MODULE 3

TUBERCULOSIS AND OTHER BACTERIAL INFECTIONS

Contents

- Tuberculosis
- Atypical mycobacteriosis
- Respiratory infections
- Enteric infections
- Other bacterial infections

Learning Objectives

When you have completed this module you should:

- Be able to recognise when to refer a patient for investigations for TB
- Know what the clinical features of atypical mycobacteriosis are
- How to manage patients who present with pneumonia
- List the common causes of diarrhoea in persons with HIV infection
- Know how to manage patients with common bacterial infections

3.1 TUBERCULOSIS AND HIV

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); about 9 million new cases of TB occur each year and each 3 million deaths occur from TB globally[2]. The annual incidence of TB in Sub-Saharan Africa is 313 per 100 000 population and in Zimbabwe, though accurate records are not available, it is estimated that annual incidence is over 700 per 100 000 of population. In persons with TB over the prevalence of HIV infection is about 70%. The main reasons for the increase in the burden of TB are the increasing levels of poverty, the erosion of family support structure, inadequate case detection, diagnosis and cure, and the HIV/AIDS pandemic. TB is probably the commonest opportunistic infection in Zimbabwe and it is estimated that over 30% of all new cases of TB diagnosed can be

[2] World Health Organization. Treatment of tuberculosis: Guidelines for National Programmes. WHO, Geneva, 1997

attributed to HIV infection. HIV infection fuels the TB epidemic.

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

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

Diagnosis

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

Latent TB is diagnosed on the finding of positive tuberculin skin test in the absence of clinical or radiological evidence of TB.

Treatment

ALL PATIENTS WITH TB OR SUSPECTED TB SHOULD BE REFERRED FOR SPECIALIST OPINION. Always follow the National TB Guidelines.

Latent TB

The current policy in Zimbabwe is not to use single drugs or dual drug combinations for treating suspected TB. If there is a need to treat patients for TB, refer the patient to a specialist for assessment. The management of such patients will be in accordance with the National TB guidelines.

Active TB

In persons not receiving antiretroviral therapy or are on ART but not receiving PIs and NNRTIs give:

RECOMMENDED TREATMENT
Active TB (in persons not receiving PIs or NNRTIs)

Antibiotic	Dose	Frequency	Route	Duration
Rifampicin	600mg	OD	PO	8 weeks
PLUS				
Isoniazid	300mg	OD	PO	8 weeks
PLUS				
Ethambutol	1600mg	OD	PO	8 weeks
PLUS				
Pyrazinamide	2g	OD	PO	8 weeks
THEN				
Ethambutol	800-1200mg	OD	PO	18 weeks
PLUS				
Isoniazid	300mg	OD	PO	18 weeks

In persons who are receiving antiretroviral therapy that includes PIs or NNRTIs give:

RECOMMENDED TREATMENT Active TB (persons receiving PIs or NNRTIs)				
Antibiotic	**Dose**	**Frequency**	**Route**	**Duration**
Streptomycin	1g	OD	IM	8 weeks
PLUS				
Isoniazid	300mg	OD	PO	8 weeks
PLUS				
Ethambutol	1600mg	OD	PO	8 weeks
PLUS				
Pyrazinamide	2g	OD	PO	8 weeks
THEN				
Streptomycin	1g	Three times a week	IM	30 weeks
PLUS				
Isoniazid	300mg	Three times a week	PO	30 weeks
PLUS				
Ethambutol	1.5g	Three times a week	PO	30 weeks

NUTRITION AND TUBERCULOSIS

People with TB infection often lose weight. While TB drugs help fight the infection, proper food is necessary to improve the health of the person with TB.

People with TB who eat plenty healthy food have less side effects from the TB drugs and have faster recovery. Some of the signs and symptoms of TB, like weight loss, cough, breathlessness and fever as well as adverse effects of TB drugs like diarrhoea, nausea and vomiting, burning skin and digestive problems can be alleviated by adjusting the diet.

DIARRHOEA IN TB

People with TB who have diarrhoea often eat little or nothing because of the distress the diarrhoea causes. The little food that is eaten is not properly absorbed as the food does not

stay long enough in the digestive system. Because of not eating enough, or not absorbing the food, people with TB often get malnourished. To break the cycle of diarrhoea, malnutrition and infection, people with TB need to eat easily digestible food. The recommendations on dietary management of diarrhoea, as explained in chapter 4 are relevant for people with TB.

WEIGHT LOSS IN TB

When the body does not get enough nutrients, or cannot absorb the nutrients it must use stored reserves. Fat and carbohydrates have stores in the body, but proteins do not. They will break down muscles to get the needed proteins. When the muscles start to break down the result is body wasting. It is of concern when ill people lose weight. Protein deficiency will affect the immune system as it also uses proteins for its performance. When the immune system is not working properly infections will hit the body more easily and more severely.

3.2 ATYPICAL MYCOBACTERIOSIS

Mycobacterium avium complex disease (MAC) is uncommonly encountered in Africa and its prevalence in HIV infected immunosuppressed persons in other parts of the developing world is not known. Symptoms include fever, weight loss, night sweats, diarrhoea, and wasting, and organisms may be found in blood, secretions and excreta of infected persons.

