MINISTRY OF HEALTH

Malawi National Tuberculosis Control Programme Manual

SEVENTH EDITION – 2012

MINISTRY OF HEALTH

National Tuberculosis Control Programme Manual

SEVENTH EDITION
JANUARY 2012

This manual was developed in collaboration with the TB CARE II project and is made possible by the generous support of the American people through the United States Agency for International Development (USAID). The contents of this manual are the sole responsibility of the National TB Control Programme and do not necessarily reflect the views of USAID or the United States Government.

Table of Contents

Foreword

Tuberculosis (TB) continues to be a public health problem in our country despite the fact that the disease can be diagnosed following standard procedures and that it can be cured even in the presence of human immunodeficiency virus (HIV) infection. The productive age group is highly affected, resulting in a reduction in their contribution to socio-economic development of the country. Tuberculosis is also compounded by the emergence of other complicated forms of TB, such as multidrug-resistant TB (MDR-TB), which are difficult and costly to cure, thus posing a serious threat to TB control.

Achieving effective TB control requires concerted efforts at all levels. Hence, in 2007 the Ministry of Health declared TB an emergency in order to raise awareness and advocate for more action by all stakeholders as a way of containing the TB problem.

This 7th Edition of the National Tuberculosis Control Programme Manual is written for all health care workers in Malawi to serve as a guideline for better TB control. It builds on previous versions of the manual, but takes into account some of the important changes that have taken place in the last few years. One of the key initiatives embarked on in 2007 is the Universal Access to TB Diagnosis and Care. This manual also clarifies issues of MDR-TB management and new TB diagnostic technologies.

The Ministry of Health (MoH) will continue to offer assistance and supervision to districts and peripheral health unit personnel. With your cooperation at all levels in following the guidelines of the manual, together we can strengthen our fight against TB and achieve our national goal.

Dr. Charles Mwansambo
Principal Secretary

Acknowledgements

Special thanks go to the following individuals who worked on revising this Manual:

Dr. James Mpunga, Mrs. Rhoda Banda, Mr. Isaiah Dambe, Dr. D.S. Nyangulu, Mr. Alick Mwale, Mr. Isaac Chelewani, Mr. Henderson Mgawi, Mr. Hastings Banda, Mr. Henry Kanyerere, Mr. Cornelious Kang'ombe, Mr. Austine Makwakwa, Mr. Bernard Mvula, Mr. Burton Upindi, Mr. Lameck Mlauzi, Mr. Laphiod Chisuwo, Mr. George Samuti, Mr. Knox Banda, Mr. Andrew Dimba, Dr. Kuzani Mbendera, Mrs. Anne Mwenye, Mr. Noel Mphasa, Mr. Manuel Nazombe, and Mr. Harry Kawonga. Many thanks to all NTP support staff for the administrative and logistical support rendered during development of this manual.

The program is also indebted to Dr. Suzanne Anderson, Dr. Bernadette O'Hare, Dr. Chris Buck, and Dr. Charlotte Adamczik for their valuable contributions on Paediatric TB Management.

The Malawi government is also indebted to several partners who financially and technically assist the country in its fight against TB. These include the Health SWAp pool donors as well as discrete donors such as DFID, USAID, CDC, HUTAP and KNCV. In particular, the following members from donor and development partners personally contributed to this manual: Dr. Richard Banda, Dr. Michael Herce, Mr. Rodrick Nalikungwi, Mr. Ishmael Nyasulu and Mr. Fidelis Sindani.

Special thanks also go to WHO and IUATLD for their continued technical assistance to the Malawi TB Control Programme.

Acronyms

3TC	Lamivudine
AFB	Acid fast bacilli
AIDS	Acquired immunodeficiency syndrome
Amk	Amikacin
Amx	Amoxycilin
ARI	Annual risk of infection
ARV	Antiretroviral therapy
BCG	Bacille Calmette-Guérin vaccine
CBO	Community-based organisation
Cfz	Clofazimine
Clv	Clavulanate
Cm	Capreomycin
CMS	Central Medical Stores
CPT	Co-trimoxazole preventive therapy
CRL	Central Reference Laboratory
Cs	Cycloserine
CXR	Chest x-ray
DFID	Department for International Development
DHMT	District Health Management Team
DHO	District Health Officer

DOT	Directly observed treatment
DOTS	Directly observed treatment short-course
DR-TB	Drug-resistant tuberculosis
DRS	Drug Resistance Survey
DST	Drug susceptibility testing
DTO	District Tuberculosis Officer
E	Ethambutol
EFV	Efavirenz
EHP	Essential Health Package
EPTB	Extra-pulmonary tuberculosis
Eto	Ethionamide
FDC	Fixed dose combination
FNA	Fine needle aspiration
H	Isoniazid
HAART	Highly active antiretroviral therapy
HTC	HIV testing and counselling
HIV	Human immunodeficiency virus
HSA	Health surveillance assistant
IEC	Information, education and communication
Ipm	Imipenem
IRIS	Immune reconstitution inflammatory syndrome

IUATLD	International Union Against Tuberculosis and Lung Disease
KS	Kaposi sarcoma
Km	Kanamycin
Lfx	Levofloxacin
LP	Lumbar puncture
LTBI	Latent tuberculosis infection
Lzd	Linezolid
KNCV	Royal Netherlands Tuberculosis Association
MCH	Maternal and child health
MDG	Millennium Development Goal
MDR-TB	Multidrug-resistant tuberculosis
Mfx	Moxifloxacin
MGIT	Mycobacteria growth indicator tube
MoH	Ministry of Health
MSTG	Malawi Standard Treatment Guidelines
MTB/RIF	(GeneXpert) *Mycobacterium tuberculosis*/rifampicin (resistance test)
NGO	Non-governmental organisation
NTP	National Tuberculosis Programme
Ofx	Ofloxacin
OPD	Outpatient department
PAS	P-aminosalicylic acid

PITC	Provider initiated testing and counselling
PLHIV	Person(s) living with HIV
PMTCT	Prevention of mother-to-child transmission (of HIV)
POW	Programme of work
PPM	Public-private mix
PTB	Pulmonary tuberculosis
Pto	Prothionamide
QA	Quality assurance
R	Rifampicin
S	Streptomycin
STI	Sexually transmitted infection
SWAp	Sector-wide approach
TAT	Turnaround time
TB	Tuberculosis
TBM	Tuberculous meningitis
TB/HIV	HIV related-TB
TDF	Tenofovir
Trd	Terizidone
TST	Tuberculin skin test (Mantoux test)
US	Ultrasound
USAID	United States Agency for International Development

USG	United States Government
UVGI	Ultraviolet germicidal irradiation
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis
Z	Pyrazinamide

CHAPTER 1

Introduction

1.1 Tuberculosis in Malawi

Tuberculosis (TB) remains one of the major public health problems in Malawi and is among the top ten killer diseases in the country. TB is therefore one of the priority diseases addressed by the Malawi Essential Health Package (EHP). The NTP strives to help Malawi achieve the TB-related Millennium Development Goal (MDG) target to halve TB prevalence and deaths by 2015. The NTP's overall goal is to dramatically reduce TB-related morbidity and mortality and eliminate TB as a public health threat in Malawi.

