



# THE NATIONAL TUBERCULOSIS AND LEPROSY PROGRAMME

## TB MANUAL

## FOREWORD

The publication of the third edition of the National Tuberculosis and Leprosy Programme (NTLP) manual marks a big step forward because it underscores the Programme's commitment to providing the latest knowledge and developments in TB and leprosy control in Zambia. It provides among other challenges, the TB/HIV collaborative activities, paediatric TB, Public-Private Mix, MDR TB and Infection prevention. The manual also provides information on integrating and decentralising NTLP services to the districts and health facility levels

Tuberculosis has rapidly become a major health problem in Zambia in the last decade. In spite of the fact that the tuberculosis control Programme has been in existence for a long period and that Short Course Chemotherapy (SCC) has been generally available in Zambia from about 1980.

The cornerstone of TB prevention and control remain early identification and adequate treatment of infectious individuals in communities. This means that it is a cardinal responsibility of general health staff as well as all people in our communities to be alert and suspect tuberculosis in persons who may exhibit symptoms suggestive of TB, such as prolonged cough, persistent fevers, weight loss, loss of appetite coughing up blood and others.

The advent of the HIV/AIDS epidemic and its hand-in-glove relationship with tuberculosis has further aggravated the difficulty of diagnosis and treating tuberculosis, especially in the urban setting where the number of cases threatens to overwhelm the capacity of the general health care system. A case in point is the problem of ensuring that Direct Observed Therapy Short Course (DOTS) is implemented in a cohesive and systematic manner so as to maintain compliance and improve treatment outcome. The decentralisation of the TB treatment services has not only been a practical imperative (in the face of an overwhelming TB caseload), but is also in line with the overall Health Reform process that emphasises a devolution of responsibilities to the lower levels of the health care system. It is our desire and vision to reduce the problem of tuberculosis to such an extent that its eventual elimination becomes a virtual possibility.

This manual therefore comes at a most opportune time when the overall health planning process is district-focused and emphasizes service delivery at the lower levels. It will enable a variety of health workers at all levels gain knowledge of TB control as well as provide guidance to clinicians, nurses, public and Community Health Workers in the improvement of management and care provided to TB patients.

This edition has incorporated a lot of new innovation in TB control and addresses more issues pertaining to TB, TB/HIV, MDR/XDR TB, Paediatric TB, Public-Private Partnerships including patient and community Involvement. It also addresses issues of infection prevention and many other important items necessary for a successful TB control Programme. It should be realized that TB is a notifiable disease in accordance with the Public Health Act, Chapter 295 of the laws of Zambia and all care providers attending to TB clients are expected to ensure that such cases are notified in line with the Government policies and guidelines.

Lastly, I wish to thank the Directorate of Public Health and Research and all the cooperating partners for making it possible to produce this third edition of the TB Manual. It is my hope that this tool will find the widest use in our institutions for a long time to come and that it will continue to be updated as new knowledge is added to the efforts in the fight against tuberculosis.

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Finally, at the Ministry of Health, I would like to thank the TB/Leprosy Specialist (National Programme Manager) Dr Nathan Kapata and all staff in the TB unit namely, Mrs. L. M Zulu, Mr. M. Malukutu, Ms. Chanda Chikwanda and Mr. C Munyandi for their dedication to ensuring the smooth running of the TB control Programme and ensuring the finalization of this manual.

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## Abbreviations

AFB	Acid fast bacilli
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral therapy
CPT	Co-trimoxazole preventive therapy
DCT	Diagnostic counselling and testing
DOT	Direct observation of therapy
DOTS	The internationally recognised strategy for TB control
DST	Drug susceptibility testing
EQA	External Quality Assurance
FDC	Fixed dose combination
HIV	Human immunodeficiency Virus
IPT	Isoniazid Preventive therapy
IQA	Internal quality assurance
MDR	Multidrug resistant TB
MOH	Ministry of Health
NGO	Non governmental organisation
NTLP	National TB and Leprosy control programme
QA	Quality assurance
QC	Quality Control
STD	Sexually transmitted disease
TB	Tuberculosis
VCT	Voluntary Counselling and Testing
WHO	World Health Organisation

## CHAPTER 1: Tuberculosis Epidemiology and Control

### Introduction

Tuberculosis (TB) is a bacterial disease caused by infection with *Mycobacterium tuberculosis*. *M. tuberculosis* is transmitted by airborne spread in infectious droplets that are produced when an infected person coughs or sneezes. The droplets containing the mycobacteria can remain in the air for a long time, their concentration is reduced by good ventilation and the bacteria are killed by exposure to ultra-violet light such as sunlight.

Primary infection with TB occurs on first exposure to the bacteria. The bacteria are inhaled and lodge in the terminal bronchioles (Ghon focus) where lymphatics drain to the hilar lymph nodes. The combination of the Ghon focus and the hilar lymphadenopathy form the primary complex. The immune response and the infectious dose determine what happens to the individual. In most cases the immune system prevents further replication of the bacteria although a few dormant bacteria persist. This is called latent TB infection. In other individuals especially with weakened immune systems, such as people living with HIV, the bacteria continue to multiply and disease occurs within a few months (up to 2 years) after infection. Individuals with latent TB infection, reactivation may occur if either their immune system becomes weakened or if they become re-infected again.

### Global Epidemiology

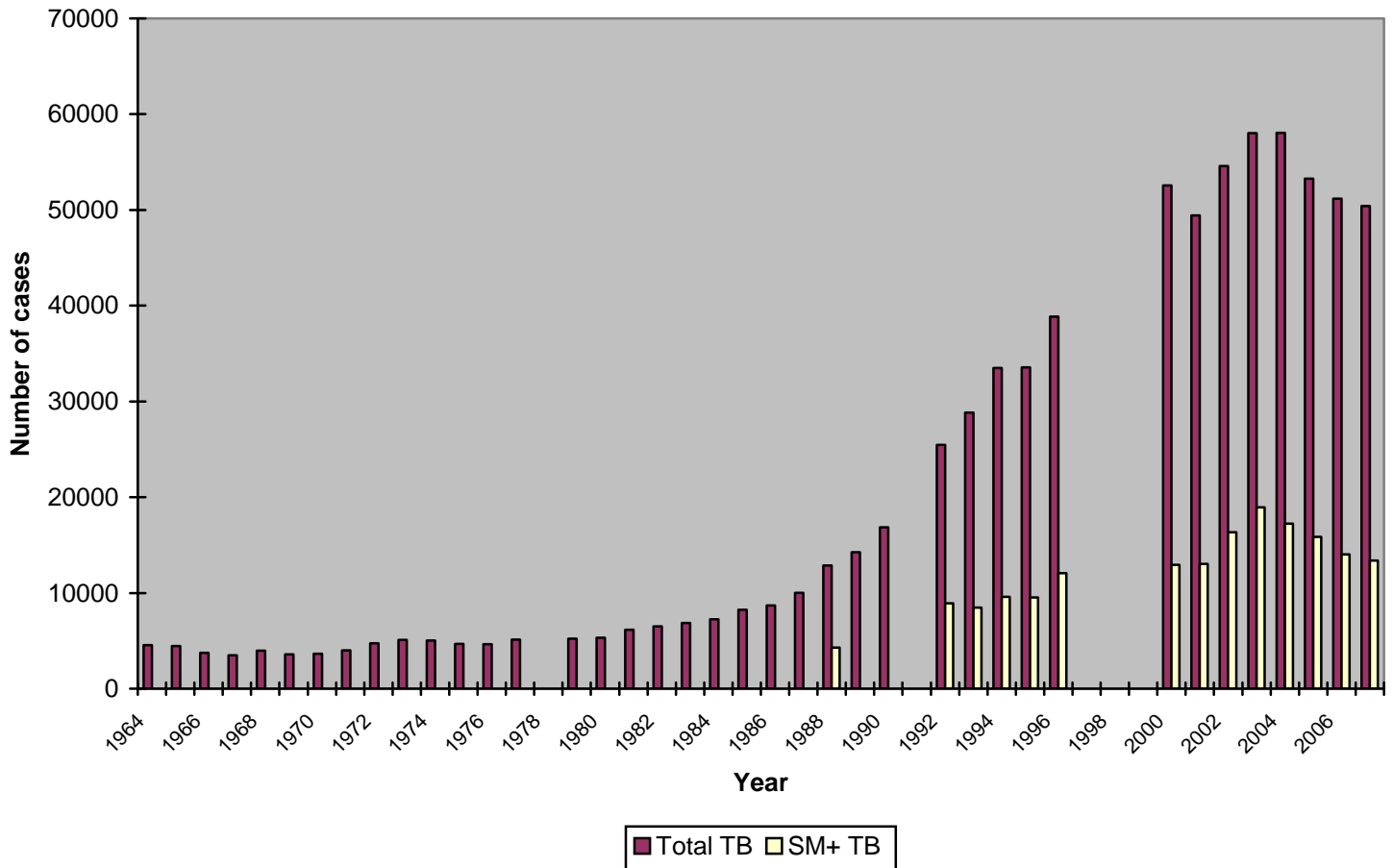
In 2006 there were 9.2 million new TB cases and approximately 2 million deaths due to TB (WHO Report 2008). All regions of the world have a stable or falling number of cases of TB except for the African region where the numbers of new cases of TB continue to rise, fuelled by the HIV epidemic.

### Zambia Epidemiology

Tuberculosis continues to be among the major public health problems in the country, more than 40 years after launching a first TB control programme. The number of tuberculosis cases has steadily increased from 4,572 cases in 1964 to 58,070 cases in the year 2004, more than ten-fold (figure 1). The majority of cases appear in young adult population groups aged 15-45 years, the same age group affected by HIV/AIDS. The rapid increase of tuberculosis in Zambia from 1985 onwards is mainly attributed to the HIV epidemic, but other factors like population growth, urban overcrowding and improved case detection have also contributed.

In 2006, Zambia notified 51,267 patients of TB (all forms), giving a notification rate of 466/100,000. This number is more than 5 times higher than the amount of TB that was found in Zambia in the pre-HIV era. The WHO estimated the TB incidence of all forms of TB to be 64,632 in 2006 and therefore, this translated into a case detection rate of all forms of TB to be 79%.

**Figure 1: Notifications of tuberculosis all forms and new smear positive cases in Zambia, 1964-2007**



### Stop TB strategy

Zambia has adopted the new Stop TB strategy which was developed in 2006. DOTS remains at the heart of the strategy to stop TB. DOTS consists of 5 main technical elements; political commitment, case detection through quality assured bacteriology, standardized treatment with supervision and patient support, an effective drug supply and management system and a monitoring and evaluation system that incorporates impact measurement. Newer elements in the strategy to stop TB include community and NGO participation in TB care, advocacy, communication and social mobilisation and improved management of TB/HIV and drug resistant TB. The full strategy is shown in figure 2.



**Table 1: The Stop TB strategy**

<b>The Stop TB Strategy</b>	
<b>Vision</b>	A world free of TB
<b>Goal</b>	To dramatically reduce the global burden of TB by 2015 in line with the Millennium Development Goals (MDGs) and the Stop TB Partnership targets
<b>Objectives</b>	<ul style="list-style-type: none"> <li>• Achieve universal access to high-quality diagnosis and patient-centred treatment</li> <li>• Reduce the human suffering and socioeconomic burden associated with TB</li> <li>• Protect poor and vulnerable populations from TB, TB/human immunodeficiency virus (HIV) and multidrug-resistant TB (MDR-TB)</li> </ul>
<b>Targets</b>	<p>Support development of new tools and enable their timely and effective use</p> <ul style="list-style-type: none"> <li>• MDG 6, Target 8: "halted by 2015 and begun to reverse the incidence" [of TB]</li> <li>• Targets linked to the MDGs and endorsed by Stop TB Partnership               <ul style="list-style-type: none"> <li>– By 2005: detect at least 70% of new sputum smear-positive TB cases and cure at least 85% of these cases</li> <li>– By 2015: reduce prevalence of and deaths due to TB by 50% relative to 1990</li> <li>– By 2050: eliminate TB as a public health problem (&lt;1 case per million population)</li> </ul> </li> </ul>
<b>Components of the strategy and implementation approaches</b>	
<ol style="list-style-type: none"> <li><b>1. Pursue high-quality DOTS<sup>a</sup> expansion and enhancement</b> <ul style="list-style-type: none"> <li>• Political commitment with increased and sustained financing</li> <li>• Case detection through quality-assured bacteriology</li> <li>• Standardized treatment with supervision and patient support</li> <li>• An effective drug supply and management system</li> <li>• Monitoring and evaluation system, and impact measurement</li> </ul> </li> <li><b>2. Address TB/HIV, MDR-TB and other challenges</b> <ul style="list-style-type: none"> <li>• Implement collaborative TB/HIV activities</li> <li>• Prevent and control MDR-TB</li> <li>• Address prisoners, refugees and other high-risk groups and special situations</li> </ul> </li> <li><b>3. Contribute to health system strengthening</b> <ul style="list-style-type: none"> <li>• Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery and information systems</li> <li>• Share innovations that strengthen systems, including the Practical approach to lung health (2)</li> <li>• Adapt innovations from other fields</li> </ul> </li> <li><b>4. Engage all care providers</b> <ul style="list-style-type: none"> <li>• Public–public and public–private mix approaches</li> <li>• International standards for tuberculosis care (3)</li> </ul> </li> <li><b>5. Empower people with TB, and communities</b> <ul style="list-style-type: none"> <li>• Advocacy, communication and social mobilization</li> <li>• Community participation in TB care</li> <li>• Patients' charter for tuberculosis care (4)</li> </ul> </li> <li><b>6. Enable and promote research</b> <ul style="list-style-type: none"> <li>• Programme-based operational research</li> <li>• Research to develop new diagnostics, drugs and vaccines</li> </ul> </li> </ol>	
<p><sup>a</sup> The internationally recommended strategy for TB control. It was launched in 1994 and later named DOTS.</p>	

## **NTLP Role and set up**

The Government of Zambia recognises TB as a major public health problem and is committed to its control. As part of this commitment it has established the National TB and Leprosy Control Programme, which falls under the Directorate of Public Health and Research within the Ministry of Health.

The National TB Programme was established in 1964 and operated as a vertical Programme in the health sector until 1993 when the Health Sector Reform was implemented. In 1993 the TB Programme was combined with the AIDS and STI Programmes to form the National AIDS/STD/TB/Leprosy Programmes. In 1997, with the implementation of the decentralized health system, the vertical TB Programme was fully integrated within the district health structure and the specific TB posts at Provincial and District levels were abolished. At the central level TB and Leprosy were part of the Directorate of Public Health and research and a TB/Leprosy Officer coordinated activities. Following the decentralisation of the health services, the TB and Leprosy control Programme almost collapsed in the late nineties resulting from a lack of focus on TB control at all levels due to loss of structure, staff trained and guidance in TB control, evidenced by lack of data and frequent drug supply interruptions. In recognition of these facts, the programme was reorganised in 2000. Assisted by the committed Government of the Republic of Zambia with increasing support from donors such as the Global Fund, United States Aid (USAID), Canadian International Development Agency (CIDA) and with the technical support of organisations such as CDC, KNCV and ZAMBART and many others, the programme has survived and has been strengthened. The current TB control in Zambia is well integrated in the primary health care services. The Programme has intensified collaborative TB/HIV activities together with the National AIDS Control Programme and other stakeholders. These activities are complimentary to and in synergy with the established core activities of tuberculosis and HIV/AIDS prevention and control Programme in the country.

The program developed a 5 year strategic plan 2006-2010 which is guided by the Global Plan to Stop TB.

## **The National TB Control Programme 5 year strategy**

**Goal:** To reduce the burden of TB in Zambia

**Main Objective:** To reduce mortality, morbidity and socio-economic burden associated with Tuberculosis so that it is no longer a major public health problem.

### **Targets**

In line with the Millennium Development Goals and the Stop TB Strategy:

- To detect at least 70% of infectious cases and cure at least 85%.
- To reduce the TB prevalence and deaths rates by 50% by 2015

### **TB Control Strategy**

To achieve the targets the NTLP has adopted the Stop TB Strategy as its TB control strategy.

The components of this strategy are:

1. Pursue high quality DOTS expansion and enhancement
2. Addressing TB/HIV, MDR TB and other challenges
3. Contributing to Health Systems Strengthening
4. Engaging all care providers
5. Empowering people with TB and communities
6. Enabling and promoting research

## **Structure and Functions of NTLP**

In its current structure the TB and Leprosy Control Programme consists of the National, Provincial, District and Health Facility levels.

### **National Level: Central Unit**

At the Ministry of Health there is a central TB unit in the Directorate of Public Health and Research headed by TB/Leprosy specialist (National TB/Leprosy Programme Manager) supported by TB/Leprosy officers.

Functions of the Central Unit

- a) Planning, co-ordinating, monitoring and evaluating standardised Tuberculosis control measures.
- b) Training and supervision of personnel involved in Tuberculosis work.
- c) Budgeting and procuring supplies e.g. drugs and laboratory equipment.
- d) Resource mobilization
- e) Coordinating TB/HIV activities through a National TB/HIV Coordinating Committee
- f) Set and support operational research agenda
- g) Supporting Reference laboratories.

### **Provincial Level**

The provincial unit is within the provincial health office. The TB/Leprosy focal person will work with the Communicable Diseases Control Specialist at this level to coordinate TB control activities at provincial level.

Functions of Provincial Level

- a) Co-ordinating Tuberculosis Control activities in the province by working closely with the Central Unit staff
- b) Supervising and training of District TB/Leprosy Control Officers and other peripheral health workers.
- c) Compiling and analyzing TB data for the province in consultation with the Central Unit.
- d) Ordering, distributing and monitoring supplies e.g. drugs and laboratory supplies.
- e) Coordinating TB/HIV activities through a Provincial TB/HIV Coordinating Committee

### **District Level**

At this level, the District TB/Leprosy control officer (DTLC) is responsible for coordinating TB control activities working in conjunction with the Clinical Care Expert, Data manager and the Manager for Planning and Development.

Functions of the District Level

- a) Implementing the NTLP activities in the district through health facility staff.
- b) Supervising health workers in case finding and chemotherapy of Tuberculosis
- c) Keeping up to date records on TB, and compiling quarterly TB reports
- d) Liaising with other stakeholders in the district
- e) Coordinating TB/HIV activities through a District TB/HIV Coordinating Committee
- f) Ordering, distributing and monitoring supplies e.g. drugs and laboratory supplies.