Treatment

ATYPICAL MYCOBACTERIOSIS First line treatment				
Antibiotic	**Dose**	**Frequency**	**Route**	**Duration**
Clarithromycin	500mg	BID	PO	12+ months
PLUS				
Ethambutol	15mg/kg	OD	PO	12+ months

ATYPICAL MYCOBACTERIOSIS Second line treatment				
Antibiotic	**Dose**	**Frequency**	**Route**	**Duration**
Azithromycin	600mg	OD	PO	12+ months
PLUS				
Ethambutol	15mg/kg	OD	PO	12+ months

PLUS				
Rifabutin	450mg	OD	PO	12+ months

3.3 RESPIRATORY INFECTIONS

Bacterial lower respiratory tract infections are common in the general population. They are more frequent and more severe in immunosuppressed persons with HIV infection. Pneumonia caused by *Streptococcus pneumonia* may often be the first indication of HIV infection. Other causes of pneumonia in persons with HIV infection include *Klebsiella pneumonia*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* and *Haemophilus influenzae* in children. Patients with bacterial pneumonia present with cough, fever, systemic symptoms of myalgia, headache and loss of appetite, they often have chest pain difficulty in breathing and tachypnoea, and they may also have haemoptysis. Patients may present with classic lobar pneumonia, bronchopneumonia or with unresponding and atypical pneumonia.

Diagnosis

The diagnosis of pneumonia is usually made on clinical grounds. Radiologic changes on chest x-ray may reveal lobar consolidation, patchy consolidation, diffuse lung infiltrates or atypical changes including cavitatory disease. 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.

Treatment

Details of treatment are given in the tables below:

FIRST LINE TREATMENT				
Antibiotic	**Dose**	**Frequency**	**Route**	**Duration**
Amoxycillin	500mg	TID	PO	7 days
OR				
Trimethoprim/sulphamethoxazole (Cotrimoxazole)	800mg/160mg	BID	PO	7 days

SECOND LINE TREATMENT				
Antibiotic	**Dose**	**Frequency**	**Route**	**Duration**
Crystalline penicillin	5Munits	QID	IV	
AND				
Chloramphenicol	500mg	QID	IV or PO	

If patients do not respond over a period of 72 hours then admission to hospital should be arranged and the patient commenced on crystalline penicillin 5 million unit intravenously 6 hourly together with chloramphenicol 500mg orally or intravenously 6 hourly. Patients may require oxygen and this may be administered by mask.

If patients do not respond to this treatment then consider changing the antibiotic regimen to ciprofloxacin 500mg to 750mg orally twice a day or clindamycin 600mg 4 times a day may be used and consider *Pneumocystis carinii* pneumonia as a possible diagnosis.

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 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.

<u>Diagnosis</u>

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.

3.4 ENTERIC INFECTIONS

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

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

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

Table 5: Gastrointestinal pathogens in persons with HIV infection

	PATHOGEN	CLINICAL FEATURES	TREATMENT
VIRUSES	Herpes simplex virus infection	Abdominal pain, diarrhoea. Diagnosis on biopsy or tissue culture.	Aciclovir 400mg orally or iv 3 times a day for 14 days
	Cytomegalovirus infection	Abdominal pain, diarrhoea, obtundation. Diagnosis on biopsy	Ganciclovir 5mg/kg IV twice a day for 2-3 weeks then 5mg/kg IV per day,OR Foscarnet may be given IV in a dose of 90mg/kg twice daily for 14 to 21 days then 90-120mg/kg/day as maintenance
	Adenovirus	Watery diarrhoea	No specific treatment

	PATHOGEN	CLINICAL FEATURES	TREATMENT
BACTERIA	Non-typhoid salmonelloses	Fever, abdominal pain, diarrhoea, diarrhoea with blood, weight loss, anorexia, hepatosplenomegaly. Diagnosis on blood or stool culture	Ciprofloxacin 500mg orally 4 times a day for 7 to 10 days
	Shigelloses	Fever, abdominal pain, bloody diarrhoea. Diagnosis on blood or stool culture	Ciprofloxacin 500mg orally 2 times a day for 5 days
	Campylobacter infection	Fever, abdominal pain, diarrhoea, diarrhoea with blood, Diagnosis on stool microscopy	Mebendazole 100mg orally twice daily for 3 days
	Clostridial infection	Diarrhoea, abdominal pain, blood in stool, pseudomembranous colitis	Metronidazole 200mg orally 4 times a day for 10 days
	Mycobacterium avium intracellulare	Fever, night sweats, malaise, weight loss, abdominal pain, diarrhoea, hepatomegaly. Diagnosis on blood culture, bone marrow or lymoh node or liver biopsy	Rifabutin PLUS Ethambutol PLUS Clarithromycin

	PATHOGEN	CLINICAL FEATURES	TREATMENT
PARASITES	Cryptosporidiosis	Watery diarrhoea, loss of appetite, afebrile. Diagnosis on stool microscopy.	Paromomycin 1g orally 2 times a day PLUS Azithromycin 600mg orally daily for 4 weeks
	Microsporidiosis	Watery diarrhoea, loss of appetite, afebrile. Diagnosis on stool microscopy.	Albendazole 400mg orally twice a day for 4 weeks
	Isosporiasis	Watery diarrhoea, loss of appetite, afebrile. Diagnosis on stool microscopy.	Trimethoprim 160mg / sulphamethoxazole 800mg orally twice daily for 2-4 weeks
	Strongyloides stercoralis	Hyperinfection and diarrhoea	Albendazole 5mg/kg orally twice daily for 3 days, OR, Thiabendazole 22mg/kg orally twice daily for 2 days

Important points to remember

- TB is by far the commonest opportunistic infection in developing countries with high HIV prevalence
- TB in persons with HIV infection responds well to the standard anti-TB treatment regimens
- There is evidence that in HIV infected persons who have positive tuberculin skin tests and no clinical or radiologic evidence of TB, i.e., latent TB, monotherapy with INH for 9 months, or, dual therapy with rifampicin and pyrazinamide for 2 months prevents the development of active TB
- TB should be looked for actively in persons with HIV infection and treated adequately if found
- Bacterial pneumonias occur commonly in persons with HIV infection and are often the cause of death in such persons
- A number of bacterial infections may be prevented by giving immunosuppressed persons cotrimoxazole on a long term basis