revealed squamous cell carcinoma of the lung



Discussion

- Why is there a need for careful diagnosis that goes beyond basic opportunistic infections when working with HIV patients?

Malignancies

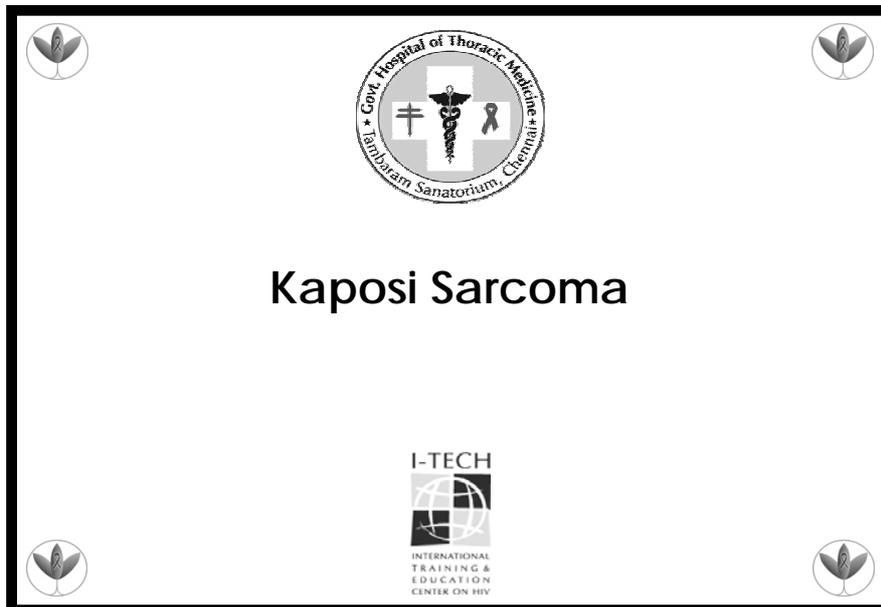
Slide 11

- It is typical for doctors to look for opportunistic infections like TB and PCP in HIV positive patients.
- It is less typical, however, to look for malignancies, which could result in an inaccurate and/or incomplete diagnosis.
- There is a saying that your eyes see only what your mind knows.
- If you are not looking for malignancies because you are assuming you will find opportunistic infections in an HIV+ patient, you will not see possible malignancies such as lymphoma or Kaposi sarcoma of the lung in this patient.
- With HIV+ patients, there must always be a high index of clinical suspicion.
- If lymphoma is a possibility in a patient, especially if the patient is HIV+, do a biopsy. Lymphoma is one of the most common malignancies present in HIV+ patients.
- You may also need to refer patient and family for counselling to address psychosocial issues related to their HIV status.
- Several malignancies have been associated with HIV infection:
AIDS DEFINING: Kaposi sarcoma
 - Non-Hodgkin's lymphoma
 - (High/intermediate grade of B lymphocyte lineage)
 - Acute leukemia (Burkitt's type)
 - Cervical carcinoma.



Session 5: Malignancies Associated with Immunosuppression

Slide 12



- Malignancies associated with HIV infection (continued):
 - Non AIDS-Defining, But Increased
 - Hodgkin's disease
 - Anal carcinoma
 - Testicular seminoma
 - Reported (no association apparent)
 - Non-Hodgkin's lymphoma (low grade of beta-cell lineage, or T-cell lineage)
 - Multiple myeloma
 - Acute leukemia (myeloid and lymphoid)
 - Melanoma
 - Colonic carcinoma
 - Gastric carcinoma
 - Oro- pharyngeal squamous cell carcinoma



Kaposi Sarcoma (KS)

- KS cancer cells form small tumors that most commonly appear as raised macules (blue or purplish papules or blotches) and can appear on the skin and inside the body
- HIV-related KS is much more common and aggressive
- Lesions are commonly found on the palate, the gastrointestinal tract, lungs or lymph nodes
- Pulmonary lesions are infiltrative and often lead to respiratory failure

Malignancies

Slide 13

- Kaposi sarcoma is a multicentric, angioproliferative disease.
- It is a unique tumour as it is thought that it begins as a growth factor dependent hyperplasia, but develops over time into a genetically mutated, independent tumour.
 - This tumour probably produces its own growth factor to maintain its proliferative capacity.
- A human Herpes virus (HHV-8) has been found in Kaposi sarcoma lesion, suggesting this as yet uncharacterized virus may be a key pathogenetic factor in KS.
- HIV proteins, particularly tat, may play an important role in tumour promotion by mimicking the action of extracellular matrix proteins on endothelial cell growth and type IV collagen expression.
 - Extracellular tat promotes both Kaposi sarcoma cells and endothelial cells to proliferate, migrate and invade surrounding tissue.
- Cytokines, particularly basic fibroblast growth factor, oncostatin-M, tumour necrosis factor, IL-6, and IL-1beta, also play a key role in KS.
- These cytokines are produced by both KS cells and activated endothelium and may therefore act in both an autocrine and paracrine manner to stimulate events required for angiogenesis: endothelial cell migration, invasion, and proliferation



How HIV Leads to Kaposi Sarcoma

- Endothelial cells infected with KSHV are activated by tat proteins, cytokines from HIV-infected cells and cells activated by infection
- Activated endothelial cells produce cytokines, which promotes further cell growth and invasion
- Cytokine stimulation and proliferation of KSHV-infected endothelial cells induces the morphological and phenotypic changes of KS

Malignancies

Slide 14

- Endothelial cells infected with KSHV (Kaposi sarcoma-related herpes virus) are activated by:
 - Tat proteins
 - Cytokines from HIV-infected cells (macrophages, CD4 cells) and
 - Cells activated by infection (CD8, B cells, dendritic cells)
- Activated endothelial cells produce cytokines, particularly basic fibroblast growth factor, which promotes further cell growth and invasion.
- Cytokine stimulation and proliferation of KSHV-infected endothelial cells induces the morphological and phenotypic changes of KS.
- An autocrine/paracrine loop is then established, whereby endothelial and Kaposi sarcoma cells continue to produce these cytokines.
- HIV proteins continue to be produced by surrounding HIV-infected cells and the uncontrolled proliferation and invasion of KS cells persists.
- Immunodeficiency allows the process to go unchecked, but beta HCG (beta human chorionic gonadotrophin) acts as an inhibitor



Session 5: Malignancies Associated with Immunosuppression

Slide 15

KS Lesions



Malignancies

Slide 15

- Kaposi sarcoma, or KS, is a multicentric neoplasm (cancer) consisting of multiple vascular lesions (overgrowth of small blood vessels).
- KS cancer cells form small tumours (spots or blotches) on the skin called lesions.
 - These lesions most commonly appear as raised macules and can appear on the skin and inside the body.
- Although some people without HIV infection can get KS, HIV-related KS is much more common and aggressive. (GMHC Fact Sheet, www.gmhc.org)
- Kaposi sarcoma is caused by the human herpes virus type 8 (HHV8), also known as the Kaposi sarcoma herpes virus (KSHV). (Zim, Malignancies)
- HHV-8 is spread primarily through saliva, but it can also be spread through semen and blood, and from mother to baby. (GMHC Fact Sheet, www.gmhc.org)
- Lesions may be found anywhere on the body and on any mucosal surface.
 - Skin lesions are hyperpigmented, blue or purplish papules or nodules and associated with lymphodema.
 - Lesions are commonly found on the:
 - Palate
 - Gastrointestinal tract
 - Lungs or
 - Lymph nodes
- Pulmonary lesions are infiltrative and often lead to respiratory failure.
- In persons with pulmonary infiltrative Kaposi sarcoma, the outcome is poor and there is a high mortality rate. (Zim, Malignancies)



Kaposi Sarcoma



Chest X-ray showing bilateral diffuse linear and nodular infiltrates

© Slice of Life and Suzanne S. Stensaas

Malignancies

Slide 16

- 32 year old injecting drug user presented with this X-ray picture.
- Fiberoptic bronchoscope and BAL were undiagnostic.
- Open lung biopsy showed spindle cells and vascular clefts, typical of KS.
- The diagnosis of Kaposi sarcoma is made on clinical suspicion and is confirmed by a histological examination (taking a biopsy of the tissue and examining how the cells look under a microscope).
- Punch biopsy of the accessible cutaneous lesions.
- Lymph node biopsy
- GI lesions- Endoscopic visualization and biopsy
- Pulmonary KS- Bronchoscopic visualization and BAL analysis and biopsy
 - In cases of pleural effusion, pleural fluid cytology and pleural biopsy.
 - The condition may be confused with bacillary angiomatosis (Bartonellosis), an infective condition commonly seen in persons with HIV/AIDS.



Session 5: Malignancies Associated with Immunosuppression

Slide 17

Discussion: Differential Diagnoses

- What are the differential diagnoses for this presentation?



Malignancies

Slide 17



Differential Diagnoses for KS (1)

- Cutaneous entities, which may include:
 - Malignant melanoma
 - Angiomas
 - Cutaneous angiosarcomas
 - Spindle cell hemangio endothelioma
 - Angio lipoma
 - Dermato fibromas
 - Pyogenic granulomas
 - Arthropod bites
 - Glomus tumours
 - Sarcoid nodules

Malignancies

Slide 18

- The clinical appearance of KS lesions may be confused with other cutaneous entities, which may include:
 - Malignant melanoma
 - Angiomas
 - Cutaneous angiosarcomas
 - Spindle cell hemangio endothelioma,
 - Angio lipoma
 - Dermato fibromas
 - Pyogenic granulomas
 - Arthropod bites
 - Glomus tumours
 - Sarcoid nodules
- Most extensive lesions may bear notable similarity to:
 - Lichen planus
 - Sarcoidosis
 - Urticaria pigmentosa
 - Popular urticaria
 - Eruptive xanthomas
 - Disseminated secondary syphilis etc.
- KS nodules appear similar to Bacillary angiomatosis.



Session 5: Malignancies Associated with Immunosuppression

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Differential Diagnoses for KS (2)

- Most extensive lesions may bear notable similarity to Lichen planus, Sarcoidosis, urticaria pigmentosa, papular urticaria, eruptive xanthomas, disseminated secondary syphilis etc.
- KS nodules appear similar to Bacillary angiomatosis

Malignancies

Slide 19



Session 5: Malignancies Associated with Immunosuppression

Slide 20

Treatment

- Surgery
- Cryotherapy
- Intralesional cytotoxic chemotherapy
- Radiation
- Interferon therapy
- Systemic chemotherapy

Malignancies

Slide 20

- Treatment:
 - **SURGERY:** Well circumscribed small lesions can be treated by excision, but the indistinct margins typical of KS may make this difficult, and recurrence may be a problem.
 - **CRYOTHERAPY:** Liquid nitrogen cryotherapy is occasionally an effective treatment for small lesions.
 - **INTRA LESIONAL CYTOTOXIC CHEMOTHERAPY:** Vinblastine intra lesional injections can be used for somewhat larger lesions and for oral lesions.
 - **RADIATION:** It is probably the most effective treatment for localized KS. Radiation techniques used: either low energy superficial X-ray or high energy X-rays (photon beams)
 - **INTERFERON THERAPY:** Interferon alpha-2a and interferon alpha-2b have been used as systemic agents in the treatment of widespread and visceral KS.
 - **SYSTEMIC CHEMOTHERAPY:** Treatment of choice for widespread cutaneous or visceral KS. The main agents used are:
 - Vinca alkaloids
 - Etoposide
 - Doxorubicin
 - Bleomycin
 - Treatment of Kaposi sarcoma requires specialist supervision. Kaposi sarcoma is a cancer, and treatment is with radiotherapy if lesions are localized and with combination cytotoxic chemotherapy for generalized disease.



Discussion: Treating KS

- How often do you see patients with Kaposi sarcoma at Tambaram Sanatorium? How would you describe a typical patient with this disease?
- What can be done to increase the comfort of patients suffering from the symptoms of this disease?
- What resources are there at Tambaram to diagnose and treat patients with KS?

Malignancies

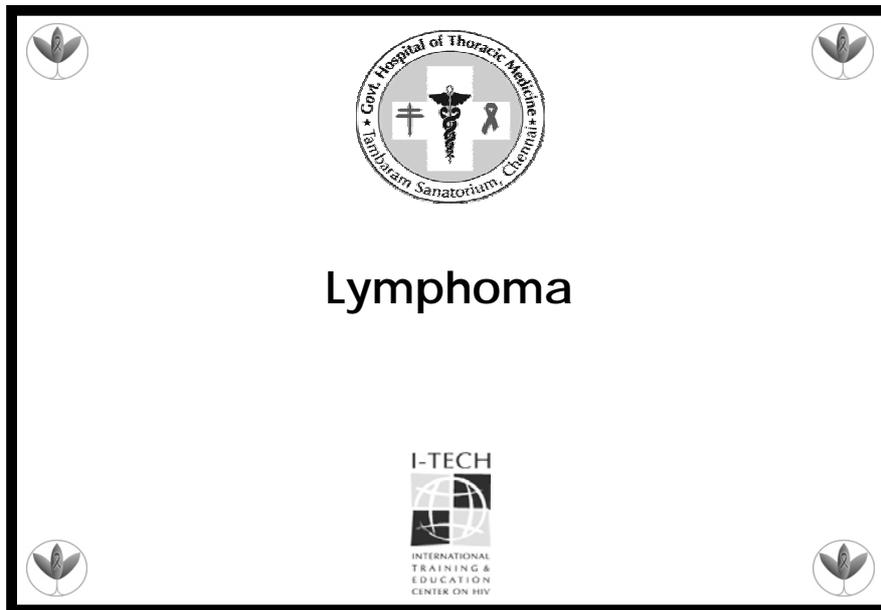
Slide 21

- Treatment (continued)
 - Cytotoxic drug combinations that have been used with varying degrees of success include:
 - Bleomycin
 - Vincristine
 - Daunorubicin
 - Vinblastine
 - Etoposide
 - Unfortunately, remission is difficult to achieve, and relapses occur commonly.
 - Localized lesions may be surgically excised or treated with liquid nitrogen, laser therapy, or radiation.
 - Intralesional injection with bleomycin has also been shown to be effective. (Zim, Malignancies)
 - Discuss participants' experience treating KS at Tambaram.
 - KS IS VERY RARE HERE IN SOUTH INDIA- SHARING EXPERIENCES IS DIFFICULT.



Session 5: Malignancies Associated with Immunosuppression

Slide 22



- HOW HIV LEADS TO LYMPHOMA:
 1. Chronic stimulation of T-cells and B-cells by HIV antigen increases production of a range of cytokines. (IL-1, IL-2, IL-4, IL-5, IL-6, IL-10)
 2. Cytokines activate B-cells which proliferate.
 - A. Adenopathy develops
 - B. Rapid cell division increases the chance of genetic changes, including the activation of oncogenes such as c-myc
 - C. EBV-infected cells are few but are at greater risk of malignancy.
 3. Malignant cells usually contain EBV, and may produce cytokines that promote proliferation.
- In the setting of HIV infection:
 - Antigen is not cleared
 - Cytokine production remains disordered
 - HIV replication continues and
 - Cells in the early stages of malignant conversion are not deleted by the host immunoregulatory mechanisms.
- Ref: Managing HIV Edited by Graeme Stewart.



Lymphoma

- Lymphoma is a disease in which cancer cells are found in the lymph system
- Can spread to almost any of the body's organs or tissues including the liver, bone marrow, spleen, or brain
- Lymphomas are divided into two general types:
 - Hodgkin's lymphomas
 - Non-Hodgkin's lymphomas

Malignancies

Slide 23

- AIDS-related lymphoma is a disease in which cancer cells are found in the lymph system in patients who have AIDS.
 - The lymph system is made up of thin tubes that branch, like blood vessels, into all parts of the body.
 - Lymph vessels carry lymph, a colorless, watery fluid that contains white blood cells called lymphocytes.
 - Along the network of vessels are groups of small, bean-shaped organs called lymph nodes.
 - Clusters of lymph nodes make and store infection-fighting cells.
- The spleen, the thymus, and the tonsils are also part of the lymph system.
- Because there is lymph tissue in many parts of the body, the cancer can spread to almost any of the body's organs or tissues including the:
 - Liver
 - Bone marrow (the spongy tissue inside the large bones of the body that makes blood cells)
 - Spleen, or
 - Brain
- Lymphomas are divided into two general types, Hodgkin's lymphomas and non-Hodgkin's lymphomas, which are classified by histology.
- Histology is also used to determine the type of non-Hodgkin's lymphoma of which there are ten.



Non-Hodgkin's Lymphoma

- Classifications:
 - Low-grade
 - Intermediate-grade
 - High-grade
- Intermediate- and high-grade types of non-Hodgkin's lymphoma are more commonly found in AIDS patients
- Epstein Barr Virus (EBV) may play a role non-Hodgkin's tumors and Burkitt-type lymphomas are also associated with HIV infection

Malignancies

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- The types of non-Hodgkin's lymphomas are classified by how quickly they spread:
 - Low-grade
 - Intermediate-grade, or
 - High-grade
- The intermediate or high-grade lymphomas grow and spread faster than the low-grade lymphomas.
- Both major types of lymphoma, Hodgkin's disease and non-Hodgkin's lymphoma, may occur in AIDS patients.
- Also, the intermediate and high-grade types of non-Hodgkin's lymphoma are more commonly found in AIDS patients. (National Cancer Institute, www.cancer.gov)
- It is thought that the Epstein Barr Virus (EBV) plays a role in the causation of non-Hodgkin's lymphoma tumours.
 - EBV has been found in biopsy specimens of lymph nodes obtained from persons with non-Hodgkin's lymphoma.
- Burkitt-type lymphomas are also associated with HIV infection and may occur before advanced immunosuppression sets in.
 - This tumour is also associated with EBV. (Zim, Viral Infections)
- NHL commonly presents as: (1) a systemic disease occurring at any stage of immunosuppression and (2) a primary cerebral lymphoma associated with markedly depressed CD4 cell counts.
- Both presentations are usually of rapid onset and require prompt assessment.
- Systemic NHL Common Presentations:
 - Systemic: Pyrexia of unknown origin, night sweats, unexplained weight loss
 - Hematological: lymphadenopathy, splenomegaly, pancytopenia
 - Gastro intestinal: gastric ulcer, bowel obstruction, ascites
 - Respiratory: lung mass, effusion
 - Neurological: aseptic meningitis, cranial nerve lesion, cord compression and nerve root lesion
 - Miscellaneous: cutaneous mass lesions, testicular mass, hypercalcemia



Session 5: Malignancies Associated with Immunosuppression

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Initial Assessment

- Confirmation of diagnosis by FNAC/excision biopsy
- Assess marrow reserve and exclude involvement (full blood count, blood film and bone marrow study)
- Assess organ function and exclude involvement
- Assess extent of disease (serum lactate dehydrogenase, CT scan chest, abdomen, and pelvis), total body gallium scan may show disease in “normal” organ: bone scan if bone involvement is suspected)

Malignancies

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- The diagnosis of lymphoma is made on histological examination of biopsied material.
- The diagnosis of intracranial lymphoma requires CT scans of the brain and tissue biopsies. (Zim, Malignancies)
- The diagnosis of Burkitt-type lymphoma is made on careful examination of lymph node biopsies. (Zim, Viral Infections)



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Poor Prognostic Factors

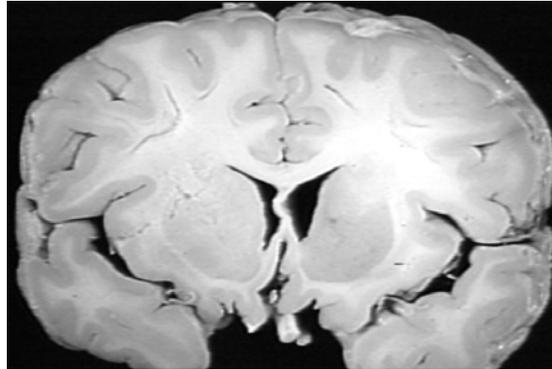
- Prior AIDS diagnosis, especially if the AIDS-defining condition is still active
- CD4 cell count below $100/\text{mm}^3$
- Poor performance status (significant debility)
- Widespread or bulky disease (mass more than 10cm diameter)

Malignancies

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CNS Lymphoma: Primary Cerebral Lymphoma



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Malignancies

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Primary CNS lymphoma is a non-Hodgkin lymphoma, usually B-cell origin, which represents 1 - 2% of all primary CNS tumors. It occurs with increased frequency in patients with AIDS, but may occur in non-AIDS patients as well. Although the tumors are radiosensitive, the overall prognosis is poor, with a median survival after diagnosis +/- of 13.5 months, with chemotherapy and radiation treatment. (www.uhrad.com)

- Brain MRI of lymphoma reveals a hyper dense lesion in the hypothalamic region.
- Definitive diagnosis is by stereotactic brain biopsy.
- Gross appearance – white, firm expansile lesion with a predilection for deep gray matter structures



Common Chemotherapy Protocols

- **CHOP:** Cyclophosphamide, Doxorubicin, Vincristine, and Prednisolone
- **CEOP:** Cyclophosphamide, Epirubicin, Vincristine, and Prednisolone
- **PEM:** Prednisolone, Etoposide, and Mitizantrone
- **MBACOD-**Methotrexate, Bleomycin, Doxorubicin, Cyclophosphamide, Vincristine and Dexamethasone

Malignancies

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- COMMON CHEMOTHERAPY PROTOCOLS FOR SYSTEMIC NHL:
 - CHOP: Cyclophosphamide, Doxorubicin, Vincristine, and Prednisolone
 - CEOP: Cyclophosphamide, Epirubicin, Vincristine, and prednisolone
 - PEM: Prednisolone, etoposide, and mitizantrone
 - MBACOD-Methotrexate, Bleomycin, Doxorubicin, Cyclophosphamide, Vincristine and Dexamethasone.
 - Additionally, clinical trials are testing the effect of giving drugs to kill the AIDS virus (antiviral therapy) in addition to treatment of lymphoma.
 - Treatment of AIDS-related lymphomas depends on the stage, histology, and grade of the disease, as well as the general health of the patient.
 - A doctor must consider white blood cell count and any other diseases caused by AIDS that the patient had or currently has. (National Cancer Institute, www.cancer.gov)



Primary Cerebral Lymphoma

- CT scan brain demonstrates a hypodense or isodense single lesion, which enhances with contrast. The prognosis is poor
- Present with signs and symptoms of intra cerebral space occupying lesion or raised intra cranial pressure.