Since Malawi began implementing the DOTS strategy, TB case notification has increased steadily, most notably from 1995 to 2003 when it reached its peak. After 2003, TB cases have trended downward, decreasing from nearly 28,000 notified cases in 2003 to about 23,000 notified cases in 2010. The country continues to register successes in the fight against TB: treatment outcomes have improved steadily over the past 5 years; access to diagnostic services has increased with the number of microscopy

centres reaching 213 nationally in 2011; and TB treatment has been scaled up to 88 initiation sites established by the end of September 2011, an increase from 44 treatment centres in 2004.

In 2007, Malawi declared TB a national emergency in order to raise awareness and improve TB case detection. Reasons for lower than expected case detection include low levels of community awareness, challenges with intensified case finding among PLHIV and limited access to sensitive diagnostic tools for smear-negative and extra-pulmonary tuberculosis. These challenges notwithstanding, rapid scale-up of ART might have contributed to the declining case notification, with over 300,000 patients on ARVs in 2010.

TB control activities are integrated into general health services with managerial and supervisory functions at national, zonal and district levels. The NTP is headed by the TB Programme Manager. Providers of TB treatment and care services include government and private for-profit as well as private not-for-profit organisations. At the community level, TB control activities are coordinated by health surveillance assistants (HSAs). Several NGOs and CBOs implement community-based TB control interventions utilizing community volunteers and community health workers that provide important linkages with health facilities.

1.2 NTP Strategy for TB Control

1.2.1 VISION

A tuberculosis-free Malawi.

1.2.2 MISSION

To ensure effective, equitable and accessible prevention, diagnosis, treatment and care for tuberculosis in Malawi.

1.2.3 GOAL

To reduce the morbidity, mortality and transmission of tuberculosis until the disease is no longer a public health problem in Malawi.

1.2.4 NTP STRATEGIC APPROACH

The NTP strategic plan is published in *National Tuberculosis Control Program Five- Year Strategic Plan 2012-2016,* January 2012. The approach is aligned with the Global STOP TB Partnership Strategy and is based on the following 7 key components:

1. To pursue high-quality DOTS expansion and enhancement;

2. To address TB/HIV, MDR-TB and the needs of poor and vulnerable populations;

3. To contribute to health system strengthening based on primary health care;

4. To engage all care providers;

5. To empower people with TB and empower communities through partnership;

6. To enable and promote research; and

7. To enhance TB programme monitoring and evaluation.

1.3 How to use this manual

This manual is intended to be a resource for NTP managers and staff as well as front-line health workers from the public and private sectors who participate in the care of TB suspects, patients and contacts. The manual covers how to identify TB suspects; diagnose TB and MDR-TB; manage TB and TB-HIV in adults and children; and use NTP reporting and recording tools to ensure proper data collection and suspect, patient and contact tracing—in short, how to optimise TB patient care.

The manual is divided into six main sections:

1. The diagnosis and management of TB in adults,

2. The diagnosis and management of TB in children,

3. The management of HIV and TB disease,

4. Special considerations for the diagnosis of MDR-TB,

5. Supervision and patient support, and

6. Monitoring and evaluation.

Within each section, individual chapters address the major technical components of TB service delivery. Each chapter contains easy-to-follow algorithms and tables to reinforce key concepts and to provide decision support to health workers.

1.4 What is new in this edition?

Advances in TB policy, TB diagnostics and international recommendations for TB control have necessitated the development of an updated version of this manual. These recommendations build on the achievements of the successful DOTS strategy implemented in Malawi. Specifically, this edition places greater emphasis on the following:

- Ensuring universal access to patient-centred treatment for all patients;
- Addressing the pressing challenges of TB/HIV co-infection, paediatric TB and multidrug-resistant TB; and
- Providing high-quality services to all TB patients, particularly patients with smear-negative and extra-pulmonary disease.

The internationally adopted Patients' Charter for Tuberculosis Care highlights these important issues, advocating that all TB patients have "the right to free and equitable access to TB care, from diagnosis through treatment completion."

CHAPTER 2

Definitions & Epidemiology

2.1 What is tuberculosis?

Tuberculosis (TB) is a communicable disease caused by a type of bacteria known as *Mycobacterium tuberculosis* (commonly referred to as TB bacilli). The bacilli usually attack the lungs, causing pulmonary TB (PTB). TB bacteria can also attack other parts of the body such as the spine, lymph nodes, brain and kidneys; this is known as extra-pulmonary TB (EPTB).

2.1.1 CAUSES AND TRANSMISSION

When infectious people cough, sneeze, talk or spit, they propel TB bacilli into the air. Transmission is more intense in crowded, poorly ventilated spaces with little ambient sunlight as it increases the likelihood of inhalation of infectious TB bacilli present in the air. If not treated, a person with active pulmonary TB disease will infect, on average, between 10 and 20 people every year.

2.1.2 INFECTION AND DISEASE

Persons infected by *M. tuberculosis* but who have no symptoms of TB disease have what is known as latent TB infection. After infection, TB bacilli can lie dormant in the body for many years.

If the immune system is somehow compromised—as in the case of HIV infection, malnutrition or other conditions—the TB bacilli can cause active disease. Many factors influence the progression from infection to disease; however, in Malawi no risk factor is more important than HIV infection. The risk of TB infection progressing to active disease is higher when the CD4+ count declines. Other factors include age, diabetes and cancer. Of note, in Malawi, the incidence of TB is highest in adults 25 to 34 years of age.

2.2 Case definitions and diagnosis

It is crucial to define TB cases properly for accurate patient registration and selection of treatment regimens. This will in turn aid standardisation of data collection and cohort analysis for treatment outcomes. The TB case definitions below are based on the level of certainty of the diagnosis and on whether or not laboratory confirmation is available.