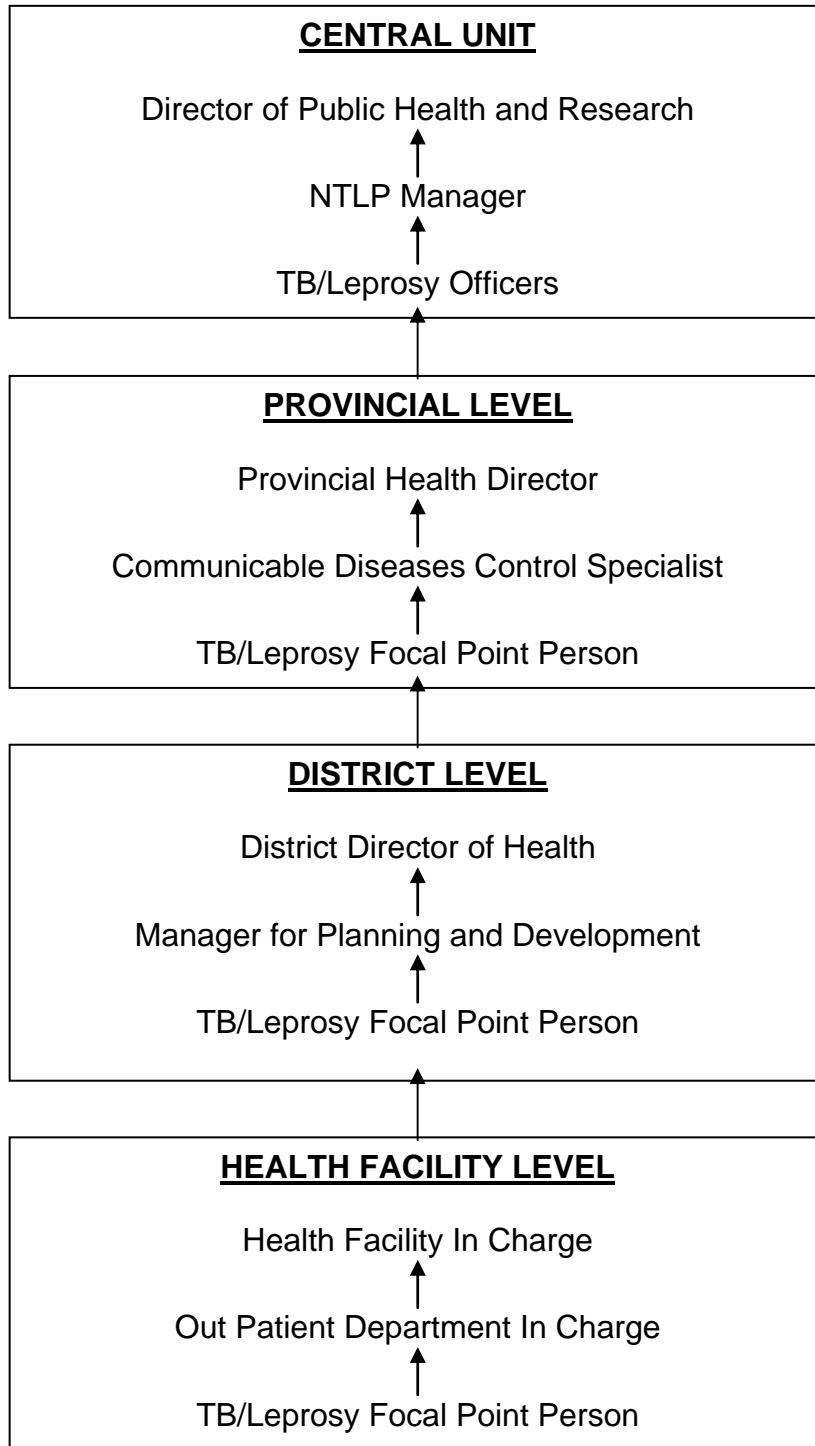
### **Health Facility Level**

A TB focal point person will coordinate NTLP activities in addition to other general duties together with other staff.

#### Functions at Health Facility Level

- a) Refer Tuberculosis suspects or their sputum specimens/smears to diagnostic (microscopy) centres for investigations.
- b) Carrying out treatment services including DOT.
- c) Tracing irregular and defaulting patients
- d) Keeping up to date TB register and compiling required TB reports for submission to the district health office.
- e) Carrying out Health Promotion activities to patients, communities and other health providers

Figure 2: Organogram of the Zambian NTLP



## CHAPTER 2: Tuberculosis in Adults

### What is tuberculosis?

Tuberculosis is a chronic infectious disease caused mainly by *Mycobacterium tuberculosis*. These micro-organisms are also known as acid-fast bacilli (AFB). The micro-organisms usually enter the body by inhalation through the lungs. Basically there are two types of tuberculosis:

**Pulmonary tuberculosis (PTB)** affects the lungs (lung parenchyma) and is the commonest form of tuberculosis.

**Extra-pulmonary tuberculosis is (EPTB)** the disease that affects organs other than the lungs, such as pleura, lymph nodes, pericardium, spine, joints, abdomen or genito-urinary tract. It may affect any part of the body.

### **Transmission**

The most important source of infection is an individual with TB of the lungs coughing (sneezing, talking, coughing) infectious droplets into the air. The transmission of these tubercle bacilli occurs by airborne spread of infectious droplets.

The concentration of infected droplets in the air and the length of time a person breathes that air determine an individual's risk of exposure. Good ventilation of the room or any other space removes nuclei droplets and so prevents nuclei to be inhaled by a person. Direct sunlight kills tubercle bacilli within minutes, but they can survive in the dark for many hours (24-48 hours).

The individual risk of infection depends on the extent of exposure to *M.tuberculosis* and the susceptibility to infection. The risk of infection for a susceptible person is therefore high with prolonged indoor exposure during the stay in a small room together with a person with smear positive pulmonary tuberculosis coughing frequently. Infectious cough particles can stay in the air for prolonged periods of time or stay alive in dust. The risk of transmission of tuberculosis from a person with smear negative PTB is low and from a person with extra-pulmonary TB even lower.

Smoke (smoking) and silicosis increase the susceptibility to infection. On the other hand good ventilation in houses dilutes the density of infected particles.

The risk of progression from infection to disease depends on the status of the immune system. The majority (90%) of people without HIV infection who are infected with *M.tuberculosis* do not develop tuberculosis disease. Their immune system is strong enough to prevent the development of disease. At this stage the only evidence of infection may be a positive tuberculin skin test. Most people infected with TB remain with so-called "dormant bacilli" that might develop into tuberculosis disease at a later stage. The development of another disease or condition that suppresses an individual's immune system triggers the dormant bacilli to become metabolically active and causes the infection to progress to tuberculosis disease.

Infection with HIV is currently the most common cause of immune suppression causing reactivation of tuberculosis in Zambia. People with TB infection and HIV have a 20-30 times higher risk of developing tuberculosis disease during their life than people without HIV infection. Other conditions like malnutrition, recurrent infections of any kind, diabetes mellitus can also cause reactivation of the TB infection.

### **Natural history of tuberculosis infection**

Droplet nuclei with TB bacilli that are inhaled are too small to be caught by the muco-ciliary defence system of the bronchi. They therefore settle in the terminal alveoli of the lungs. The tubercle bacilli favour high oxygen concentration, which stimulates the multiplication of the bacilli in the lung; the preferable area in the lung is the

apex. The multiplication of the bacilli leads to formation of a primary lesion called Ghon focus. From this lesion the bacilli spread to the nearest lymph-stations, which in most cases are hilar lymph nodes. The primary lesion combined with the hilar lymphadenopathy is called Primary Complex. The bacilli can also spread through the blood system to any other organ in the body, which can result in disseminated disease such as lymphadenopathy, meningitis, pericarditis, miliary disease etc.

The immune response develops about 4-6 weeks after the infection. The number of bacilli that have been inhaled and the strength of the immune system determine if the infection is stopped or develops into full tuberculosis disease.

In the majority of cases the immune system is strong enough to combat this primary attack. Most of the bacilli are eliminated but a few persist in a dormant stage.

**Post Primary TB** occurs after a latent period of months to many years. It is either a re-activation of the dormant bacilli that remained after primary infection or a re-infection.

**Re-activation** of dormant bacilli is seen in individuals with weakening of the immune system due to conditions such as malnutrition, chronic/ recurrent infections, HIV infection and old age.

**Re-infection** is a second infection following primary infection. This was rarely seen in the past but is now commonly seen in HIV infected individuals.

### **Signs and symptoms of TB**

Pulmonary TB is suspected in any patient presenting with some or all of the following symptoms;

- Cough which may or may not be productive of sputum for more than 3 weeks.
- Haemoptysis (coughing up blood)
- Chest pain
- Shortness of breath (dyspnoea)
- Loss of body weight
- Fever and night sweats
- Other non-specific symptoms like loss of appetite, general malaise and weakness.

In TB, the history of cough lasts only for a few months. If the cough has been going on for more than 6 months, other causes are more likely.

Extra-pulmonary TB often presents with the non-specific symptoms described above, e.g. fever, night sweats and weight loss as well as symptoms specific to the organ involved.

- Abdominal TB – ascites, intestinal obstruction
- TB meningitis – headache, neck stiffness, mononeuropathies especially of the cranial nerves
- Renal TB – haematuria, proteinuria
- Spinal TB – backache, deformity of spine (gibbus), neurological signs
- Musculoskeletal System – pain, effusions.

Tuberculosis should be considered in the differential diagnosis of any localized inflammatory process that does not respond well to general antibiotic or surgical treatment. A history of contact with an infectious TB case should be sought.

## Physical Examination

All TB suspects should have a thorough examination of the chest. TB may cause many abnormalities on chest examination but the most common are:

- Signs of consolidation – decreased air entry, dullness to percussion, increased vocal resonance and bronchial breathing
- Crepitations
- Pleural effusion - stony dullness, decreased vocal resonance, decreased air entry.

Other signs of TB may include lymphadenopathy, ascites, jaundice, hepatomegaly, neck stiffness and neurological abnormalities.

Patients will often have a marked fever and evidence of weight loss.

## Diagnosis of TB

Any patient with signs or symptoms of TB **MUST** be investigated to confirm or exclude the disease. Sputum smear examination is essential for all cases suspected of pulmonary tuberculosis

**Sputum smear examination must be done on ALL TB suspects**

Only if the results of three sputum smear examination are negative should further diagnostic tests be ordered.

Sputum-smear microscopy should be carried out at ALL levels of laboratory service. If sputum smear is NOT possible either due to lack of reagents or staff then TB suspects should be referred to the centres where laboratory facilities exist. Consideration should be given to developing a system of transporting the sputum samples to the nearest centre where laboratory facilities exist within 5 days of collection.

## Collection of sputum specimens from suspects

**The results of sputum smear can be improved by good sample collection**

### **Before collecting any sputum:**

- Explain to the patient the reason for sputum collection.
- Fill the laboratory request form as completely as possible.
- Write the patient's name on the side **and** lid of the sputum container

**Three** specimens should be collected and sent for direct microscopy

- **Spot specimen** is collected from the patient at the time of request
- **Morning specimen** The patient is then given one sputum container for collection of an early morning specimen the next day at home



- **Spot Specimen** As the patient brings the morning specimen, he/she is asked to produce a second specimen on the spot

Note:

1. If a suspect lives far away, it may be necessary to keep him/her overnight in the facility or with nearby relatives
2. Should the first specimen be positive and the suspect does not return for the second visit, the suspect must be followed-up to prevent infection in the community and further deterioration of the suspect's condition.

### **Technique for collecting sputum:**

General rules:

- A specimen collected under the supervision of a member of the health staff is likely to be better than a specimen collected without supervision.
- Sputum collection should take place in a well ventilated area or outside,
- You need to explain to the patient that saliva is not the same as sputum and that it is sputum which is needed. Patients usually co-operate better if they are out of sight of other patients at the time of collection.
- Patients who have had some food shortly before sputum collection should rinse their mouths with water first.

### **How to collect a sputum specimen**

- Sputum specimen should be collected in the open air as far away as possible from other people or in separate well ventilated room.
- Ask the patient to cough deeply (demonstration is usually more effective than words).
- Simple deep breathing techniques (10 deep slow breaths in and out) or walking around/exercising can improve sputum production
- Avoid contaminating the outside of the sputum container with sputum. If the outside is contaminated, discard the container and repeat the collection with a fresh one.
- If the specimen is not suitable (e.g. if the quantity is insufficient or if it contains saliva), ask the patient to repeat the coughing until a sufficient amount of sputum has been obtained (3 to 5 ml).

### **After collecting the sputum specimen**

- Place the lid on the container and close it firmly.
- Ensure that the patient's details are clearly written on the container (NOT on the lid)
- Wash your hands with soap and water
- Store the sputum specimens in a cool and dark place, such as cupboard or refrigerator, that can be locked and which is used solely for this purpose.
- Send the specimens to the laboratory as soon as possible (within 5 days of collection).
- Accompany each specimen with a properly completed laboratory request form.

### **Transport of sputum specimens**

Sputum specimens in containers must be suitably packed and sent by any means available to the microscopy centre together with the request form for sputum examination. Every staff member in every health unit is responsible for seeing that specimens are sent to the laboratory as soon as possible. This is particularly important for specimen for culture since viability suffers rapidly if

transit time is prolonged.

### **Sputum smear microscopy**

Mycobacteria are “acid-fast bacilli” (AFB) seen as red rods when properly stained using Ziehl Neelsen (ZN) technique and visualized under bright field microscopy using an immersion magnification (x 100) . In large diagnostic centres, smear is stained using auramine-O and observed using fluorescence microscopy, whereby the bacilli appear as bright yellow rods against a dark background.

The number of bacilli seen in a smear reflects the infectiousness of the disease. It is estimated that 5,000 - 10,000 bacilli need to be present in 1 ml of sputum to be able to detect them under a light microscope. A minimum of 100 fields should be examined before a smear is declared negative.

The results of positive sputum examination should be recorded in red ink on the laboratory register for easy identification. The laboratory staff is responsible to provide feedback of positive smear results to the clinician or TB/Leprosy coordinator for registration and initiation of treatment. Sputum results must be reported within 24 hours after the last sample is collected. If any of the sputum specimens is positive and the patient does not come back to collect the result, health staff should trace the patient using the address on the laboratory request form.

The following WHO recommended method of reporting of smear microscopy results should be used.

**Table 2: Reporting of smear results**

<b>Number of bacilli seen in smear</b>	<b>Results</b>	<b>Result Reported</b>
No AFB per 100 immersion fields	Negative	0
1 – 9 AFB per 100 immersion fields	Positive	Record exact number ( 1 – 9)
10-99 AFB per 100 immersion fields	Positive	1+
1-10 AFB per 1 immersion fields	Positive	2+
>10 AFB per 1 immersion field	Positive	3+

It is extremely important that the process of sputum collection, labeling, staining, administration and recording is accurately done. Mistakes in this process are a common cause for false positive or false negative results and might either harm the patient or endanger the community.

### **False positive sputum smear microscopy result**

This means that the sputum result of the patient is positive but the patient does not have smear positive pulmonary tuberculosis. The common causes for false positive results are:

- Red staining of scratches on the slide
- Accidental transfer of AFBs from a positive slide to a negative one, usually in the laboratory
- Contamination of the slide or smear by environmental mycobacteria
- Contamination of the slide with food particles that are acid fast and stain red
- Mislabeling of specimens and recording errors
- Mix up of specimens at clinic level.

## **False negative sputum smear microscopy result**

This means that the sputum result of a patient is negative even though the patient really has smear-positive pulmonary tuberculosis. This may arise from:-

- Sputum collection and storage problems
  - Patient provides inadequate sample
  - Sputum stored too long before smear microscopy, with overgrowth of other organisms
- Sputum processing in laboratory
  - Faulty sampling from specimen
  - Faulty smear preparation and staining
- Sputum smear examination problems
  - Inadequate time on examining the smear
  - Inadequate training of laboratory staff
- Administrative errors
  - Misidentification of patients
  - Incorrect labeling of specimens
  - Mistakes in documentation.

N.B. The sensitivity of sputum smear microscopy can be increased by concentrating the specimen by centrifugation at 3000g after decontamination with 5% sodium hypochlorite for 30 minutes. This method is highly recommended in diagnostic facilities with appropriate centrifuge machine.

## **Sputum culture**

Culture is a more sensitive method to detect mycobacteria than AFB microscopy and can detect as low as 10 bacilli/ml of sputum. However, culture methods are slow and expensive.

Depending on the technique, it takes two to eight weeks before a result is obtained. Materials and equipment needed to perform culture are costly and require complex facilities with highly skilled staff. In Zambia sputum culture for isolation of mycobacterium is performed on both a solid egg enriched medium (LJ) and liquid medium (MDGT): Normally sputum culture is done for:

- Follow-up of tuberculosis patients who fail to cure, relapse or become chronic excretors after a standardized course of treatment and who may be at risk of harbouring drug resistant organisms.
- All previous treated patients at start of retreatment
- Surveillance of tuberculosis drug resistance as an integral part of evaluation of NTLP performance.

## **Other microbiological techniques**

- serological techniques
- BacTec
- molecular techniques – PCR, DNA probes

These methods are rapid and results can be obtained from hours up to 14 days. However, these techniques need more advanced and sophisticated infrastructure and their introduction in the country requires careful planning and additional human and financial resources.

## **Other methods to support the diagnosis of TB**

### **Chest X-ray**

Diagnosis of tuberculosis using chest X-ray is not reliable because there are other chest diseases that may produce similar changes. In addition, HIV infection further diminishes the reliability of chest x-ray in the diagnosis of pulmonary TB, as it often presents with an atypical pattern. Tuberculosis, therefore, should be diagnosed whenever possible by sputum examination. Chest x-ray findings suggestive of pulmonary tuberculosis in patients with a smear negative microscopy should always be supported by clinical findings and a medical officer experienced in TB should decide on the diagnosis. However, the utility of x-ray to hasten the diagnosis of smear negative pulmonary among HIV positive should be encouraged wherever available.

**Remember there is no chest X-ray appearance typical for PTB.**

Most times a chest X-ray is not necessary when the sputum result is positive. However, there are certain condition which x-ray and clinical information are important. These include the diagnosis of pulmonary smear negative tuberculosis, pulmonary tuberculosis of small children and other complicated cases of tuberculosis such as miliary tuberculosis.

Other conditions indicative of chest X-ray are when a patient is short of breath and is suspected to have conditions that need specific treatment - such as pneumothorax, a large pleural effusion, pericarditis etc. A chest X-ray taken simultaneously with the collection of a sputum specimen is then justified.

### **Tuberculin skin test**

Tuberculin is a purified protein derived from attenuated mycobacteria. A person who has been infected with tuberculosis develops hypersensitivity to tuberculin, which is measured in millimetres of induration 48-72 hours after the tuberculin injection has been given in the skin. The test does not indicate the presence of tuberculosis disease; it only indicates mycobacterial infection. The test can be positive in a person who received BCG vaccination and who has never been infected with *M. tuberculosis*. It is often positive in individuals infected with environmental Mycobacteria Other Than Tuberculosis (MOTT) but are not infected with TB. On the other hand, a negative test does not exclude tuberculosis infection or disease. Immunosuppressive conditions such as HIV infection, malnutrition, severe bacterial infections e.g. TB itself, viral infections e.g. measles, cancers, and incorrect injection of PPD may suppress the tuberculin reaction.

The tuberculin skin test is valuable as a diagnostic tool in young children. In a child who did not receive a BCG, an induration of 10 mm or more is interpreted as positive. If the child did receive a BCG, the induration should be at least 15 mm to be positive. A positive tuberculin skin test should only be one clue to be interpreted in combination with other findings to favour the diagnosis of TB (see diagnosis of TB in children). Tuberculin test cannot be used to diagnose tuberculosis in adults for two reasons:

- A high proportion of adults is already infected with mycobacterium and therefore will test positive without suffering from tuberculosis
- People with impaired immune system due to various conditions such as those mentioned above may well have a negative tuberculin skin test despite of having active tuberculosis

## **Erythrocyte Sedimentation Rate (ESR)**

The measure of the ESR is non-specific and should not be used as a routine diagnostic tool for tuberculosis. In most patients with bacterial infection (including TB) the ESR is raised but a normal ESR does not exclude TB disease.