Malignancies

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- For non-Hodgkin's lymphoma, the EPOCH regimen that includes:
 - Etoposide
 - Vincristine
 - Daunorubicin
 - Cyclophosphamide
 - Prednisolone
 - Together with HAART has been ALSO shown to be effective.
- For intracranial lymphoma, cranial radiation together with cytotoxic chemotherapy and steroids are advised.
 - This regimen may also be used in the treatment of Burkitt-type lymphoma. (Zim, Malignancies)



Therapy of Primary Cerebral Lymphoma *

- Radiotherapy: Only consider combined radiotherapy/chemo therapy in patients with relatively preserved immune function
- Consider not treating comatose patients or those with severe pre-existing conditions
- Consider stopping therapy if there is no improvement with measures to decrease intracranial pressure or if neurological signs of disease progress during therapy

** Measures to reduce raised intracranial pressure (corticosteroids and mannitol).*

Malignancies

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- Measures to reduce raised intracranial pressure (corticosteroids and mannitol)
- Radio therapy: Only consider combined radiotherapy/chemo therapy in patients with relatively preserved immune function
- Consider not treating comatose patients or those with severe pre-existing conditions.
- Consider stopping therapy if there is no improvement with measures to decrease intracranial pressure or if neurological signs of disease progress during therapy.

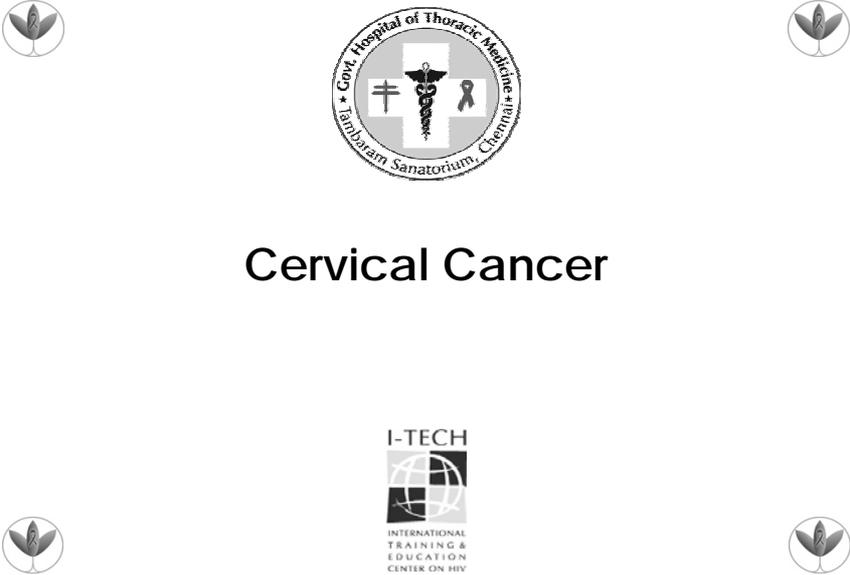


Session 5: Malignancies Associated with Immunosuppression

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Cervical Cancer





Cervical Cancer (1)

- Malignant cells form slowly in the tissues of the cervix and surrounding areas
- Human papilloma virus (HPV) infection is associated with cervical cancer
- Common cancer of women throughout the world, accounting for about 30% of all cancers and 80% of all gynecologic cancers
- Incidence of cervical dysplasia is increased in HIV-infected women

Malignancies

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- Cervical cancer is a disease in which malignant cells form in the tissues of the cervix.
- It usually develops slowly over time.
- Before cancer appears in the cervix, the cells of the cervix go through changes known as dysplasia, in which cells that are not normal begin to appear in the cervical tissue.
- Later, cancer cells start to grow and spread more deeply into the cervix and to surrounding areas. (National Cancer Institute, www.cancer.gov)



Cervical Ectopy: Stages

- Cervical ectopy (ectropian) is present on the outer surface at birth
- 1 yr. after birth size of the ectropian decreases
- At puberty it again becomes displaced on to the portio surface of the cervix
- Squamous metaplasia occurs



Cervical Ectopy (1)



Seattle STD/HIV Prevention Training Center

Source: Claire E. Stevens

Malignancies

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- When viewed with the naked eye, the endocervical mucosa of the cervical ectopy appears as a red, velvety zone, sharply contrasting with the neighboring pink and shiny squamous portio epithelium.
- This is a cervical ectopy
- With time, cervical ectopy becomes reduced, as pink, metaplastic squamous epithelium replaces the red columnar epithelium.
- Tongues of metaplastic epithelium are seen growing into the cervical ectopy.
- In older women, the process of squamous metaplasia totally replaces the cervical ectopy, and the external surface of the portio cervix becomes covered by a stratified squamous epithelium



Cervical Ectopy (2)

- Cervical cancer is a common cancer of women throughout the world, accounting for about 30% of all cancers and 80% of all gynaecologic cancers
- The mean age of cervical cancer diagnosis is about 38 years
- It is a common cause of death among women
- There has been an increase in the incidence of cervical cancer in the past 15 years
- The cancer is most prevalent in women who have multiple partners or in those monogamous women whose partners have multiple partners

Malignancies

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- Human papilloma virus (HPV) infection is the leading causal agent in the development of premalignant and malignant lower genital tract disease including cervical cancer.
- The incidence of cervical dysplasia is increased in HIV-infected women.
- The incidence of cervical dysplasia increases with progressive immunosuppression.
- Cervical dysplasia is associated with more rapid and aggressive cervical disease.
- Invasive cervical cancer is regarded as an AIDS – defining illness.
- HPV (type 16, 18, 35) is associated with a ten fold increased risk of squamous intra-epithelial carcinoma.



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Role Play: HIV and Cervical Cancer Education

- The purpose of this exercise is to determine whether a patient is at risk of having cervical cancer
- Find a partner. Each partner will have a chance to role-play a health care provider and an HIV-infected patient
- Refer to Worksheet 5.2 “Role Play: HIV and Cervical Cancer Education”
- After you have had a chance to play both roles, we will have a group discussion

Malignancies

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- *Refer to Worksheet 5.2, “Role Play: HIV and Cervical Cancer Education.”*
- *Following the instructions, each partner should have a chance to role-play an HIV-infected patient and a health care provider.*



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Role of Health Care Provider (1)

- You will need to ask the patient about her lifestyle and state of health so that you can determine whether she is at greater risk of contracting cervical cancer
- Refer to your worksheet for co-factors that have been determined to increase risk of this disease
- What questions will you need to ask?

Malignancies

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Role of Health Care Provider (2)

- At the same time, consider how it might feel to be the patient
- What concerns might she have?
- How can you do this in a way that will encourage honest responses and decrease anxiety or discomfort for the patient?

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Role of Patient (1)

- Choose one of these characters to portray:
 - HIV-infected woman, age 45 years old. Married, lower socioeconomic status. Although you are married, you are having an affair with a man other than your husband. You think that this man has had 4-5 other sexual partners, but you aren't sure. Aside from HIV, you have had no previous STIs. Your first sexual encounter was at age 24 when you were first married. You are a non-smoker

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Role of Patient (2)

- Choose one of these characters to portray:
 - HIV-infected woman, age 33. Single, middle-class. Before you were diagnosed with HIV, you had many sexual partners, but you are currently in a monogamous relationship. Your first sexual encounter was at age 22. Aside from HIV, you have had no previous STIs. You are a non-smoker

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Role of Patient (3)

- Choose one of these characters to portray:
 - HIV-infected female, age 16. Single, lower socioeconomic status. You have had many sexual partners since you worked in the sex industry until your recent diagnosis of HIV. Your first sexual encounter was at age 13. You don't know if you have had any previous STIs. You are a cigarette smoker

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Role Play: Discussion Questions

- Were you comfortable assessing the patient's risk?
- How did you handle this sensitive subject matter?
- What personal interaction methods did you use to ask the patient about their sexual history?
- When you played the patient, how did you feel?

Malignancies

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Role Play Teaching Points (1)

- Provider questions should cover:
 - Life style of the patient
 - State of health
 - HIV infection
 - Herpes simplex infection
 - Previous STI's
 - Multiple sex partners
 - Sexual history, including post coital bleeding
 - Socioeconomic status
 - Smoking
 - Oral contraceptive usage and pregnancy details
 - Pap smear intervals if done

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Role Play Teaching Points (2)

- Patient concerns:
 - Confidentiality issues
 - Cancer phobia
 - Sex and sexuality issues
 - Anxiety
 - Discomfort
 - Breach of privacy
- Personal interaction methods to ask the patient about her sexual history:
 - Effective communication skills with a non-judgmental attitude and good knowledge

Malignancies

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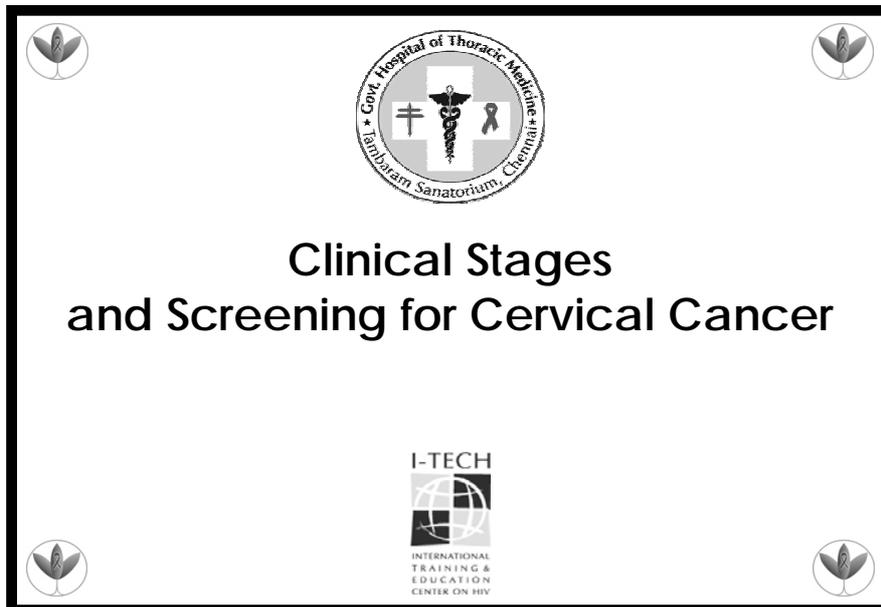
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Role Play Teaching Points (3)

- Ways to encourage honest responses and decrease patient anxiety or discomfort:
 - Effective communication (Content, process, and perceptual skills)
 - Confidentiality assurance
 - Adequate time spent on interview
 - Appropriate body language
 - Non-judgmental attitude
 - Removal of physical barriers during history elicitation
 - Knowledge and past experience

Malignancies

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- Early stages of cervical cancer may not cause symptoms.
- The early feature of cervical cancer is cervical dysplasia. This is not visible with the naked eye, cases are diagnosed by cytology.
- Cervical dysplasia can progress to invasive cancer if left untreated.
- Once the epithelial basement membrane has been breached, the malignant cells have the potential to invade locally and then spread through lymphatic channels.
- With the development of cancer, symptoms may occur.
 - These include abnormal vaginal bleeding and discharge and postcoital spotting.
- The patient also can experience symptoms related to impingement upon the surrounding structures as the cancer becomes larger.
 - This may lead to:
 - Urinary frequency
 - Dysuria
 - Haematuria
 - Urinary retention
 - Hydronephrosis
 - Renal failure
 - Lower limb oedema
 - Deep vein thrombosis
 - Lower backache, constipation, and rectal obstruction



Gross Appearance-Cervical Cancer

- No reported difference in the gross appearance of invasive cancers between HIV-infected and uninfected women
- On physical examination, cervical cancer can appear as a red, friable, exophytic lesion or as an ulcer
- Early cancers may be mistaken for a normal cervical ectropion (the presence of endocervical glands on the exocervix)
- A pap smear that is obscured with blood or inflammatory cells in a woman with a history of abnormal bleeding requires that a cervical biopsy is performed
 - Careful vaginal and cervical palpation will reveal a hard, friable cervix that may be enlarged
- A rectovaginal examination allows evaluation of the parametria for nodularity and induration, both of which are signs of an advanced lesion

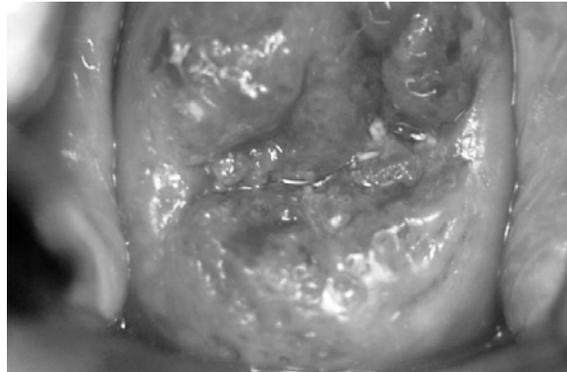
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- Advanced cancer usually causes intractable pain from perineural invasion.
- Death occurs due to uremia from urethral obstruction or haemorrhage from invasion of cancer into large pelvic vessels. (Zim, Malignancies)
- Services for routine screening for cervical cancer decrease mortality and the incidence of invasive disease.
- The treatment options and prognosis depend on:
 - Stage of the cancer, whether it affects:
 - Part of the cervix
 - Involves the whole cervix, or
 - Has spread to the lymph nodes or other places in the body
 - Type of cervical cancer
 - Size of the tumour
 - Patient's desire to have children.
- (Lymph nodes are small, bean-shaped structures found throughout the body. They filter substances in a fluid called lymph and help fight infection and disease.)



Low Grade Cervical Intraepithelial Carcinoma



Courtesy of Public Health Image Library, CDC

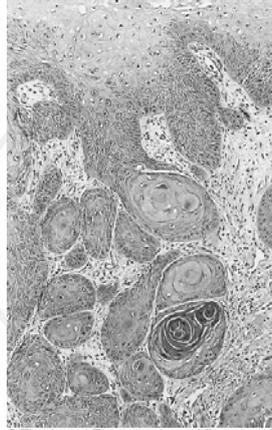
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- Treatment of cervical cancer during pregnancy depends on the stage of the cancer and the stage of the pregnancy.
 - For cervical cancer found early or for cancer found during the last trimester of pregnancy, treatment may be delayed until after the baby is born.
- After cervical cancer has been diagnosed, tests are done to find out if cancer cells have spread within the cervix or to other parts of the body.
- The process used to find out if cancer has spread within the cervix or to other parts of the body is called staging.
 - The information gathered from the staging process determines the stage of the disease.
 - It is important to know the stage in order to plan the best treatment.
- The following tests and procedures may be used in the staging process:
 - Chest X-ray
 - CT scan (CAT scan)
 - Lymphangiography
 - Pretreatment surgical staging
 - Ultrasound
 - MRI (magnetic resonance imaging)
- *Note: Only chest x-ray and ultrasound are presently available at Tambaram.*
- The results of these tests are viewed together with the results of the original tumour biopsy to determine the cervical cancer stage. (National Cancer Institute, www.cancer.gov)
- The stages of cervical cancer are shown in Handout 5.1, "Stages of Cervical Cancer".



Pap Smear-Squamous Intraepithelial Lesion



© The Armed Forces Institute of Pathology Electronic Fascicles Atlas of Tumor Pathology

Malignancies

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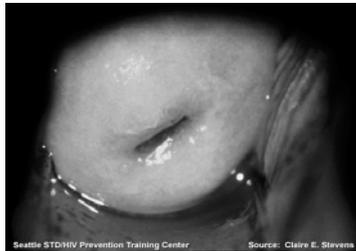
- A Pap smear from a HIV-infected woman diagnosed with a low-grade squamous intraepithelial lesion. There are prominent koilocytes and multi nucleated cells present.
- Koilocytes are the cells with prominent perinuclear halos and dense atypical nuclei.
- Papanicolaou (Pap) smear: is the standard and single most effective screening test for lower genital tract neoplasia.
 - In order to perform a Papanicolaou smear, the cervix is scraped circumferentially using a spatula or a curved brush.
 - All women who are or who have been sexually active or who have reached the age of 18 should undergo an annual Pap test and pelvic examination.
 - After a woman has had three or more consecutive normal Pap tests, this test may be performed less frequently in a low-risk woman.
 - However, even in low-risk women, a Pap smear needs to be repeated within one year if the patient has a new sexual contact.
- HIV positive women:
 - It is recommended that a gynaecologic evaluation with pelvic examination and Pap smear at the time of diagnosis in HIV-infected women be performed.
 - The examination and Pap smear should be repeated at six months and then annually.
 - Patients with Pap smear reports of dysplasia or intraepithelial neoplasia should be evaluated by colposcopy (which examines the tissues of the vagina and cervix using a lighted magnifying instrument called a colposcope).
 - Immediate colposcopic evaluation and, if a lesion is not visible, a cone biopsy are recommended for women with a Pap smear report of carcinoma. (Zim, Malignancies)
 - (A cone biopsy involves the removal of a cone-shaped sample of cervical tissue for examination under a microscope.) (National Cancer Institute, cancer.gov)



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Normal, Ectopic, Cancerous Cervices



Malignancies

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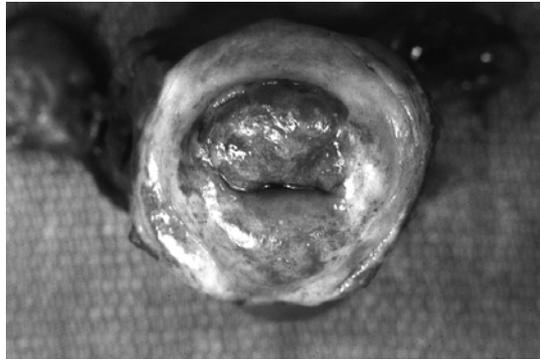
- Normal cervix, ectopic cervix, cancerous cervix



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High Grade Intraepithelial Neoplasia



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- Colpophotograph-Flat, dense, acetowhite lesion with sharp margins.
- There are prominent blood vessels forming a mosaic pattern in the lesional tissue.