2.2.1 CASE OF TB

A case of TB is:

- A patient with pulmonary symptoms having at least one sputum-smear examination positive for acid-fast bacilli (AFB) by either conventional or fluorescent microscopy;
- A patient with *M. tuberculosis* complex identified from a clinical specimen, either by culture or by a molecular diagnostic method such as Xpert MTB/RIF; or

- A patient in whom a health worker or a clinician has diagnosed TB and has decided to treat with a full course of TB treatment.

Cases of TB are also classified according to the:

1. Anatomical site of disease,
2. Bacteriological results (including drug resistance),
3. History of previous treatment, and
4. HIV status.

2.2.2 ANATOMICAL SITE OF TB DISEASE

In general, recommended treatment regimens are similar, irrespective of the anatomical site of disease. Defining the site is important for recording and reporting purposes and to identify the more infectious patients—those with pulmonary involvement (who will be further subdivided by smear status).

Pulmonary tuberculosis (PTB)

- This is a form of tuberculosis that involves the lung tissues.
- Miliary tuberculosis is classified as pulmonary TB because there are lesions in the lungs as well.
- A patient with both pulmonary and extra-pulmonary TB should be classified as a case of *pulmonary* TB.

Extra-pulmonary tuberculosis (EPTB)

- This type of TB involves one or more organs other than the lungs, for example, the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones and/or meninges.
- Both intrathoracic tuberculous lymphadenopathy (e.g. involving the mediastinal and/or hilar lymph nodes) and tuberculous pleural effusion, when radiographic abnormalities in the lungs are absent, constitute cases of *extra-pulmonary* TB.

2.2.3 BACTERIOLOGICAL STATUS

Bacteriological status refers to the detection of *M. tuberculosis* by smear, culture or molecular methods, and to the detection of drug sensitive and drug resistant cases. Any case with a positive bacteriological result (microscopy, culture or molecular method) is defined as a "bacteriological positive TB case". If the bacteriological tests are all negative or not done the case is defined as a "bacteriological negative TB case". TB cases are sub-classified as "smear-positive" or "smear-negative", which is useful because it best correlates with infectiousness.

- **Smear-positive pulmonary TB:** Patient with at least one sputum smear-positive sample (at least one AFB is found in at least one sputum sample: scanty results are considered as positive).
- **Smear-negative pulmonary TB:** Pulmonary TB that are negative for AFB and for whom a clinician prescribes anti-TB treatment.

When possible, culture and DST (and/or molecular resistance testing) should be done as indicated in Sections 8.4 to 8.6 to determine if the strain is susceptible or resistant. The different types of drug resistance are defined in Chapter 8.

2.2.4 HISTORY OF PREVIOUS TREATMENT

TB cases can also be defined according to whether or not a patient has a new infection or has previously received TB treatment. It is important to identify previously treated patients because they are at increased risk of having drug-resistant TB. At the start of treatment specimens for culture and DST should be obtained from all previously treated patients.

TABLE 2.1 TB categories

Category		Definition
New		A patient who has never been treated previously for TB or who has taken TB treatment for less than one month. This could be a PTB (smear-positive or smear-negative) or EPTB case.
Previously Treated	Relapse	A patient who presents positive bacteriologically (by smear, culture or molecular method) after previously undergoing TB treatment with a successful outcome (cured or completed treatment).
	Failure	A patient whose sputum smear or culture is positive at 5 months or later whilst on anti-TB chemotherapy. (Of note, also included in this definition are patients found to have MDR-TB at any point during treatment, regardless of whether they were initially smear-negative or -positive).
	Treatment after default	A bacteriologically positive patient who is started on treatment after previous treatment was interrupted for at least 2 consecutive months (default).

CONTINUED >

TABLE 2.1 TB categories (CONTINUED)

Category	Definition
Transfer-in	A patient who has been transferred from another treatment unit to continue treatment.
Other	All cases that do not fit the above definitions, such as patients: For whom it is not known whether they have been previously treated; Who were previously treated but with unknown outcome of that previous treatment; and/or Who have returned to treatment with smear-negative pulmonary TB or bacteriologically negative EPTB.

2.2.5 HIV STATUS

Determining and recording the patient's HIV status is critical for treatment decisions (see Chapter 7) as well as for monitoring trends and assessing programme performance. The TB Treatment Card and TB Register include dates of HIV testing, starting cotrimoxazole, and starting ART.

2.3 Tuberculosis suspect

A TB suspect is defined as any person who reports any one of the following current symptoms of any duration:

- Cough
- Fever
- Weight loss or
- Night sweats

If a person has a negative HIV test result documented within the previous 3 months, the following alternative definition applies:

- Productive cough or fever for more than 2 weeks with or without the following:
  - Respiratory symptoms (shortness of breath, chest pains, haemoptysis); or
  - Constitutional symptoms (loss of appetite, weight loss > 5% of baseline weight, night sweats).

Symptoms that may localise TB to the lungs include coughing up blood or sputum and pain in the chest.

Symptoms or signs due to EPTB depend on the site involved. Regardless of the site of disease, there are usually constitutional symptoms present such as fever, night sweats and weight loss.

CHAPTER 3

Tuberculosis Diagnosis

3.1 Approach to tuberculosis diagnosis

Early identification and treatment of TB cases is important for TB control. Direct sputum smear examination should be done on all tuberculosis suspects, especially among PLHIV having TB symptoms of *any* duration and HIV-negative suspects with cough lasting two weeks or more.

In high-risk institutions where people live under crowded conditions, such as prisons, patients coughing for more than one week should submit sputum for smear microscopy. If the results at one week are negative and symptoms persist after a course of empiric antibiotic treatment, the test should be repeated at 3 weeks.

To improve TB diagnosis, the NTP is introducing new, rapid molecular tests (Xpert MTB/RIF) and MGIT liquid culture that detect TB bacilli with greater speed and sensitivity than traditional laboratory methods.

3.2 Clinical presentation

Active TB disease causes a variety of symptoms depending on the anatomical site(s) involved. In settings such as Malawi with high HIV prevalence, up to two-thirds of TB patients may present with symptoms suggestive of extra-pulmonary disease or *both* pulmonary and extra-pulmonary disease.

Patients should be highly suspected of TB and undergo a thorough investigation for TB if:

- They are children who have been in close contact with a known TB patient;
- They are HIV positive; or
- They were treated for TB in the past.

Pulmonary tuberculosis (PTB)
In the early stages of the disease, symptoms are non-specific. Symptoms classically consist of fever, weight loss, loss of appetite, night sweats, general malaise and weakness. Absence of fever or cough does not exclude a diagnosis of tuberculosis, particularly in patients with HIV or malnutrition. Many patients may have no abnormalities detected on chest auscultation whereas others may have crackles overlying the involved areas.