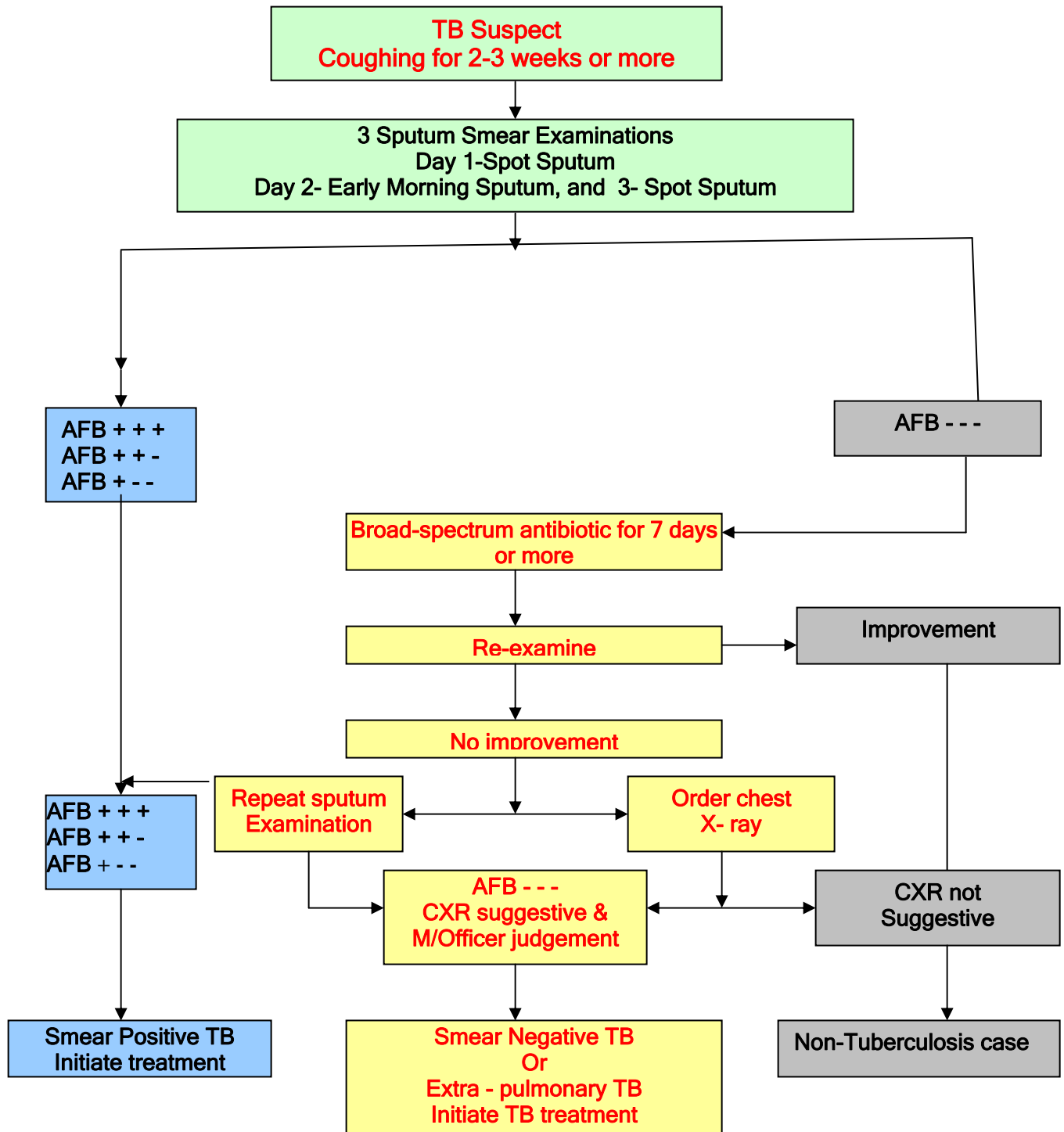
## **Biopsy**

Biopsy can play a role in the confirmation of the diagnosis of extra-pulmonary tuberculosis (e.g. lymph node biopsy). Fine needle aspiration is another method used to obtain tissue/fluid for histopathology/cytology.

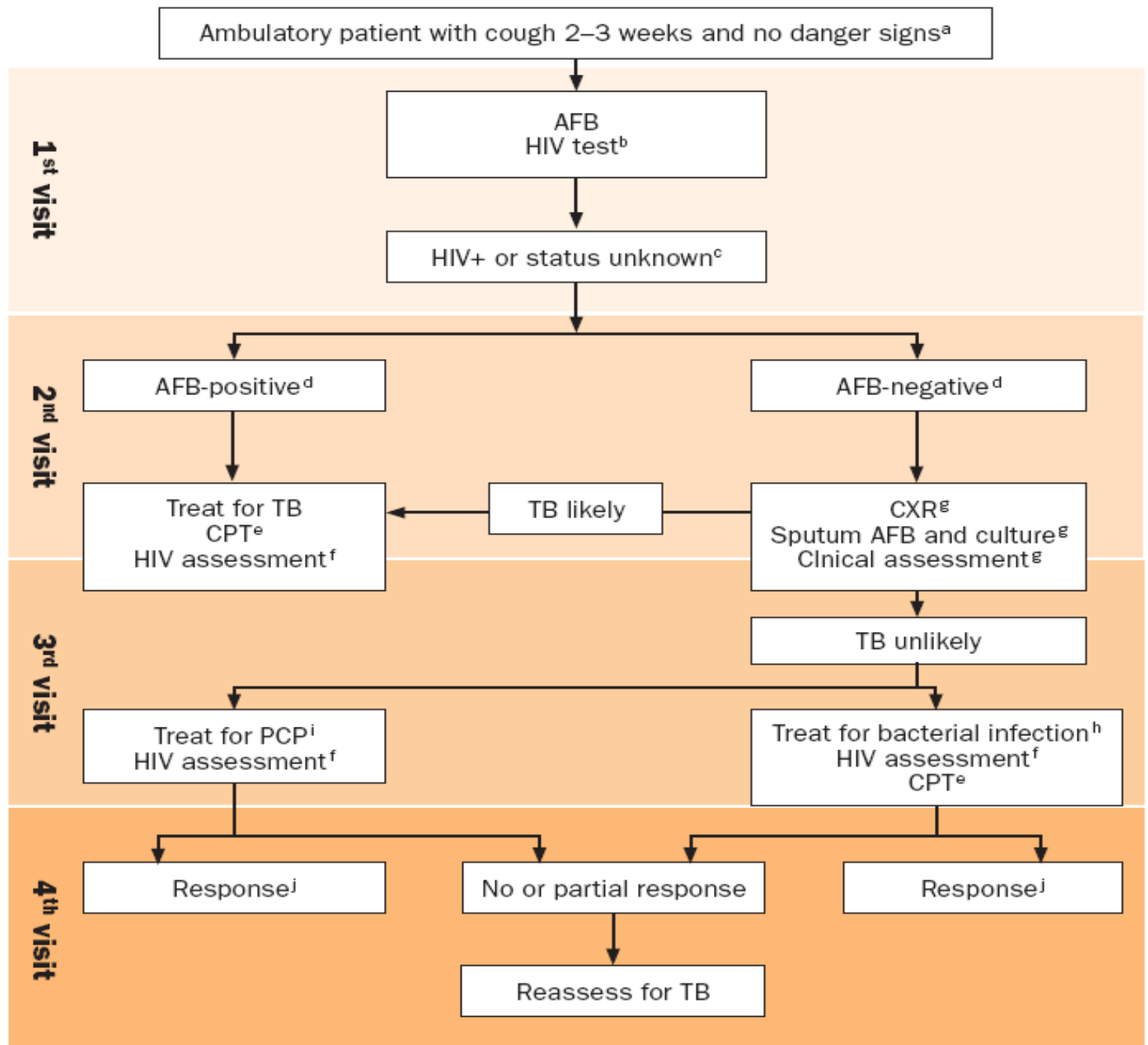
## **Diagnostic algorithms**

On the following three pages different algorithms (flowcharts) for the diagnosis of TB in adults have been presented. The main aim of these algorithms is to assist clinical decision-making in HIV-prevalent and resource-constrained settings, to expedite the diagnostic process and minimize incorrect diagnosis and mortality. The algorithms will have significant implications for both tuberculosis and HIV/AIDS service providers in these settings, and should contribute to the integration of HIV and tuberculosis interventions at the point of service delivery. The algorithms are aimed at adult and adolescent patients presenting with cough of 2-3 weeks' duration and differ according to the clinical condition of the patient (ambulatory or seriously ill).

Figure 3: Flowcharts on the diagnosis of pulmonary tuberculosis in adults



## Algorithm for the diagnosis of tuberculosis in ambulatory HIV-positive patient



<sup>a</sup> The danger signs include any one of: respiratory rate >30/minute, fever >39 °C, pulse rate >120/min and unable to walk unaided.

<sup>b</sup> For countries with adult HIV prevalence rate ≥1% or prevalence rate of HIV among tuberculosis patients ≥5%.

<sup>c</sup> In the absence of HIV testing, classifying HIV status unknown as HIV-positive depends on clinical assessment or national and/or local policy.

<sup>d</sup> AFB-positive is defined as at least one positive and AFB-negative as two or more negative smears.

<sup>e</sup> CPT = Co-trimoxazole preventive therapy.

<sup>f</sup> HIV assessment includes HIV clinical staging, determination of CD<sub>4</sub> count if available and referral for HIV care.

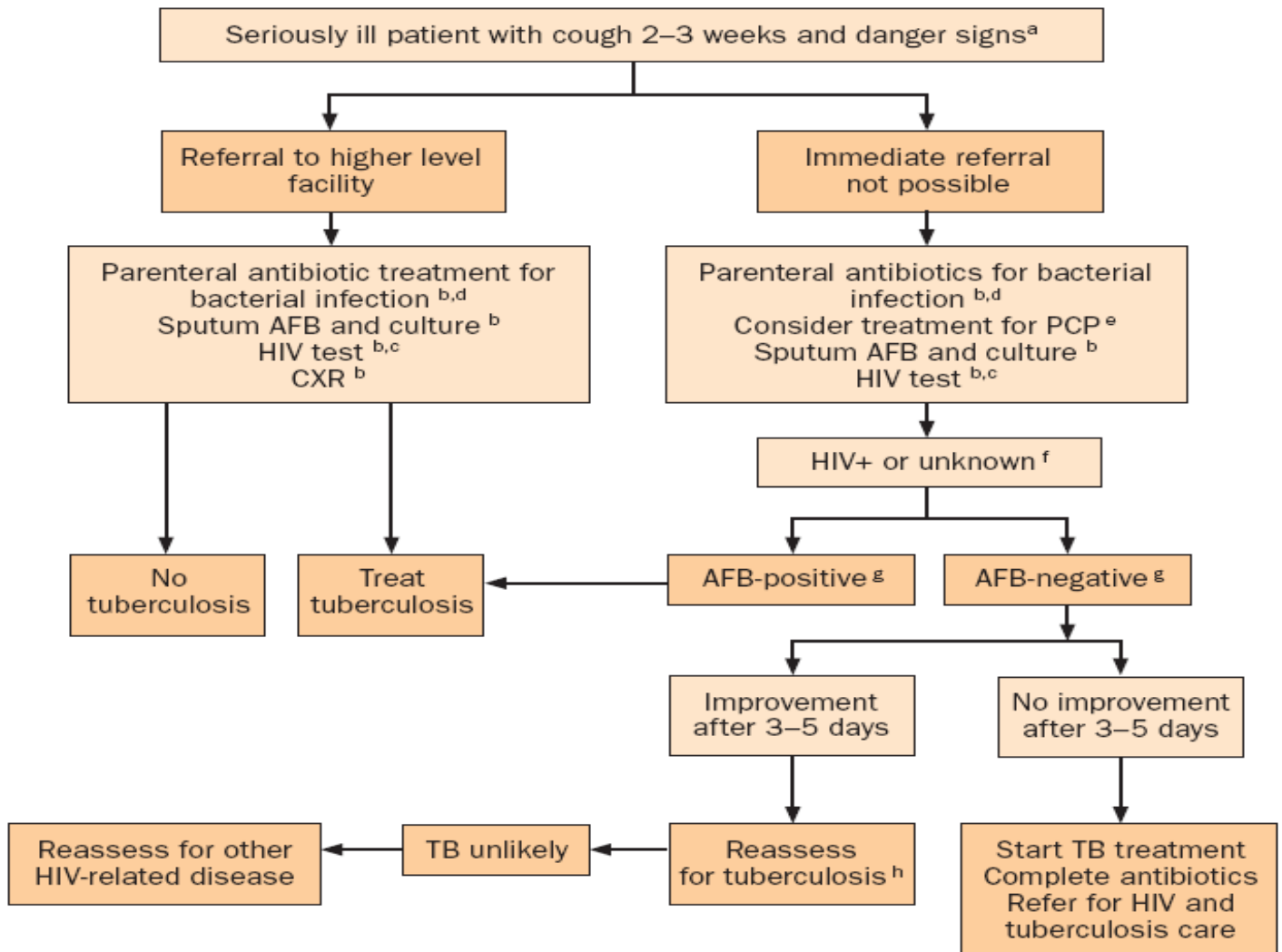
<sup>g</sup> The investigations within the box should be done at the same time wherever possible in order to decrease the number of visits and speed up the diagnosis.

<sup>h</sup> Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.

<sup>i</sup> PCP: *Pneumocystis carinii* pneumonia, also known as *Pneumocystis jirovecii* pneumonia.

<sup>j</sup> Advise to return for reassessment if symptoms recur.

## Algorithm for the diagnosis of tuberculosis in seriously ill HIV-positive patient



<sup>a</sup> The danger signs include any one of: respiratory rate >30/min, fever >39 °C, pulse rate >120/min and unable to walk unaided.

<sup>b</sup> The investigations within the box should be done at the same time wherever possible in order to decrease the number of visits and speed up the diagnosis.

<sup>c</sup> For countries with adult HIV prevalence rate  $\geq 1\%$  or prevalence rate of HIV among tuberculosis patients  $\geq 5\%$ .

<sup>d</sup> Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.

<sup>e</sup> PCP: *Pneumocystis carinii* pneumonia, also known as *Pneumocystis jirovecii* pneumonia.

<sup>f</sup> In the absence of HIV testing, classify HIV status unknown into HIV-positive depends on clinical assessment or national and/or local policy.

<sup>g</sup> AFB-positive is defined as at least one positive and AFB-negative as two or more negative smears.

<sup>h</sup> Reassessment for tuberculosis includes AFB examination and clinical assessment.



## **Extrapulmonary TB**

In high HIV prevalent settings like Zambia, extrapulmonary tuberculosis is more strongly HIV-related than pulmonary tuberculosis, with a combination of the two being especially suggestive of underlying HIV-infection. HIV-related extrapulmonary tuberculosis is a WHO clinical stage 4 (advanced AIDS) diagnosis and patients with HIV-related extrapulmonary tuberculosis often have disseminated disease and are at high risk of rapid clinical deterioration and death. The accurate diagnosis of extrapulmonary tuberculosis is complex and difficult, particularly in peripheral health facilities with limited support and diagnostic infrastructure.

If a patient has extra-pulmonary TB as well as pulmonary TB should be classified as a pulmonary tuberculosis case. It is therefore important to examine sputum specimens from patients with extra-pulmonary TB.

### **TB-lymphadenitis:**

Usually TB lymphadenitis presents as a group of firm to fluctuant, tender lymph nodes that might break through the skin. This can result in a chronic sinus but most heal leaving a scar behind. The differential diagnosis for TB lymphadenitis is persistent generalized lymphadenopathy (PGL), lymphoma, Kaposi sarcoma, metastases, and sarcoid or drug reaction.

TB lymphadenitis can be diagnosed by aspirating a little material from a fluctuant lymph node using a standard G19 needle. The material is deposited on a slide where a routine ZN staining can detect AFB in 50-70% of the cases. Where possible, patients should be referred to a larger centre for biopsy and histological investigations. The observation of any caseation is enough for the diagnosis of TB. If there is no caseation the content of the lymph node can be smeared on a slide and stained using the ZN technique for examination of AFB.

### **Pleural effusion, pericardial effusion, tuberculous ascites :**

Inflammatory tuberculous effusion may occur in the pleural, pericardial or peritoneal cavities. These conditions are more frequently seen in HIV positive individuals. The main differential diagnoses are malignancy, post-pneumonic effusion, congestive heart failure and amoebic abscess.

The diagnosis is usually by exclusion of other conditions. Aspirated fluid, which is most times clear yellow straw coloured, can be investigated on AFB (rarely seen), protein level and cells. High protein level (>30 g/l) with predominant lymphocytes in the fluid aspirate is suggestive of tuberculosis.

In Tanzania, where there are limited diagnostic facilities, exudative pleural and pericardial effusion and ascites are suggestive of tuberculosis.

### **Spinal TB:**

Tuberculosis of the spine (Pott's disease) is a severe form of tuberculosis. The TB infection starts from the inter-vertebral disc and spreads along the anterior side to the adjacent vertebral bodies. The collapse of the vertebral bodies might compress the spine causing paralysis.

The diagnosis is made with a plain X-ray of the spine that shows anterior erosion of two adjacent vertebral bodies with a narrowing or disappearance of the disc space. The main differential diagnosis is a malignancy, which most times erode the spine bodies leaving the inter-vertebral disc space intact.

### **Miliary TB:**

Miliary TB is blood-borne dissemination of tuberculosis from either a primary infection or erosion of a secondary tuberculous lesion into a blood vessel (TB bacteraemia). Miliary TB is common in late stage of HIV/AIDS disease. The patient presents with signs and symptoms of a septicaemia with fever, wasting, confusion etc.

The diagnosis is sometimes made with the help of a chest X-ray that shows uniformly distributed miliary (like millet seeds) shadows. However, this is seen in only approximately 25% of the cases. Bacteriological confirmation is sometimes possible from sputum, blood, CSF or bone marrow.

**TB meningitis:**

TB of the meninges may occur from a rupture of a cerebral tuberculoma into the subarachnoid space or blood born dissemination from active infection from elsewhere in the body.

Most times, patients present with headaches, decreased consciousness and neck stiffness. The diagnosis usually rests on clinical grounds and microscopic examination of cerebrospinal fluid and biochemical tests.

It is worthy mentioning that most forms of extra-pulmonary tuberculosis are paucibacillary, it is therefore much more difficult to confirm the diagnosis by demonstration of bacilli on microscopy. However, culture can be performed if a biopsy is taken or an exudate or caseating material is sampled.

If there is no access to laboratory where culture or histology can be performed the diagnosis is based on strong supportive (clinical, biological and radiological) evidence which is used to decide on what treatment to give.