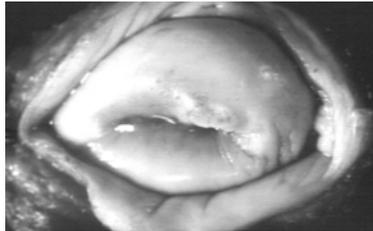


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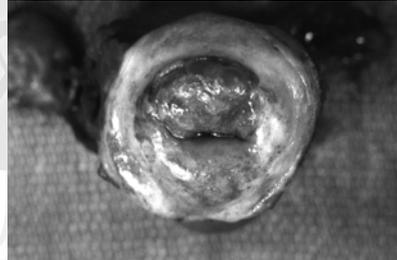
Gross Appearance of Intraepithelial Carcinoma

Low grade



© Slice of Life and Suzanne S. Stensaas

High grade



© University of Alabama at Birmingham, Department of Pathology

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- Low grade and high grade intra epithelial carcinoma



Session 5: Malignancies Associated with Immunosuppression

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Stages of Cervical Cancer: Stage 0

Stage	Test Results	Treatment Options
Stage 0	<ul style="list-style-type: none">• Cancer found in the first layer of cells lining the cervix only and has not invaded the deeper tissues of the cervix. Stage 0 is also called carcinoma in situ	<ul style="list-style-type: none">• Loop electrosurgical procedure (LEEP)• Laser surgery• Conization• Cryosurgery• Hysterectomy (for women who cannot or no longer want to have children)• Internal radiation therapy (for women who cannot have surgery)

Malignancies

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- Refer to “Stages of Cervical Cancer” (Handout 5.1) in the Participant’s Handbook.
- Share experiences treating cervical cancer with HIV-infected patients.



Session 5: Malignancies Associated with Immunosuppression

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Stages of Cervical Cancer: Stages I-IA

Stage	Test Results	Treatment Options
Stage I	<ul style="list-style-type: none">In stage I, cancer is found in the cervix only. Stage I is divided into stages IA and IB, based on the amount of cancer that is found	
Stage IA	<ul style="list-style-type: none">A very small amount of cancer that can only be seen with a microscope is found in the tissues of the cervix. The cancer is not deeper than 5 millimeters and not wider than 7 millimeters	<ul style="list-style-type: none">Hysterectomy with or without bilateral salpingo-oophorectomyConizationRadical hysterectomy and removal of lymph nodesInternal radiation therapy

Malignancies

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Stages of Cervical Cancer: Stage IB

Stage	Test Results	Treatment Options
Stage IB	<ul style="list-style-type: none">● In stage IB, the tumour is still within the cervix and either:<ul style="list-style-type: none">○ Can only be seen with a microscope and is deeper than 5 millimeters (less than 1/4 inch) or wider than 7 millimeters (about 1/4 inch)○ Can be seen without a microscope and may be larger than 4 centimeters (about 1 1/2 inches)	<ul style="list-style-type: none">● Combination of internal radiation therapy and external radiation therapy● Radical hysterectomy and removal of lymph nodes● Radical hysterectomy and removal of lymph nodes followed by radiation therapy plus chemotherapy● Radiation therapy plus chemotherapy

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Session 5: Malignancies Associated with Immunosuppression

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Stages of Cervical Cancer: Stages II-IIA

Stage	Test Results	Treatment Options
Stage II	<ul style="list-style-type: none">• Cancer has spread beyond the cervix but not to the pelvic wall. Stage II is divided into stages IIA and IIB, based on how far the cancer has spread from the cervix into nearby tissue	
Stage IIA	<ul style="list-style-type: none">• Cancer has spread beyond the cervix to the upper two thirds of the vagina but not to tissues around the uterus	<ul style="list-style-type: none">• Combination of internal radiation therapy and external radiation therapy• Radical hysterectomy and removal of lymph nodes• Radical hysterectomy and removal of lymph nodes followed by radiation therapy plus chemotherapy• Radiation therapy plus chemotherapy

Malignancies

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Session 5: Malignancies Associated with Immunosuppression

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Stages of Cervical Cancer: Stages IIB-III

Stage	Test Results	Treatment Options
Stage IIB	<ul style="list-style-type: none">• Cancer has spread beyond the cervix to the upper two thirds of the vagina and to the tissues around the uterus	<ul style="list-style-type: none">• Internal and external radiation therapy combined with chemotherapy
Stage III	<ul style="list-style-type: none">• Cancer has spread to the lower third of the vagina and may have spread to the pelvic wall and nearby lymph nodes. Stage III is divided into stages IIIA and IIIB, based on how far the cancer has spread	

Malignancies

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Stages of Cervical Cancer: Stages IIIA-III B

Stage	Test Results	Treatment Options
Stage IIIA	<ul style="list-style-type: none">• Cancer cells have spread to the lower third of the vagina but not to the pelvic wall	<ul style="list-style-type: none">• Internal and external radiation therapy combined with chemotherapy
Stage IIIB	<ul style="list-style-type: none">• Cancer cells have spread to the pelvic wall and/or the tumour has become large enough to block the ureters. This blockage can cause the kidneys to enlarge or stop working. Cancer cells may also have spread to lymph nodes in the pelvis	<ul style="list-style-type: none">• Internal and external radiation therapy combined with chemotherapy

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Stages of Cervical Cancer: Stage IV

Stage	Test Results	Treatment Options
Stage IV	<ul style="list-style-type: none">• Cancer has spread to the bladder, rectum, or other parts of the body. Stage IV is divided into stages IVA and IVB, based on where the cancer is found	

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Stages of Cervical Cancer: Stages IVA-IVB

Stage	Test Results	Treatment Options
Stage IV	<ul style="list-style-type: none">• Cancer has spread to the bladder or rectal wall and may have spread to lymph nodes in the pelvis	<ul style="list-style-type: none">• Internal and external radiation therapy combined with chemotherapy
Stage IVB	<ul style="list-style-type: none">• Cancer has spread beyond the pelvis and pelvic lymph nodes to other places in the body, such as the abdomen, liver, intestinal tract, or lungs	<ul style="list-style-type: none">• Radiation therapy as palliative therapy to relieve symptoms caused by the cancer and improve quality of life• Chemotherapy

Malignancies

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Treatment of Cervical Cancer (1)

- Surgery
 - Conization
 - Hysterectomy
 - Bilateral salpingo-oophorectomy
 - Radical hysterectomy
 - Pelvic exenteration

Malignancies

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- Three types of standard treatment are used:
 1. Surgery: sometimes used to treat cervical cancer. The following surgical procedures may be used:
 - Conization:
 - Surgery to remove a cone-shaped piece of tissue from the cervix and cervical canal for biopsy. Also called cone biopsy.
 - Hysterectomy:
 - The uterus and cervix are removed in a hysterectomy.
 - If the uterus is taken out through the vagina, the operation is called a vaginal hysterectomy.
 - If the uterus is taken out through an incision (cut) in the abdomen, the operation is called a total abdominal hysterectomy.
 - Bilateral salpingo-oophorectomy:
 - The removal of both ovaries and both fallopian tubes.
 - Radical hysterectomy:
 - This surgery involves removing the cervix, uterus, fallopian tubes, ovaries, and part of the vagina.
 - Lymph nodes may also be removed.
 - Pelvic exenteration:
 - If the cancer has spread throughout the pelvis, then the lower colon, rectum, or bladder (depending on where the cancer has spread) may be removed along with the cervix, uterus, and vagina.
 - Plastic surgery may be needed to make an artificial vagina after this operation.



Treatment of Cervical Cancer (2)

- Surgery (continued)
 - Cryosurgery
 - Laser surgery
 - Loop electrosurgical excision procedure (LEEP)
- Radiation
- Chemotherapy

Malignancies

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1. Surgery (continued)
 - Cryosurgery:
 - An instrument is used to freeze and destroy the abnormal tissue. This procedure is also called cryotherapy. *Carcinoma in situ* may be treated with cryosurgery.
 - Laser surgery:
 - A laser beam (a narrow beam of intense light) is used as a knife to remove the cancer. A laser beam can also be used to kill the cancer cells. This may be called laser therapy.
 - Loop electrosurgical excision procedure (LEEP):
 - An electrical current passed through a thin wire loop is used as a knife to remove abnormal tissue.
 2. Radiation Therapy: the use of X-rays or other types of radiation to kill cancer cells and shrink tumours. Radiation therapy may use external radiation (using a machine outside the body) or internal radiation.
 - Internal radiation involves putting radioisotopes (materials that produce radiation) through thin plastic tubes into the area where cancer cells are found.
 - Both external and internal radiation are used for cervical cancer.
 3. Chemotherapy: the use of drugs to kill cancer cells.
 - Chemotherapy may be taken by mouth, or it may be put into the body by inserting a needle into a vein or muscle.
 - Either type of chemotherapy is called systemic treatment because the drugs enter the bloodstream, travel through the body, and can kill cancer cells throughout the body. (National Cancer Institute, cancer.gov)
- *Note: Presently, none of the treatments described are available at Tambaram.*
- *Go over treatment options shown on Handout 5.1, "Stages of Cervical Cancer". Ask participants to share other experiences treating cervical cancer with HIV-infected patients.*



Session 5: Malignancies Associated with Immunosuppression

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Key Points (1)

1. Physicians must think in terms of not only the possibility of opportunistic infections but also malignancies when diagnosing and treating HIV positive patients
2. Kaposi sarcoma is a type of cancer which is more aggressive and common in HIV-infected persons than in the general populace. Kaposi sarcoma is very rare in South India

Malignancies

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Key Points (2)

3. AIDS-related lymphoma, a disease in which cancer cells are found in the lymph system in patients who have AIDS, can be difficult to treat because of patients' compromised immune systems
4. The incidence of cervical dysplasia, a precursor to cervical cancer, is increased in HIV-infected women
5. Kaposi sarcoma, lymphoma, and cervical cancer can be treated through radiation therapy, chemotherapy, and surgery

Malignancies

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Clinical Management of Opportunistic Infections

Participant's Handbook

Session 6

Prevention of Opportunistic Infections

Session 6: Prevention of Opportunistic Infections

Aim: The aim of this unit is to introduce participants to strategies to prevent opportunistic infections.

Learning Objectives: By the end of this unit, participants will be able to:

- Describe environmental protection strategies that minimize the risk of acquiring specific opportunistic infections.
- Compare the advantages and disadvantages of using chemoprophylaxis.
- Explain which vaccinations and immunisations can be administered to HIV-positive patients.
- Describe environmental factors that can help prevent opportunistic infections.

Key Points

1. A number of opportunistic infections are preventable using a single antimicrobial agent.
2. Cotrimoxazole, if taken regularly, has been shown to prevent a number of infections that occur frequently in HIV-infected persons.
3. TB may be prevented through vaccination and through prophylactic treatment of latent infection.
4. The advantages and disadvantages of chemoprophylaxis should be weighed.
5. Safe and hygienic practices in the health-care facility and in the home may prevent the transmission of infections.



Handout 6.1

Vaccination of Children Who Have HIV Infection

Vaccine	Recommendation for	
	Asymptomatic Child	Symptomatic Child
Bacille Calmette Guerin (BCG)	Yes	No
Diphtheria Pertussis Tetanus	Yes	Yes
Oral Polio Vaccine	Yes	Yes
IM Polio Vaccine	Yes	Yes
Measles	Yes	Yes
Hepatitis B Virus	Yes	Yes
<i>Haemophilus influenzae</i> B	Yes	Yes
Yellow Fever	No	No
Influenza	No	No



Preventable Infections

	Infection	Method of prevention
Viruses	Hepatitis B	Vaccination
	Influenza	
	Polio	
	Measles	
Bacteria	Diphtheria	Vaccination EPI Programme
	Pertussis	
	Tetanus	
	Tuberculosis	BCG Vaccination at birth (EPI Programme) Chemotherapy with INH
	<i>Haemophilus influenza B</i>	Vaccination
	Streptococcal pneumonia	Vaccination with conjugated vaccine, to be repeated every five years Chemotherapy with cotrimoxazole
Protozoa	Non-typhoid salmonellosis	Chemotherapy with cotrimoxazole
	Nocardiosis	
	Isosporiasis	
Fungi	<i>Cyclospora</i> Infection	Chemotherapy with cotrimoxazole
	Toxoplasmosis	
	<i>Pneumocystis pneumonia</i>	
	Candidiasis	
	Cryptococcosis	
Fungi	Coccidioidomycosis	Chemotherapy with fluconazole



Worksheet 6.1

The Impact of a Reduced OI Caseload

Instructions for Group

- Read the scenario below.
- As a class, discuss and answer the questions that follow.

Scenario

Imagine that the number of patients at Tambaram Sanatorium that require diagnosis and/or treatment of HIV-related opportunistic infections (OIs) was cut by ONE HALF.

- What impact would that have on the hospital as a whole? Consider what that would mean in terms of resources, workloads, facilities, quality of patient care, etc.
- What impact would that have in the unit/department(s) that you work in?
- How would this impact you personally and the work that you do?



Worksheet 6.2

Developing Guidelines for Environmental Protection

Instructions for the Group

- As a group, discuss and answer the questions below.
- Appoint someone to write on the flip-chart.
- Appoint a presenter to report your group's results.
- You will have 5 minutes to present to the rest of the group.

Your group will be assigned a category of infection: _____

Questions

1. Review the infections in this category listed on the handout entitled, "Table: Preventable Infections." What other HIV-related opportunistic infections could be added to this list (which may or may not be preventable using chemoprophylaxis)?

2. Go through the list of infections in this category (including the ones in the table and the ones you've added). To the best of your group's ability, identify the behavioural, environmental, and lifestyle factors that increase the probability of contracting the infection.

3. Now that you've identified factors that increase risk, what guidelines could you give to patients that would help them reduce their risk of contracting the infection? In other words, if possible, how could they alter their behaviours, environments, or lifestyles to try to avoid contracting the disease? Write your guidelines on the flip-chart paper to present to your colleagues later.



References

Central TB Division. (2003). *TB India 2003: Revised National Tuberculosis Control Programme (RNTCP) Status Report*. New Delhi, India: Directorate General of Health Services, Ministry of Health and Family Welfare. Available online at <http://www.tbcindia.org/documents.asp>.

Clinical Epidemiology Resource & Training Centre (2003), *Prevention of Opportunistic Infections: A Training Course for Doctors and Nurses*. Harare, Zimbabwe: University of Zimbabwe College of Medicine.

The Foundation for Professional Development (2001). *Course in HIV/AIDS Management*. Pretoria, South Africa: The Foundation for Professional Development.

 **Notes**



**Prevention of
Opportunistic Infections**
Session Six





Learning Objectives

- By the end of this session, you will be able to:
 - Describe environmental protection strategies that minimize the risk of acquiring specific opportunistic infections
 - Compare the advantages and disadvantages of using chemoprophylaxis
 - Explain which vaccinations and immunizations can be safely administered to HIV positive patients
 - Describe environmental factors that can help prevent opportunistic infections

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- *The aim of this session is to introduce participants to strategies to prevent opportunistic infections.*



Discussion

- Imagine that the number of patients at Tambaram Sanatorium that require diagnosis and/or treatment of HIV-related opportunistic infections (OIs) was cut by ONE HALF
 - What impact would that have on the hospital as a whole? Consider what that would mean in terms of resources, work loads, facilities, quality of patient care, etc.
 - What impact would that have in the unit/department(s) that you work in?
 - How would this impact you personally and the work that you do?

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- *Read the scenario in “The Impact of a Reduced OI Caseload” (Worksheet 6.1) in the Participant’s Handbook.*



Discussion: Impact on Hospital

- Better utilization of resources in quality care
- While work load may decrease, more patients may seek medical advise because of better care & support
- Facilities can be improved
- Quality of patient care will improve



Discussion: Impact on Unit or Department and Self

- Unit or department:
 - Improvement of patient care quality
 - More time can be spent on each patient
 - Better utilization of available resources
- Self:
 - Can spend more time with the patient to give quality and evidence-based care to patients
 - Allows better utilization of available resources



Introduction (1)

- With antiretroviral (ARV) drugs, it is possible to delay the onset of AIDS and the development of opportunistic infections
- The period of susceptibility to opportunistic infections correlates well with CD4+ lymphocyte levels

Prevention of Opportunistic Infections

Slide 6

- Persons with HIV infection and AIDS are prone to life threatening infections as a result of their immune suppression.
- With the advent of effective antiretroviral (ARV) drugs, and their appropriate use in combinations, it is possible to delay the onset of AIDS and the development of opportunistic infections and also to allow PLHAs to enjoy a better quality of life.
- As antiretroviral therapy cell mediated immunity gradually improves and as the HIV plasma viral load decreases, the peripheral blood CD4+ lymphocyte counts increase.
- Individuals with HIV infection and immunosuppression develop, and often succumb to, a number of bacterial, viral, protozoal and fungal infections.
 - Many of these are treatable with appropriate antimicrobial agents.
 - A large number of infections that commonly occur in immunosuppressed individuals may be prevented with antimicrobial agents used on a long-term basis.



Introduction (2)

- With successful ARV therapy, the levels of peripheral blood CD4+ lymphocytes gradually increase
- Studies have shown that a number of infections may be prevented with chemoprophylaxis

Prevention of Opportunistic Infections

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- With the introduction of ARV therapy, it has become evident that chemoprophylaxis for opportunistic infections need not be a lifelong process.
- The period of susceptibility to opportunistic infections correlates well with CD4+ lymphocyte levels.
 - With successful ARV therapy, the levels of peripheral blood CD4+ lymphocytes gradually increase.
 - Although studies are limited, it is generally felt that chemoprophylaxis be continued while the peripheral blood CD4+ lymphocyte counts remain less than 200/mm³.
- Infections such as:
 - Tuberculosis
 - *Pneumocystis jiroveci pneumonia* (PCP)
 - Toxoplasmosis
 - Bacterial lower respiratory tract infections
 - Recurrent meningitis and septicaemia
 - Chronic diarrhoeal diseases including cryptosporidiosis and
 - Bacterial skin infections occur commonly in HIV-infected patients.
- Studies have shown that a number of infections may be prevented with chemoprophylaxis.



Cotrimoxazole Chemoprophylaxis (CTZ)

- CTZ can potentially prevent the following life-threatening infections:
 - *Streptococcus pneumoniae* pneumonia
 - *Pneumocystis jiroveci* pneumonia
 - Non-typhoid salmonellosis
 - Cerebral toxoplasmosis
 - Nocardiosis
 - Isosporiasis
 - *Cyclospora* infection

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- Long-term chemoprophylaxis with cotrimoxazole (CTZ) can potentially prevent the following life-threatening infections:
 - *Streptococcus pneumoniae* pneumonia
 - *Pneumocystis jiroveci* pneumonia
 - Non-typhoid salmonellosis
 - Cerebral toxoplasmosis
 - Nocardiosis
 - Isosporiasis
 - *Cyclospora* infection



Treatment with CTZ

- Recommended that all persons with symptomatic HIV infection and those with CD4+ lymphocyte counts of less than 200/mm³ should receive:
 - Cotrimoxazole (sulphamethoxazole 800 mg and trimethoprim 160 mg) once daily orally
 - Should be given in the form of two tablets of regular strength or one tablet of the double strength orally daily
 - Treatment is continued indefinitely
 - Clinical guidelines:
 - If CD4 count is not available, all symptomatic patients should be given prophylaxis

Prevention of Opportunistic Infections

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- It is therefore recommended that all persons with symptomatic HIV infection and those with CD4+ lymphocyte counts of less than 200/mm³ should receive:
 - Cotrimoxazole (sulphamethoxazole 800 mg and trimethoprim 160 mg) once daily orally.
 - This may be given in the form of two tablets of the regular strength or one tablet of the double strength orally daily.
 - Treatment is continued indefinitely.
- Cotrimoxazole is a relatively inexpensive drug; it is rarely associated with side effects (except in persons who are allergic to sulphonamides) and is easily administered orally.
- The effect of long-term cotrimoxazole prophylaxis has been the improvement of quality of life, the prolongation of life, and the reduction in the incidence of opportunistic infections.
- This is an intervention that has been shown to work and programmes for the provision of cotrimoxazole to persons with HIV infection who have evidence of immunosuppression should be developed and implemented as a priority.