Extra-pulmonary tuberculosis (EPTB)
EPTB may affect any organ outside of the lungs. Commonly involved sites include: the pleura, lymph nodes, meninges, bones and joints, spine, genitourinary tract, peritoneum and pericardium.

TABLE 3.1 Clinical features of the most common EPTB presentations

TB Lymphadenitis	• Commonly affects posterior cervical and supraclavicular lymph nodes; • Usually painless enlarged lymph nodes early in course.
Pleural TB	• Pleuritic chest pain and shortness of breath; • An effusion around the lungs.
Spinal TB	• Tender swelling of the back, sometimes with weakness of the legs due to compression of the spinal cord; • Most frequently affects the thoracic or lumbar portions of the spine.
Osteoarticular	• Slow onset (> 4 weeks) of monoarthritis with little or no pain; • Usually hip, knee, elbows or wrists; • Signs of joint destruction (clinical or radiological); • Often associated with pulmonary TB.

CONTINUED >

TABLE 3.1 Clinical features of the most common EPTB presentations (CONTINUED)

TB Meningitis	• Presents subtly with headache and mental status changes after 1-2 weeks of low-grade fever, loss of appetite and irritability; • May progress acutely to severe headache, confusion/coma and neck stiffness.
Pericardial TB	• May present suddenly with shortness of breath, fever, oedema and retrosternal chest pain.
Gastrointestinal TB	• Abdominal pain, abdominal swelling (ascites), bowel obstruction, fever, weight loss and bloody stools are common.

3.3 Laboratory diagnosis of TB

Whenever possible, bacteriologic confirmation of TB by one of the laboratory methods described below should be used to make a definitive diagnosis of TB disease. Bacteriology refers to using smear, culture or newer methods to definitively identify *M. tuberculosis* in a clinical sample from a TB suspect. Smear microscopy and culture remain the cornerstones of bacteriologic confirmation of TB in Malawi. Culture and drug susceptibility testing are discussed in further detail in Chapter 8.

It is important to note that the absence of bacteriologic confirmation of TB should *not* delay treatment of a TB suspect with a history and clinical findings compatible with TB disease, especially in seriously ill patients, children and PLHIVs. In 10 – 20% of adults and in an even higher percentage of children, a culture or molecular test may be negative even though the patient clinically has TB disease (on the basis of clinical, radiographic and histopathologic findings or response to anti-TB treatment).

The laboratory diagnosis of TB begins with the collection of a quality clinical specimen. In the majority of cases this is a sputum specimen.

3.3.1 SPUTUM COLLECTION

Patients and guardians should be counselled and advised properly on how to produce quality sputum specimens. To minimise the number of patient visits, only two sputum specimens should be collected using the **'spot-morning' approach**. The first specimen should be collected at the time when the patient

first presents to the clinic. During the patient's visit, a second labelled sputum container should be given to the patient and/or guardian so that his or her sputum can be collected the next morning. The NTP will evaluate a 'spot-spot' approach in selected districts and will communicate any change in sputum collection strategy by circular.

Before collecting sputum

- Patients should be well informed about the diagnostic process and the reason for collecting sputum.
- Sputum collection should be done in the open air (or ventilated room) away from other people to avoid infecting them.
- Patients should clean their mouths if they have been eating.
- A health worker should demonstrate how to cough and how to open and close the sputum container.
- The laboratory request form should be filled out accurately and completely.
- Clearly label the sputum container with the patient's name and the date of collection. Label the container itself, not the lid.
- Make sure that the patient's details have been recorded in the TB suspect register.

How to collect a quality sputum specimen

1. Tell the patient that the best specimens come from deep inside the lungs after coughing, not from saliva.

2. Demonstrate how to cough deeply.

3. Ensure that no one is standing in front of a patient producing sputum.

4. Instruct the patient to:

    a. Inhale deeply 2 to 3 times and to breathe out hard each time,

    b. Cough deeply from the chest,

    c. Place the open container close to the mouth to collect the sputum, and

    d. Screw the lid tightly.

5. 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 container.

6. The volume of the sputum should be about 3 to 5 ml.

After collecting a sputum specimen

- Double check to ensure that the container is labelled properly,
- Ensure that the container is firmly closed, and
- Wash your hands with soap and clean water.

- The two sputum specimens should be sent to a microscopy site ***within 24 hours***.
- Store sputum specimens for culture, preferably in a refrigerator or in a cool, safe and dark place.
- Sputum specimens for culture should be sent to the laboratory ***within 4 days.***
- Do not use laboratory request forms for wrapping specimens.

Who should collect sputum specimens?

- **It is the responsibility of health workers and community volunteers to collect sputum specimens from TB suspects.**
- For in-patients, the ward nurse should check with the patient and/or guardian each morning to encourage sputum production and to collect samples for submission to the laboratory.
- At health centre and community levels, HSAs and community volunteers should follow up with TB suspects to ensure sputum specimens are collected.
- Should the patient not return after submission of the first spot specimen, the HSA, community volunteer or DTO must follow up with the patient immediately.

3.3.2 TRANSPORTATION OF SPUTUM SPECIMENS

- Every health worker is responsible for sending sputum specimens to the laboratory as soon as possible to ensure examination is done within 4 days of collection.
- Use any available means of transport.
- The specimens should be packed carefully, preferably in a transport box.
- Make sure that every specimen goes to the laboratory with a laboratory request form.
- A cold chain should be maintained throughout the transportation process, especially when sending samples for culture.

Trained health workers and community volunteers may prepare smears at peripheral sites prior to transportation to the microscopy centre. In order to do so, health workers must have been trained on how to properly prepare and fix sputum smears as well as how to safely package fixed slides for transportation.

NOTES TO LABORATORY PERSONNEL

- Sputum specimens should be delivered to hospital laboratories as soon as possible.
- Sputum microscopy can be done by Ziehl-Neelsen conventional light microscopy or by fluorescent microscopy.
- Laboratory personnel should perform sputum examination the same day samples are submitted, aiming to return a result to the patient within 24 hours.
- Sputum samples should **not be "batched"** for microscopy.

3.3.3 SPUTUM SMEAR MICROSCOPY

- Sputum smear microscopy is the primary test for the diagnosis of pulmonary tuberculosis (PTB).
- Diagnosis of TB by smear microscopy is made by visual identification of acid-fast (AFB) or fluorescent bacilli under direct examination of a stained sample by conventional light or fluorescent microscopy, respectively.
- Fluorescent microscopy is a new way to detect TB bacilli using a specialised microscope. It is a more sensitive and less-time consuming technique than traditional light microscopy.
- Laboratory personnel report results based on the number of TB bacilli seen when evaluating areas visualised under the microscope called "fields" (see Table 3.2).