**Table 3. Diagnosis and immediate management of suspected extrapulmonary tuberculosis**

LYMPH NODE TUBERCULOSIS (PERIPHERAL)	PLEURAL EFFUSION	DISSEMINATED TUBERCULOSIS	PERICARDIAL EFFUSION	TUBERCULOUS MENINGITIS
<p><b>Essential investigations</b></p> <ul style="list-style-type: none"> <li>HIV test (rapid if possible)</li> <li>Sputum smears if coughing</li> <li>Needle aspirate for AFB ( 18 to 21 gauge)</li> </ul> <p><b>High suspicion of tuberculosis if:</b></p> <ul style="list-style-type: none"> <li>2 cm or more in size</li> <li>Asymmetrical/localized</li> <li>Painless swelling</li> <li>Firm/fluctuant/fistulated</li> <li>Cervical location</li> <li>Weight loss, night sweats, fever</li> </ul> <p><b>Findings that suggest a non-tuberculosis diagnosis</b></p> <ul style="list-style-type: none"> <li>KS<sup>a</sup> in skin or mouth (probable KS nodes)</li> <li>Symmetrical (probable lymphoma or HIV lymphadenopathy)</li> <li>Tender, inflamed, purulent (bacterial or fungal)</li> <li>Site other than cervical</li> </ul> <p><b>Immediate management</b></p> <ul style="list-style-type: none"> <li>Aspirate for cytology and AFB microscopy</li> <li>Excision biopsy if aspirate non-diagnostic unless                         <ul style="list-style-type: none"> <li>HIV+ with possible disseminated tuberculosis (e.g. rapid clinical deterioration)</li> </ul> </li> <li>Tuberculosis considered the most likely clinical diagnosis, and biopsy not available within 2 weeks</li> </ul>	<p><b>Essential investigations</b></p> <ul style="list-style-type: none"> <li>HIV test (rapid if possible)</li> <li>CXR</li> <li>Sputum smears if coughing</li> <li>Aspirate &amp; inspect fluid<sup>b</sup></li> <li>Differential white blood cell count and protein determination (if possible) of aspirate</li> </ul> <p><b>High suspicion of tuberculosis if:</b></p> <ul style="list-style-type: none"> <li>Unilateral effusion</li> <li>Aspirate of fluid<sup>b</sup> is:                         <ul style="list-style-type: none"> <li>Clear and straw coloured and</li> <li>Clots on standing in a tube without anticoagulants</li> </ul> </li> <li>Weight loss, night sweats, fever</li> <li>Evidence for tuberculosis elsewhere</li> </ul> <p><b>Findings that suggest a non-tuberculosis diagnosis</b></p> <ul style="list-style-type: none"> <li>Bilateral effusion (possible heart failure or pneumonia)</li> <li>Clinical KS<sup>a</sup>/other malignancy</li> <li>Aspirate of fluid is:                         <ul style="list-style-type: none"> <li>Cloudy/pus (probable empyema)</li> <li>Fails to clot (does not exclude tuberculosis, but send fluid for protein and differential cell count, and consider heart failure)</li> </ul> </li> </ul> <p><b>Immediate management</b></p> <ul style="list-style-type: none"> <li>Features of tuberculosis only                         <ul style="list-style-type: none"> <li>Start tuberculosis treatment</li> </ul> </li> <li>Features of non-tuberculosis diagnosis                         <ul style="list-style-type: none"> <li>Send aspirate for differential cell count, protein and, if available, cytology: ≥50% lymphocytes and protein &gt;30 g/L suggests tuberculosis</li> <li>Treat for tuberculosis if the only unusual feature is failure of aspirate to clot, or no other diagnosis by 7 days</li> </ul> </li> </ul>	<p><b>Essential investigations</b></p> <ul style="list-style-type: none"> <li>HIV test (rapid if possible)</li> <li>CXR</li> <li>Malaria blood film</li> <li>Sputum smears if coughing</li> <li>Blood cultures, full blood count and cryptococcal antigen</li> </ul> <p><b>High suspicion of tuberculosis if:</b></p> <ul style="list-style-type: none"> <li>Weight loss, fever and cough</li> <li>Abnormal CXR (which can include miliary pattern)</li> <li>Large spleen/liver</li> <li>Night sweats</li> <li>Anaemia</li> </ul> <p><b>Findings that suggest a non-tuberculosis diagnosis</b></p> <ul style="list-style-type: none"> <li>if HIV+ consider Salmonella, pneumococcus, malaria, Cryptococcus</li> <li>Rigors</li> <li>Very breathless (respiratory rate &gt;30/min)</li> <li>Severe diarrhoea</li> <li>Blood in stool</li> <li>Positive cryptococcal antigen, malaria smear or likely pathogen isolated from blood culture</li> </ul> <p><b>Immediate management</b></p> <ul style="list-style-type: none"> <li>Features of tuberculosis only                         <ul style="list-style-type: none"> <li>Start tuberculosis treatment (add antibiotics if critically ill)</li> </ul> </li> <li>Features of non-tuberculosis diagnosis                         <ul style="list-style-type: none"> <li>Investigate other causes</li> <li>Start both tuberculosis treatment and antibiotics if critically ill</li> </ul> </li> </ul>	<p><b>Essential investigations</b></p> <ul style="list-style-type: none"> <li>HIV test (rapid if possible)</li> <li>CXR</li> <li>Sputum smears if coughing</li> <li>Cardiac ultrasound (ideally)</li> <li>Electrocardiogram if ultrasound not available</li> </ul> <p><b>High suspicion of tuberculosis if:</b></p> <ul style="list-style-type: none"> <li>Lung fields clear (but may have bilateral pleural effusion)</li> <li>Weight loss, night sweats, fever</li> <li>Evidence of tuberculosis elsewhere</li> </ul> <p><b>Findings that suggest a non-tuberculosis diagnosis</b></p> <ul style="list-style-type: none"> <li>Streaky shadowing of lung fields and/or heart shape not symmetrical (probable heart failure)</li> <li>High blood pressure</li> <li>Electrocardiogram suggests another cause for enlarged heart (e.g. high blood pressure, valve disease, dilated cardiomyopathy)</li> <li>Murmur (probable valvular disease)</li> <li>Rigors (probable bacterial pericarditis)</li> </ul> <p><b>Immediate management</b></p> <ul style="list-style-type: none"> <li>Features of tuberculosis only                         <ul style="list-style-type: none"> <li>Refer tuberculosis treatment</li> <li>Refer for urgent aspiration if very breathless/unwell</li> </ul> </li> <li>Features of non-tuberculosis diagnosis                         <ul style="list-style-type: none"> <li>Investigate other causes (urea and cardiac ultrasound)</li> <li>Treat for tuberculosis if ultrasound confirms effusion and no other diagnosis made by 7 days</li> </ul> </li> </ul>	<p><b>Essential investigations</b></p> <ul style="list-style-type: none"> <li>HIV test (rapid if possible)</li> <li>Lumbar puncture</li> <li>Microscopy (Gram stain and AFB)/ protein/glucose in cerebrospinal fluid</li> <li>Cryptococcal antigen/stain</li> <li>Sputum smears if coughing</li> </ul> <p><b>High suspicion of tuberculosis if:</b></p> <ul style="list-style-type: none"> <li>Weight loss, night sweats, fever</li> <li>Cerebrospinal fluid clear with high protein, low glucose and lymphocytes</li> <li>Cryptococcal antigen (or India ink and fungal culture) –ve in cerebrospinal fluid</li> <li>Evidence of tuberculosis elsewhere</li> </ul> <p><b>Findings that suggest a non-tuberculosis diagnosis</b></p> <ul style="list-style-type: none"> <li>HIV test +ve (cryptococcal disease more likely than tuberculosis)</li> <li>Cerebrospinal fluid cloudy or neutrophils on microscopy (probably bacterial)</li> <li>Cryptococcal tests +ve</li> <li>Rapid onset</li> <li>Very high cerebrospinal fluid pressure (probably cryptococcal)</li> </ul> <p><b>Immediate management</b></p> <ul style="list-style-type: none"> <li>Features of tuberculosis only                         <ul style="list-style-type: none"> <li>Start tuberculosis treatment</li> <li>Admit</li> </ul> </li> <li>Features of non-tuberculosis diagnosis                         <ul style="list-style-type: none"> <li>Treat for cryptococcal disease if crypto tests +ve or if HIV+ and no other diagnosis made</li> </ul> </li> </ul>

<sup>a</sup> KS-Kaposi's sarcoma

<sup>b</sup> The aspirate should be put in a plain tube (with no anticoagulant) in order to observe its appearance and clotting. A second aliquot should be placed into an anticoagulated tube, so that a differential white blood cell count and protein determination can be requested if necessary.

## CHAPTER 3: Management of TB

### Introduction

Early case finding and adequate treatment of tuberculosis patients is the cornerstone of TB control. Management of TB cases uses standardised short-course chemotherapy provided under direct observation at least in the initial phase of treatment for all identified smear positive TB cases, the main sources of infection. The aims of treatment are:

- To cure TB patients to prevent further transmission of TB in the communities
- To prevent death from active TB or its late effects.

It is always necessary to use combinations of specific anti-tuberculosis drugs in all treatment regimens to avoid the emergence of drug resistant TB. **At no time should monotherapy (use of a single anti-TB drug) be employed at any stage of treatment.**

Once a decision is made to treat as TB, it is the responsibility of the health care provider to ensure that the patient is notified and completes the full course of TB treatment.

Due to the tremendous increase in the TB caseload, TB patients should be treated on an ambulatory basis with the exception of seriously ill, MDR/ Extreme Drug Resistance (XDR) TB patients.

The Ministry of Health Policy is that all patients diagnosed with tuberculosis are entitled to anti-TB drugs free of charge.

The only effective treatment of TB:

- An appropriate combination of anti-TB drugs,
- Given in the correct dosages,
- Taken daily and uninterrupted by the patient under supervision,
- For the stipulated duration of treatment

### Disease classification

Tuberculosis cases are classified as either Pulmonary Tuberculosis (PTB) or Extra-Pulmonary Tuberculosis (EPTB). Patients with pulmonary tuberculosis are further subdivided into sputum smear-positive and sputum smear-negative cases.

#### *Pulmonary Tuberculosis*

##### **Smear positive pulmonary tuberculosis (PTB+)**

Tuberculosis in a patient with at least one initial smear examinations positive by direct microscopy for Acid Fast Bacilli (AFB+)

##### **Smear negative pulmonary tuberculosis (PTB-)**

Tuberculosis in a patient with three initial negative smear examinations by direct microscopy for Acid Fast Bacilli (AFB-) **and** non-response to a course of broad-spectrum antibiotics, **and** again three negative smear examinations by direct microscopy, **and** X-ray abnormalities suggestive of active tuberculosis as determined by the treating Medical Doctor.

OR

Tuberculosis in a patient with three initial smear examinations negative by direct microscopy but positive by culture for mycobacterium.

### ***Extra-pulmonary tuberculosis***

#### **Extra-pulmonary tuberculosis (EPTB)**

Tuberculosis in organs other than the lungs proven by one culture positive specimen from an extra-pulmonary site or histopathological evidence from a biopsy.

OR

Tuberculosis based on strong clinical evidence, including macroscopic evidence of specimen inspection, consistent with active extra-pulmonary tuberculosis **and** the decision by a Medical Doctor to treat with a full course of anti-tuberculosis therapy.

Note that in all suspect extra-pulmonary cases three sputum specimens should be examined in order to rule out pulmonary tuberculosis. In addition note that cases of pleurisy should be classified as extra-pulmonary tuberculosis, if sputum smears are negative.

#### **Case definitions**

Patients who have taken anti-tuberculosis drugs for one month or more at any time in the past have an increased chance of having drug-resistant tuberculosis. Therefore, it is essential that all patients, especially those with positive smears, are carefully questioned about previous anti-tuberculosis treatment before current treatment is started, to ensure that the treatment is as effective as possible. Cases are therefore further defined by treatment history as:

- *New case*: tuberculosis in a patient who has never taken anti-tuberculosis drugs for more than one month.
- *Relapse*: Smear positive tuberculosis in a patient who has been declared cured from tuberculosis or completed treatment and is now diagnosed with a fresh episode.
- *Treatment failure (smear-positive)*: tuberculosis in a newly diagnosed patient who *remains smear-positive* 5 months or more after the start of chemotherapy.
- *Treatment after default*: smear positive patient who had taken treatment for a month or more before default in intensive phase.
- *Transfer in*: patient who has been transferred from another tuberculosis register to continue treatment.
- *Chronic case*: tuberculosis in a patient who remains smear-positive after completing a re-treatment regimen under supervision.

**Note** that if a patient is smear negative but has been treated for TB before they do not fit any of the criteria above and should be defined as *other retreatment*. It is important for such cases that a proper diagnosis is made rather than just assuming this to be a recurrence of TB as often there are underlying problems such as HIV disease.

## Treatment of Tuberculosis

### Basic principles of TB control

Early case finding and adequate treatment of tuberculosis patients is the corner-stone of tuberculosis control. The aim of treatment is to cure TB patients, to prevent death from active TB or its late effects and to prevent further transmission of tuberculosis to the community. The DOTS strategy is the gold standard to achieve these aims and to prevent the development of anti-TB drug resistance.

In order to achieve effective treatment of tuberculosis, adequate chemotherapy should be prescribed in appropriate combination of at least three anti tuberculosis drugs (Mono-therapy must be avoided). Every confirmed tuberculosis patient should take the drugs regularly for a sufficient period of time.

In the past some clinicians advocated the so called "treatment trial" as a diagnostic manoeuvre. This approach leads to unnecessary treatment of many patients due to the tendency to jump too quickly to treatment trial without the necessary careful and thoughtful approach to diagnosis. Clinicians have to come to a decision on whether to put a patient on treatment or not. No trials of therapy should be entertained. A patient either has TB and should be treated as such, or does not have TB and should not be treated.

### Short-course chemotherapy

Providing short-course chemotherapy is an important component of the DOTS strategy. It is the most effective way to ensure rapid sputum conversion of infectious patients, thereby stopping further transmission of *M. tuberculosis* to the community. The first short-course regimen of 8 months was introduced in Zambia in 1986 for sputum smear positive patients only. Non-infectious patients also receive a short-course regimen since the late nineties. A six months short-course regimen for new smear positive, smear negative and extrapulmonary TB will be introduced in 2009.

Short-course chemotherapy has a very high success rate if properly applied in a patient with tuberculosis, diagnosed in time. The length of the regimen varies from 6 to 8 months depending on the category of disease. The six months regimen, which contains rifampicin throughout, is slightly more effective in preventing re-activation of dormant bacilli, reducing relapse especially in HIV positive tuberculosis patients.

### First Line Anti TB Drugs

There are five first-lines anti TB drugs.

These drugs have three main properties: bactericidal activity, sterilizing and the ability to prevent resistance. The first line anti-TB drugs possess these properties to different extent.

**Isoniazid (H)** is bactericidal with a high potency, kills more than 90% of the total population of TB bacilli during the first few days of treatment.

**Rifampicin (R)** is bactericidal with a high potency; it is the most effective sterilising anti-TB drug and makes short course chemotherapy possible.

**Pyrazinamide (Z)** achieves its sterilising action within 2-3 months. It is bactericidal with a low potency.

**Ethambutol (E)** is bacteriostatic with a low potency.

**Streptomycin (S)** is bactericidal with a low potency.

## **Fixed Dose Combination**

To ensure that the correct combinations of drugs are used at the correct dose, Zambia has 2, 3 and 4 Fixed Dose Combinations of drugs available for use in all facilities.

Advantages of fixed-dose combination:

- Prevention of drug resistance (when given under DOT)
- Simplification of treatment
- Simplification of drug management
- Reduction of misuse of the drugs for treatment of other conditions other than TB

However, a limited stock of single-dose formulation is available at higher level facilities for management of patients with major side effects.

All TB treatment is considered in 2 phases:

### **1. Intensive Phase**

The intensive phase is designed for the rapid killing of actively growing bacilli and the killing of semi-dormant bacilli. This means a shorter duration of infectiousness. The duration of the phase is two (2) to three (3) months.

### **2. Continuation Phase**

The continuation phase eliminates bacilli that are still multiplying and reduces the risk of failure and relapses. The duration is between four (4) and ten (10) months depending on disease site and drugs used.

## Treatment Regimens in Adults

### Category I Patients:

All new patients (Smear positive, negative and extra pulmonary).

**Intensive Phase:** 2(RHZE)

**Continuation Phase:** 6(HE) or 4(RH)

**Table 4: Dose-body weight relation for patients treated with category I treatment regimen containing EH.**

Weight in Kg	Intensive Phase 2 months	Continuation Phase 6 months
	RHZE 150/75/400/275	EH 400/150
30-37	2	1
38-54	3	2
55-70	4	3
>71	5	3

**Table 5: Dose-body weight relation for patients treated with category I treatment regimen containing RH.**

Weight in Kg	Intensive Phase 2 months	Continuation Phase 4 months
	RHZE 150/75/400/275	RH 150/75
30-37	2	2
38-54	3	3
55-70	4	4
>71	5	5

### Category II Patients:

All previous treated patients including smear positive retreatment, smear negative retreatment and treatment failures, treatment after default and relapse cases.

**Intensive Phase:** 2S(RHZE)/ 1(RHZE)

**Continuation Phase:** 5(RHE)



**Table 6: Dose-body weight relation for patients treated with category II treatment regimen.**

Weight in Kg	Intensive Phase 3 months			Continuation Phase 5 months
	2 months		1 month	
	RHZE 150/75/400/275	+ S 1 g	RHZE 150/75/400/275	RHE 150/75/275
30-37	2	0.5 g	2	2
38-54	3	0.75g	3	3
55-70	4	1g	4	4
>71	5	1g	5	5

The re-treatment regimen is the last opportunity for a patient to get cured. Therefore re-treatment must be administered under strict DOT during the entire treatment. The NTLP recommends three months admission during intensive phase especially for those patients with a history of poor adherence. The continuation phase is administered under two weekly supervision (DOT) on ambulatory bases.

Patients with a relapse or failure might possibly harbour resistant bacilli. It is therefore important that before any patient is started on a category II re-treatment regimen, at least one sputum sample is collected and sent to Chest Diseases Laboratory (CDL) for culture and susceptibility testing (see drug-resistance).

### **Possible Outcomes Of Treatment**

- **Cured (C):** A tuberculosis patient who was initially sputum-smear-positive and has a negative result in the last month of treatment and on at least one previous occasion.
- **Treatment Completed (TC):** A tuberculosis patient who was initially smear positive on diagnosis and completed treatment without sputum examination at the end of treatment or a patient who was initially sputum-smear negative or had extra-pulmonary tuberculosis and completed treatment.
- **Failure (F):** A tuberculosis patient who was sputum-smear-positive at the onset of treatment and has a positive sputum-smear 5 or 8 months after the start of anti-tuberculosis treatment or a smear negative patient at diagnosis who becomes sputum positive after 2 months of treatment.
- **Transfer Out (TO):** A patient who is transferred to another District to continue treatment there. The patient will be recorded as Transferred In (TI) in the receiving District.
- **Defaulter (OC):** A patient who fails to attend 14 consecutive days during the intensive treatment phase or who fails to attend two consecutive monthly clinics during the continuation phase
- **Died (D):** A patient who dies for any reason during the course of treatment

### **Patient Compliance and Defaulter Tracing**

**Patient compliance is a key factor in treatment success.**

Promoting compliance through a patient centred approach, which includes facilitating access to treatment, choosing with the patient the most convenient time and place for direct observation of treatment and, when possible providing other social and medical services, is much more effective than spending resources on defaulter tracing. It is vital for health staff and community workers to offer polite and efficient attention and to consider the needs of the patient at every contact with them.

- **Intensive phase** treatment should be administered under the direct observation of a trained designated treatment supporter either at the health centre or in the community.
- **Continuation phase** treatment is usually self-administered by the patient under monthly supervision by the health centre.
- Patients on **re-treatment** regimens should be closely monitored (supervised) for the duration of the treatment

## **Daily Observed Treatment (DOT)**

- Drugs are administered under direct observation of designated trained observer- this may include health care worker, community volunteer or trained relative.
- Drug intake is recorded daily immediately after each intake
- The identity and address of the patient is properly recorded
- The patient and his relatives are well aware of the importance of daily observed treatment for the sake of the patient's own health
- Health staff are available for tracing irregular and defaulting patients in collaboration with local community based organisations
- The treatment centre is supervised by the District TB/Leprosy Officer, at least once monthly

## **Patient education**

It is the task of health staff to educate tuberculosis patients about their disease. Education is essential for obtaining the patient's co-operation over the required treatment

It is important to keep in mind that patient education is

- A dialogue, not a lecture
- Essential to attain a high cure rate and good compliance
- Essential to prevent disabilities/complications

Education messages should include:

- Duration of treatment
- Importance of compliance
- How to deal with circumstances such as travel, loss of tablets etc
- Possible side effects.
- Importance of eating a balanced diet
- Avoidance of alcohol and smoking during and after treatment
- Cough hygiene (spitting into handkerchief or tissue papers or containers, covering the mouth when coughing)

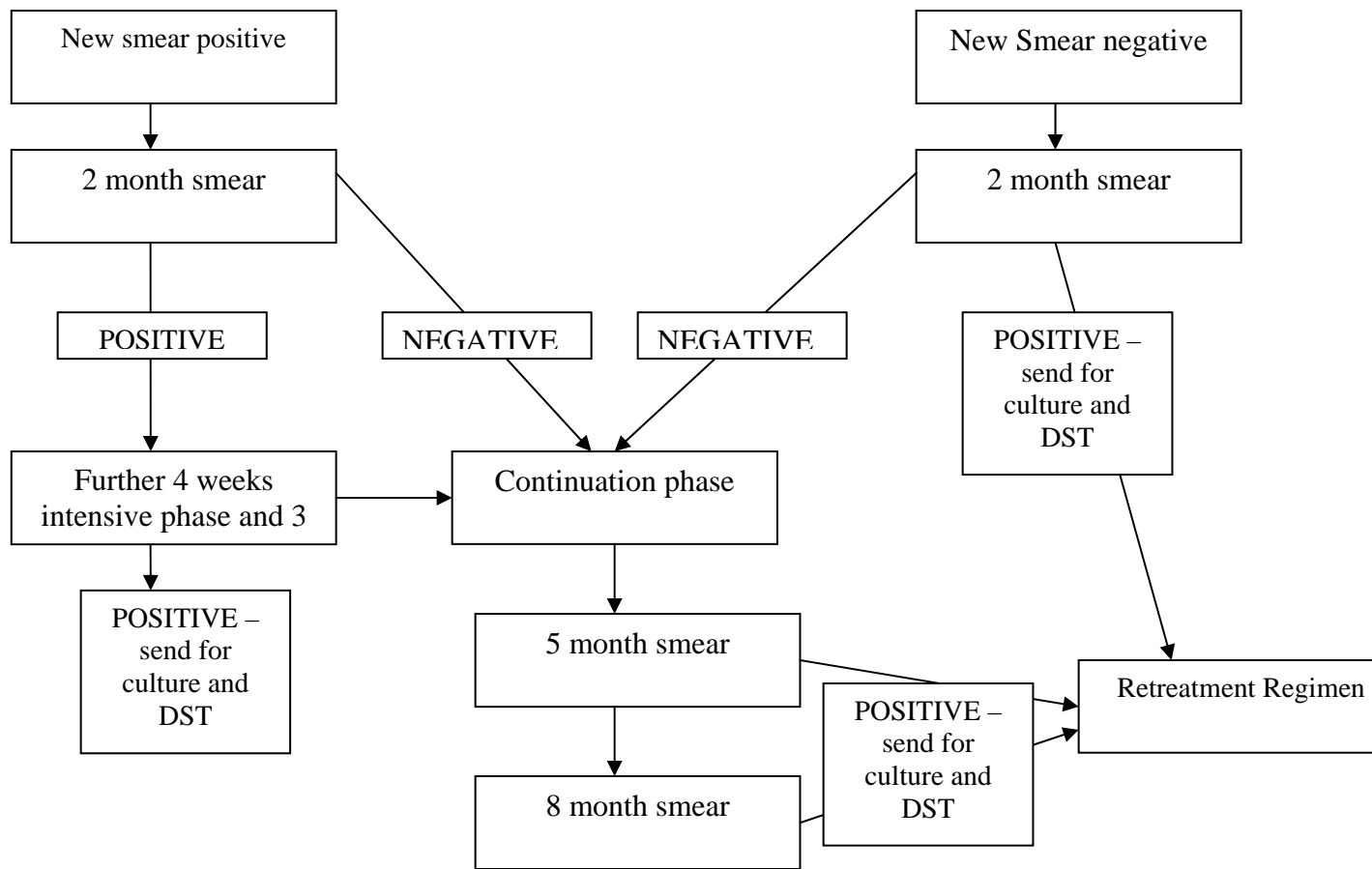
## **Patient Monitoring and Follow-Up**

### **New Patients**

All patients should have 2 sputum specimens taken for AFB smear at **2, 5 and 8 months** in case of an eight month treatment and at 2 and 6 months in case of 6 months treatment.