Giving CTZ to Children and Pregnant Women

- Cotrimoxazole chemoprophylaxis may also be used in pregnant women in regular doses
- Use the following regimen when prescribing CTZ to young children:
 - Children < 6 months old, quarter tablet of single strength of CTZ once a day
 - Children ages 6 to 12 months, half a tablet once a day
 - Children >12 months, one tablet a day

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- Cotrimoxazole chemoprophylaxis may also be used in pregnant women in the doses stated.
- In children, the dose is based on the trimethoprim dose of 15mg/kg/day.
- Use the following regimen when prescribing CTZ to young children:
 - Children < 6 months old give a quarter tablet of single strength of CTZ once a day.
 - Children ages 6 to 12 months, give half a tablet once a day.
 - Children >12 months, give one tablet a day.
- The success of this intervention in preventing infections is dependent upon adherence to the treatment regimen.
 - Hence all patients with HIV infection should be educated, counselled, and encouraged to comply with the treatment. (Zim, Prevention of OI).
- If patients develop hypersensitive reactions to CTZ, 100 mg of Dapsone per day should be prescribed.
- Tamaram has also successfully tried desensitization for CTZ in a few patients.
 - If the patients also have hypersensitivity to Dapsone, the alternatives are either to prescribe 300 mg per week of nebulised Pentamidine or the newer drug, Atovaquone.



Tuberculosis Testing (1)

- Active TB should first be excluded by carrying out:
 - Clinical examination
 - Performing chest X-ray
 - Microscopic examination of sputa

Prevention of Opportunistic Infections

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- Tuberculosis occurs very commonly in persons with HIV infection.
- The infection is easily treated with the standard anti-TB drug regimens and all efforts need to be made to identify and treat persons with possible HIV/TB co-infection.
- In offering chemoprophylaxis for TB, all attempts should be made to exclude active TB first.
 - Active TB may be excluded by carrying out a thorough clinical examination and by performing a chest X-ray and microscopic examination of sputa.
 - If active TB is discovered, the patient should be treated for TB according to the TB guidelines developed by the Revised National Tuberculosis Control Programme (RNTCP).



Tuberculosis Testing (2)

- WHO recommends all HIV positive persons have tuberculin skin test (Mantoux test)
 - If tuberculin test is positive (equal to or greater than 5mm using 5TU in a Mantoux test), patients should have chest x-ray and sputum examinations
 - Individuals having positive tuberculin test and no clinical, microbiologic or radiological evidence of TB, should be considered to have latent TB
- Refer to NACO Guidelines on Tuberculosis

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- The World Health Organization recommends that in all HIV positive persons a tuberculin skin test (Mantoux test) should be performed.
 - If the tuberculin test is positive, i.e., equal to or greater than 5mm using 5TU in a Mantoux test, patients should have a chest X-ray and sputum examinations.
 - Those that have a positive tuberculin test and no clinical, microbiologic or radiologic evidence of TB should be considered to have Latent TB.
 - Such patients may be treated for latent TB
- Care should be taken not to treat active TB with one or two anti-TB drugs only. (Zim, Prevention of OIs)



INH Chemoprophylaxis for TB (1)

- Preventive therapy for TB reduces risk of development of active TB in HIV-infected individuals
- However, in India, the durability of this effect may be limited by high rates of re-infection with TB



INH Chemoprophylaxis for TB (2)

- WHO recommends TB preventive therapy if possible where diagnostic testing, (e.g. chest X-rays) is available to exclude active TB and where PPD skin testing is feasible
- In such situations, isoniazid therapy (with pyridoxine supplementation) for 6 months in tuberculin skin test reactors should be given after exclusion of active disease

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- In India, however, the issue of INH prophylaxis is complicated due to the following reasons:
 - Difficulty in excluding active TB disease in those with HIV/TB co-infection.
 - In a country like India where the burden of TB is high, chemoprophylaxis may not prevent the reinfection.
 - Widespread use of INH for chemoprophylaxis may contribute to an increase in INH resistance.
 - PPD skin test may not be feasible and is also not reliable in severely immunocompromised patients.
- BCG Vaccination
 - Vaccination with BCG in HIV patients is effective in preventing the progression of infection with *M. tuberculosis* with TB disease provided it's given before infection.
 - But complications from vaccination have been reported as microbacterial meningitis, cervical, axillary lymphadenopathy, and disseminated BCG disease.
 - WHO does not recommend BCG for children who show symptoms of HIV, but recommends vaccination of healthy infants of HIV infected mothers.
 - If some complication does occur, it can be treated with anti-TB treatment.



Prevention of Cryptococcal Meningitis

- For preventing recurrences of cryptococcal meningitis:
 - Fluconazole 200mg orally daily for life
- For preventing oro-pharyngeal candidiasis and oesophageal candidiasis and histoplasmosis:
 - Fluconazole 200mg orally daily
- For secondary prevention of fungal infections:
 - Itraconazole given in a dose of 200mg orally daily

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- Secondary prevention of cryptococcal meningitis and prevention of other mycoses:
 - In persons with HIV infection who have had an episode of cryptococcal meningitis, it has been demonstrated that this life-threatening infection may be suppressed through the long-term use of Fluconazole after the initial episode has been adequately treated appropriately with antimycotic agents, such as:
 - Amphotericin B
 - Flucytosine and Fluconazole, or
 - Itraconazole
 - For preventing the recurrence of cryptococcal meningitis give the patient Fluconazole 200 mg orally daily for life.
 - For preventing oro-pharyngeal candidiasis and oesophageal candidiasis and histoplasmosis, give the patient Fluconazole 200mg orally daily.
 - However, this is not routinely used in India because of resistance issues and good response to Fluconazole.
 - Other antifungal agents have also been shown to be effective in the secondary prevention of fungal infections.
 - These include Itraconazole given in a dose of 200mg orally daily. (Zim, Prevention of OIs)



Other Secondary Infections and Complications (1)

- Anal genital herpes:
 - Acyclovir, 400 mg BID
 - Famciclovir*, 250 mg BID
 - Valacyclovir*, 500 mg BID

** Not available at Tambaram*

Prevention of Opportunistic Infections

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- The following drugs are recommended for other secondary infections and complications related to HIV:
 - Prophylaxis for Herpes Simplex is advocated for patients with frequent outbreaks of anal genital herpes. The drugs commonly used are:
 - Acyclovir, 400 mg BID
 - Famciclovir*, 250 mg BID
 - Valacyclovir*, 500 mg BID



Other Secondary Infections and Complications (2)

- If the CD4 < 50:
 - Oral Ganciclovir*, 1 g TID for cytomegalovirus prophylaxis is advocated
- If the CD4 < 100:
 - Toxoplasma prophylaxis is advocated and drugs available are:
 - CTZ
 - Dapsone, 200 mg per week and Pyrimethamine, 75 mg per week
 - Atovaquone* with or without Pyrimethamine

** Not available at Tambaram*

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- If the CD4 is less than 50, oral Ganciclovir*, 1g TID for cytomegalovirus prophylaxis is advocated.
- If the CD4 is less than 100, Toxoplasma prophylaxis is advocated. The drugs available are:
 - CTZ
 - Dapsone, 200 mg per week and Pyrimethamine, 75 mg per week
 - Atovaquone* with or without Pyrimethamine
- **Not available at Tambaram*



Risks and Benefits of Prophylaxis (1)

- Risks and benefits of prophylaxis should be carefully considered
- Advantages of long-term anti-fungal therapy: improved quality of life and nutrition for patients with advanced AIDS

BUT



Risks and Benefits of Prophylaxis (2)

- Cryptococcal meningitis is uncommon
- Prophylactic treatment is expensive, and it may interfere with other more important treatments
- Concerns about the effect of increased use of fluconazole on drug-resistance in *Cryptococcus* and in *Candida*

Prevention of Opportunistic Infections

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- It may interfere with other more important treatments (for example, there could be a drug interaction with rifampin and rifabutin).
- Source: (Foundation for Professional Development)



Discussion: Risks and Benefits of Chemoprophylaxis

- What might be an example of when you think chemoprophylaxis would be warranted for a patient with cryptococcal meningitis?
- Why do you think it would be warranted in this case?
- In what situations would you not recommend chemoprophylaxis?
- What about with patients with oro-pharyngeal candidiasis or oesophageal candidiasis?

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- *Discuss the risks and benefits of chemoprophylaxis using the questions on the corresponding slide in the PowerPoint presentation.*



Vaccinations in HIV+ Patients

- Babies born to mothers with HIV infection should be immunized according to the National Guidelines of the Expanded Programme on Immunizations (EPI)
- These children will receive BCG vaccination at birth and vaccination against polio, pertussis, diphtheria, tetanus, and measles during the first nine months of life
- Hepatitis B vaccine, Haemophilus influenza B vaccine, and the conjugate pneumococcal vaccine may also be given

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- Babies born to mothers with HIV infection should be immunized according to the National Guidelines of the Expanded Programme on Immunizations (EPI).
- These children will receive BCG vaccination at birth and vaccination against:
 - Polio
 - Pertussis
 - Diphtheria
 - Tetanus, and
 - Measles during the first nine months of life.
- This policy should be encouraged and continued.
- Hepatitis B vaccine, *Haemophilus influenza B* vaccine, and the conjugate pneumococcal vaccine may also be given.
- BCG vaccine should not be given to symptomatic HIV/AIDS patients and a booster should not be given to the pre-school child until the child's HIV status is known.
- Vaccination against Yellow Fever should be avoided.
- Children with HIV infection and AIDS may be vaccinated in accordance with the National EPI guidelines provided that live vaccines are avoided in symptomatic children.
- *Handout 6.1 "Vaccination of Children Who Have HIV Infection" summarizes the vaccination recommendations. (Zim, Prevention of OIs)*



Vaccination of HIV+ Children (1)

	Yes	No
Bacille Calmette Guerin (BCG)	Yes	No
Diphtheria Pertussis Tetanus	Yes	Yes
Oral Polio Vaccine	Yes	Yes
IM Polio Vaccine	Yes	Yes
Measles	Yes	Yes

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- Refer to “Vaccination of Children Who Have HIV Infection” and “Preventable Infections” (Handouts 6.1-6.2) in the Participant’s Handbook.



Vaccination of HIV+ Children (2)

Hepatitis B Virus	Yes	Yes
Haemophilus influenzae B	Yes	Yes
Yellow fever	No	No
Influenza	No	No



Preventable Infections (1)

Viruses	Hepatitis B	Vaccination
	Influenza	
	Polio	
	Measles	
Bacteria	Diphtheria	Vaccination EPI Programme
	Pertussis	
	Tetanus	
	Tuberculosis	BCG Vaccination at birth (EPI Programme) Chemotherapy with INH
	Haemophilus influenza B	Vaccination

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- *Handout 6.2 summarizes the infections that may be preventable and the methods of prevention.*
- *These include the vaccines used in the Expanded Programme of Immunization (EPI). (Zim, Prevention of OIs)*



Preventable Infections (2)

Bacteria	Streptococcal pneumonia	Vaccination with conjugated vaccine, to be repeated every five years Chemotherapy with cotrimoxazole
	Non-typhoid salmonellosis	Chemotherapy with cotrimoxazole
	Nocardiosis	
Protozoa	Isosporiasis	Chemotherapy with cotrimoxazole
	Cyclospora Infection	
	Toxoplasmosis	



Preventable Infections (3)

	Pneumocystis pneumonia	Chemotherapy with cotrimoxazole
Fungi	Candidiasis	Chemotherapy with fluconazole
	Histoplasmosis	
	Cryptococcosis	
	Coccidioidomycosis	



Guidelines for Environmental Protection Exercise (1)

- Break into four groups, one for each of the following categories of infection: virus, bacteria, protozoa, fungi
- In your groups brainstorm ways in which patients could reduce their risk of contracting infections by changing their environment, behaviours, or lifestyles

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- In addition to chemoprophylaxis, there are other ways in which patients can reduce their risk of contracting opportunistic infections:
 - Making changes to their environments, behaviours, and lifestyle choices may reduce their chances of contracting infection.
- *Refer to Worksheet 6.2, "Developing Guidelines for Environmental Protection."*



Guidelines for Environmental Protection Exercise (2)

- Refer to Worksheet 6.2, “Developing Guidelines for Environmental Protection”, using a piece of flipchart paper and a marker to answer the questions
- Choose one group member to write down your guidelines and another member to share the guidelines with the rest of the class



Environmental Protection Small Group Questions

1. What other HIV-related opportunistic infections could be added the list of preventable infections?
2. What behavioral, environmental, and lifestyle factors increase the probability of contracting an infection?
3. How can patients alter their behaviors, environments, or lifestyles to try to avoid contracting an infection?



Environmental Protection Large Group Discussion Questions (1)

1. Does anyone have any additional suggestions for guidelines to prevent this type of infection?
2. How receptive do you think patients would be to making these kinds of behavioural (environmental, lifestyle) changes? What might be some barriers?



Environmental Protection Large Group Discussion Questions (2)

3. What factors are within the patient's control?
4. What resources can you offer or refer patient to?
5. How could you best present the guidelines so that patients would be encouraged to take the steps you advised?



Environmental Protection Exercise Teaching Points (1)

- HIV-related OIs that can be added to the list of preventable infections:
 - TB
 - PCP
 - Toxoplasmosis
 - Cryptosporidiosis
 - Isospora
 - Microsporidiosis
 - Cryptococcosis
 - Candidiasis
 - Bacterial pneumonias
 - Non tryphoidal salmenellosis
 - Nocardiosis
 - Histoplamosis



Environmental Protection Exercise Teaching Points (2)

- Factors that increase the probability of contracting an infection:
 - Coughing without covering the mouth
 - Inadequate hand washing
 - Rearing pet animals without proper preventive measures
 - Noncompliance with immunization schedule/vaccinations and infection control measures
 - Misuse or failure to use personal protective equipment



Environmental Protection Exercise Teaching Points (3)

- Factors that increase the probability of contracting an infection (continued):
 - Lack of training in infection control measures or handling and disposal of infectious materials
 - Failure to implement occupational accidental exposure policies
 - Failure to follow personal and environmental safety measures
 - Drinking water without adequate infection control procedures
 - Failure to follow safe sex practices



Environmental Protection Exercise Teaching Points (4)

- Ways that patients can reduce the risk of contracting an infection:
 - Adequate hand washing
 - Following universal immunization schedule or vaccination whenever necessary
 - Following infection control measures
 - Following cough hygiene
 - Proper use of personal protective equipment
 - Consuming safe drinking water
 - Adherence to environmental and personal hygiene
 - Adequate safety measures when rearing pet animals



Environmental Protection Exercise Teaching Points (5)

- Barriers to making changes:
 - Poor knowledge/ignorance
 - Poverty
 - Resistance to change behaviours & life style
- Factors within patient's control:
 - Knowledge
 - Behavior change
 - Life style modifications



Environmental Protection Exercise Teaching Points (6)

- Resources for patients:
 - Education about opportunistic infections
 - IEC materials
 - Training on infection control measures and immunisation schedule



Health Care Worker Practices

Preventing the Spread of Opportunistic Infections



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Safe Practices: Avoiding Injuries (1)

- HIV is not spread through droplet inhalation, but a health worker may become infected via needle stick or scalpel blade injuries
- All needle stick injuries should be reported and post-exposure prophylaxis treatment should begin

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- HIV infection and infection with the Hepatitis B and C viruses may rarely be transmitted to health workers, managing persons with these infections.
- Safe practices and guidelines for Standard Precautions should be strictly adhered to in order to minimize the risk.
- HIV is not spread through droplet inhalation, but a health worker may become infected by the accidental introduction of infected material obtained from an infected person through needle-stick and scalpel blade injuries.



Safe Practices: Avoiding Injuries (2)

- Average risk of transmission of HIV through a needle stick is about 0.3%
- The risk is higher if:
 - The injury was a deep intramuscular stab
 - The needle had been used in a patient with advanced HIV infection
 - The needle had been used to draw venous or arterial blood
 - Blood was visible on the needle

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- It is important to prevent the introduction of infected material into the body, and certain safe practices should always be adhered to. These include:
 - Developing a policy for the prevention of occupational accidental exposure to blood borne pathogens.
 - Implementing standard precautions for the prevention of exposure to potentially infectious material.
 - Educating all personnel of the risks involved in improper handling of infectious materials. The steps necessary for preventing exposure should be clearly displayed in posters.
 - Training of all employees in the handling and disposal of infectious material.
 - Training all personnel on how to safely handle sharp objects and how to safely dispose of them.
 - Messages should promote avoiding re-capping of needles, using “sharps bins” for disposing of sharps, and taking care in performing procedures.
 - Ensuring an uninterrupted supply of:
 - Education materials
 - Disposable needles and syringes, and
 - Sharps bins



Safe Practices: Basic Care

- Wash hands regularly
- Wear rubber apron under gown
- Wear facemask
- Wear goggles if there is likelihood of splashing
- Dispose of infectious waste and needles appropriately
- Do not recap needles

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- Hand washing is an important method of preventing transmission of infection.
- When carrying out procedures, it is advisable to wear a rubber apron under the gown.
- A face mask should also be worn.
- If there is likelihood of splashing, goggles should also be used.
- Health personnel should be conscious that blood and secretions from patients may be infectious and that simple contamination of unbroken skin does not comprise a significant risk but contamination of intact mucous surfaces of the mouth and eyes does.
- All needle-stick injuries should be reported and post-exposure prophylaxis should begin.

Note: See the Infection Control curriculum for more guidelines and training.



Discussion: Safe Practice Policies & Procedures

- What policies does Tambaram Sanatorium have in place to help prevent exposure to potentially infectious material?
- What are the procedures for handling and disposing of infectious materials?
- Is there education and training available for employees on such procedures?
- In what ways could the hospital improve in providing safe practice policies and procedures?



Key Points (1)

1. A number of opportunistic infections are preventable using a single antimicrobial agent
2. Cotrimoxazole, if taken regularly, has been shown to prevent a number of infections that occur frequently in HIV-infected persons
3. TB may be prevented through vaccination and prophylactic treatment of latent infection

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- For homework, divide into three groups according to your place of work. Review the model algorithms in Session 7.
- The facilitator will assign two algorithms to each group, which you will finalize and share with the rest of the class during Session 7.
- If time permits and participants are willing, tour wards within Tambaram to observe cases.
- Then reconvene to discuss what participants have seen.



Key Points (2)

4. The advantages and disadvantages of chemoprophylaxis should be weighed carefully
5. Safe and hygienic practices in the health care facility and in the home may prevent the transmission of infections



Clinical Management of Opportunistic Infections

Participant's Handbook

Session 7

Clinical Management of
Common Medical Problems

Session 7: Clinical Management of Common Medical Problems

Aim: The aim of this unit is to introduce participants to the management of common medical problems.

Learning Objectives: By the end of this unit, participants will be able to:

- Advise HIV-infected patients on how they can care for symptoms of common opportunistic infections and support their bodies' immune systems.
- Provide appropriate clinical care for persons with HIV infection who present with some common medical problems related to HIV and opportunistic infections.

Key Points

1. A number of opportunistic infections are preventable using a single antimicrobial agent.
2. Cotrimoxazole, if taken regularly, has been shown to prevent a number of infections that occur frequently in HIV-infected persons.
3. TB may be prevented through vaccination and through prophylactic treatment of latent infection.
4. The advantages and disadvantages of chemoprophylaxis should be weighed.
5. Safe and hygienic practices in the health-care facility and in the home may prevent the transmission of infections.



Handout 7.1

Educating Your Patient about Common Side Effects of ARV Therapy

All antiretroviral drugs, as well as drugs used to treat and prevent OIs, have some side effects. These side effects may vary from person to person. Some may experience few or no side effects, while others have mild to severe side effects. Side effects often occur after starting a new drug or therapy; they may decrease or disappear entirely after several weeks or may persist throughout the therapy.

Below are the more common side effects associated with first-line regimen ARVs. In addition, advice a caregiver can give to the patient on managing these side effects is included. Local practices and remedies should be assessed and integrated as appropriate.

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, or may suffer depression, anxiety, and/or stress).
- Fatigue may result from sleep problems (having trouble falling asleep, staying asleep, suffering sleep disturbances).
- Fatigue can also be a symptom of anaemia.