TABLE 3.2 Reporting laboratory results

Result Reported	Interpretation
Negative	No bacilli seen in 100 fields
"Scanty" or actual number counted	1 to 9 bacilli seen (either acid-fast or fluorescent) in 100 fields*
1+	10 to 99 bacilli seen (either acid-fast or fluorescent) in 100 fields
2+	1 to 10 bacilli seen (either acid-fast or fluorescent) per 1 field
3+	> 10 bacilli seen (either acid-fast or fluorescent) per 1 field

*A finding of 3 or fewer bacilli in 100 fields does not correlate well with culture positivity.

3.3.4 INTERPRETATIONS OF SPUTUM SMEAR RESULTS

3.3.4.1 SMEAR-POSITIVE PULMONARY TB

Identifying just one positive sputum smear with even one bacilli detected at the start of treatment meets criteria for classifying a patient as a "smear-positive" case. Smear-positive patients are the most infectious and most likely to transmit the disease to people in their surroundings; as such, they have historically been the primary focus of infection control measures and contact tracing efforts. The NTP has expanded the definition of an index case for contact tracing purposes to include all cases of PTB.

3.3.4.2 SMEAR-NEGATIVE PULMONARY TB

Smear-negative PTB is the most common form of TB in Malawi. It is important to identify, especially in persons living with HIV, because the mortality is higher than in smear-positive PTB cases. For this reason, aggressive early TB treatment and close follow-up of HIV-positive TB suspects, especially those who are seriously ill, is critical to prevent unnecessary TB deaths. For diagnostic algorithms for smear-negative PLHIV, please refer to Chapter 7.

A patient is a smear-negative TB case if one of the following criteria is met:

- Negative smear on microscopy, an inconclusive chest x-ray but a decision by a clinician to treat with a full course of anti-TB drugs based on a positive HIV test or clinical evidence of HIV and a clinical presentation compatible with TB.
- Negative smear on microscopy and a decision by a clinician to treat with a full course of anti-TB drugs based on abnormalities on chest x-ray consistent with active pulmonary TB plus one of the following:
  - Positive HIV test or strong clinical evidence of HIV infection, OR
  - If HIV-negative, no improvement with a course of broad-spectrum antibiotics.

KEY POINTS

- A sputum smear result is positive if at least one tubercle bacillus (acid-fast OR fluorescent) is detected on one or more sputum smears.
- The patient should be registered as a smear-positive case and should be started on TB treatment immediately.
- If both sputum smears are negative, the patient should be investigated further for TB.
- The patient should receive a thorough clinical evaluation and undergo further testing by chest x-ray and/or Xpert MTB/RIF.
- Please refer to the diagnostic algorithm for details.

3.3.5 THE ROLE OF CHEST X-RAYS IN THE DIAGNOSIS OF PULMONARY TUBERCULOSIS

Chest x-ray findings especially in patients with a negative sputum smear should be correlated with clinical findings, history and physical examination. Whenever possible, an experienced clinical officer should assist in interpreting the x-ray and making a TB diagnosis based on x-ray. Chest x-ray appearances alone do not always help diagnose PTB. In 10 to 20% of HIV-positive patients with PTB, the chest x-ray is negative. A normal x-ray does not rule out TB in a patient with compatible symptoms and clinical findings. Patients with a normal x-ray who remain symptomatic should be referred to a clinician for further investigations.

Classic radiographic findings suggestive of TB, particularly in patients who are not immunocompromised, include:

- Upper lobe infiltrates
- Cavitary lesions
- Hilar and/or paratracheal lymphadenopathy

In patients with primary PTB and HIV infection, the x-ray findings can be quite different:

- Lower lobe infiltrates
- A miliary or “scattered seed” like pattern

The following figures illustrate common x-ray findings seen in patients with TB.

FIGURE 3.1 Normal chest x-ray and anatomic landmarks in a healthy person without TB

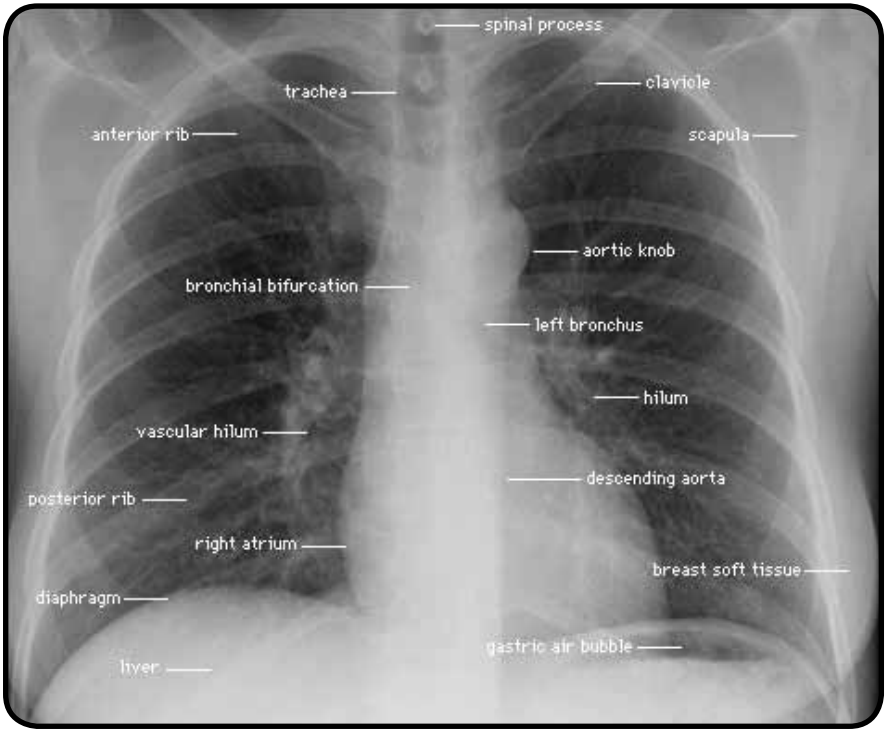


FIGURE 3.2 X-ray findings in an immunocompromised TB patient (note the miliary or "scattered seed" appearance of the lungs)