Results should be available at these visits and must be recorded on the patient treatment cards and in the registers.

The continuation phase can only start after **2 months supervised intensive treatment**, if the sputum specimens are negative for AFB.



**Retreatment patients**

Before the start of the re-treatment regimen, two sputum specimens must be collected and sent as soon as possible to the nearest Reference Laboratory for sputum-smear and culture and drug susceptibility tests.

A re-treatment case is at risk of developing multi-resistant disease and should receive fully supervised treatment for the whole duration of treatment. Should the sputum smear be positive at 3 months, the 4 oral drugs are continued for another 4 weeks. If the patient is still smear positive at the end of the fourth month, all drugs are stopped for 3-4 days, when sputum specimens are taken for culture and sensitivity testing. The patient is then started on the continuation phase.

Sputum specimens should be examined for AFB two months after start of the continuation phase and at the end for confirmation of the treatment result. Patients who are smear positive after the completion of the continuation phase are no longer eligible for the re-treatment therapy.

If the pre-treatment sensitivity pattern shows resistance to either Isoniazid or Rifampicin alone, there is still a good chance of cure provided that the patient takes the drugs under full supervision until the end of treatment. If the pre-treatment specimen showed resistance to both Isoniazid and Rifampicin, the chance to achieve sputum conversion is limited. This patient should be notified as a potential case of MDR TB to the district Tb officer for further investigation and management.

### **Regularity of treatment**

Health staff at the health units should ensure that the patient collects his drugs regularly. They should organise the tracing of patients if they do not attend regularly or default from treatment. Priority should be given to sputum smear-positive pulmonary tuberculosis patients.

To make any patient tracing easy, it is essential that patients are fully and correctly registered in the tuberculosis treatment register. Where available, community health workers should be involved in the supervision and tracing of defaulters.

### **Defaulter Prevention**

Irregular patients should be followed as soon as possible and returned to treatment to prevent defaulting. Priority should be given to smear positive and re-treatment cases

- Intensive phase of treatment: as soon as the patient fails to attend two consecutive clinic days.
- Continuation phase treatment: two weeks after the patient fails to attend a clinic.

Defaulter action should be recorded in the Tuberculosis Treatment Register by writing the date of the tracing under the section "**Remarks**" with the annotation "DT".

### **Contact Tracing**

Contact invitation, investigation and treatment should be encouraged. Where close family contacts of the index case develop respiratory symptoms the contact should be advised to attend the clinic.

### **Side Effects of First Line Anti TB Drugs**

Most TB patients complete their treatment without any significant drug side effects. However, a few patients do develop side effects. So clinical monitoring of all TB patients for side-effects is important during TB treatment. Side effects can be grouped into minor and major categories. In general a patient who develops minor side effects should continue the TB treatment; the patient should also receive symptomatic treatment at primary health facility level. If a patient develops a major side effect, the TB treatment should be stopped and the patient referred to a higher level of care.

**Table 7: Side Effects Of Anti TB Drugs and Their Management**

<b>SIDE EFFECTS</b>	<b>DRUG(S) PROBABLY RESPONSIBLE</b>	<b>MANAGEMENT</b>
<b>Minor</b>		<b>Continue anti-TB drugs, check drug doses</b>
Anorexia, nausea, abdominal pain	Pyrazinamide Rifampicin	Give drugs with small meals or last thing at night
Joint Pains	Pyrazinamide	Aspirin
Burning sensation in the feet	Isoniazid	Pyridoxine 100 mg daily
Orange/red urine	Rifampicin	Reassurance.
Itching	S, H, R, Z	Antihistamines and emollients, observe
<b>Major</b>		<b>Stop responsible drug(s) and refer</b>
Skin rash	S, H, R, Z	Stop anti-TB drugs (see below)
Deafness (no wax on auroscopy)	Streptomycin	Stop streptomycin, use Ethambutol
Dizziness (vertigo and nystagmus)	Streptomycin	Stop streptomycin, use Ethambutol
Jaundice (other causes excluded) Hepatitis	Isoniazid Pyrazinamide Rifampicin	Stop anti-TB drugs (see below)
Confusion (suspect drug-induced acute liver failure if jaundice present)	Most anti-TB drugs	Stop anti-TB drugs. Urgent liver function tests and Prothrombin time.
Visual impairment (other causes excluded)	Ethambutol	Stop Ethambutol
Shock, purpura, acute renal failure	Rifampicin	Stop Rifampicin

## **Re- introduction of TB Drugs after severe side effects (Drug Challenge)**

The idea of drug challenging is to identify the drug responsible for the reaction. Drug challenge starts with the anti tuberculosis drug least likely to be responsible for the reaction (i.e. Isoniazid). The idea of starting with a small dose is that if a reaction occurs to a small challenge dose, it will be less severe than to a full dose. The dose is gradually increased over three days. The procedure is repeated, adding one drug at a time. A reaction after adding in a particular drug identifies that drug as the one responsible for the reaction. There is no evidence that this challenge process gives rise to drug resistance. If the drug responsible for the reaction is Pyrazinamide, Ethambutol or Streptomycin, TB treatment is resumed without the offending drug. If the offending drug is Rifampicin or Isoniazid, if possible, the offending drug is replaced with another drug. It may be necessary to extend the treatment regimen. This prolongs the total time of TB treatment, but decreases the risk of relapse.

**Table 8: Re introduction of TB drugs following a drug reaction**

Anti-TB Drug	Day 1 (challenge dose)	Day 2	Day 3	Day 4
Isoniazid	50 mg	100 mg	200 mg	300 mg
Rifampicin (RH)	75 mg	150 mg	300 mg	Full dose
Pyrazinamide	250 mg	500 mg	1 g	Full dose
Ethambutol	100 mg	200 mg	400 mg	Full dose
Streptomycin	125 mg	250 mg	500 mg	Full dose

## **Management of drug-induced hepatic**

Most anti tuberculosis drugs can damage the liver. Isoniazid, Pyrazinamide and Rifampicin are most commonly responsible, Ethambutol rarely. When a patient develops hepatitis during treatment, the cause may be the TB treatment or something else. It is important to rule out other possible causes before deciding that the hepatitis is drug-induced. If the diagnosis is drug-induced hepatitis, the anti tuberculosis drugs should be stopped. The drugs must be withheld until liver function tests have reverted to normal. Sometimes it is not possible to perform liver function test; in these situations, it is advisable to wait an extra 2 weeks after the jaundice has disappeared before recommencing TB treatment. Asymptomatic jaundice without evidence of hepatitis is probably due to Rifampicin. Once drug-induced hepatitis has resolved, the same drugs are reintroduced one at a time. However, if the hepatitis produced clinical jaundice, it is advisable to avoid Pyrazinamide. A suggested regimen in such patients is a 2-month initial phase of daily streptomycin, Isoniazid and Ethambutol, followed by a 10-month continuation phase of Isoniazid and Ethambutol (2 SHE/10 HE). A severely ill TB patient with drug-induced hepatitis may die without anti tuberculosis drugs. In this case, the patient should be treated with two of the least hepatotoxic drugs, streptomycin and Ethambutol. After the hepatitis has resolved, usual TB treatment should be restarted.

## CHAPTER 4: Tuberculosis and the Human Immunodeficiency Virus (HIV)

### Introduction

People who are infected with both HIV and *M. tuberculosis* have a considerably higher risk of developing TB. This risk is estimated to be in the order of 5-10% per year

The presence of HIV and TB co-infection affects outcomes in both TB Control Programmes and in HIV/AIDS Care and Treatment Programmes.

- TB is a leading cause of illness and death among people living with HIV/AIDS
- TB in combination with HIV infection has a higher risk of relapse and mortality
- HIV increases the risk of progression of *M. tuberculosis* infection to TB disease
- Adverse drug reactions to anti-TB medications are more common in HIV-infected TB patients
- Smear-negative pulmonary TB and extra pulmonary TB are more common in HIV-infected TB patients

Evidence shows that HIV TB co-infection rates in Zambia are 50 - 70%, or higher. The majority of TB patients are infected with HIV, and likewise patients identified with HIV infection are likely to have TB co-infection

### Clinical Presentation

Studies have shown that HIV-infected tuberculosis patients may present more frequently with extra-pulmonary tuberculosis and smear-negative tuberculosis than patients who are HIV- negative. Overall HIV-positive individuals with TB are probably less infectious than HIV-negative individuals both due to the higher proportion of smear negative and extrapulmonary TB and also due to the fact that they often have less caseating disease and so cough up less TB bacilli.

Clinicians both under-diagnose and over-diagnose tuberculosis in patients with AIDS.

- All patients suspected or known to be HIV-positive should be examined for tuberculosis, in particular when there is a cough. **Sputum smear is still the first line of diagnosis**
- Several pulmonary diseases can mimic pulmonary tuberculosis on chest X-ray. Take care not to diagnose pulmonary tuberculosis in every patient with AIDS, an abnormal chest X-ray, signs and symptoms of chest disease and negative sputum-smears. Keep Kaposi's Disease in mind!
- Signs and symptoms of severe progressive tuberculosis are very similar to those of clinical AIDS, in particular chronic fever, loss of body weight and cough
- Tuberculosis is often the first disease to develop in a HIV-seropositive person

Algorithms for the diagnosis of TB in HIV- positive individuals were given in chapter 3.

### TB/HIV Integration

The objectives of TB/HIV integration are:

1. To establish mechanism of collaboration between tuberculosis and HIV/AIDS Programmes
2. To decrease the burden of tuberculosis in people living with HIV/AIDS
3. To decrease the burden of HIV in tuberculosis patients.

## Guidelines for TB – HIV Integration

1. TB/HIV collaborating committees should be established at all levels of health care service provision. These committees allow all stakeholders to share experience and to identify barriers to the implementation of TB/HIV collaborative activities. TB Programmes should create formal linkages with HIV care Programmes (e.g., regular team meetings; data recording, sharing, and reporting; joint review and analyses of facility level data; strategies for clinical management and monitoring of HIV-TB co-infected patients; referral mechanisms; etc.).

TB registers and data forms should include fields to indicate whether patients have been offered DCT, have been tested for HIV, the results (indicated in such a way as to maintain confidentiality), have been successfully referred for HIV care (e.g., recording their HIV patient number in the TB records)

VCT registers and HIV data forms should include fields to indicate whether patients have been screened for TB and the result. And allow tracing to TB registers if they have been started on treatment.

2. All HIV positive individuals should be screened for TB initially when their HIV is diagnosed and subsequently during HIV follow up
3. Diagnostic counseling and testing (DCT)<sup>1</sup> for HIV should be offered to all TB patients.
  - a. CT services should be integrated into TB services to avoid loss of patients when referred to another service delivery point for CT
  - b. TB patients who have not received DCT services (patients in continuing therapy, or patients who opt-out of CT in earlier contacts) should continue to be offered these services at subsequent contacts
  - c. Group sensitization should take place in the TB corner regarding the advantages of HIV testing and counselling and all currently enrolled patients should be offered the opportunity to test.
4. Linkages between TB and HIV care services should be established so that HIV+ patients can be promptly and effectively referred for HIV assessment and care

To minimize the risk of transmitting TB to other immunocompromised HIV/AIDS patients, TB/HIV patients should complete at least the initial 2-3 weeks of TB treatment before being seen in the HIV care service site

TB services should have the ability to assess HIV disease status

CD4 testing should be provided, where possible, for any TB patient diagnosed with HIV upon diagnosis of HIV infection. Where CD4 is not available, initial clinical diagnosis and staging of HIV based on clinical evidence and total lymphocyte count (TLC) will facilitate early entry into HIV care

5. TB patients with pulmonary TB who are diagnosed with HIV should:
  - a. Start TB treatment immediately



b. Start ART according to the guidelines (Table 9)

Patients on TB and ART co-treatment need to be carefully monitored and managed by a competent clinician, to ensure that the correct drug regimens are selected and potential side-effects, toxicities and drug interactions are identified and managed.

- a. Rifampicin and nevirapine [NVP] should not be combined: if a patient is on a NVP containing-regimen, and is not pregnant, substitute the NVP with efavirenz [EFV]
- b. Patients on INH and ART (especially stavudine [d4T] and didanosine [ddI] containing regimens) have a higher probability of peripheral neuropathy
- c. Patients on INH and NVP together may have increased incidence of severe hepatitis
- d. If a patient's clinical condition deteriorates, and he/she has started ART relatively recently (usually within 3-6 months), consider immune reconstitution syndrome and treat or refer accordingly

- 6. Clinical monitoring, pharmacy / drug supply, and laboratory visits for patients on TB and HIV treatment should be coordinated to simplify care for the patient and improve adherence to care for both TB and HIV
- 7. TB DOTS and community TB support systems should integrate ART adherence support and treatment monitoring:
  - a. Provide integrated adherence support at the facility level
  - b. Notify community-based DOTS and treatment support Programmes and assist them to provide comprehensive adherence support and monitoring for potential side-effects and toxicities

**Table 9: Initiation of ART in TB patients**

<b>Scenario 1: Newly diagnosed TB (category I) and HIV co-infection</b>	
No CD4 count facility (patient clinically stable and no history of any other stage 2 or 3 conditions).	<ul style="list-style-type: none"> <li>• Start category I TB treatment immediately</li> <li>• Reassess monthly and consider initiation of ART if clinical condition of patient deteriorates while on TB treatment or refer patient to higher level of care</li> <li>• If patients condition stable consider ART after TB treatment</li> </ul>
No CD4 count facility (patient seriously ill or with history of other stage 3 or 4 conditions)	<ul style="list-style-type: none"> <li>• Start category I TB treatment immediately</li> <li>• Start ART as soon as TB medications are tolerated (usually within 2-3 weeks)</li> </ul>
CD4 count available (>350/mm <sup>3</sup> )	<ul style="list-style-type: none"> <li>• Start category I TB treatment immediately</li> <li>• Reassess as per TB review schedule and consider initiation of ART if clinical condition of patient deteriorates while on TB treatment or refer patient to higher level of care</li> <li>• If patients condition stable consider ART after TB treatment</li> </ul>
CD4 count available (200-350/mm <sup>3</sup> )	<ul style="list-style-type: none"> <li>• Start category I TB treatment immediately</li> <li>• Reassess monthly and consider initiation of ART if clinical condition of patient deteriorates while on TB treatment or refer patient to higher level of care</li> <li>• If patients condition stable consider ART after category I TB treatment</li> </ul>
CD4 count available (50-200/mm <sup>3</sup> )	<ul style="list-style-type: none"> <li>• Start category I TB treatment immediately</li> <li>• Start ART as soon as TB medications are tolerated (usually within 2-3 weeks) or at the end of intensive phase of TB treatment</li> </ul>
CD4 count available (<50/mm <sup>3</sup> )	<ul style="list-style-type: none"> <li>• Start category I TB treatment immediately</li> <li>• Start ART as soon as TB medications are tolerated (usually within 2-3 weeks)</li> </ul>
<b>Scenario 2: Newly diagnosed TB (category II) and HIV co-infection</b>	
	<ul style="list-style-type: none"> <li>• Evaluate eligibility for ART as in scenario 1 above</li> <li>• Commence category II TB treatment</li> <li>• Choice of ART regimen should take into account that patients would be on rifampicin throughout TB treatment</li> </ul>
<b>Scenario 3: PLHIV on ART who develops TB</b>	
Develops TB while on ART	<ul style="list-style-type: none"> <li>• Start TB treatment immediately and if ART regimen includes nevirapine, substitute nevirapine with efavirenz and continue ART</li> <li>• If patient's clinical condition deteriorates, consider immune reconstitution syndrome and give steroid therapy or refer to higher level of care</li> <li>• <b>OR</b> refer the patient for TB treatment if TB service is situated in another facility</li> </ul>
<b>Patient on TB treatment is diagnosed HIV positive</b>	
HIV diagnosed during intensive phase of category I or II TB treatment	<ul style="list-style-type: none"> <li>• Refer to instructions in scenario 1 and 2 above.</li> </ul>
HIV diagnosed during the continuation phase of TB treatment	<ul style="list-style-type: none"> <li>• If patient is clinically stable consider initiating ART after completion of TB treatment</li> <li>• If patient has other evidence of stage 3 or 4 condition refer to instructions in scenario 1 and 2 above.</li> <li>• If ART is required immediately avoid nevirapine in patients on category II TB treatment or category I with abnormal liver function</li> </ul>
<b>HIV and TB treatment in pregnancy</b>	
HIV pregnant woman on ART develops TB	<ul style="list-style-type: none"> <li>• Reassess ART regimen in view of potential drug-drug interaction with anti-tuberculosis drugs or refer to higher level of care</li> <li>• Thereafter commence anti-tuberculosis treatment</li> </ul>
Pregnant woman on TB treatment tested positive for HIV	<ul style="list-style-type: none"> <li>• Continue TB treatment</li> <li>• Refer for PMTCT or ART clinic to determine eligibility and choice of ARV regimen</li> <li>• Where possible defer ART until end of TB treatment or in the second trimester of pregnancy</li> </ul>

## **Immune Reconstitution Syndrome**

Occasionally patients with HIV related TB may experience a temporary exacerbation of symptoms or radiographic manifestations of TB after beginning anti-TB treatment. This paradoxical reaction in HIV-infected patients with TB is thought to be a result of immune reconstitution. This occurs as a result of the simultaneous administration of ART and anti-TB drugs. Symptoms and signs may include high fever, lymphadenopathy, expanding central nervous system lesions and worsening of CXR findings. A thorough evaluation is necessary to exclude other causes particularly TB treatment failure, before diagnosing a paradoxical reaction. For severe paradoxical reactions, prednisolone

(1-2 mg/kg for 1-2 weeks, then gradually decreasing doses) may help, although there is no evidence for this.

## **Isoniazid Preventive Therapy (IPT)**

Isoniazid preventive therapy (IPT) has been demonstrated to be effective in delaying the development of clinical disease in an HIV infected individual with latent TB infection by up to two years. Though WHO has recommended that IPT be provided to all people living with HIV in whom active TB has been excluded, the Ministry of Health is currently not recommending its use in adults on a programmatic basis due to the following reasons:

- difficulties in exclusion of active TB in individuals with dual TB/HIV infection;
- avoidance of the development of INH resistance

This position will be reviewed as further evidence becomes available of the impact of programmatic implementation of IPT in other settings.

However, IPT is recommended for use in children under the age of 5 years who are contacts of smear positive TB cases (see Chapter: TB in children).

## **Cotrimoxazole Preventive Therapy (CPT)**

The use of cotrimoxazole preventive therapy for HIV infected TB patients will follow the guidelines for the HIV/AIDS Programme.