Advise the patient to:

1. Try going to sleep at night and waking in the morning at the same time every day; changes in sleep patterns can make a person feel more tired.
2. Avoid caffeine, alcohol, or nicotine for 4 to 6 hours before going to bed. A light snack, chamomile tea, warm milk, and relaxation techniques before bedtime are often helpful.
3. Try to get a little exercise. Exercise eases stress and makes a person feel stronger and more alive.
4. Have someone help with day-to-day chores such as cooking. Keep easy-to-prepare foods on hand for times when cooking is too tiring.
5. Eat snack foods throughout the day and fresh fruits that don't require preparation.

Anaemia

- Anaemia may be caused by HIV itself or be a side effect of drugs.
- Give intramuscular injections of vitamin B12 every 1 to 2 weeks, if necessary or feasible.

Advise the patient to:

1. Return to the clinic to check haemoglobin count regularly.
2. Eat a diet of locally available foods that are high in folic acid, including spinach and other green leafy vegetables, and foods high in iron and vitamin B12, such as fish, red meat, and poultry, if available.
3. Take multivitamins and/or supplements of folic acid or iron.



Handout 7.1 (continued)

Educating Your Patient about Common Side Effects of ARV Therapy (continued)

Headache

• Headaches are generally treatable with nonprescription drugs and through stress reduction.

Advise the patient:

1. For on-the-spot relief, try resting in a quiet, dark room with your eyes closed; place cold washcloths over your eyes; massage the base of your skull with your thumbs and massage both temples gently; take hot baths or showers.
2. To prevent headaches from recurring, try to anticipate when the pain will strike. Avoid or limit those foods known to trigger headaches, especially caffeine (in coffee, tea, and soft drinks), chocolate, alcohol, citrus fruit (if more than half a cup a day), food additives (monosodium glutamate), nuts, onions, hard cheeses, and vinegar.

Nausea and vomiting

• Persistent vomiting can lead to serious medical problems, such as dehydration, chemical imbalances, or even tearing of the oesophagus. Advise the patient to come to the clinic if nausea or vomiting persists and/or interferes with his or her taking their medications.

• Give anti-nausea medications, as needed.

• Nausea often improves if antiretrovirals are taken with food, and most ART drugs can be taken with a meal or snack. Ritonavir or saquinavir should be taken with foods that are high in fat. Indinavir can be taken with a light, fat-free, low-protein meal or snack. Only ddI must absolutely be taken on an empty stomach.

Advise the patient to:

1. Eat a diet of bananas, rice, applesauce, toast, and tea, if possible (known as the BRAT diet).
2. Eat small amounts of bland, odourless foods such as toast, crackers, clear soup, or broth, which are easier to keep down. Eat simple boiled foods such as porridge, potatoes, and beans.
3. Avoid hot, spicy, strong-smelling, and greasy food.
4. Keep some dry crackers at your bedside. Before getting out of bed in the morning, eat a few dry crackers and sit in bed for a few moments.
5. Eat small snacks throughout the day, and avoid large meals.
6. Try peppermint, chamomile, or ginger tea (or the local equivalent).

Diarrhoea

• Watch for signs of dehydration and weight loss. If the patient is dehydrated, teach him or her how to make an oral rehydration solution.

Advise the patient to:

1. Eat a diet high in soluble fiber (which slows the diarrhoea by absorbing liquid). These include the BRAT diet (see d. above) and soft white rice, oatmeal (or oat bran), cream of wheat, or other locally available porridge and soft bread (not whole-grain).



Handout 7.1 (continued)

Educating Your Patient about Common Side Effects of ARV Therapy (continued)

2. Avoid foods high in insoluble fiber, such as corn, popcorn, fruits (dried and raw), vegetables, nuts, seeds, and most grains. These can make diarrhoea worse.
3. Decrease high-fat foods.
4. Avoid milk products and greasy, high fiber or very sweet foods. These tend to aggravate diarrhoea.
5. Prevent dehydration by drinking a lot of fluids. If dehydrated, drink rehydration solution.
6. Drink rice or barley water made by boiling a half-cup of rice or barley in one litre of water. Once the rice or barley is cooked, pour off the water and drink it in small sips.

Rash

- Many people get a rash when starting antiretrovirals, 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 antiretroviral medications than among men. Nevirapine appears to be the main culprit, along with abacavir, efavirenz and amprenavir, as well as cotrimoxazole, isoniazid, 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.
- Be sure to monitor a patient's skin for discolouration and changes in its surface, as well as for signs of hypersensitivity, especially after starting a new medication; teach the patient to watch for such signs.

Advise the patient to:

1. Use creams, moisturisers or a topical ointment such as Benadryl diphenhydramine to soothe and comfort the skin, if a rash should develop.
2. Use unscented, non-soap cleansers or oatmeal soaps.
3. Avoid taking very hot showers or baths; they tend to irritate the skin.
4. If a rash should develop, protect skin from sun exposure; the ultraviolet (UV) rays of the sun may exacerbate a rash.

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.
- Look for these signs during a patient's follow-up visits and advise the patient to watch out for these signs and report them to his or her caregiver.
- Treatment of peripheral neuropathy includes stopping or decreasing the offending drug. Once there is damage to the nerves, it cannot be reversed, therefore be sure to monitor for signs of peripheral neuropathy from the start of therapy.



Handout 7.1 (continued)

Educating Your Patient about Common Side Effects of ARV Therapy (continued)

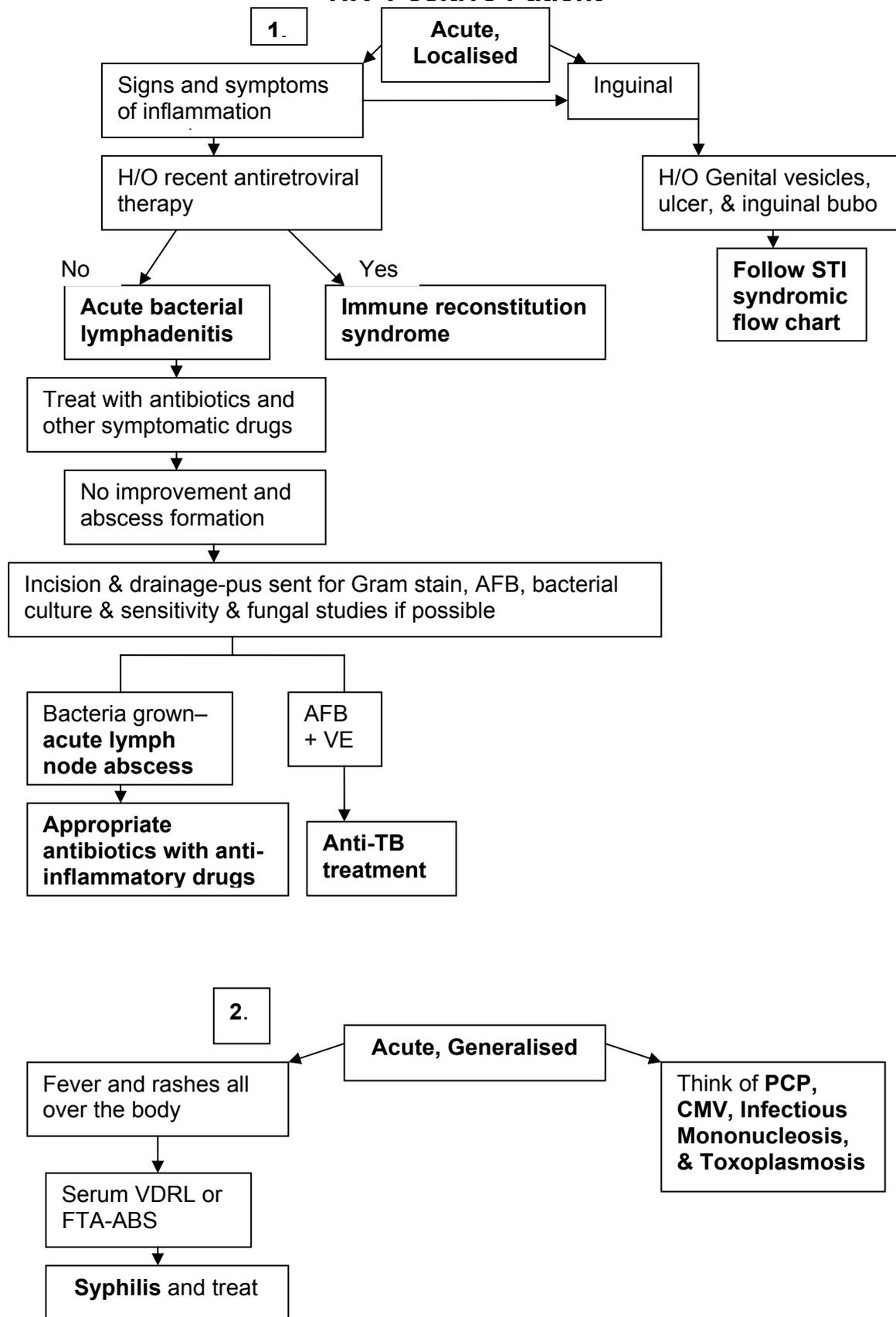
- Because vitamin B deficiency can contribute to peripheral neuropathy, prescribe a B-complex supplement containing thiamine (B1), riboflavin (B2), niacin, pyridoxine (B6) and cobalamin (B12). Consider giving the patient a weekly B12 injection.

Advise the patient to:

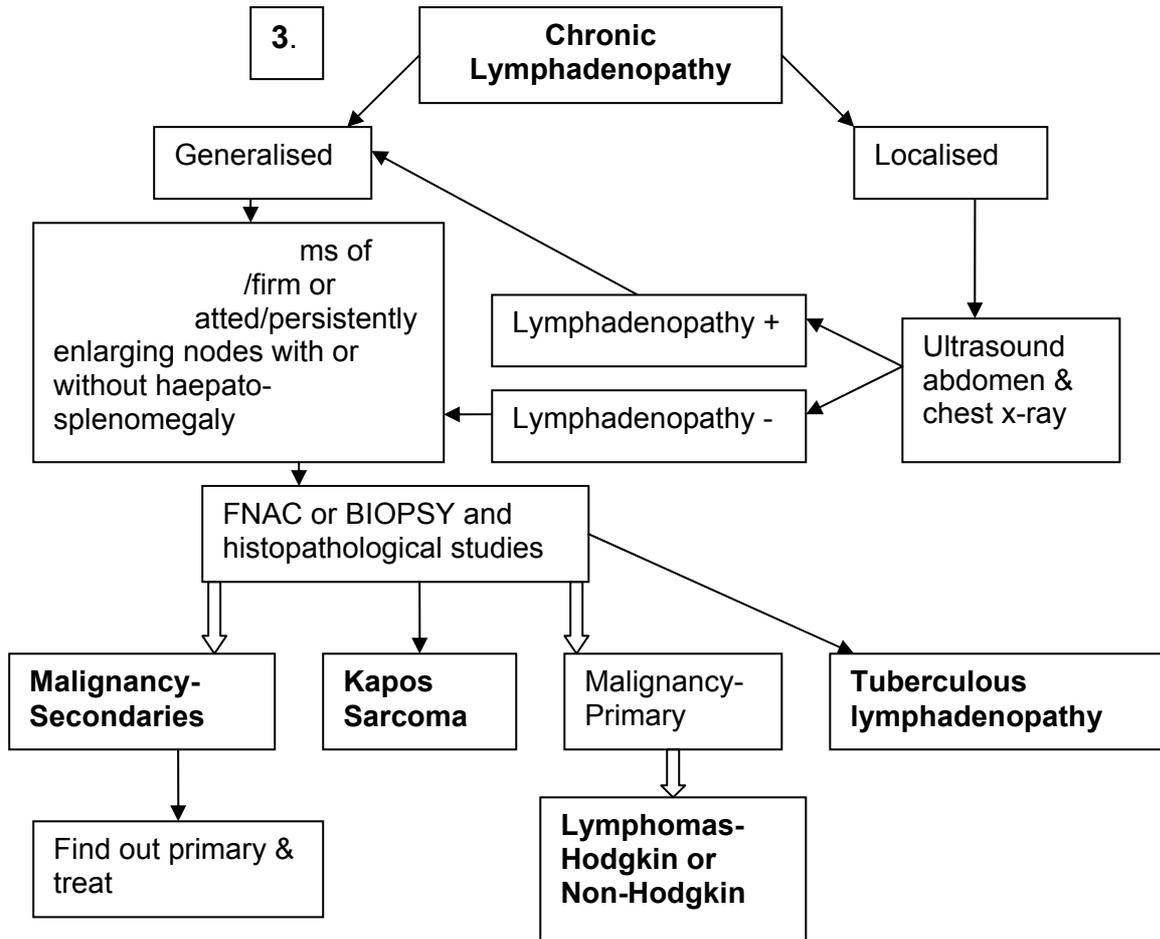
1. Wear loose-fitting shoes, roomy cotton socks, and padded slippers around the house. Good air circulation around the feet helps.
2. Keep feet uncovered in bed. Bedding that presses down on the toes can add to the problem.
3. Walk around, but not too much. Walking helps blood to circulate in the feet, but too much walking or standing can make the problem worse.
4. Soak feet in ice water (or the coldest water available) to reduce foot pain.
5. Massage the feet; this reduces foot pain temporarily.
6. Try ibuprofen (or the equivalent) to reduce pain and swelling
7. Take vitamin B complex supplements.

Adapted from: Family Health International (2003), *HIV/AIDS Care & Treatment: A Clinical Course for People Caring for Persons Living with AIDS*; Arlington: USA. Visit www.fhi.org.

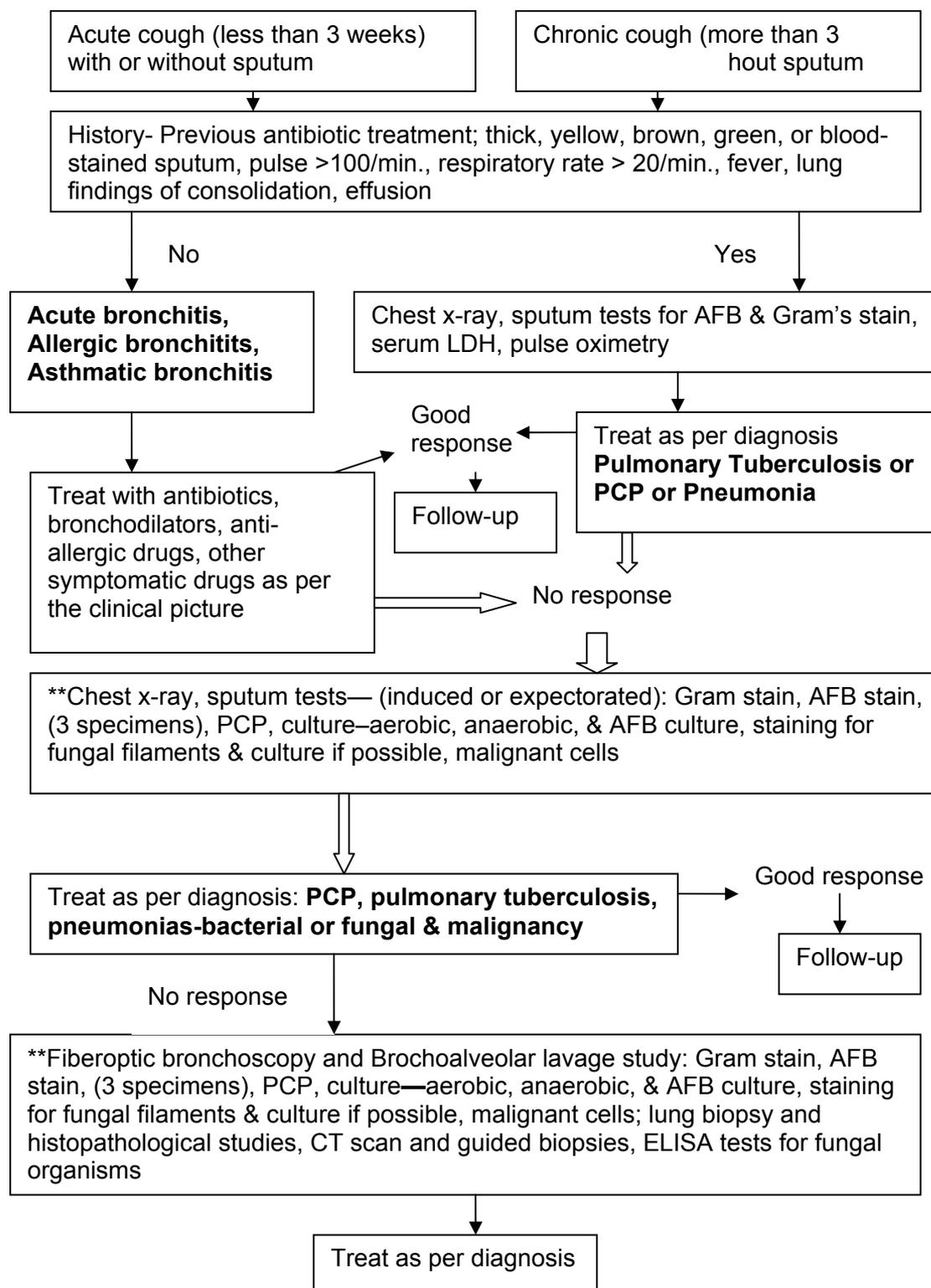
Management of Lymphadenopathy in an HIV-Positive Patient



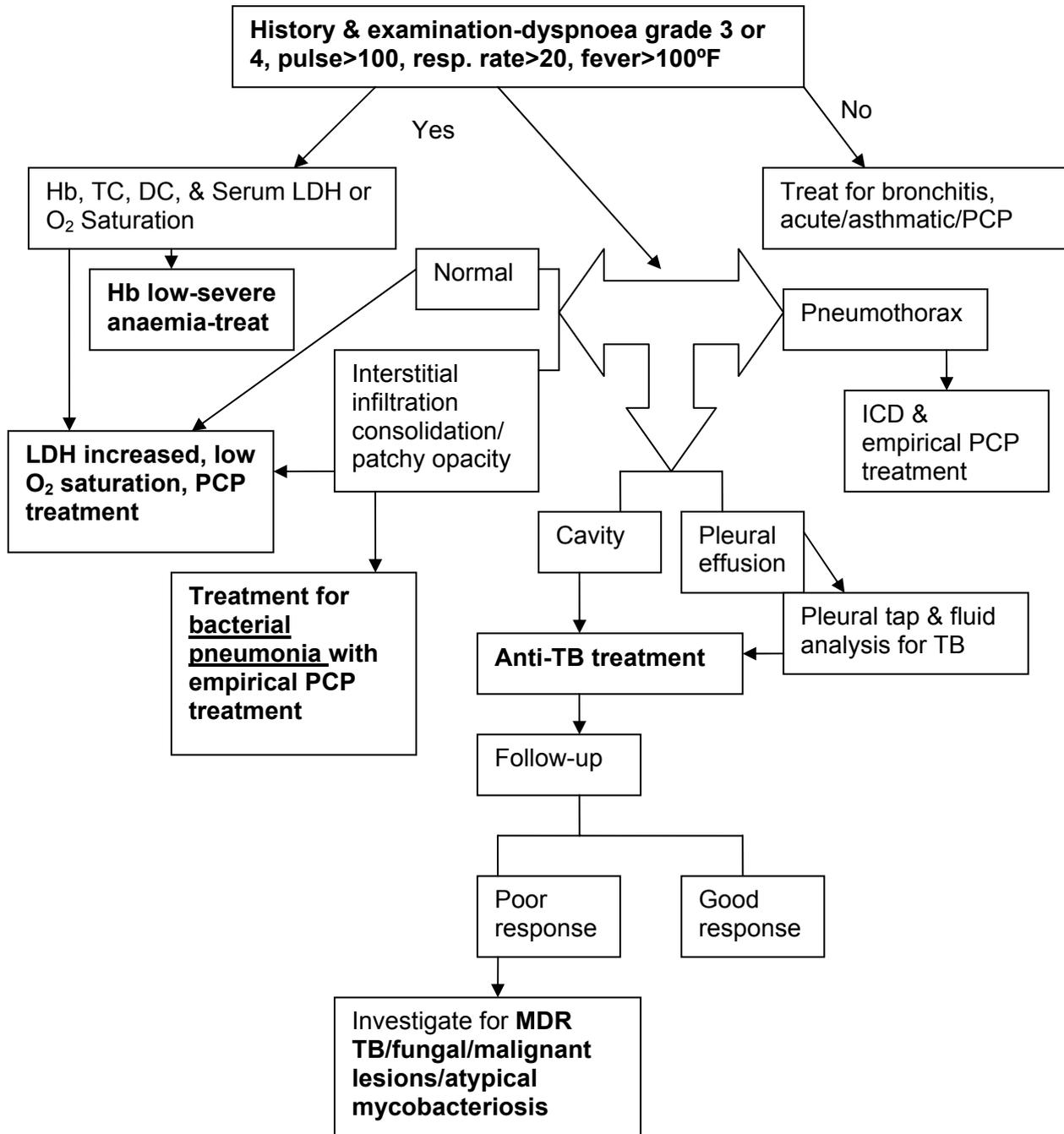
Management of Lymphadenopathy in an HIV-Positive Patient (continued)