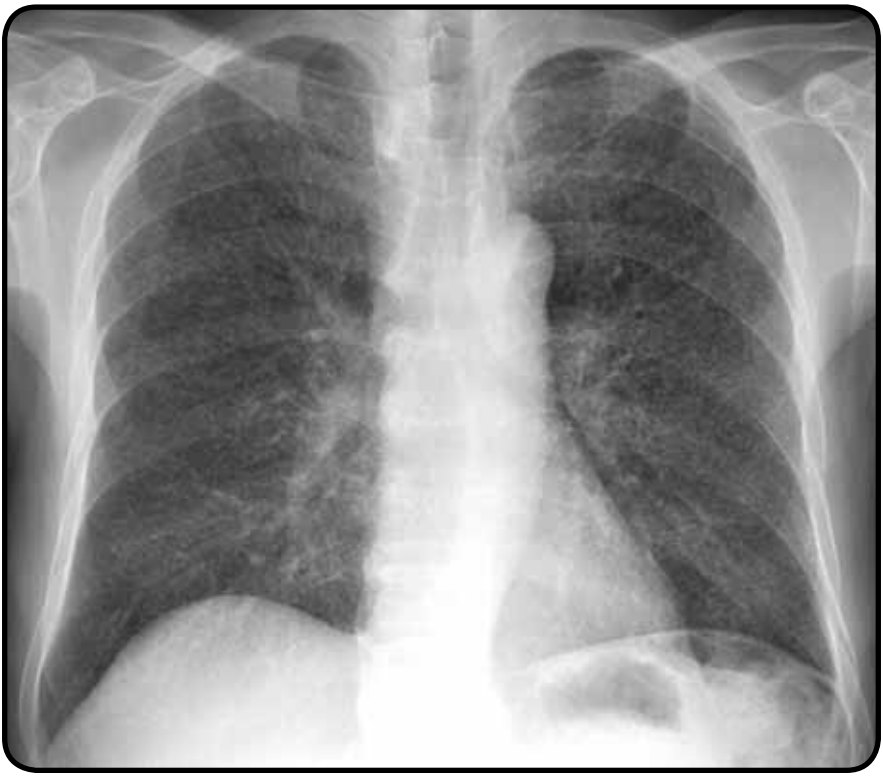


FIGURE 3.3 X-ray findings in a paediatric TB patient (note the characteristic Ghon focus of primary TB in children located in the right hilum)

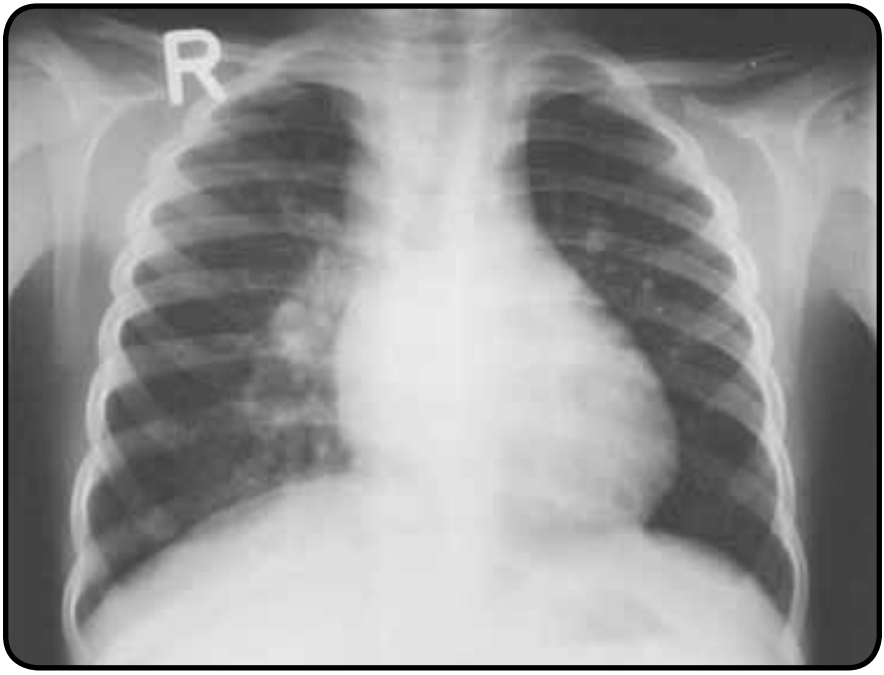
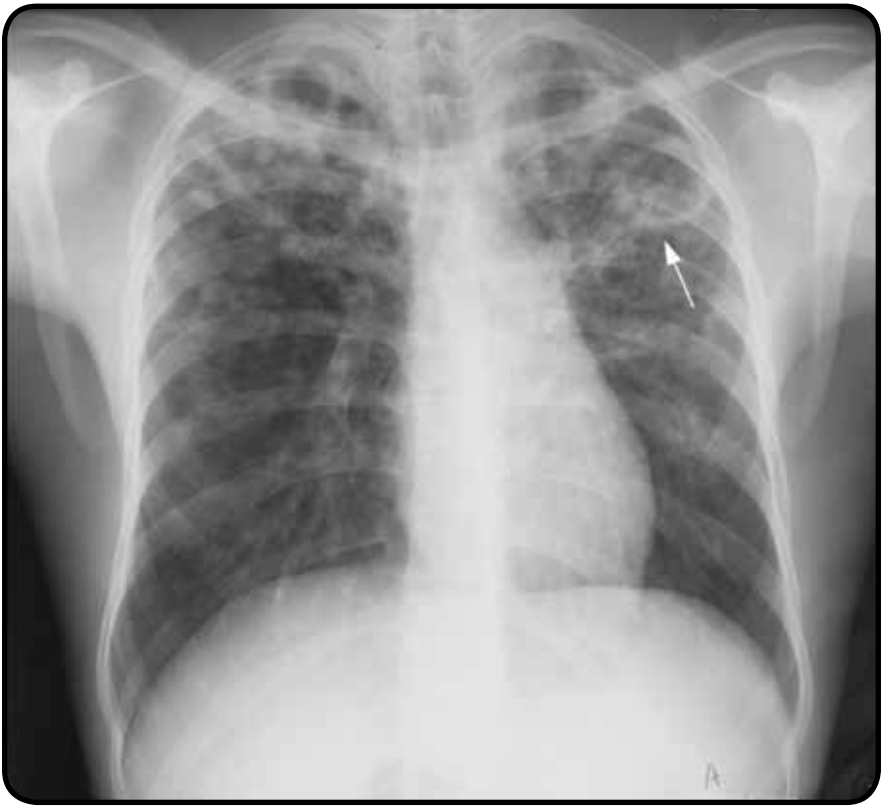


FIGURE 3.4 Classical x-ray findings in a TB patient



3.3.6 EXTRA-PULMONARY TB (EPTB)

The common sites of involvement of EPTB in adults are the lymph nodes in the neck and armpits, the pleura lining the lungs, the meninges lining the brain and spinal cord and the pericardial space around the heart. Patients with TB found in the blood, bone marrow or two non-neighbouring organs are said to have a particularly severe form of EPTB known as **disseminated TB**.