## **CHAPTER 5: Tuberculosis In Children**

### **Introduction**

Tuberculosis in children (under 15 years of age) accounts for approximately 11% of the total number of cases of TB notified every year.

The source of transmission to a child is usually an adult (often a family member) with sputum smear positive PTB. Therefore TB in children is mainly an indication of failure to control TB in adults, as children rarely have sputum positive TB and are unlikely to be a source of transmission.

Though the priority of TB control is to cure infectious cases, it is still important to cure childhood TB as this will result in: improved well being through decreased morbidity and mortality; improved credibility and reputation of the NTP; and less chance for children to have reactivation with cavitation in later life.

### **Diagnosis**

#### **Approach to the Diagnosis of TB in Children**

The diagnosis of TB in children is difficult. It is easy to over diagnose TB, but also easy to miss the diagnosis and presume the clinical presentation is due to malnutrition or AIDS. Bacteriological confirmation is usually not possible, and so the diagnosis of TB in children is nearly always presumptive.

#### **Clinical assessment**

Respiratory symptoms and disease are extremely common in childhood, particularly before 5 years of age. In most cases of suspected TB, the child has been treated with a broad-spectrum antibiotic, with no clinical response. Always look for three important clues to TB in children:

- Contact with an adult or older child with smear-positive PTB.
- Failure to thrive or weight loss (growth faltering). This is a good indicator of chronic disease in children, but is not specific.
- Respiratory symptoms such as cough lasting for more than two to three weeks in a child who has received a course of broad-spectrum antibiotics.

#### **Differential diagnosis of chronic respiratory symptoms**

Other conditions that present with chronic respiratory symptoms include:

- Pertussis (whooping cough)
- Asthma
- HIV infection
- Aspirated foreign body
- Bronchiectasis
- Cystic fibrosis
- Cardiac disease
- Severe gastro-oesophageal reflux
- Severe cerebral palsy

## Laboratory confirmation

It is important to confirm diagnosis of TB in a child using whatever specimens and laboratory facilities are available. Specimens can be obtained in the following ways:

### 1. Expectoration

Sputum should always be obtained in older children (10 years of age or older) who are pulmonary TB suspects. Among younger children, especially children under 5 years of age, sputum is difficult to obtain and most children are sputum smear-negative. However, in children who are able to produce a specimen, it is worth sending it for smear microscopy (and mycobacterium culture if available). Bacterial yields are higher in older children (more than 5 years of age) and adolescents, and in children of all ages with severe disease. As with adult TB suspects, three sputum specimens should be obtained: an on-the-spot specimen (at first evaluation), an early morning specimen and a second on-the-spot specimen (at a follow-up visit).

### 2. Gastric aspiration

Gastric aspiration using a naso-gastric feeding tube can be performed in young children who are unable or unwilling to expectorate sputum. Gastric aspirates should be sent for smear microscopy and mycobacterium culture. A gastric aspirate should be obtained on each of three consecutive mornings.

### 3. Sputum induction

Several recent studies have found that sputum induction is safe and effective in children of all ages and the bacterial yields are as good as or better than for gastric aspirates. However, training and specialized equipment are required to perform this procedure properly.

### 4. Lymph node aspirates

Lymph nodes should be aspirated with a medium to large bore needle attached to a small syringe. Any material obtained should be sprayed onto a slide, air dried and stained for acid fast bacilli

In addition to increasing the yield of confirmed TB cases, mycobacterium culture is the only way to differentiate *M. tuberculosis* from other non-tuberculosis mycobacterium. Bacteriological confirmation is especially important for children who have:

- Suspected drug-resistant TB
- HIV infection
- Complicated or severe cases of disease
- Uncertain diagnosis.

## Investigations relevant for suspected TB in Children

### a. Suspected pulmonary TB

Chest X-rays are useful in the diagnosis of TB in children. In the majority of cases, children with pulmonary TB have CXR changes suggestive of TB. Patients with persistent opacification that does not improve after a course of antibiotics should be investigated for TB.

Adolescent patients with TB have CXR changes similar to adult patients with large pleural effusions and apical infiltrates with cavity formation being the most common forms of presentation. Adolescents may also develop primary disease with hilar adenopathy and collapse lesions visible on CXR.

### b. Suspected extra pulmonary TB

Table 1 shows the investigations usually used to diagnose the common forms of extra pulmonary TB. In most of these cases, TB will be suspected from the clinical picture and confirmed by histology or other special investigations.

**Table 10: Common forms of extra pulmonary TB in children**

Site	Practical approach to diagnosis
Peripheral lymph nodes (especially cervical)	Lymph node biopsy or fine needle aspiration
Miliary TB (e.g. disseminated)	Chest X-ray and lumbar puncture (to test for meningitis)
TB meningitis	Lumbar puncture (and computerized tomography where available)
Pleural effusion (older children and adolescents)	Chest X-ray, pleural tap for biochemical analysis (protein and glucose concentrations), cell count and culture
Abdominal TB (e.g. peritoneal)	Abdominal ultrasound and ascitic tap
Osteoarticular	X-ray, joint tap or synovial biopsy
Pericardial TB	Ultrasound and pericardial tap

### Treatment In Children

Treatment outcomes in children are generally good, even in young and immunocompromised children who are at higher risk of disease progression and disseminated disease, provided that treatment starts promptly. There is a low risk of adverse events associated with use of the recommended treatment regimens.

### **Recommended treatment regimens**

When using child formulations, the following treatment regimens should be used. There are more weight bands to optimize accurate dosage.

**Table 11: Recommended doses of first-line anti-TB drugs for children**

Drug	Daily dose	
	Dose and range (mg/kg body weight)	Maximum (mg)
<b>Isoniazid (H)</b>	5 (4–6)	300
<b>Rifampicin (R)</b>	10 (8–12)	600
<b>Pyrazinamide (Z)</b>	25 (20–30)	–
<b>Ethambutol (E)</b>	children 20 (15–25)*	–
<b>Streptomycin (S)</b>	15 (12–18)	–

\*WHO recommends a dosage of 20 mg/kg to be safe in children.

## Treatment Regimens in Children

### Category I Patients:

All new patients (Smear positive, negative and extra pulmonary)

**Intensive Phase:** 2(RHZ)

**Continuation Phase:** 4(RH)

**Table 12: Dose-body weight relation for children treated with category I treatment regimen using CHILD formulations of FDCs.**

Weight in Kg	Intensive Phase 2 months	Continuation Phase 4 months
	RHZ (60/30/150)	RH (60/30)
5-9	1	1
10-14	2	2
15-19	3	3
20-25	4	4
> 25	Use adult formulation RHEZ	Use adult formulation RH
26-37	2 tablets	2 tablets

### Category II Patients:

All previous treated patients including smear positive re-treatment, smear negative retreatment and treatment failures, treatment after default and relapse cases.

**Intensive Phase:** 2S(RHZ)/

**Continuation Phase:** 10(RH)

**Table 13: Dose-body weight relation for children treated with category II treatment regimen using CHILD formulations of FDCs.**

Weight in Kg	Intensive Phase 2 months		Continuation Phase 4 months
	RHZ 60/30/150	+ S 1 g	RH 60/30
5-9	1	0.1 g	1
10-14	2	0.2 g	2
15-19	3	0.3 g	3
20-25	4	0.4 g	4
> 25	Use adult formulation RHEZ		Use adult formulation RH
26-37	2 tablets	0.5 g	2 tablets

**IF CHILD FORMULATIONS ARE NOT AVAILABLE CHILDREN CAN BE TREATED USING ADULT FORMULATIONS FOLLOWING EXISTING NATIONAL TB MEDICATION GUIDELINES**

**Notice the different weight bands!**

**Table 14: Dose-body weight relation for children treated with category I treatment regimen using ADULT formulations of FDCs.**

Weight in Kg	Intensive Phase 2 months		Continuation Phase 4 months
	RH	+ Z	RH
6-11	½	½	½
12-18	1	1	1
19-25	1 ½	1	1 ½
>25	Use adult formulation RHEZ		Use adult formulation RH
26-37	2 tablets		2 tablets

**Table 15: Dose-body weight relation for children treated with category II treatment regimen using ADULT formulations of FDCs.**

Weight in Kg	Intensive Phase 2 months			Continuation Phase 10 months
	RH	+ Z	+ S	RH
6-11	½	½	0.1 g	½
12-18	1	1	0.2 g	1
19-25	1 ½	1	0.5 g	1 ½
>25	Use adult formulation RHEZ			Use adult formulation RH
26-37	2 tablets			2 tablets

**Corticosteroids**

Corticosteroids may be used for the management of some complicated forms of TB, e.g. TB meningitis, complications of airway obstruction by TB lymph glands, and pericardial TB. In cases of advanced TB meningitis, corticosteroids have been shown to improve survival and decrease morbidity, and thus are recommended in all cases of TB meningitis. The drug most frequently used is prednisone, in a dosage of 2 mg/kg daily, increased up to 4 mg/kg daily in the case of the most seriously ill children, with a maximum dosage of 60 mg/day for 4 weeks (see Annex 4). The dose should then be gradually reduced (tapered) over 1–2 weeks before stopping.

**Administering treatment and ensuring adherence**

Children, their parents and other family members, and other caregivers should be educated about TB and the importance of completing treatment. The support of the child's parents and immediate family is vital to ensure a satisfactory outcome of treatment. Often a health-care worker can observe or administer treatment, but if this arrangement is not convenient for the family, a trained community member (preferably someone other than the child's parent or immediate family) can undertake this responsibility.



Children with severe forms of TB should be hospitalized for intensive management where possible. Conditions that merit hospitalization include:

- (i) TB meningitis and miliary TB, preferably for at least the first 2 months,
- (ii) respiratory distress,
- (iii) spinal TB
- (iv) severe adverse events, such as clinical signs of hepatotoxicity (e.g. jaundice).

If it is not possible to ensure good adherence and treatment outcome on an outpatient basis, some children may require hospitalization for social or logistic reasons.

### **TB/HIV Co-infection in Children**

HIV makes the diagnosis and management of TB in children even more difficult than usual, for the following reasons:

1. Several HIV-related diseases, including TB, may present in a similar way.
2. The interpretation of tuberculin skin testing is less reliable. An immunocompromised child may have a negative tuberculin skin test despite having TB.
3. In some countries HIV infection is very common in adults with TB. If there is a history of contact with an adult with smear-positive PTB and that adult is the child's parent, then the child has an increased chance of being HIV infected as well. In addition, the child with TB, even if not HIV-infected, may come from a household where one or both parents have died. This situation makes compliance and completion of treatment more difficult.

For these reasons and those mentioned above, many of the clinical features that are used to suggest a diagnosis of childhood TB are less useful in the presence of HIV infection.

### **Differential diagnosis in HIV-infected children**

In addition to the differential diagnosis for chronic respiratory symptoms, include:

- Bacterial pneumonia
- Lymphocytic Interstitial Pneumonitis (LIP)
- Bronchiectasis
- Pulmonary Kaposi's sarcoma
- Pneumocystis Carinii Pneumonia

### **Continued respiratory problems / poor response to TB treatment in children with HIV**

HIV-infected children with TB are more susceptible to other respiratory diseases and more likely to die despite TB treatment. An important reason for a poor response to TB treatment is that the child does not have PTB. The difficulties in diagnosing PTB in children mean that it may be confused with other causes of HIV-related lung disease. Most children who receive treatment for PTB are smear-negative cases. If they do not improve on TB treatment, consider other diagnoses, e.g. LIP or cardiac disease. In all cases, consider poor treatment adherence as a cause of poor treatment response.

Mixed respiratory infections are a particular feature of HIV-infected children. It is common for children with TB to develop bacterial pneumonia as a complication. Treatment should follow Integrated Management of Childhood Illness (IMCI) guidelines.

TB – HIV Integration Guidelines, 14 April 2006 8

## HIV testing

**HIV counselling and testing is indicated for all TB patients as part of their routine management**

### **Contact screening for Children living with an infectious TB patient**

It is recommended that household contacts of smear positive TB are screened for symptoms of disease and Isoniazid preventive therapy (i.e. daily Isoniazid 5mg/kg for at least 6 months) is offered to children aged less than 5 years, who do not have symptoms or signs of active TB disease.

Clinical assessment alone is sufficient to decide whether the contact is well or symptomatic. Routine assessment of exposed contacts does not require CXR or TST

Follow-up should be carried out at least every 2 months until treatment is complete. If TB is suspected at initial assessment or at subsequent follow-up the child should be treated for TB as above. Referral to a district or tertiary hospital may be necessary when there are uncertainties of diagnosis. Contacts with TB disease should be registered and treated.

### **Special circumstances**

#### **Child contacts of infectious MDR-TB cases**

The only chemo prophylaxis regimens to have been studied are based on Isoniazid and, to a lesser extent, on rifampicin. Since by definition MDR-TB is resistant to both of these drugs, it is unlikely that use of these drugs to treat latent infection caused by an MDR tuberculosis strain will prevent the development of active TB disease. Close contacts of MDR-TB patients should receive careful clinical follow-up for a period of at least 2 years. If active disease develops, prompt initiation of treatment with a regimen designed to treat MDR-TB is recommended. On the basis of the currently available evidence, WHO does not recommend second-line drugs for chemoprophylaxis in MDR-TB contacts.

#### **Management of a baby born to a mother with infectious pulmonary TB**

If a mother is found to have pulmonary TB, then the baby, and if possible, the placenta, should be investigated for evidence of congenital TB infection and the baby treated. Once the mother has been on treatment for at least 2–3 weeks, she is generally no longer infectious. If a mother has been on treatment for TB for several weeks before delivery, it is less likely that the baby will become infected. The risk is highest if a mother is diagnosed at the time of delivery or shortly thereafter.

A breastfeeding infant has a high risk of infection from a mother with smear-positive pulmonary TB, and has a high risk of developing TB. The infant should receive 6 months of Isoniazid preventive therapy, followed by BCG immunization. Breastfeeding can be safely continued during this period

#### **BCG vaccination in children**

BCG is a live attenuated vaccine derived from *M. Bovis*. The WHO Expanded Programme on Immunization recommends BCG vaccination as soon as possible after birth in countries with a high TB prevalence.

## CHAPTER 6: Multi-Drug Resistant Tuberculosis

### Introduction

Resistance of Mycobacterium tuberculosis to anti-TB drugs is a man-made problem. Wild strains of M. tuberculosis that have never been exposed to anti-TB drugs are almost never clinically resistant. Prevention of drug resistance is important because treatment will not succeed if the tubercle bacilli are resistant to the drugs used. One of the aims of effective management of tuberculosis (TB) is to minimise development of drug resistance.

Multi-drug-resistant TB (MDR-TB) has not been a major problem in TB control in Zambia. The National TB control Programme conducted a national drug surveillance survey in 2000 that showed a low prevalence of both drug resistance and MDR-TB. According to the survey, the prevalence of MDR-TB among new cases was 1.8% and 2.3% in re-treatment cases.

### Causes of MDR-TB

- Prolonged shortages of drugs
- Use of anti-TB drugs of unproven quality (sale of such medications over the counter and on the black-market).
- Incorrect management of individual cases by clinicians
- Poor adherence to treatment by patients
- Sub-optimal dosage
- Poor drug absorption

### DOTS-Plus Framework Approach

The framework approach consists of an essential core of five components based on fundamental principles of TB control (DOTS)

The five components are:

- Sustained government commitment
- Accurate, timely diagnosis through quality assured culture and drug susceptibility testing
- Appropriate treatment utilizing second-line drugs under strict supervision
- Uninterrupted supply of quality assured anti-TB drugs
- Standardized recording and reporting system.

### Definitions of resistance

- **Initial Resistance:** Drug resistance in a newly diagnosed patient who has never received anti-TB drugs. It occurs when a patient develops tuberculosis after being infected by another person who has resistant tubercle bacilli.
- **Acquired or Secondary Resistance:** Drug resistance occurring in patients who have a history of previous TB treatment (re-treatment cases)
- **Multi-Drug Resistant –TB (MDR-TB):** Occurs when there is resistance to both Isoniazid and Rifampicin
- **Extreme Drug Resistant TB (XDR-TB):** This is MDR TB that is resistant to flouroquinolones and at least one of the injectables (capreomycin, kanamycin)

## **Case detection:**

Case detection for MDR-TB is similar to that of TB in general. The basis for identification of MDR-TB cases is bacteriological examination, which includes smear microscopy, culture, Drug Susceptibility Testing (DST) as well as previous history of treatment.

## **Groups at Risk of MDR-TB**

- **Failures of Category II (chronic TB cases).** Patients in whom Category II treatment (Re-treatment regimen) have failed almost always have MDR-TB. Chronic TB cases, defined as patients who are sputum positive at the end of a re-treatment regimen, have perhaps the highest MDR-TB rates of any other group
- **TB patients who are close contacts of MDR-TB cases.** Most studies have shown close contacts of MDR-TB patients to have very high rates of MDR-TB, particularly in institutions that have MDR-TB outbreaks or high MDR-TB prevalence e.g. Prisons, health care workers from health facilities that tend to have high MDR-TB rates. This may be particularly important if the contact cases are HIV positive and many outbreaks of MDR and XDR TB have been reported from such settings

## **Case Definitions**

### **Drug resistant case:**

A patient is confirmed as having drug resistant TB **only** by the laboratory.

Anti-TB drug resistance is classified according to the following definitions:

- **Confirmed mono-resistance:** TB due to bacilli that are resistant in vitro to only one anti-TB drug.
- **Confirmed poly-resistance:** TB due to bacilli that are resistant in vitro to more than one anti-TB drug, with the exception of both isoniazid and rifampicin.
- **Confirmed MDR-TB:** TB due to bacilli that are resistant in vitro to both isoniazid and rifampicin.

## **Management of suspected MDR-TB patients**

If a patient is suspected to have MDR-TB, the following should be done:

- Collect at least 2 sputum specimens to send for microscopy, culture and DST
- Do not admit patient to a general ward (especially in high HIV settings as HIV positive individuals can easily get infected). If hospital admission is necessary, the patient should be admitted to a special ward (side ward), which has good ventilation.
- At home advise patient to sleep in a separate room from others (if possible)
- If MDR is confirmed by the laboratory the patient should be referred for treatment at a designated institution under strict supervision.

## **CHAPTER 7: Use of Anti-TB Drugs in Special Situations**

### **TB In Pregnancy**

TB is one of the major causes of maternal mortality in Zambia. Pregnant women diagnosed with tuberculosis should start anti-tuberculosis treatment immediately. Women who become pregnant during treatment should continue with their treatment. However, streptomycin should not be used because of the risk of toxicity to the unborn child.

Women on tuberculosis treatment should avoid pregnancy because of the potential risk of damage to the foetus. Women using oral contraceptives and taking Rifampicin should use alternative methods of contraception such as condoms because Rifampicin lowers blood concentration of the contraceptive drug thereby increasing the risk of unplanned pregnancy.

### **Breast Feeding**

Breastfeeding should not be stopped when the mother is on tuberculosis chemotherapy. There is some transfer of anti-tuberculous drugs in the breast milk and therefore if the baby develops complications that may be caused by tuberculosis drugs, alternative feeding may be necessary.

### **Renal Failure**

Rifampicin, Isoniazid, and Pyrazinamide are safe and can be given in normal dosages. Patients with severe renal failure should receive pyridoxine (Vitamin B6) with Isoniazid to prevent peripheral neuropathy.

The excretion of streptomycin is renal and that of Ethambutol is partially renal therefore avoid streptomycin and Ethambutol if there are alternatives. Otherwise give the drugs in reduced doses at less frequent intervals.

The safest regimens to give to patients in renal failure is; 2 HRZ/4 HR

### **Liver Disease**

Most anti-TB Drugs can cause liver damage and therefore care is needed in treating TB patients.

- Do not give Pyrazinamide because this is the most hepatotoxic anti-TB drug.
- Isoniazid, Rifampicin plus 1 or 2 non-hepatotoxic drugs such as streptomycin or Ethambutol can be used for total treatment duration of 8 months.
- If the patient has severe liver damage, an alternative regimen is streptomycin plus Isoniazid plus Ethambutol in the initial phase followed by Isoniazid and Ethambutol in the continuous phase with a total of 12 months.
- Recommended regimen is 2 S(RHE)/4 (RH) or 2 S(EH)/10 (EH).