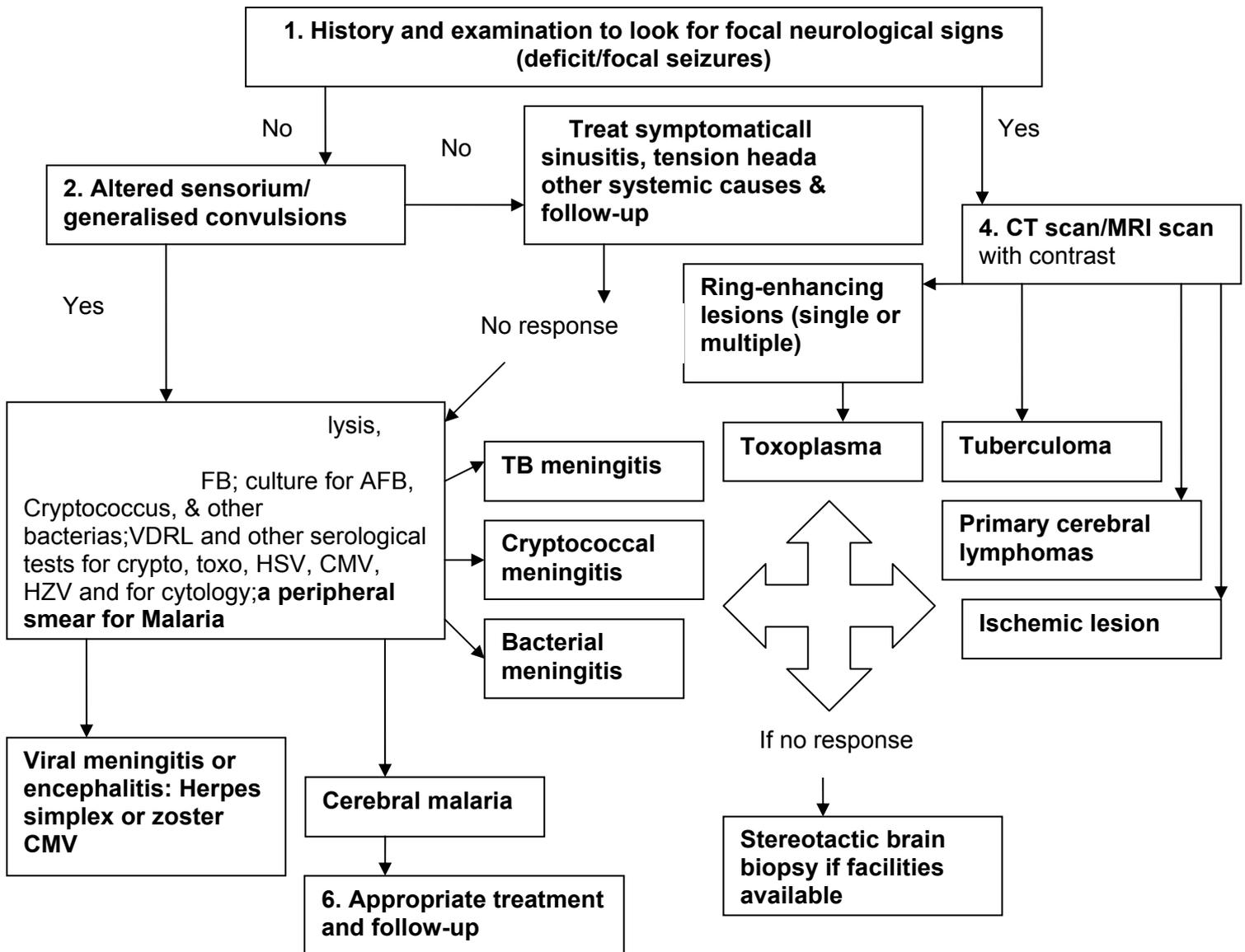
Management of Cough in an HIV-Positive Patient



Management of Dyspnoea in an HIV Positive Patient



Management of Headache in an HIV-Positive Patient





Management of Seizures in an HIV-Positive Patient

Differential Diagnosis:

1. Syncope
2. Brain stem ischemia
3. Pseudo-seizures
4. TIA
5. Rage attacks
6. Panic attacks

Treatment for the Seizure Disorders:

Partial Seizures and Generalised Seizures

Treat with:

Drug	Dose	Frequency
Phenytoin	200-400 mg	qd
Carbamazepine	600-1200 mg/day	2 or 3 divided doses
Valproic Acid	1500-2000 mg/day	3 divided doses
Phenobarbital	100-200 mg	qd
Primidone	750-1500 mg/day	3 divided doses
Felbamate	1200-3600 mg/day	3 divided doses
Gabapentin	900-1800 mg/day	3 divided doses

Absence (Petit-Mal) Seizures

Drug	Dose	Frequency
Ethosuximide	100-1500 mg	2 divided doses
Valproic Acid	1500-2000 mg/day	3 divided doses
Clonazepam	0.04-0.2 mg/kg/day	2 divided doses

Status Epilepticus

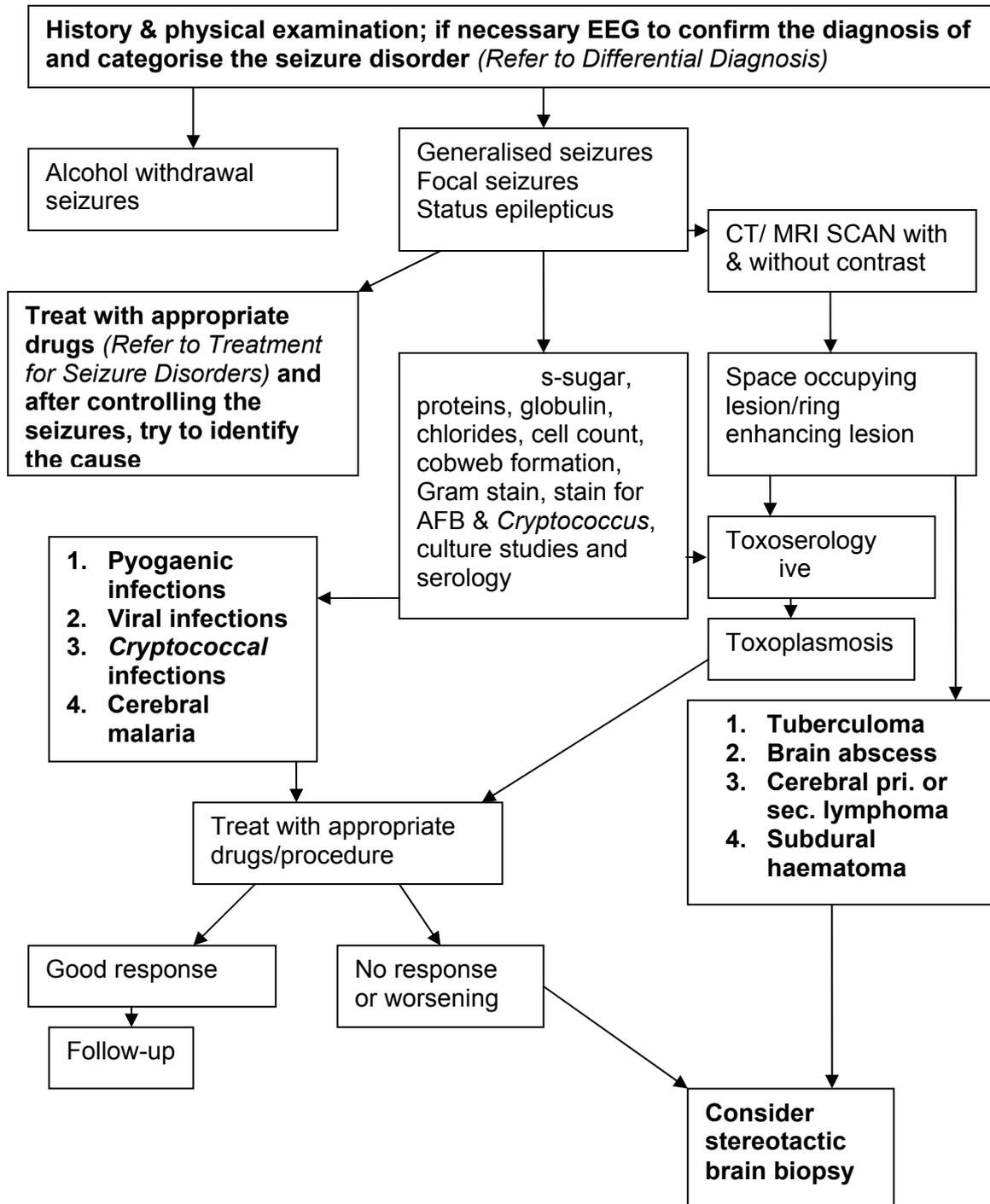
1. Maintenance of airway
2. If seizures continue, 50% dextrose (25-50 ml) IV
3. If necessary, 10 mg of diazepam IV, over a period of 2 min., and repeated after 10 mtes, OR 4 mg of IV bolus of lorazepam, repeated after 10 min.
4. Regardless of the response to (3), phenytoin 18-20 mg/kg, given as IV at the rate of 50 mg/min. (to provide initiation of long-term control)
5. If seizures continue, Phenobarbital given at the loading dose of 10-20 mg/kg IV SLOWLY (Beware of respiratory depression.)
6. Alternatively, IV midazolam can be used. Dose is 0.2 mg/kg, followed by 0.05–0.2 mg/kg/hour
7. If these measures fail, general anaesthesia with ventilatory assistance and neuromuscular junction blockade may be used.

 **Handout 7.6 (continued)**

Management of Seizures in an HIV-Positive Patient (continued)Alcohol Withdrawal Seizures

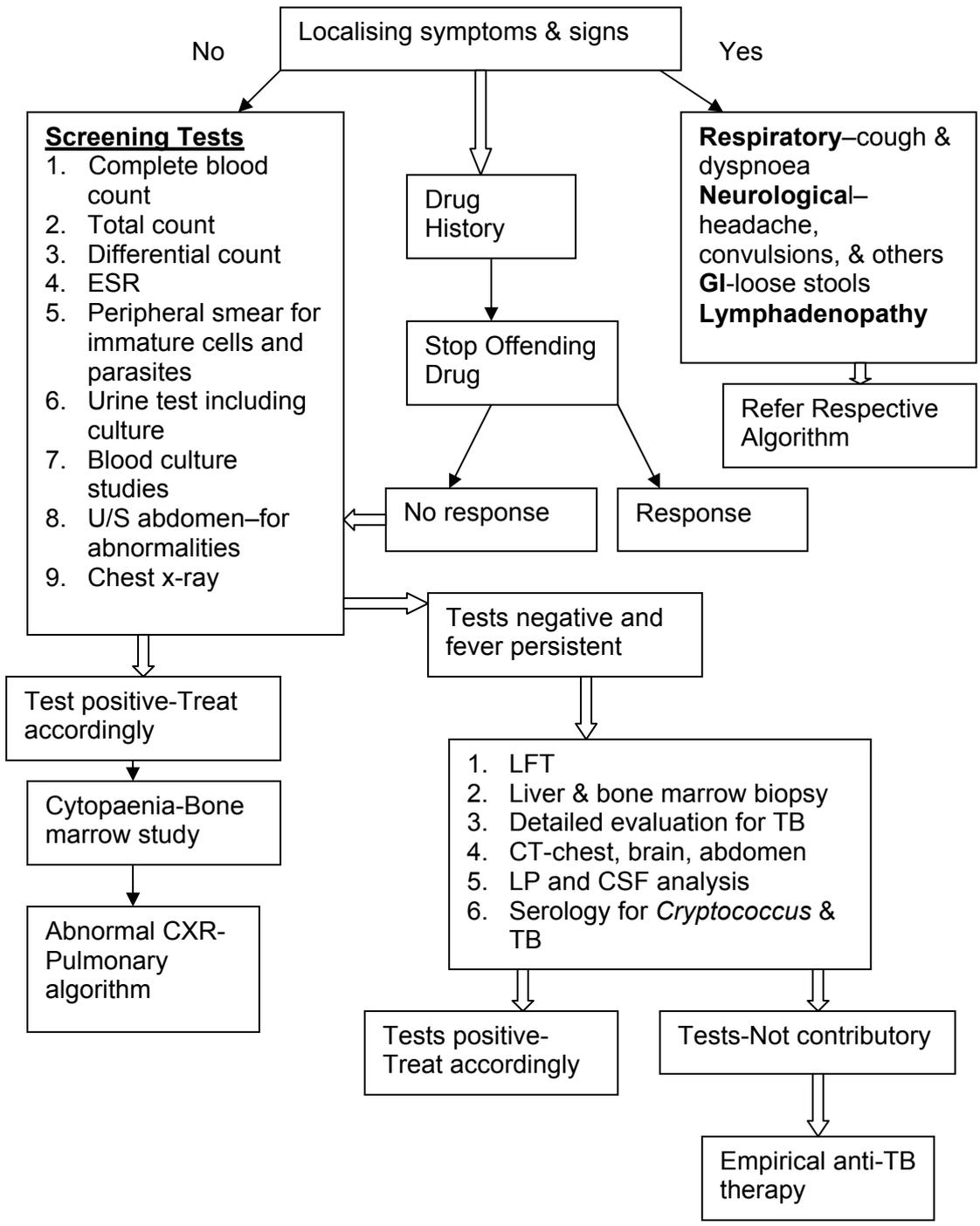
Treatment with anticonvulsants is usually not required, since they are self-limited. Status epilepticus may follow and is managed as above. Thiamine can be given.

**Management of Seizures in an HIV-Positive Patient
(continued)**





Management of Persistent Fever in an HIV-Positive Patient





Case Study: Lymphadenopathy

Case Study Instructions:

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
3. Discuss the case together and answer the related questions in the time you

Case 1

An HIV-positive patient that you have been following for 6 months and who has been taking cotrimoxazole regularly as prescribed presents with generalised lymphadenopathy.

He has lost 5 kg since his last visit 1 month ago. He has an enlarged lymph node in the left neck measuring 5 x 4-cm and lymph nodes in the right neck and axillae measuring 1.5 x 2-cm.

Question:

1. How do you manage him now?



Case Study: Common Medical Problems

Case Study Instructions:

1. Choose a presenter for your group. The presenter will share your group's decisions and answers with the larger group.
2. Choose a recorder for your group. The recorder may write on notepaper or flip-chart paper.
case together and answer the related questions in the time you are given.

Case 1

A 27-year-old previously healthy man presents with a history of headache that has not responded to paracetamol, which he has been taking 3 times a day for the last 3 days.

He has been taking cotrimoxazole regularly and has been visiting the hospital each month for the last 3 months. He states that the headache affects the entire cranium and is worse when he bends down.

He has not been able to go to work for the last 3 days because of the worsening headache. He has not had any fits but states that he may have a "bit of fever." His appetite has been poor and because he has felt nauseated for the last 3 days, has eaten almost nothing.

He has been using condoms whenever he has sex since he was told he was HIV-positive.

Examination shows an ill-looking man who weighs 65 kg (5 kg down from a month ago). Axillary temperature is 37.5° C.

He has bilateral cervical lymphadenopathy and some neck stiffness.

Questions:

1. What are the likely diagnoses for this patient?



Worksheet 7.2 (continued)

Case Study: Common Medical Problems (continued)

2. What would be your immediate diagnosis?

3. What investigations would you perform?



Microteaching Exercise: Types of Opportunistic Infections and Opportunistic Diseases

Instructions

For this exercise, you will divide into 4 groups. Each group will cover a different category of opportunistic infection/disease: Gastrointestinal infections, respiratory infections, neurological manifestations, or cancers associated with HIV infections.

Each group should select 1 member to serve as the reporter and another member to be the facilitator. You will read the information provided in the handouts, then work as a group to present the information to the other participants as a case study. Use flip-chart paper and a marker to present the case and to record class findings and present teaching points at the time of discussion.

In addition to the material provided, you may also want to draw upon your own knowledge and experiences. You can also use the paper and markers to present key pieces of information about the type of infection or disease. In particular, you should be prepared to teach the following to your colleagues:

1. What are the common infections in your category associated with HIV?
2. What are the clinical features in a person with HIV infection that may indicate the presence of these types of infections?
3. What facilities do you have in your place of work for making a diagnosis of this type of infection?
4. What experiences, if any, have you had working with these types of infections?



Microteaching Exercise: Respiratory Infections and HIV

Your group will be in charge of providing an overview of respiratory infections and HIV to your colleagues. Read through the information presented in this handout. Then discuss as a group what you think would be important to teach your colleagues so that they would have a general introduction to these kinds of infections. Also, draw upon your own knowledge and experiences with respiratory infections. Be prepared to teach a case study to your colleagues that covers the following:

1. What are the common respiratory infections associated with HIV?
2. What are the clinical features in a person with HIV infection that may indicate the presence of respiratory infections?
3. What facilities do you have in your place of work for diagnosing respiratory infections?
4. What experiences, if any, have you had working with these types of respiratory infections?

Use the paper and markers provided to create visual aids to help you present this information to your colleagues.

Information on Respiratory Infections in Persons with HIV

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

***Up to two thirds of people with HIV will have a respiratory illness associated with HIV infection. Many of these illnesses are treatable AND few are preventable. Aggressive investigation of pulmonary symptoms and signs is essential.

Bacterial Respiratory Infections

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

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

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

Microteaching Exercise: Respiratory Infections and HIV (continued)

***Pneumocystis Carinii* Pneumonia**

Pneumocystis carinii pneumonia (PCP) is an opportunistic infection. It is commonly encountered in immunosuppressed persons with HIV infection and commonly causes death in persons with AIDS. Patients usually present with cough, shortness of breath, and fever. Often patients with PCP have features of respiratory failure. Symptoms may be very severe, and an attack of PCP may lead to the death of the patient if not treated early and effectively.

Other Causes of Lower-Respiratory-Tract Infections in Immunosuppressed Persons

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

Tuberculosis

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

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

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

The typical symptoms and signs of pulmonary TB are cough with or without fever, night sweats, and weight loss. Chest x-ray may show upper lobe infiltrates with or without cavitation. In immunosuppressed persons, the diagnosis may be difficult to make as TB



Worksheet 7.3A (continued)

Microteaching Exercise: Respiratory Infections and HIV (continued)

in such hosts may present with atypical symptoms, lack of typical symptoms, and minimal changes on chest x-ray. In addition, in persons with AIDS, the presence of other opportunistic infections and extrapulmonary TB may complicate the diagnosis. Sputum should always be examined for the presence of acid-fast bacilli (AFBs) indicative of mycobacteria. Sputum may also be cultured for mycobacteria and cultured colonies can be tested for antimicrobial resistance. (Zim, Module 1)

OTHER HIV-ASSOCIATED RESPIRATORY ILLNESSES***

MALIGNANCIES:

- A. Kaposi sarcoma
- B. Non-Hodgkin lymphoma
- C. Lung carcinoma

MECHANICAL:

- A. Airway diseases/Emphysema
- B. Pneumothorax

VASCULAR

- A. Pulmonary hypertension

INTERSTITIAL LUNG DISEASES

- A. Lymphoid interstitial pneumonitis



Microteaching Exercise: Gastrointestinal Infections and HIV (Oral, Gastrointestinal, and Hepatobiliary Diseases)

Your group will be in charge of providing an overview of gastrointestinal infections and HIV to your colleagues. Read through the information presented in this handout. Then discuss as a group what you think would be important to teach your colleagues so that they would have a general introduction to these kinds of infections. Also, draw upon your own knowledge and experiences with gastrointestinal infections. Be prepared to teach a case study to your colleagues.