All patients suspected of EPTB should be offered HIV testing and counselling. If HIV positive, they should start co-trimoxazole preventive therapy (CPT) immediately and antiretroviral therapy (ART) according to national guidelines.

FIGURE 3.5 Summary of the most common clinical findings to assist in EPTB diagnosis

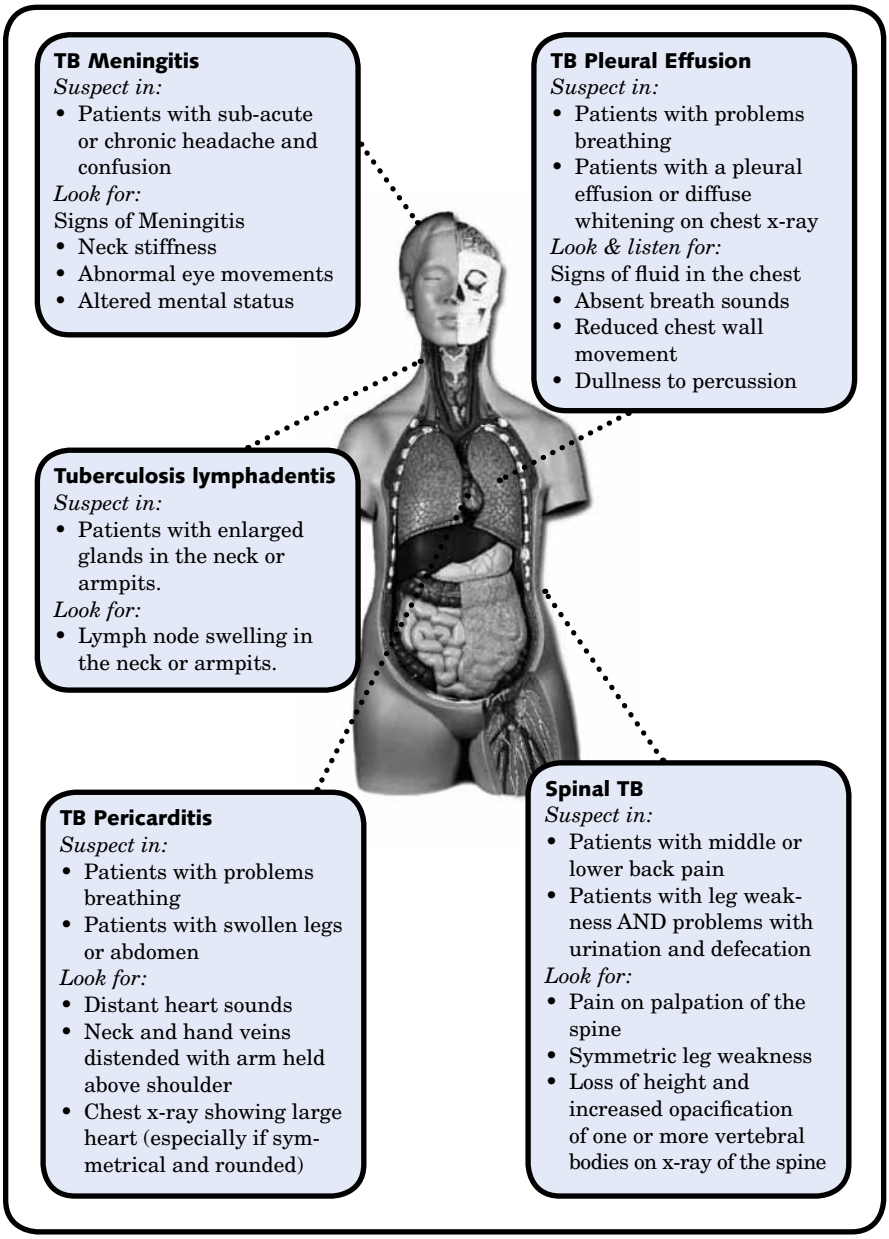


TABLE 3.3 Summary of the diagnostic approach to EPTB

Type of EPTB	Recommended investigations	Findings HIGHLY suggestive of TB	Findings suggestive of NON-TB diagnosis
Pleural TB	• Rapid HIV test • Chest x-ray (CXR) • Sputum smear or Xpert MTB/ RIF • Aspiration & inspection of pleural fluid • Differential white blood cell count and protein determination (if possible) of aspirate	• One-sided effusion: TB is one of the most common causes of a unilateral pleural effusion in Malawi • Aspirated fluid is clear and straw-coloured • Lymphocytes comprise ≥ 50% of WBCs in pleural fluid • Weight loss, night sweats, chest pain, fever • Evidence of TB in other part of the body	• Bilateral pleural effusions • Clinical evidence of Kaposi sarcoma (KS) or other cancer • Aspirated fluid is pus (empyema) or bloody (usually cancer)

Lymph Node TB	• Rapid HIV test • Sputum smear or Xpert MTB/RIF • Needle aspiration for AFB (18 – 21 gauge needle) • Lymph node excisional biopsy	• Lymph nodes (LN) > 2 cm in size • Painless swelling • Asymmetrical/localised • Posterior cervical location • Firm/fluctuant/ presence of fistula	• KS in skin or mouth • Symmetrical (concern for lymphoma or HIV) • Tender or red/inflamed
TB Pericarditis	• Rapid HIV test • Sputum smear or Xpert MTB/RIF • CXR • Ultrasound (US) examination	• Fever, chest pain and night sweats • Evidence of TB in other part of the body • Pericardial effusion or pericardial thickening on US	• Streaky shadowing of lung fields on CXR • Murmur • High blood pressure

CONTINUED >

TABLE 3.3 Summary of the diagnostic approach to EPTB (CONTINUED)

Type of EPTB	Recommended investigations	Findings HIGHLY suggestive of TB	Findings suggestive of NON-TB diagnosis
Disseminated TB	• Rapid HIV test • CXR • Sputum smear or Xpert MTB/RIF • Aspiration of ascitic fluid	• Abnormal CXR including "miliary" pattern • Fever, cough, night sweats & weight loss • Large spleen and/or liver	• Rigors • Severe diarrhoea or blood in stool • Shock/sepsis (very low BP) • Pathogen from blood culture
Spinal / Bone disease	• Rapid HIV test • Appropriate x-rays • FNA or biopsy for AFB	• Signs of spinal cord compression (paraplegia, urinary and bowel incontinence) • Fever, night sweats and weight loss	• Clinical evidence of cancer • Clinical evidence of rheumatologic disease (e.g., rheumatoid arthritis)