### **The Role of Steroids in the Treatment of Tuberculosis**

Common indications for steroids:

- TB meningitis (decreased consciousness, neurological deficits, spinal block)
- TB pericarditis (with effusion or constriction)
- TB pleural effusion (large with severe symptoms). Note that the drainage through a wide-bore intravenous cannula often relieves the acute distress.
- Massive lymphadenopathy with pressure effects
- Severe hypersensitivity reactions to anti-TB drugs
- More rarely:
  - Hypo-adrenalism
  - Renal tract TB (to prevent ureteric scarring)
  - TB laryngitis with life threatening airway obstruction

**Table 16: Recommended doses of adjuvant steroid therapy (drug of choice is Prednisolone)**

Indication	Prednisolone (Dosage)
TB meningitis	1-2 mg/kg (max 60 mg) for 4 weeks then taper off over several weeks
TB pericarditis	1-2 mg/kg (max 60 mg) for 4 weeks, then half for 4 weeks (max 30 mg/d), then taper off over several weeks
TB pleural effusion (severe)	0.5-1mg/kg (max 30mg) for 1-2 weeks then taper off over several weeks.

Note: Steroids are immunosuppressant and may theoretically increase the risk of developing opportunistic infections in TB/HIV patients. However, used as indicated above, the overall benefit of steroid outweighs the potential risk.

## **CHAPTER 8: Tuberculosis Infection Control**

### **Introduction**

TB is the most common opportunistic infection and a leading cause of death in persons living with HIV/AIDS (PLWHA). Persons with undiagnosed, untreated and potentially contagious TB are often seen in clinical care settings especially HIV care settings.

In this era of increasing access to HIV counseling and testing, care, and treatment for people living with HIV, more people living with HIV-associated immunosuppression are attending health care and community facilities than ever before. Persons, including health care workers, with HIV-associated immunosuppression are particularly vulnerable to developing TB disease if they become infected with *Mycobacterium tuberculosis* (*M. tuberculosis*, the germ that can cause TB) as a result of exposure in these settings.

The risk of patients and health care workers (HCWs) acquiring TB could be significantly reduced if governments, health authorities, and HCWs themselves make infection control a high priority.

There are two main ways to reduce TB transmission:

- Work practice and administrative control measures
- Environmental control measures

### **Infection Control Measures For Health Facility**

#### **Work practice and administrative measures**

There are five components to good work practice and administrative controls:

- Infection control plan;
- Administrative support for procedures in the plan, including quality assurance;
- Training of staff;
- Education of patients and increasing community awareness; and
- Coordination and communication between TB and HIV/AIDS care Programmes.

#### **Infection Control Plan**

Each facility should have a written TB infection control plan that outlines a protocol for the prompt recognition, separation, provision of services, investigation for TB and referral of patients with suspected or confirmed TB disease.

The TB Focal Person is responsible for ensuring the infection control procedures are implemented and should be a member of the health facility's infection control committee. The plan will include, but not be limited to, the following policy areas:

1. Screening all patients as soon as possible after arrival at the facility to identify persons with symptoms of TB disease or persons who are being investigated or treated for TB disease.

2. Instructing all patients in respiratory hygiene/cough etiquette. This includes instructing them to cover their nose and mouth when coughing or sneezing, and when possible providing face masks or tissues to assist them in covering their mouths.

Face masks help prevent the spread of *M. tuberculosis* from the patient to others. The face mask can capture large wet particles near the mouth and nose of the patient, preventing the bacteria from being released into the environment. Face masks could be provided to persons who have a positive symptom screen to wear until they leave the facility. Cloth masks can be sterilized and reused. Paper tissues provided to these persons, with instructions to cover their mouths and noses when coughing or sneezing, are less costly and also less likely to identify people as TB suspects with attendant risk of stigma. However, they are less likely to be used effectively.

Tissues and face masks should be disposed in bins to be later incinerated. Clients and especially staff should be encouraged to wash their hands after contact with respiratory secretions. TB cannot be spread from the hands, but other serious lung infections such as influenza can.

3. Placing TB suspects and cases in a separate well-ventilated waiting area such as a sheltered open-air space.

4. Prompt management of these TB suspects so that they spend as little time as possible at the facility.

5. Ensuring rapid diagnostic investigation of TB suspects, including referring TB suspects to TB diagnostic services if not available on site; and ensuring that persons reporting TB treatment are adhering with their treatment.

6. Using and maintaining environmental control measures (see Environmental Control Measures).

7. Training and educating all staff on TB and the TB infection control plan (training should include special risks for TB for HIV-infected persons, and need for diagnostic investigation for those with signs or symptoms of TB).

8. Providing routine, confidential HIV counseling and testing for staff, with adequate access to treatment.

9. Monitoring the TB infection control plan's implementation and correcting any inappropriate practices or failure to adhere to institutional policies.

### **Administrative Support**

Administrative support and resources must be made available to institutions to allow them to carry out their infection control plan. Regular checking and quality assurance should be in place.

### **Training of Staff**

Infection control is effective only if all staff working in a facility understands the importance of the infection control policies and their role in implementing them. . Training should be conducted before initial assignment and continuing education should be provided to all employees and volunteers annually

### **Education of Communities**

Communities need to be educated about infection control and cough etiquette. Communities should understand the reasons for the use of masks/tissues to avoid stigmatisation.

### **Coordination and Communication between TB and HIV/AIDS Care Programmes**



Coordination and communication between HIV/AIDS and TB Programmes is vital to ensure good infection control Facilities with both TB and HIV programmes must ensure that all HIV positive individuals are screened for TB **before** they are referred for HIV care to avoid the spread of infection in HIV congregate settings such as ART clinics. (see chapter 4)

## **Environmental Control Measures**

Environmental control methods range from inexpensive methods such as maximising natural ventilation and mechanical ventilation, to more costly methods such as ultraviolet germicidal irradiation and HEPA filtration.

Simple environmental control measures available in Zambia include:

- Open all doors and windows to increase natural ventilation
- Arrange for patient waiting areas to be outside with maximum natural ventilation and sunlight (UV light kills TB bacilli)
- Ask patients to provide sputum specimens outside or in well ventilated spaces away from others

**It is important to recognize that if work practice or administrative controls are inadequate, environmental controls will not eliminate the risk.**

## **Protection of Health Care Workers and Staff**

### **Increasing Awareness of TB in Health Care Workers and Staff**

There is increased risk of TB disease or infection in health care workers compared with the general population<sup>1</sup>. Other people at risk include volunteers, peer educators, adherence supporters, and volunteers working as counselors or in support groups who have contact with persons with TB who have not yet been diagnosed and started on treatment. PLWHA in these roles are at particular risk of rapid progression to TB disease if they become infected or re-infected due to exposure to *M. tuberculosis* in the facility.

It is recommended that staff be investigated for TB if they have a cough for two weeks or more. The infection control plan should indicate who staff can contact to initiate TB investigations, and reinforce that all services are confidential.

### **Increasing Access to Voluntary HIV Counseling and Testing**

Providing accessible, acceptable, confidential VCT, including periodic retesting, to staff, can facilitate encouraging and enabling health care workers and all staff to know their HIV status. Policies, which prioritize ART for health care workers who need it, can motivate them to know their HIV status.

**Immunocompromised health care workers should be given opportunities to work in areas with a lower risk of exposure to TB.**

## **Personal Respiratory Protection**

Respirators can protect health care workers from inhaling M. tuberculosis only if standard work practice and environmental controls are in place. They are expensive to purchase and require specialized equipment to determine proper fit. They are generally unavailable in Zambia.

Respirators are different from face masks, such as surgical masks made of cloth or paper. **Use of a face mask does not protect health care workers, other staff, patients, or visitors against TB.** Therefore, it is **NOT** recommended that health care workers and other staff or visitors wear them.

## Multi-Drug Resistant TB (MDR-TB)

**Because of the risk of severe morbidity and mortality to HIV-infected persons from MDRTB, persons with known MDRTB should receive routine care outside of normal HIV care settings at an established centre.**

## Laboratory Safety

### AFB Smear Preparation

Many laboratories, which process infectious sputum, perform only direct smear microscopy:

- Performing direct smear microscopy has not been documented to result in the transmission of M. tuberculosis
- Direct smear microscopy can be safely performed on the open bench in a **well ventilated** room
- Neither environmental controls nor personal respiratory protection are necessary during the preparation of smears.
- In laboratories performing only smear preparation, the greatest threat to the personnel is contact with coughing patients.

### Preparation of Liquid Suspensions of Mycobacterium Tuberculosis

Laboratories, which process liquid preparations of, suspended M. tuberculosis (e.g. Centrifugation, cultures, and drug susceptibility testing), have a higher risk for nosocomial M. tuberculosis transmission. Only designated laboratories with appropriate biosafety cabinets (BSC I or BSC II) and experienced staff may work with liquid suspensions of M. tuberculosis Biosafety cabinets must be regularly serviced and used correctly to ensure that they protect staff.

## Waste Management

The purpose of waste management is to:

- Protect people who handle waste items from accidental injury
- Prevent the spread of infection to healthcare workers and to the local community

## Intermediate Handling of Waste (Within the Health Facility)

- Have separate waste containers for contaminated and non-contaminated waste
- Use non-corrosive washable containers with covers for contaminated waste
- Wash all waste containers with 0.5% chlorine solution every time emptied
- Wear utility gloves when handling contaminated waste
- Avoid splashes when disposing of liquid contaminated waste

### **Disposal of Waste (Incineration, Burial)**

- Use heavy-duty (utility) gloves and appropriate personal protective equipment when handling wastes; decontaminate and clean gloves between uses.
- Always wash hands after handling contaminated wastes.
- Handle wastes carefully to avoid spills or splashes. Avoid transferring contaminated waste from one container to another.
- Incineration is the preferred method for waste disposal, as the heat will generally be sufficient to destroy infectious micro-organisms and will also prevent scavenging and re-use of discarded items.
- If incineration is not possible, then careful burial is the next best alternative.
- Remaining waste after burning or incineration, should be buried in a deep pit and covered over with dirt; the pit should not be accessible to the public
- Culture plates and culture specimen containers and slides should be sterilized in an autoclave before disposal

### **Tips for Safe Handling and Disposal of Infectious Waste:**

- Use plastic or galvanized metal containers with tight-fitting covers.
- Use puncture-resistant sharps containers for all disposable sharps.
- Place waste containers close to where the waste is generated and where convenient for users.
- Ensure that equipment that is used to hold and transport wastes is not used for any other purpose.
- Regularly wash all waste containers with a disinfectant cleaning solution (0.5% chlorine solution plus soap), rinse with water, and air-dry.

## **CHAPTER 9: Logistics and Supplies**

### **Introduction**

Continuous provision of diagnosis and treatment is a pre-requisite for successful control of tuberculosis. In order to prevent the interruption of services it is important to have a comprehensive logistic management information system (LMIS) in place that will ensure a full supply of both drugs and laboratory reagents and supplies at all levels. The basic purpose of an LMIS is to collect and report information to other levels in the system in order to make decisions regarding quantification, procurement and distribution of drugs, medical and laboratory supplies. Logistics management information system is therefore the responsibility of every staff.

### **TB Central Unit**

The central unit is responsible for quantifying, procurement and providing guidance to medical stores on the distribution of supplies. The unit is also responsible for provision of LMIS tools.

### **Provincial Level**

The province will receive and compile consumption data from the districts and order supplies based on this data from the Central Unit. The province will receive supplies on behalf of the districts, distribute and supervise on supply management.

### **District Level**

The district will receive and compile consumption data from the facilities and order supplies from the Provincial Office. The district will receive supplies on behalf of the facilities and distribute.

### **Health Centre**

The facility will submit consumption data on laboratory information and demand form to the district

### **Tuberculosis Laboratory reagents and supplies**

The quantity of laboratory supplies required is based on number of suspected TB cases seen at the facility and subsequent follow up patients. The fraction of follow up patients can be determined from TB laboratory registers. Of all suspects examined, 10% (1 out of 10) are expected to be sputum smear positive. A proportion of those that are smear negative may still have TB. The number of smear negative cases has increased due to the TB/ HIV co-infection. In Zambia the NTP will also follow up these patients at 2, 5 & 8 months. Therefore for quantification purposes, these will have to be taken into consideration.

## **Quantification of Supplies**

- (A) (Required Slides/Containers (Z)) = number of TB suspects (n) x no of slides/containers used per suspect (3) Therefore  $Z = n \times 3$
- (B) Out of the above 40% (both smear positive and negative) will require follow up at 2, 5, and 8 months

For smear positive patients supply requirements (Q) = 40% of Z x 3 (2mth) + 3 (5mth) + 3 (8mths)

$$Q = 40\% \text{ of } Z \times 9$$

$$\text{Total required} = Z + Q$$

**NOTE: Assuming that 10% of all suspects are smear positive and are followed up at 2, 5 & 8 Months**

**Assuming that 30% of all the suspects have smear negative TB and are followed up  
A total of 40% will then be used to calculate TB requirements for follow up as shown above.**

### Quantification for Laboratory Reagents

A form has been designed for easy calculation of laboratory reagents. Instruction on how the form should be filled is provided below.

1	2	3	4	5	6	7	8
Item	Amount required for 1000 slides	Number of Patients/ 3 Months	Factor	3 Month running required	6 Months reserve required	Currently in stock	Total Order
			x Factor	A	B=Ax2	C	D=A+B+C
Basic fuchsin	15 gm		0.5	0	0		0
Methylene blue	15 gm		0.5	0	0		0
Immersion oil	100 ml		3	0	0		0
Sulphuric acid	1250 ml		38	0	0		0
Phend	250 gm		7.6	0	0		0
Xylene	1000 ml		30	0	0		0
Alcohol	1500 ml		45	0	0		0
Hydrochloric acid	50 ml		1.5	0	0		0
Spirit	1000 ml		1.5	0	0		0
Slides	1000		66	0	0		0
Sputum containers	1000		66	0	0		0

**Instructions for filling in the laboratory supply order form**

The calculation is performed as follows:

The sum of smear positive patients (new cases and relapses) recorded on the quarterly report. On case findings of the previous two, quarters are entered under the column headed "No of patients".

The requirements for the quarterly (A) are calculated by multiplying the number of patients by the factor (the quantity required for a single examination).

The reserve stock requirement (B) is equal to the quantity required for 3 months.

The quantity of materials presently available (C) is determined by counting the materials in the store at the unit.

The total order (D) is the sum of the quantity required for the quarter year (A) plus the quantity required for reserve stock (B) minus the quantity in the store (C) at the time that the order form is completed.

## Frequency of ordering

**Table 17: Frequency for ordering of laboratory reagents and other supplies**

Level	Frequency
Health Centre from District	Quarterly
District from Province	Quarterly
Province from central	Half yearly
Central Unit from Source	Annually – 18 months (including lead time)

## TB drug supply management

### District

Ordering of TB drugs will be done using Drug Order Form . Ordering should be done quarterly, before supplies run out. The quantities of TB drugs needed for the following quarter can be calculated, by means of multiplying the registered number of TB patients from the last quarter, with the total number of drugs needed to complete the whole period of treatment.

The total requirements needed will be multiplied with factor '2'; to ensure that there will be enough drugs to cover the following quarter, in case the number of patients will increase, there will be enough drugs.

From the total of 'running requirements plus reserve requirements', the remaining stock balances at the last day of the previous quarter in the district pharmacy will be deducted, and the result will be the "total order" for the District.

Sign the form before you send it.

**ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM**

**QUARTERLY ORDER FORM FOR TB DRUGS WITH AT HEALTH FACILITY**

Name of Facility: \_\_\_\_\_ quarter of year \_\_\_\_\_

Name of Request Officer: \_\_\_\_\_ Date of completion of this form: \_\_\_\_\_

Signature: \_\_\_\_\_

**Anti-TB drugs tablets - needs based on morbidity (case notification)**

Drug / Item	Cat 1 and 3: 2(RHZE)/6EH			Cat2: 2(RHZE)/S/1(RHZE)/5(RHE)			Paediatric 2(RHZ) 4(RH)			Paediatric 2(SR)	
	Cases	Factor	Total A	Cases	Factor	Total B	Cases	Factor	Total C	Cases	Factor
<b>Unit tablets/vials</b>											
(R150/H75/Z400/E275)		x 180			x 360						
E400/H150)		x 360									
(R150/H75/E275)					x 450						
S1g					x 60						x 40
RH 150/75								x 360			x 540
Z 400								x 360			x 210
Syringes needles					x 60						x 60
Water for injection					x 60						x 60

Drug / Item	Running requirement of last quarter = E	Required buffer stock F=E/4	Stock last day previous quarter G	Total order E + F - G
(R150/H75/Z400/E275)				
E400/H150)				
(R150/H75/E275)				
S1g				
RH 150/75				
Z 400				
Syringes needles				
Water for injection				

These assumptions are an over-estimate since a significant number of patients use lower dosages, and others die during treatment or default. This extra supply provides you with a surplus for treating patients who are not reported in the quarterly report (in the columns transfer in, treatment resumed and others) and patients who are sputum-smear negative but have TB meningitis, military tuberculosis and other severe forms of tuberculosis which require short-course Treatment.

**Health Centre**

The Health Centre is required to complete a monthly drug order form (as above) to order TB drugs from the District Pharmacy Stores.

**Table 18: Frequency for ordering of drugs**

Level	Frequency
Health Centre from District	Monthly
District from Province	Quarterly
Province from Central Level	Quarterly
Central Unit from Source	Annually – 18 months (including lead time)

**Maintenance of buffer stocks**

Adequate buffer stocks should be maintained at all levels as shown the table below. Minimum drug stock at different levels

**Table 19: Required buffer stock levels at the different levels**

<b>Level</b>	<b>BUFFER STOCK</b>
Peripheral health unit	1 month
District level	3 months
Provincial Level	6 months
National level	12 months

It is important to maintain this level of stock in order to ensure that drugs do not completely run out in the event that there are delays in the arrival of the normal running requirements.

### **Receipt of TB drugs and laboratory reagents and supplies**

The following should be observed when receiving drugs, reagents and supplies:

- The quantity and quality is checked at all levels.
- All discrepancies should be reported on the appropriate discrepancy form, which should be signed by both the person receiving the order and the person delivering.
- Fill in a Goods Received Note
- Fill in or update the stock control card for the drugs, reagents and supplies received.
- Never start using supplies from a consignment before checking, unpacking and entering on stock control cards.

### **Drug and reagent shelf life**

Pharmacy and laboratory staff should ensure that the stocks expiring earlier are utilised first before stocks with a longer shelf life ("first expire first out"). Whatever can not be used before the expiry date, should be redistributed through the Provincial Office

### **Accountability**

Accountability for drugs and other supplies is the responsibility of all health staff. At each point where supplies are used, health staff must maintain daily records. Interrelated records should be consistent with each other and recorded balances should tally with physical counts. Ensure the following:

- Stock control cards should be maintained for each of the drugs and supplies.
- All information on the stock control card is current and correct.
- A physical count is done and recorded on a monthly basis. .
- Drug log books are maintained at dispensing point and in the ward.



## Monitoring

Monitoring is essential in order to prevent interruption of services.

The supervisor must ensure that:

- Supplies are stored in a dry and secure place
- Drugs and supplies are utilized before expiry –
- Supplies are used in accordance with TB control policy
- Drugs and supplies at any level should be recorded on stock cards and placed together with the supplies on the shelves
- Records of supplies are properly maintained
- Interrelated records are consistent with each other
- All transfers of drugs and supplies are recorded.
- Supplies are ordered and delivered **timely**

## CHAPTER 10: Recording and Reporting System

### Introduction

Accurate keeping of records on all individual patients, maintenance and regular reporting are minimum requirements that need to be met by all staff involved in TB control services. All documents used in the TB Programme should be maintained confidential as any other health records. Examples of the main documents are given at the back of the manual as annexes.

#### **a) TB Suspect Register**

This should be at every facility preferably in the out patient department. All those suspected of TB are written in this register before requesting the examinations.

#### **b) TB Laboratory Request Form for Microscopy**

This should be kept in all health facilities. This form is to be used to request for sputum examination in all TB suspects and for patients on treatment for follow up.