1. What are common gastrointestinal infections associated with HIV?
2. What are the clinical features in a person with HIV infection that may indicate the presence of gastro-intestinal infections?
3. What facilities do you have in your place of work for diagnosing gastrointestinal infections?
4. What experiences, if any, have you had working with these types of gastrointestinal infections?

Use the paper and marker provided to create visual aids to help you present this information to your colleagues.

Information about Gastrointestinal Infections and HIV

***Oral manifestations of HIV infection often represent the first clinical signs of this disease. Diseases of the gastrointestinal and hepatobiliary tracts are a major source of morbidity and mortality in patients with HIV infection. Abdominal pain, dysphagia, diarrhoea, gastrointestinal bleeding, jaundice, and hepatomegaly may reflect underlying opportunistic infection, AIDS-related neoplasia, adverse reactions to medications, or the effect of HIV infection alone.

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

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

Perianal lesions such as bacterial skin infections, anal warts, and herpes may occur. Persons with HIV infection may have anorexia, nausea and vomiting, and are prone to gastrointestinal infection with a number of pathogens. These are shown in Table 1.

Oropharyngeal and Oesophageal Candidiasis

The 2 main types of candidiasis are localised disease (of the mouth and throat, and of the vagina), and systemic disease (of the oesophagus, skin and nails, and other

Microteaching Exercise: Gastrointestinal Infections and HIV (continued)

viscera). The mouth and throat variant (oropharyngeal candidiasis or OPC) is believed to occur at least once in the lifetime of all HIV-infected patients. This does not lead to death but can cause pain and odynophagia. The symptoms of oesophageal candidiasis are difficulty in swallowing and pain in the chest that increases with swallowing. Disseminated candidiasis causes fever and symptoms in the organs affected by the disease (for example, blindness when it affects the eyes).

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

Table 1: Gastrointestinal Pathogens in Persons with HIV Infection

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

Oral lesions in persons with HIV infection

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

- Oral candidiasis
- Oral and labial herpes
- Kaposi sarcoma
- Oral hairy leukoplakia



Worksheet 7.3B (continued)

Microteaching Exercise: Gastrointestinal Infections and HIV (continued)

- Aphthous ulcers
- Stomatitis
- Histoplasmosis
- Gingivitis, pyorrhoea, and periodontitis
- Cheilitis

Lymphoma**

Human papilloma virus**

Each of these conditions should be looked for when managing persons with HIV infection. (Zim, Module 1)

Oesophageal Diseases***

Oesophageal disorders occur in about 40% of AIDS patients.

- A. Candida oesophagitis can occur in any stage of HIV infection.
- B. CMV ESOPHAGITIS also causes odynophagia.

Diarrhoea is the most common gastrointestinal symptom in HIV infection. Most patients have some degree of malabsorption and many are malnourished; diarrhoea and weight loss are independent predictors of mortality. Gastrointestinal infections are the predominant cause of diarrhoea, although certain medications and, rarely, malignancy may also be causes.

***Anorectal diseases are common in homosexual men and may include anal fistulas, anal ulcers secondary to herpes simplex virus, and CMV, NONSPECIFIC IDIOPATHIC ULCERATION, LYMPHOMA, AND SQUAMOUS CELL CARCINOMA.

***Haepatobiliary diseases

Haepatomegaly with variable degree of serum alkaline phosphatase and amino transferases is the common picture and jaundice is also a presenting feature. CMV infection(disseminated), fungal infections may affect the liver. Hepatitis A, hepatitis B and hepatitis C infections do occur in HIV patients. Drug-induced liver diseases also are encountered in HIV patients. Ascites is also a presenting feature in HIV patients and it is due to opportunistic infections like tuberculosis, and chronic viral hepatitis and can also be due alcoholic liver disease.



Microteaching Exercise: Neurological Manifestations and HIV

Your group will be in charge of providing an overview of neurological manifestations and HIV to your colleagues. Read through the information presented in this handout. Then discuss as a group what you think would be important to teach your colleagues so that they would have a general introduction to these kinds of infections. Also, draw upon your own knowledge and experiences with neurological manifestations. Be prepared to teach a case study to your colleagues that covers the following:

1. What are common neurological manifestations associated with HIV?
2. What are the clinical features in a person with HIV infection that may indicate the presence of neurological infection?
3. What facilities do you have in your place of work for diagnosing neurological manifestations?
4. What experiences, if any, have you had working with these types of neurological manifestations?

Use the paper and marker provided to create visual aids to help you present this information to your colleagues.

Information about Neurological Manifestations and HIV

***Neurological manifestations are common in HIV disease and they can occur at any stage of the disease.

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

Cryptococcal Meningitis

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

Toxoplasmosis

This disease, though fairly frequently encountered in PLHA in industrialised nations, is diagnosed infrequently in developing countries. This is probably the result of the lack of diagnostic facilities in developing countries. The infection leads to the development of multiple cystic lesions in the brain. In HIV-infected persons, toxoplasmosis mainly appears as encephalitis or as disseminated disease.

Microteaching Exercise: Neurological Manifestations and HIV (continued)**Herpes Simplex Virus**

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

Herpes Zoster Infections

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

Cytomegalovirus Infection (CMV)

Cytomegalovirus may affect multiple systems and organs in the body in immunosuppressed individuals. The incidence of CMV disease varies between geographical locations, but CMV causes significant suffering in HIV-infected persons worldwide. Symptoms include fever and diarrhoea from CMV colitis, dyspnoea from CMV pneumonitis, and blindness caused by CMV retinitis. (Zim, Module 1)

***HIV-related headaches may develop due to aseptic meningitis, cryptococcal meningitis, cerebral toxoplasmosis, or lymphoma. Headaches are more common in advanced HIV disease but may occur at any stage.

***Convulsive disorders can occur newly in HIV infected patients, mostly in those with AIDS.

***Cerebrovascular disorders also can occur due to either cerebral infarction or haemorrhage.



Microteaching Exercise: Cancers Associated with HIV Infections

Your group will be in charge of providing an overview of cancers associated with HIV to your colleagues. Read through the information presented in this handout. Then discuss as a group what you think would be important to teach your colleagues so that they would have a general introduction to these kinds of diseases. Also, draw upon your own knowledge and experiences with cancers associated with HIV. Be prepared to teach a case study to your colleagues that covers the following:

1. What are the common cancers associated with HIV?
2. What are the clinical features in a person with HIV infection that may indicate the presence of a cancer?
3. What facilities do you have in your place of work for cancers associated with HIV?
4. What experiences, if any, have you had working with these types of cancers?

Use the paper and marker provided to create visual aids to help you present this information to your colleagues.

Information about Cancers Associated with HIV Infections

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

- Kaposi sarcoma
- Carcinoma of the cervix
- Squamous cell carcinoma of the conjunctiva
- Burkitt-type lymphoma
- Non-Hodgkin lymphoma
- Intracranial lymphoma
- Squamous cell carcinoma of the genital tract

Kaposi's Sarcoma

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

Non-Hodgkin Lymphoma and Intracranial Lymphoma

Non-Hodgkin lymphoma and intracranial lymphoma have been described frequently in association with HIV infection. Non-Hodgkin lymphoma is often generalised and can



Worksheet 7.3D (continued)

Microteaching Exercise: Cancers Associated with HIV Infections (continued)

only be diagnosed by histologic examination of biopsied material. Intracranial lymphoma is associated with advanced immune suppression and is diagnosed after examining biopsies of tumor found on CT scans or MRI scans of the brain.

Carcinoma of the Cervix

Carcinoma of the cervix is associated with HIV infection, and there has been an increase in the annual incidence of this cancer in areas where the prevalence of HIV infection is high. It is advisable therefore to perform annual Pap smears on all women with HIV infection. There is a strong aetiologic association between carcinoma of the cervix and human papilloma virus (HPV). HPV types 16 and 18 are most commonly associated with cervical carcinoma, accounting for 64% of cases (HIV Insite).

Squamous Cell Carcinoma

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

Intraepithelial neoplasia of the uterine cervix, the anus, penis, and vulva has also been described in association with HIV infection. (Zim, Module 1)



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 **Notes**



**Clinical Management of
Common Medical Problems**
Session Seven



I-TECH
INTERNATIONAL
TRAINING &
EDUCATION
CENTER ON HIV



Learning Objectives

- By the end of this session, you will be able to:
 - Advise HIV-infected patients on how they can care for symptoms of common opportunistic infections and support their bodies' immune systems
 - Provide appropriate clinical care for persons with HIV infection who present with some common medical problems related to HIV and opportunistic infections

Management of Common Medical Problems

Slide 2

- *The aim of this session is to introduce participants to the management of common medical problems.*



Non-Drug Therapy
in Patients with HIV/AIDS



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Introductory Exercise

- The purpose of this exercise is to help you think about what steps HIV-infected patients can take to manage their health
- Take some time to think about the questions on the next slide, then we will discuss them as a group

Management of Common Medical Problems

Slide 4

- While some drugs can slow down the onset of symptoms of HIV-related disease and can help strengthen the body's defense system, it is not always possible to use drug therapies.
 - These drugs are expensive and not affordable to the average person.
 - They can also have a number of side effects.



Introductory Exercise Questions

- What can HIV-infected patients do to support their bodies' immune systems?
- What are some options for caring for symptoms of common medical problems associated with HIV and OIs that don't involve drug therapy?



Non-Drug Measures (1)

- Avoid stress
- Eat a balanced diet
- Avoid alcohol, smoking, and tobacco and get plenty of rest
- Engage in a moderate amount of exercise daily
- Adopt safer sex practices
- Get treatment for symptoms or infections as soon as possible
- Consume fresh, home-cooked meals

Management of Common Medical Problems

Slide 6

- Patients should **avoid stress** as much as possible.
- To **strengthen their immunity**, they should try to:
 - Eat a balanced diet
 - Avoid alcohol and tobacco, and
 - Get plenty of rest and exercise
- Patients should **not remain sedentary**; they should engage in a moderate amount of exercise daily.
- Patients should **adopt safer sex practices**. By practicing safer sex, the person with AIDS can avoid introducing more HIV into their body (an increase in virus will speed up the process of that person's disease progression).
- Patients should try to **treat symptoms or infections as soon as possible**.
 - While there is no cure for HIV, a nurse or doctor can treat most of the opportunistic infections.
 - It is particularly important to seek care if a person has symptoms of TB, since TB can be cured.
 - Stay away from crowded areas where there may be greater exposure to opportunistic infections like TB.
- Patients should **consume fresh, home-cooked meals** instead of canned or pre-packaged food.
 - Partially cooked items should not be consumed so that digestion is not adversely affected.



Non-Drug Measures (2)

- Avoid animals and birds or adapt appropriate preventive measures when rearing pet animals and birds
- Practice yoga, meditation
- Live with hope
- Ensure personal & environmental hygiene
- Associate with a positive network

Management of Common Medical Problems

Slide 7

- Patients can help themselves by maintaining a **positive attitude**.
 - For most individuals, receiving a positive HIV test result is devastating, and it is natural and appropriate that they respond as such.
 - By saying that one should adopt a positive approach does not mean that one does not react emotionally to the discovery of infection.
 - Rather, a patient with a positive attitude tries as much as possible to “live” with HIV.
 - A diagnosis of HIV infection means that the patient could still have a number of asymptomatic years left.
- A patient should try to adopt an attitude towards HIV with the perspective of fighting the disease with the right kind of tools (such as the healthy lifestyle issues mentioned above) and not letting HIV and AIDS get the better of her or him. (HIV/AIDS Training Course, S. Africa)
- Associate with a positive HIV network to update themselves about HIV/AIDS
- Many of the clinical management procedures that we will go over involve drug therapy, but you may want to keep in mind these other ways that patients can use to improve their health that don't involve drugs.



Non-Drug Measures (3)

- Go to the hospital if s/he exhibits any of the following symptoms:
 - High fever for at least two to four days that does not respond to usual medication
 - Severe breathlessness and dizziness
 - Chest pain
 - Headache
 - Uncontrolled diarrhoea



Persistent Generalised Lymphadenopathy

- More than 3 separate extra inguinal lymph node groups (like axillary or cervical) are affected
- At least 2 nodes, more than 1.5 cm in diameter, at each site
- Duration more than 1 month
- No local or contiguous infection that might explain the adenopathy

Source: NACO

Management of Common Medical Problems

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- PGL is defined as palpable lymphadenopathy (lymph node enlargement of >1 cm) at two or more extra inguinal sites persisting for more than 3 months in the absence of a concurrent illnesses or condition other than HIV infection to explain the condition
- NACO definition:
 - More than 3 separate lymph node groups extra inguinal- axillary or cervical are affected
 - At least 2 nodes more than 1.5 cm in diameter at each site
 - Duration more than 1 month
 - No local or contiguous infection that might explain the adenopathy.



Lymphadenopathy in HIV/AIDS

- Lymphadenopathy of PGL should be distinguished from other causes
 1. Infections:
 - a. Bacterial-TB, Syphilis
 - b. Fungal-Histoplasmosis
 - c. Viral-Cytomegalo virus
 2. Malignancies:
 - a. KS
 - b. Lymphomas
 3. Dermatological conditions:
 - a. Seborrhoeic dermatitis
 - b. Chronic pyoderma
 4. Other causes
 - a. Toxoplasmosis
 - b. Drug reactions



Treatment of Generalised Lymphadenopathy (1)

- If a person has enlarged lymph nodes, look carefully for an infective cause
- The patient may have generalised infected eczema and hence has lymphadenopathy
- If a local infective cause is found, patient should be given:

Amoxicillin	500 mg	QID	PO	10 days
Erythromycin	500 mg	QID	PO	10 days

Management of Common Medical Problems

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- Refer to the algorithm on “Management of Lymphadenopathy in an HIV+ Patient” (Handout 7.2) in the Participant’s Handbook.
- If a local cause is found, then the patient should be given a course of antibiotics such as:
 - Amoxicillin 500mg PO orally 4 times a day for 10 days, and
 - Erythromycin 500 mg orally four times a day for 10 days.



Treatment of Generalised Lymphadenopathy (2)

- Patients should be reviewed a month after treatment is completed and if improved, they could be discharged
- If the lymphadenopathy persists or is getting worse, then continue the management according to the flowchart



Treatment of Generalised Lymphadenopathy (3)

- If a VDRL test is positive, treat the patient for syphilis as follows:
 - Give benzathine penicillin 2.4 M units IM
 - Educate, counsel, promote and provide condoms.
 - Arrange for partner treatment
 - If the patient with PGL and a positive VDRL test is a pregnant woman, she should receive benzathine penicillin 2.4 M units IM once weekly for 3 weeks

Management of Common Medical Problems

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- Note: In persons allergic to penicillin, give the patient doxycycline 100 mg orally twice daily for 14 days.
- Or, if the patient who is allergic to penicillin is a pregnant woman, give erythromycin 500 mg orally four times daily for 14 days.



Treatment of Generalised Lymphadenopathy (4)

- Look carefully for symptoms suggestive of TB, including:
 - Chronic cough or history of TB contact
 - Fever, night sweats, weight loss
 - Asymmetrically enlarged lymph nodes
 - Matted or fluctuating lymph nodes
 - Lymph nodes enlarging over a period of observation
 - Evidence of hilar lymphadenopathy on chest X-ray



Treatment of Generalised Lymphadenopathy (5)

- If any of these features are present, there is a need to investigate for TB or malignancy
- Any HIV-positive individual who has TB symptoms should be referred for assessment and possible biopsy of lymph nodes



Lymphadenopathy Case Study

- An HIV-positive patient you have been following for 6 months and who has been taking cotrimoxazole regularly as prescribed presents with generalized lymphadenopathy

He has lost 5 kg since his last visit a month ago. He has an enlarged lymph node in the left neck measuring 5 x 4 cm and lymph nodes in the right neck and axillae measuring 1.5 x 2 cm

- Question for discussion:
 - How would you manage him now?

Management of Common Medical Problems

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- *The purpose of this exercise is to give you a chance to apply the procedures for clinical management of generalised lymphadenopathy.*
- *Refer to “Lymphadenopathy Case Study” (Worksheet 7.1) in the Participant’s Handbook.*



Case Study Teaching Points (1)

- This patient needs a thorough clinical examination for other lymph node group involvement (inguinal, supra trochlear, occipital, etc.), hepatosplenomegaly, and appropriate investigations, including:
 - Ultrasound examination of abdomen for retroperitoneal and para aortic lymph node enlargements
 - Chest X-ray for mediastinal lymph node enlargement
 - FNAC

Management of Common Medical Problems

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- *Management should be discussed along with Handout 7.2 (the algorithm for Management of Lymphadenopathy.)*
- In this patient, the lymphadenopathy is significant since the sizes of the lymph nodes are more than 2 cm.
- It is also generalized because cervical nodes on both sides and the axillary nodes are enlarged.
- It is chronic because it is of 6 months duration.



Case Study Teaching Points (2)

- Aspirated material can be studied for various pathological abnormalities, especially for tuberculosis and malignant cells, and stained for AFB (Mycobacterium tuberculosis)
- If the diagnosis is achieved, appropriate treatment is started
- If the diagnosis is not made, lymph node biopsy can be tried, and histopathological studies can be done to make out a definitive diagnosis. An appropriate treatment can be given



Management of Persistent Cough

- Patients with HIV infection who present with cough lasting more than 3 weeks should be carefully assessed for:
 - Lower respiratory tract infections such as bronchitis and pneumonia
 - TB or other opportunistic infection

Management of Common Medical Problems

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- *Refer to the algorithm on “Management of Cough in an HIV+ Patient” (Handout 7.3) in the Participant’s Handbook.*



Causes of Coughs in Patients with HIV/AIDS (1)

- Bacterial, viral, fungal, protozoal (PCP) and parasitic infections/infestations of the respiratory tract, malignancies of the respiratory tract, and allergic diseases
- Acute and transient cough may be due to:
 - Viral-induced lower respiratory tract infections
 - Post nasal drip due to:
 - Sinusitis or rhinitis
 - Secondary to pharyngitis or laryngitis

Management of Common Medical Problems

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- HIV/AIDS patients presenting with a cough should be assessed for the following:
 - Bacterial
 - Viral
 - Fungal
 - Protozoal (PCP) and parasitic infections/infestations of the respiratory tract,
 - Malignancies of the respiratory tract, and
 - Allergic diseases
- Cough may be acute or chronic.
- Acute cough can also occur due to more serious diseases like pneumonitis, pulmonary embolism etc.



Causes of Coughs in Patients with HIV/AIDS (2)

- Chronic cough can occur due to:
 - Tuberculosis
 - Fungal infections
 - Parasitic infections
 - Malignancies
 - PCP also can occur



Respiratory Failure

- Respiratory failure results from a disorder in which lung function is inadequate for the metabolic requirements of the individual
- Depending upon the presence or absence of hypercapnia (raised PaCO₂), the respiratory failure is divided into Type-1 or Type-2

Management of Common Medical Problems

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- Refer to the algorithm on “Management of Dyspnoea in an HIV+ Patient” (Handout 7.4) in the Participant’s Handbook.
- Severe respiratory distress means that the patient is in respiratory failure and if he/she is not treated urgently death will occur.
- If any of the following are present, then respiratory distress is most likely present:
 - Rapid respiratory rate (fast breathing) (> 30 per minute)
 - Central cyanosis
 - Inability to talk as a result of dyspnoea
 - Pulse rate >120 beats per minute in a person with cough and shortness of breath and/or localised persistent chest pain.



Assessment of Respiratory Failure

- Conscious level
- CO₂ retention
- Airway obstruction
- Right heart failure
- Background functional status and quality of life
- Signs of precipitating event

NOTE: Patient may not appear distressed despite being critically ill.

Management of Common Medical Problems

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- Conscious level: response to commands, ability to cough
- CO₂ retention: warm periphery, bounding pulses, flapping tremor
- Airway obstruction: intercostals indrawing, wheezing, pursed lips and tracheal “tug”
- Right heart failure: peripheral oedema, raised JVP, hepatomegaly, ascites
- Background functional status and quality of life
- Signs of precipitating event: brochospasm, infections, pulmonary embolism, pneumothorax, CNS depression (narcotic drugs)
- Investigations: Chest X-ray and arterial blood gases
 - In persons with a large pleural effusion or a pneumothorax, you will not be able to hear breath sounds in the lung field. Listen carefully with your stethoscope.
 - Pleural Effusion: Clinical examination reveals classical signs and symptoms. The signs are:
 - Tracheal shift to opposite side
 - Diminished movements and breath sounds on the same side
 - VF and VR decreased or absent on the same side, and
 - Stony dull note on the same side.
 - In HIV patients the fluid is aspirated and tested for various infections. The commonest etiology is tuberculosis.



Management of Respiratory Failure

- Maintenance of airway
- Treatment of specific precipitating event
- Frequent physiotherapy and pharyngeal suction
- Nebulized bronchodilators
- Controlled oxygen therapy
- Antibiotics
- Diuretics

Management of Common Medical Problems

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- Investigations (continued):
 - Pneumothorax: Clinical examination reveals classical signs and symptoms. The signs are:
 - Tracheal shift to opposite side
 - Diminished movements on the same side
 - VF and VR decreased or absent on the same side
 - Hyper-resonant note on the same side and
 - Amphoric breathing may be present.
 - The commonest cause is tuberculosis.
 - The following are clinical features suggestive of TB:
 - Chronic cough or history of TB contact
 - Fever, night sweats, weight loss
 - Asymmetrically enlarged lymph nodes
 - Matted or fluctuating lymph nodes



Symptoms and Causes (1)

- May be persistent or worsening cough, and/or dyspnoea, and/or localized chest pain
- Symptoms of cough and dyspnoea are very common; follow guidelines for the management of acute respiratory infection (ARI) or asthma

Management of Common Medical Problems

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- Symptoms of cough and dyspnoea are extremely common, and in general, the guidelines for the management of acute respiratory infection (ARI) or for asthma should be followed.



Symptoms and Causes (2)

- Most common cause of cough and dyspnoea is asthma
- The ideal management of asthma includes the following:
 - Oxygen
 - Intravenous hydrocortisone 200 mg
 - Inhaled nebulised salbutamol

Management of Common Medical Problems

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- Most common cause of cough and dyspnoea is asthma, and if the patient has the features of asthma then he/she should be treated for asthma.
- Asthma features:
 - Rapid respiratory rate
 - Wheezing on expiration
 - Prolongation of expiration
 - History of periodic attacks, or
 - Family history of asthma, eczema or hay fever
- Management of Bronchial Asthma:
 - Chronic Persistent Asthma:
 - Step 1-Use of inhaled short acting beta-2 adrenoreceptor agonists: salbutamol, terbutaline
 - Step 2-Low dose inhaled steroids or other anti-inflammatory agents: beclometasone, dipropionate, budesonide, fluticasone propionate
 - Step 3-High dose inhaled steroids or low dose inhaled steroids plus long acting inhaled beta-2 adrenoreceptor agonists
 - Step 4-High dose inhaled steroids and regular bronchodilators
 - Step 5-Addition of regular steroid therapy
 - Management of Acute Severe Asthma
 - Hospitalization
 - Oxygen
 - Nebuliser therapy
 - Steroids
 - IV access and other measures



Headache and Other Neurological Problems (1)

- Non HIV-related causes of headache:
 - Migraine, tension headache, sinusitis, dental disorders, anaemia, and refractive disorders (in the eye)
 - Hypertension and certain antihypertensive drugs, e.g., nifedipine
 - Fever alone can also cause a headache

Management of Common Medical Problems

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- *Refer to the algorithm on “Management of Headache in an HIV+ Patient” (Handout 7.5) in the Participant’s Handbook.*



Headache and Other Neurological Problems (2)

- HIV-related causes of headache:
 - Encephalitis or dementia
 - Discrete mass lesions/abscess
 - Meningitis
- Headache can also accompany systemic infections and will resolve with the treatment of the systemic infection

Management of Common Medical Problems

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- Encephalitis or dementia:
 - Subacute encephalopathy
 - HSV
 - CMV
 - Progressive Multifocal Leukoencephalopathy
 - HZV
 - Treponema pallidum
 - MAC
- Discrete mass lesions/abscess:
 - Toxoplasma gondii
 - KS
 - Primary or metastatic lymphoma
 - Cryptococcus neoformans
 - Coccidioides immitis
 - Candida albicans
 - Mycobacterium tuberculosis
 - Nocardia asteroides
- Meningitis:
 - Cryptococcal meningitis
 - Aseptic meningitis
 - Pyogenic meningitis
 - TB Meningitis
 - Fungal meningitis
 - HSV, HZV
 - CMV



Headache and Other Neurological Problems (3)

- Adverse reaction to medications, including acute hypersensitivity reactions, may include headache
- HIV headache is a new onset headache in late stages of HIV-1 infection due to uncertain pathogenesis

Management of Common Medical Problems

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- HIV headache: At times this type of headache indicates the onset of systemic infections like Toxoplasma
- The common causes of headache, not related to HIV infection, are:
 - Nervous tension
 - Migraine
 - Dental caries
 - Refractive disorders
 - Sinusitis
 - Anaemia
 - Hypertension
 - Fever
 - Drugs such as nifedipine and indomethacin



Neurological Signs

- The patient should be examined for the following neurological signs:
 - Dementia
 - Hemiplegia
 - Paraplegia
 - Sensory neuropathy
 - Speech impairment
 - Blindness
 - Deafness
 - Neck stiffness
 - Facial nerve paralysis

Management of Common Medical Problems

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- *Refer to the algorithm on “Management of Seizures in an HIV+ Patient (Handout 7.6) in the Participant’s Handbook.*
- A history of fits or convulsions may indicate a brain lesion.
- Note that changes in mental state may be very subtle but may indicate dementia.
- Such changes include:
 - Changes in behaviour
 - Confusion
 - Lack of concentration
 - Difficulties in learning and remembering.
- Also note that patients with no previous history of severe prolonged headache, even without neurologic signs, should be referred.



Persistent Fever

- Defined as a body temperature of more than 38°C lasting for more than two weeks
- If the patient has been in a malaria endemic area, take blood slide and if positive, treat for malaria
- To treat possible urinary tract or enteric infections:

Management of Urinary Tract or Enteric Infections				
Amoxicillin	500 mg	TID	PO	10 days
Cotrimoxazole <i>(if allergic to penicillin)</i>	2 tablets	BID	PO	10 days

Management of Common Medical Problems

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- Refer to the algorithm on “Management of Persistent Fever in an HIV+ Patient” (Handout 7.7) in the Participant’s Handbook.
- Refer to Handout 7.7 Management of Persistent Fever in an HIV+ Patient
- To treat possible urinary tract or enteric infections:
 - Give ten-day course of amoxicillin 500mg orally three times a day.
 - If allergic to penicillin, give cotrimoxazole 2 tablets orally twice daily for 10 days.
 - Quinolones like norfloxacin can also be included.



Algorithm Exercise

- Using the sample algorithms provided as a model, you have developed two of your own
- In your groups, please finalize the two algorithms that can be applied in your institution
- Each group will then share their algorithms with the rest

Management of Common Medical Problems

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- *Finalize the algorithms you have been assigned in your groups.*
- *Each group can then share the algorithms they have developed with the rest of the class.*



Chronic Diarrhoea (1)

- Defined as passing more than 3 liquid stools daily for 14 days
- HIV-related causes of diarrhoea include:
 - HIV enteropathy
 - Cryptosporidiosis
 - Isosporiasis
 - Strongyloidiasis
 - Malabsorption syndrome
 - Intestinal TB
 - Intestinal lymphoma

Management of Common Medical Problems

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- Diarrhoea in persons with HIV infection may be intermittent with acute exacerbations or may be chronic in nature.



Chronic Diarrhoea (2)

- Patient may be dehydrated, anaemic, and wasted
- In addition, there may be:
 - Skin and hair changes
 - Hypopigmentation of the lips, while the nails may be darkly pigmented
 - Oral thrush, hairy leukoplakia, and lymph node enlargement



Key Points in Treating Chronic Diarrhoea

- Assessment of state of hydration
- Immediate correction of established dehydration
- Prevention of dehydration with oral fluids and rehydration solutions



Treatment (1)

- Mild or moderate dehydration may be corrected by administering oral rehydration solution
- Severely dehydrated patients and those unable to take oral fluids because of vomiting may require fluids intravenously
- Advise patient to take extra fluids (200 mls) whenever diarrhoea occurs

Management of Common Medical Problems

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- Mild or moderate dehydration
 - may be corrected by administering oral rehydration solution as follows:
 - Give 200 ml of ORS solution every 15 minutes for the first 4 hours
 - Then give 500 ml of ORS solution every hour while the diarrhoea continues
 - Once diarrhoea stops, the patient should take 5 litres of ORS solution daily together with 250 ml of ORS after passing each stool.
 - This is continued until the patient is passing normal stools and is taking a normal diet
- Severe dehydrated patients and those unable to take oral fluids because of vomiting
 - require fluids intravenously as follows:
 - 1.5 litres Ringers Lactate IV in the first hour and, if tolerated, 500 ml ORS solution orally every hour
 - Continue IV fluids so that the patient receives 2 litres Ringers Lactate in the next 12 hours and then 3 litres every 24 hours together with ORS as described above.
 - Advise patient to take extra fluids whenever diarrhoea occurs. Up to 200mls of fluid should be taken each time a watery stool is passed.



Treatment (2)

- Advise patient on potassium supplementation
- To treat possible bacterial infection or amoebiasis:
 - Cotrimoxazole two tablets twice daily orally for 7 days
 - AND
 - Metronidazole 400 mg orally thrice daily for 7 days

Management of Common Medical Problems

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- Advise patient on potassium supplementation. Potassium-containing foods include vegetables and fruits, particularly ripe bananas and fruit juice.
- To treat possible bacterial infection or amoebiasis:
 - Cotrimoxazole two tablets twice daily orally for 7 days, and,
 - Metronidazole 400 mg orally 3 times a day for 7 days in order to treat possible bacterial infection or amoebiasis. (Zim, Mgmt of Common Medical Problems)



Severe Weight Loss

- Severe involuntary weight loss in a person with HIV infection is known as "HIV-associated wasting syndrome" or "slim disease"
- Defined as weight loss of greater than 10% body weight
- Possible reasons for weight loss include:
 - Chronic and recurrent diarrhoea
 - Malabsorption, HIV-induced myopathy
 - Intestinal parasitic infestations
 - Poor appetite

Management of Common Medical Problems

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- HIV infection leads to weight loss that is often severe in the more advanced stage of the disease.
- The cause of the wasting is not fully understood. It is possible that patients with AIDS lose weight as part of chronic debility.
- Other possible reasons for the weight loss include:
 - Chronic and recurrent diarrhoea
 - Malabsorption
 - HIV-induced myopathy
 - Intestinal parasitic infestations
 - Poor appetite.
- None of these factors have been substantiated as the exact cause of the severe weight loss.



Symptoms

- Most common symptoms of HIV-related severe weight loss include reduction of appetite with or without fever and diarrhoea
- Other symptoms:
 - Feverish and dehydrated
 - Dry skin, possibly dry hyperpigmented rash
 - Kaposi sarcoma
 - Anaemia, cheilitis, and hyperpigmented nails
 - Neurologic involvement such as encephalopathy.
 - Skin and hair changes
 - Oral and oesophageal thrush
 - Oral candidiasis or oral hairy leukoplakia
 - TB and other respiratory conditions
 - Encephalopathy and AIDS dementia complex

Management of Common Medical Problems

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- The most common symptoms of severe weight loss include reduction of appetite with or without fever and diarrhoea.
- The patient's clothes may also very obviously no longer fit them.
- The patient is usually so debilitated that he/she can no longer cope with work.
- Patients with HIV-associated wasting disease may also exhibit other symptoms



Diet

- All persons with HIV infection should have a balanced diet
- Most important feature is that it should be high in calories and should consist of both carbohydrates and protein
- A diet can be made calorie rich by adding oil and sugar to the staple starch base of maize, sorghum, cassava or rice



Proteins and Fats

- Protein rich foods include:
 - Milk and milk products such as cheese or sour milk
 - Eggs
 - Beans
 - Groundnuts
 - Meat
 - Fish
 - Soya beans
- Fat containing foods include:
 - Cooking oil
 - Groundnuts
 - Milk and milk products
 - Meat
 - Fish
 - Soya beans

** Patients should also eat cooked fresh vegetables and fruits that are easily available*

Management of Common Medical Problems

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- In patients with severe stomatitis and difficulty in chewing or swallowing, this diet should be made into a palatable liquid or porridge.
- Very ill patients may be given a high-energy supplement made of soya bean meal, sunflower oil, and sugar.
 - This is made up into a soft liquid porridge and the patient is fed this four to six times a day.
 - Soya bean milk may not be affordable by all patients and hence a high-energy drink may be made up at home by adding sugar (50g) and cooking oil (20ml) to 500 ml of milk.
 - This high-energy milk could be further fortified by beating up one egg into the mixture if eggs are available and are tolerated.
- An adult should drink 500 ml of high-energy milk daily until he is able to take a full normal diet. Children should be fed and treated according to the IMCI guidelines. (Zim, Mgmt of Common Medical Problems)
- Guidelines for the approach to the management of involuntary weight loss in adults with HIV infection appear in Handout 7.11, "Management of Involuntary Weight Loss."
- Severe weight loss is defined as loss of weight that results in emaciation and evidenced by the fact that patient's clothes no longer fit. The weight loss should amount to over 10% of the total body weight.
- Follow the guidelines for the management of persistent diarrhoea as we discussed earlier in the training.
- Advise the patient to eat a balanced diet, as we discussed earlier.
- Follow the guidelines for the management of fever as we discussed earlier in the training. What were some of the key aspects of managing fever?
- If it is suspected that the patient may have an opportunistic infection, such as TB or cryptococcal meningitis, the patient may require a further work-up and appropriate treatment. Nevertheless, the patient should receive treatment for HIV wasting syndrome. (Zim, Mgmt of Common Medical Problems)



Brainstorming Discussion: Foods for Weight Gain

- What are some common, locally-available, low-cost ingredients that patients should consider using?
- What are some specific dishes that we could recommend that are high in calories and have both carbohydrates and protein?



Stevens-Johnson Syndrome

- Skin condition caused by an adverse reaction to a medication, usually:
 - Penicillins (e.g., amoxicillin, ampicillin, penicillin, Augmentin)
 - Sulfa drugs (e.g., Bactrim)
 - Barbiturates
 - NNRTIs
 - More common with nevirapine than efavirenz
- Usually classified as a severe form of a skin rash known as erythema multiform, although it is unknown if the two are truly related

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- Stevens-Johnson is an occasional adverse reaction to the NNRTIs, especially nevirapine.
 - The risk is reduced somewhat by properly dosing nevirapine initially at 200 mg once daily for two weeks, then increasing the dose to 200 mg twice daily.



Stevens-Johnson Syndrome Examples



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- Extensive exfoliative, blisters involving the different parts of the body-typical of Stevens-Johnsons syndrome.



Symptoms (1)

- Development of large blisters in the mouth, in the throat, on the skin, around the anus or genitals, or even on the eyes
 - Blisters may rupture, leaving the immature layers underneath exposed, which may cause severe pain or discomfort
 - Eye inflammation can be severe and may result in scarring and even blindness



Symptoms (2)

- Affected persons may develop reddish skin rashes in various shapes, sizes, and locations in addition to joint pains, fever, and itching
- A wide range of distribution and severity of symptoms may occur, sometimes making the diagnosis difficult



Diagnosis (1)

- Most recognizable cause of Stevens-Johnson syndrome is medications
 - When within two weeks of starting a medication
 - Occurs in less than 1 out of every 2000 people who take a form of penicillin, the most likely drug to cause this reaction
 - Mild rashes develop in roughly one to two percent of people who take penicillin



Diagnosis (2)

- Second possible cause is infections:
 - Viruses, especially Herpes simplex virus
 - Bacteria that cause pneumonia
 - Vaccines are a very rare cause of the syndrome



Treatment

- Treatment of Stevens-Johnson involves stopping any recently started drugs, treating any underlying infections, and tending to the affected areas of the body
- Sores can be cleaned with topical antibiotics and dressings
- Intravenous fluids and systemic antibiotics or anti-inflammatory medications may also be required
- Itching can also be treated with medications
- Most cases resolve on their own whether or not a cause is found

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- Once a person develops a reaction to a medication, they should not take that medication or similar medications again unless absolutely needed for a life-threatening condition.
- Areas of skin where blisters have ruptured leave open sores on the skin, which can become infected.
- The following may also be required:
 - Observation for worsening symptoms
 - Intravenous fluids and systemic antibiotics or
 - Anti-inflammatory medications
- Itching can also be treated with medications to relieve this annoying symptom.
- Skin biopsies may be required to make a diagnosis in difficult or atypical cases.
- In rare instances, death can occur from a severe case due to widespread skin involvement and infection. (Brochert, Steven Johnson's Syndrome)



Case Study (1)

- A 27-year-old previously healthy man presents with a history of headache that has not responded to paracetamol, which he has been taking three times a day for the last 3 days
- He has been taking cotrimoxazole regularly and has been visiting the hospital each month for the last three months. He states that the headache affects the whole cranium and is worse when he bends down

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- *Refer to “Common Medical Problems Case Study” (Worksheet 7.2) in the Participant’s Handbook.*



Case Study (2)

- He has not been able to go to work for the last 3 days because of the worsening headache. He has not had any fits but states that he may have a “bit of fever”. His appetite has been poor and because he has felt nauseous for the last three days, has eaten almost nothing
- He has been using condoms whenever he has sex since he was told he was HIV positive



Case Study (3)

- Examination shows an ill looking man who weighs 65 kg (5 kg down from a month ago). Axillary temperature is 37.5 C
- He has bilateral cervical lymphadenopathy and some neck stiffness



Questions for Discussion

- What are the likely diagnoses for this patient?
- What would be your immediate management?
- What investigations would you perform?



Case Study Teaching Points (1)

- Likely diagnoses:
 - Sinusitis
 - Pharyngitis
 - Malarial fever
 - Enteric fever
 - Meningitis (cryptococcal, tuberculous, bacterial or viral)
 - Other acute viral & bacterial infections
- Immediate management:
 - Symptomatic treatment for fever
 - Headache with analgesics
 - Anti emetics for nauseous
 - Appropriate nutrition (orally or intravenously)
 - Continuation of cotrimoxazole

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- This patient has acute headache, fever, stiffness of neck and bilateral cervical lymphadenopathy.
- The likely diagnoses are:
 - Sinusitis
 - Pharyngitis
 - Malarial fever
 - Enteric fever
 - Meningitis (cryptococcal, tuberculous, bacterial or viral), and
 - Other acute viral & bacterial infections



Case Study Teaching Points (2)

- Investigations:
 - Total count
 - Differential count
 - ESR
 - Peripheral smear for malarial parasite (and other parasites depending upon the area where the patient is residing), and immature cells
 - Widal test
 - Urine examination
 - Chest X-ray PA view
 - X-ray of para nasal sinuses
 - Cerebrospinal fluid analysis after ophthalmic fundus examination
 - Ultrasound examination of abdomen
- Depending upon the findings other tests can be requested



Microteaching Exercise (1)

- Divide into 4 groups. Each group will cover a different category of opportunistic infection/disease
- Select one member of your group to serve as the reporter and another member to be the facilitator
- Read the information provided in the handouts, then work as a group to present the information to the other participants as a case study

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- Refer to “*Microteaching Exercise: Types of Opportunistic Infections and Opportunistic Diseases*” (Worksheets 7.3-7.3D) in the *Participant’s Handbook*.



Microteaching Exercise (2)

- Use flip chart paper and a marker to present the case and to record class findings and present teaching points at the time of discussion
- In addition to the information provided, you may also want to draw upon your own knowledge and experiences



Key Points

1. Persons with HIV should be counseled about what they can do to care for themselves by changing behaviour and making healthy choices
2. Common medical ailments associated with HIV and opportunistic infections can be clinically treated without the use of antiretroviral therapy

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- *If time permits and participants are willing, tour wards within Tambaram to observe cases.*
- *Then reconvene to discuss what participants have seen.*