#### **c) TB Laboratory Request Form for Culture and Drug susceptibility testing**

This should be kept in all facilities and to be used for patients who are still sputum positive at 2, 5 or 8 months of treatment. It should also be used for patients being diagnosed as relapses and any other special cases

#### **d) Laboratory Register for Microscopy**

This should be maintained at all diagnostic centres. All details for each patient should be entered in this register. This register provides information on the number of suspects examined, the numbers of smear positive cases detected and the number and results of smear examination for follow up.

#### **e) Laboratory Register for Culture and Drug susceptibility testing**

This register is maintained at the Reference laboratories. Staff should enter all details. This register provides information on the number of suspects examined, the number of smear positive cases and number of positive cultures detected and the number and results of drug susceptibility tests.

#### **f) TB Patient Identity Card**

This is issued to the patient upon notification and is to be kept by the patient. This should be updated regularly by the treatment supporter when patient is observed taking the drugs and presented at the health facility on each visit. It also provides patient with dates of the next clinic visit.

#### **g) TB Treatment Card**

Maintained at the patient's treatment centre and should be updated regularly by health centre staff. All details should be filled in. This card contains information on sputum examination and HIV test results and HIV care information for co infected patients.

#### **h) Health Facility TB Register**

Maintained in all health facilities treating TB patients, information entered in this register is for monitoring and evaluating treatment outcome. Also keeps data on patients HIV status. This register is necessary for preparing TB Quarterly Reports.

#### **i) TB Transfer Form**

This should be filled in by the health facility from which the patient is being transferred for use at his/her new treatment centre and feedback slip at the bottom of the form should be sent back to the referring centre.

**j) Quarterly Report on TB Case Registration**

To be compiled quarterly by all diagnostic centres using a standardised form. Information required is obtained from the TB suspects' register, Laboratory and TB Health Facility Registers

**k) Quarterly Order Form For TB Drugs at Health Facility**

This form is filled in to request for drugs for patients notified in that quarter. It also indicates current stock position.

**l) Quarterly Report On TB/HIV Activities**

Information requested in this report is to be obtained from the TB Health Facility Register

**m) Quarterly Report On TB Outcomes**

This report gives treatment outcomes for patients notified 12 months ago. Information is obtained from the TB Health Facility Register.

## **Supervision**

For the proper functioning of the Programme, it is essential that there is **regular supervision** at all levels of health delivery.

The aim of supervision at all levels can be summarized as follows:

- To check if national TB management guidelines are followed
- To identify weaknesses and address them
- To provide opportunities for strengthening the Programme through technical support

## **Central Unit**

Supervision is an integral component of TB control Programme and should be done on regular basis. Staff from the Central Unit should visit the provinces at least twice a year and any district as need arises. They should use a standardized approach to supervising using a checklist, and should give feedback to Provincial Health Management Team and the District Health Management Team. At the end of each visit a written report of the supervision visit should be sent to the Provincial Health Management Team and District Health Management Team. The Director of Public health and Research should be briefed and receive a copy of supervisory visit report.

## **Provincial Level**

- The Provincial TB/Leprosy Focal Point Person should regularly supervise the district TB/Leprosy Focal Point person through field visits and quarterly through Provincial integrated supervisory visits.
- The Provincial TB/Leprosy Focal Point Person should provide support supervision to the district TB Coordinator. The Provincial TB/Leprosy Focal Point Person should brief the **DHMT** and make a report of supervision. Copy of the report should be sent to the Central Unit and to **DHMT** (TB focal point person).
- The provincial TB focal point person should supervise the clinical management of TB patients admitted in the wards in their respective district/provincial hospitals.

## District Level

- The District TB/Leprosy Focal point person will conduct at least monthly supportive visits to facilities in his/her district health facilities. During these visits, he should use a standardised checklist (SEE ANNEX).
- After each visit he should compile a report on the visit to be submitted to the facility, a copy of which should be kept at the DHMT and sent to the province.
- The district TB focal point person should supervise the clinical management of TB patients admitted in the wards in their respective district hospitals

## Health Facility

- Health centre staffs are responsible for the supervision of all community based TB activities. They should conduct regular (preferably fortnightly) visits and compile reports for submission to the district.

## Laboratory Services Supervision

### Quality Assurance

Quality Assurance Programme is dynamic and ongoing process of monitoring **reliability** and **reproducibility** of results that permits corrective action when established criteria are not met. It is good that all laboratories performing TB testing procedures establish and implement a QA Programme to monitor and evaluate laboratory functions and services throughout the total process i.e. through internal quality control, external quality assessment and standardization. Chest Diseases Laboratories has been mandated to oversee and manage QA activities pertaining to TB Microscopy, culture and drug susceptibility testing.

For implementation of QA activities for sputum smear microscopy the two specialised TB laboratories (University Teaching Hospital and TDRC) have been allocated provinces to supervise and they are to send all reports to CDL:

- UTH is responsible for Lusaka Province
- TDRC responsible for the Northern and North Western provinces

In TB smear microscopy Quality assurance consists of three components:

**Quality Control (QC)** - Also called internal quality control includes all means by which the TB smear microscopy laboratory controls operation, including instrument checks and checking new lots of staining solutions.

**External Quality Assessment (EQA)** - A process which allows participating laboratories to assess their capabilities by comparing their results with those in other laboratories in the network (intermediate and central laboratory) through panel testing and blinded rechecking. EQA also includes on-site evaluation of the laboratory to review quality of performance and should include on-site re-reading of smears. EQA is an expansion of the panel testing as described by EQA Guidelines.

**Quality Improvement (QI)** - A process by which the components of smear microscopy diagnostic services are analyzed with the aim of looking for ways to permanently remove obstacles to success. Data collection, data analysis and creative problem solving are the key components of this process. It involves continued monitoring, identifying defects, followed by remedial action including retraining when needed, to prevent recurrence of problems. QI often relies on effective on-site evaluation visits.

# ANNEXES

Form 1.

## ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAMME DISTRICT HEALTH OFFICE TUBERCULOSIS TREATMENT CARD

Name \_\_\_\_\_

District/Patient No. \_\_\_\_\_

Address: \_\_\_\_\_

Date of Registration \_\_\_\_\_

Sex: M:  F:  Age: \_\_\_\_\_

Health Facility \_\_\_\_\_

Name and Address of Community treatment supporter: \_\_\_\_\_

Sputum Smear Microscopy				Culture			DST	
Month	Date	Smear	Lab No.	Date Culture	Result	Lab No.	Date	
0								
2								
3								
5								
8								
>8								

X-ray Done	Yes	No
Date _____		
Results		
Normal	Abnormal	

Disease Site	
Pulmonary <input type="checkbox"/>	Extra pulmonary <input type="checkbox"/>
Specify _____	
Type of Patient	
New <input type="checkbox"/>	Treatment after default <input type="checkbox"/>
Relapse <input type="checkbox"/>	Treatment after failure <input type="checkbox"/>
Transfer in <input type="checkbox"/>	Other (Specify) _____

HIV Counseling and Testing			
Accepted	Place/Date of Test	Results	Post-test Counseling
Yes <input type="checkbox"/> No <input type="checkbox"/>			Yes <input type="checkbox"/> No <input type="checkbox"/>

HIV Care		
CPT	Date Start	
HIV Care	Reg No	
	Date	
ARV	Eligible	
	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
	Date:	
	Start Date ARV	

### INITIAL INTENSIVE PHASE - 2 MONTHS

Enter No. of Tablets to Appropriate Regimen below:

Adult:	Category I 2 (RHZE)	Category II 2 S(RHZE)/1(RHZE)	Child:	Paediatric I	Paediatric II
	RHZE	S inj RHZE		RHZ	S inj RHZ

Other \_\_\_\_\_

ADMINISTRATION OF DRUGS: one line per month. Mark in the boxes: X = directly observed; N = Not supervised; 0 = Not taken

Day Month	W E I G H T																															ADULTS								
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	RHZE 150/75/400/275	S 1g	Weight (Kg)	RHZ 60/30/150	S 1g			
																																			Weight	No. Tabs		5-9	1	0.1g
																																			26 - 37kgs	2	0.5 g	10-14	2	0.2g
																																			38 - 54kgs	3	0.75 g	15-19	3	0.3g
																																			55 - 70kgs	4	1g	20-25	4	0.4g
																																			> 71kgs	5	1g			

Dot

C	V	R	N
---	---	---	---

Plan

Dot Score: \_\_\_\_\_



--

Weight	RH	RHZE
30-37 KG	1	2
38-54 KG	2	3
55-70 KG	3	4
> 70 KG	3	5

Child:	RHZ Child	RH Child
5-9 KG	1	1
10-14 KG	2	2
15-19 KG	3	3
20-25 KG	4	4

### Patient Identity Card

INTENSIVE PHASE: Dot Plan: \_\_\_\_\_ Start Weight: \_\_\_\_\_  
 Start Date: \_\_\_\_\_ Observer: \_\_\_\_\_

\*Other explanation:

1	2	3	4	5	6	7	
8	9	10	11	12	13	14	
15	16	17	18	19	20	21	
22	23	24	25	26	27	28	
29	30	31	32	33	34	35	
36	37	38	39	40	41	42	
43	44	45	46	47	48	49	
50	51	52	53	54	55	56	
57	58	59	60	61	62	63	
64	65	66	67	68	69	70	
71	72	73	74	75	76	77	
78	79	80	81	82	83	84	
85	86	87	88	89	90	91	
92	93	94	95	96	97	98	
99	100	101	102	103	104	105	
106	107	108	109	110	111	112	

*Goal: 60 DOT days (new), or 90 DOT days (re-treatment)*

Observer initials each DOT day patient was **observed swallowing** drugs.

Or - writes reason code on each missed day, & explains:

**D** = Drugs not available **S** = Sick **M** = Missed Observation **\*Other**

### CONTINUATION PHASE:

Date	Drugs supplied	Amount	Wt	Planned Next Appt

Remark: \_\_\_\_\_



**IDENTITY CARD**

TB CASE NUMBER: \_\_\_\_\_  
 (Orig.DxCentre ID/Serial No./YR)

Use this card to help get yourself the very best care!

Name: \_\_\_\_\_ District/Patient NO: \_\_\_\_\_  
 Address: \_\_\_\_\_

Date of Registration: \_\_\_\_\_  
 Sex: M:  F:  Age: \_\_\_\_ Health Facility: \_\_\_\_\_

**Disease Site**  
 Pulmonary  Extrapulmonary   
 Specify: \_\_\_\_\_

**Type of Patient**  
 New  Treatment after default   
 Relapse  Treatment after Failure   
 Transfer in  Other (Specify): \_\_\_\_\_

Date Treatment Started:  
 \_\_\_\_\_  
 Day Month Year

**TREATMENT REGIMEN**

	Initial Phase		Continuation Phase
2 RHEZ	<input type="text"/>	6 EH/4 RH	<input type="text"/>
2 SRHEZ/1HREZ	<input type="text"/>	5 RHE	<input type="text"/>
CHILD: 2 RHZ	<input type="text"/>	4 RH	<input type="text"/>
2 SRHZ	<input type="text"/>	10 RH	<input type="text"/>

**DATE TREATMENT STARTED**

day     month     year

**Appointment Dates**

\_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

**REMEMBER**

1. Take care of your card
2. Bring your card at every clinic
3. Take your medicines every day.
4. Come for review as advised.

**TYPE OF TUBERCULOSIS**

PTB SMEAR POS  SMEAR NOT DONE   
 PTB SMEAR NEG  EPTB   
 Non-Pulmonary TB

Treatment Outcome		Date of Decision
Cured <input type="checkbox"/>	Transferred Out <input type="checkbox"/>	
Died <input type="checkbox"/>	Rx Failed <input type="checkbox"/>	
Completed <input type="checkbox"/>	Defaulted <input type="checkbox"/>	

## **ANNEX : NTP TECHNICAL SUPPORT/ SUPERVISORY CHECK LIST**

### **Introduction**

Supervisory visits at any level should be conducted by the Ministry of health staff who may be accompanied or supported by other stakeholders. The TB/Leprosy Specialist is responsible for coordinating visits to the Provinces as relates to the TB/Leprosy control programme. At Provincial/ District levels the respective TB/Leprosy officers will coordinate these activities.

### **Preparation for the supervision:**

- TB/Leprosy coordinator to give a brief to outline the ministry's vision to the team
  - Desk review of data for respective region/ area
  - Make brief summary of the findings on the data reports
  - Desk review on immediate past visit reports if available
  - Make short summaries of the trip reports ( strengths and weaknesses)
  - Arrange any supplies/drugs/reagents etc that need to be taken to the facility

Teams are expected to work within the MOH structure and are therefore supposed to report to the respective Health Offices (PHOs/ DHOs) before conducting any activities and share their reason for the visit including discussions on:

- Main TB Control strategies
- Programme achievements from previous quarter
- Resources available (additional supplies, drugs, reagent, IEC materials, etc.)
- New development
- NTP plans

On completion of the supervision there has to be a debriefing process that has to be done at each level (i.e., at facility, district and provincial levels).

It is important that the debriefing must be supportive and encouraging. It has to highlight the strengths, successes and areas of improvement as part of standard reporting.

## STOP TB TECHNICAL SUPPORT/ SUPERVISORY CHECK LIST

Checklist - based on the components of the Stop TB Strategy	
Pursue high quality DOTS expansion and enhancement	Comment
<p><b>1 Political commitment</b>            TB Coordinator/ Focal point person available            Focal person has desk at PHO/ DHO            Focal person participates in management meetings            Plan of action contains TB/ Leprosy activities            TB/Leprosy activities being supported (Resources available?)            Trainings conducted (number staff trained in previous quarter)</p> <p><b>2 Diagnosis through Quality Assured bacteriology</b>            Case detections: proportion of smears done, SS+? Vs Total            Lab supplies: Are they adequate or suspect load? Stock outs in past month?            Courier / transport system for sputum? Patients referred?            Feedback mechanism on sputum results?            Feedback on referred patients?            Lab staffing? Microscopists? EQA?</p> <p><b>3 Standardized treatment with patient support</b>            Guidelines available?            Number of activities treatment supporters (reports/meetings available)            Number of community supporters trained in previous quarter</p> <p><b>4 Uninterrupted drug supplies</b>            Drug stock outs in last 1 month?            Check drug stock-control cards            Compare drug requirement to available stocks</p> <p><b>5 Standardized reporting and recording systems</b>            Examine completeness and correctness on a sample of 5 or 10 treatment cards and compare with the documentation on the same in the register            Update the incomplete parts on registers and cards (discuss importance/ need to update cards and register regularly)            Compile quarterly report for previous quarter (or latest available) including report of treatment outcomes for the respective cohort and compare with what was reported and submitted (Analyse the data together with staff and brainstorm solutions to challenging issues)</p>	

Address TB/HIV, MDR TB and other challenges	Comment
<p><b><i>TB/HIV</i></b>            Provincial/ District Coordinating committee in place? (check reports/minutes)            DCT/PITC Provided?            HIV testing in TB Corners or referred?            TB/HIV data sharing meetings held?            TB/HIV guidelines available? DCT Trainings conducted? Number?            ICF? IPT?</p> <p><b><i>MDR TB</i></b>            Any confirmed cases            Number of sputum sent for Culture and DST</p> <p><b><i>Special situations</i></b>            Any programme in prisons? Displaced persons?            Infection control guidelines in place? Plans?</p>	
Contribute to health System strengthening	Comment
<p>Adequate Human resource for TB/Control activities?            Infrastructure needs: labs? TB Corners?</p>	
Engage all care providers	Comment
<p>Any collaboration with NGOs? CBOs?            International Standards for TB care available? (Provide copy if not available-discuss)            Community activities? Reports?</p>	
Empower people with TB and Communities	Comment
<p>Do they have a TB support group? (reports)            What activities done by support groups? IGAs? IEC?            Patients' charter for TB Care</p>	

TB/HIV ACTIVITIES			Weight	Date Tx Started	Treatment								DOT Plan	Outcome of Treatment and Date
HIV Result	ART Yes/No	CPT Yes/NO	Start KG	Regimen									DOT Score	
HIV Reg No	ART Start Date/ART Reg No	Start Date	End KG			1	2	3	4	5	6	7	8	
					wk									
					mo									
					wk									
					mo									
					wk									
					mo									
					wk									
					mo									
					wk									
					mo									
					wk									
					mo									
					wk									
					mo									

**OUTCOME of TREATMENT**

**C = Cure: Sputum-smear positive patient with negative smear result at end of treatment**

**TC = Treatment Complete (no smear result)**

**F = Failure: Sputum-smear positive patient with positive smear at 5 months or later during treatment**

**OC = Out of Control: Patient did not attend two consecutive clinics despite several attempts to trace the patient and motivate him/her to attend**

**TO = Transferred Out: Patient continues treatment in another district (write date & district)**

**D = Died; write date of Death.**

**ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM**

**QUARTERLY REPORT ON TB CASE REGISTRATION**

Name of Facility / District: \_\_\_\_\_  
 quarter \_\_\_\_\_

Name of Reporting Officer: \_\_\_\_\_  
 \_\_\_\_\_

Date of completion: \_\_\_\_\_

Signature: \_\_\_\_\_

**CASES NOTIFIED**

Cases by Type @ Dx:	New Cases N= 30								Old Cases N=						Total		
	S-POS		S-Neg		EPTB		R-POS		R-AFTER DEFAULT		RX-failure		Other previously Rx			Total	
Age	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Total
< 15	30														30	0	30
>15							0								0	0	0
Total	30	0	0	0	0	0	0	0	0	0	0	0	0	0	30	0	30

**NEW SMEAR POSITIVE BY SEX AND AGE GROUP**

	0 - 14	15 - 24	25 - 34	35 - 44	45 - 54	55 - 64	65 >	TOTAL
MALE								
FEMALE								
TOTAL								

**LABORATORY ACTIVITY**

No of suspects examined by microscopy	No of suspects found smear positive

### Quarterly Report on TB/HIV activities

		No Tested for HIV			No. HIV positive		
		Males	Females	Total	Males	Females	Total
	New Smear Positive PTB cases						
	Other TB cases						

Cases by TB Regimen						
	Adult: age more than 14			Paediatric: age 0 - 14		
	2 EHRZ / 6 EH or 2 EHRZ / 4 RH	2 SHRZE / 1 EHRZ / 5 HRE		2 HRZ / 4 RH	2 SHRZ / 10 RH	Total
Total	0	0		30	0	30



**ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM  
QUARTERLY ORDER FORM FOR TB DRUGS WITH AT HEALTH FACILITY**

Name of Facility: \_\_\_\_\_ *quarter of year* \_\_\_\_\_

Name of Request Officer: \_\_\_\_\_ Date of completion of this form: \_\_\_\_\_

Signature: \_\_\_\_\_

**Anti-TB drugs tablets - needs based on morbidity (case notification)**

Drug / Item	Cat 1 and 3: 2(RHZE)/6EH			Cat2: 2(RHZE)S/1(RHZE)/5(RHE)			Paediatric 2(RHZ) 4(RH)			Paediatric 2(SRHZ) 10(RH)		
	Cases	Factor	Total A	Cases	Factor	Total B	Cases	Factor	Total C	Cases	Factor	Total D
<b>Unit tablets/vials</b>												
(R150/H75/Z400/E275)	0	180	0	0	270	0						
E400/H150)	0	360	0									
(R150/H75/E275)				0	450	0						
S1g				0	60	0				0	60	0
RH 150/75	0	360	0				0	360	0	0	540	0
Z 400							0	180	0	0	180	0
RHZ 60/30/150 Child							0	180	0	0	180	0
RH 60/30							0	360	0	0	840	0
Syringes needles				0	60	0				0	60	0
Water for injection				0	60	0				0	60	0

Drug / Item	Running requirement of last quarter = <b>E</b>	Required buffer stock	Stock last day previous quarter	Total order
		<b>F=E</b>	<b>G</b>	<b>E + F - G</b>
(R150/H75/Z400/E275)	0	0		0
E400/H150)	0	0		0
(R150/H75/E275)	0	0		0
S1g	0	0		0
RH 150/75	0	0		0
Z 400	0	0		0
Syringes needles	0	0		0
Water for injection	0	0		0

**Total Cases                    30**