TB Meningitis	• Rapid HIV test • Lumbar puncture • Laboratory tests on Cerebrospinal Fluid (CSF) – including Gram stain, AFB, cell count & differential, protein & glucose on CSF, cryptococcal CSF antigen or India ink	• Fever, weight loss, night sweats • CSF with between 100 – 500 cells/mm3 with lymphocyte predominance • CSF with high protein and low glucose • India Ink and/or cryptococcal antigen negative • Evidence of TB in other part of the body	• If HIV-positive, cryptococcal meningitis is more likely than TB • Rapid onset • Very high opening CSF pressure (more likely cryptococcal) • CSF cloudy or with neutrophilic predominance (more likely bacterial) • India ink or cryptococcal antigen test positive

3.4 TB diagnostic pathway

Early identification of TB cases and putting patients on effective treatment is important for TB control and reducing TB-related mortality, particularly in TB/HIV co-infected patients. Diagnosis of tuberculosis depends on the identification of the tubercle bacilli in sputum by microscopy, culture or newer molecular tests OR strong suspicion of TB based on sound clinical judgement.

3.4.1 MICROSCOPY

Sputum smear microscopy is the mainstay of TB diagnosis in Malawi. The two main techniques include:

- Conventional microscopy using Ziehl-Neelsen staining
- Fluorescent microscopy

3.4.2 XPERT MTB/RIF

Xpert MTB/RIF is a new rapid test for detecting TB in sputum. Xpert MTB/RIF simultaneously tests for drug resistance to rifampicin, enabling earlier diagnosis and treatment initiation for MDR-TB patients. Testing with Xpert MTB/RIF requires only one sputum specimen and can detect both TB and rifampicin-resistance in less than 2 hours.

To optimise the use of Xpert MTB/RIF, the NTP has developed a national diagnostic algorithm to assist providers with identifying patients who should be prioritised for Xpert MTB/RIF testing and to guide clinical decision making (Annexes).

The NTP has prioritised the following patients for Xpert MTB/RIF testing:

- All smear-negative TB suspects
- All hospitalised TB suspects
- All confirmed retreatment cases and MDR-TB suspects

Despite the introduction of Xpert testing, sputum microscopy remains the backbone of the TB diagnostic network and along with culture and drug susceptibility testing (DST) continues to be the method of choice for monitoring patient response to anti-TB therapy.

3.5 Approach to TB diagnosis in the ambulatory or seriously ill patient

There are two TB algorithms that provide a general approach to assist with clinical decision making. The algorithms are intended to assist with TB diagnosis in adult and adolescent suspects in HIV-prevalent settings and differ based on the clinical condition of the patient – whether the patient is ambulatory (or slightly sick) or seriously ill. Footnotes are provided in the Annexes.

FIGURE 3.6 Approach to TB diagnosis in the ambulatory patient

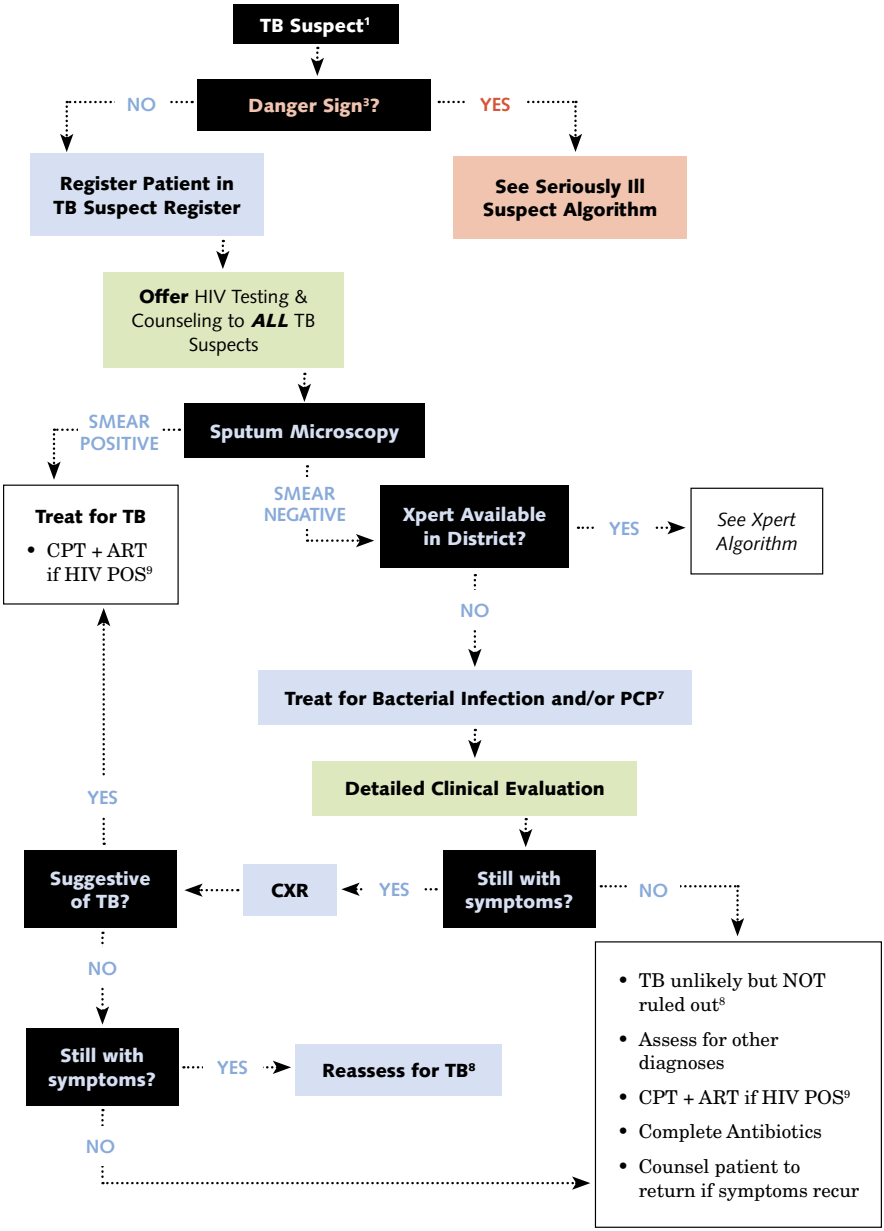
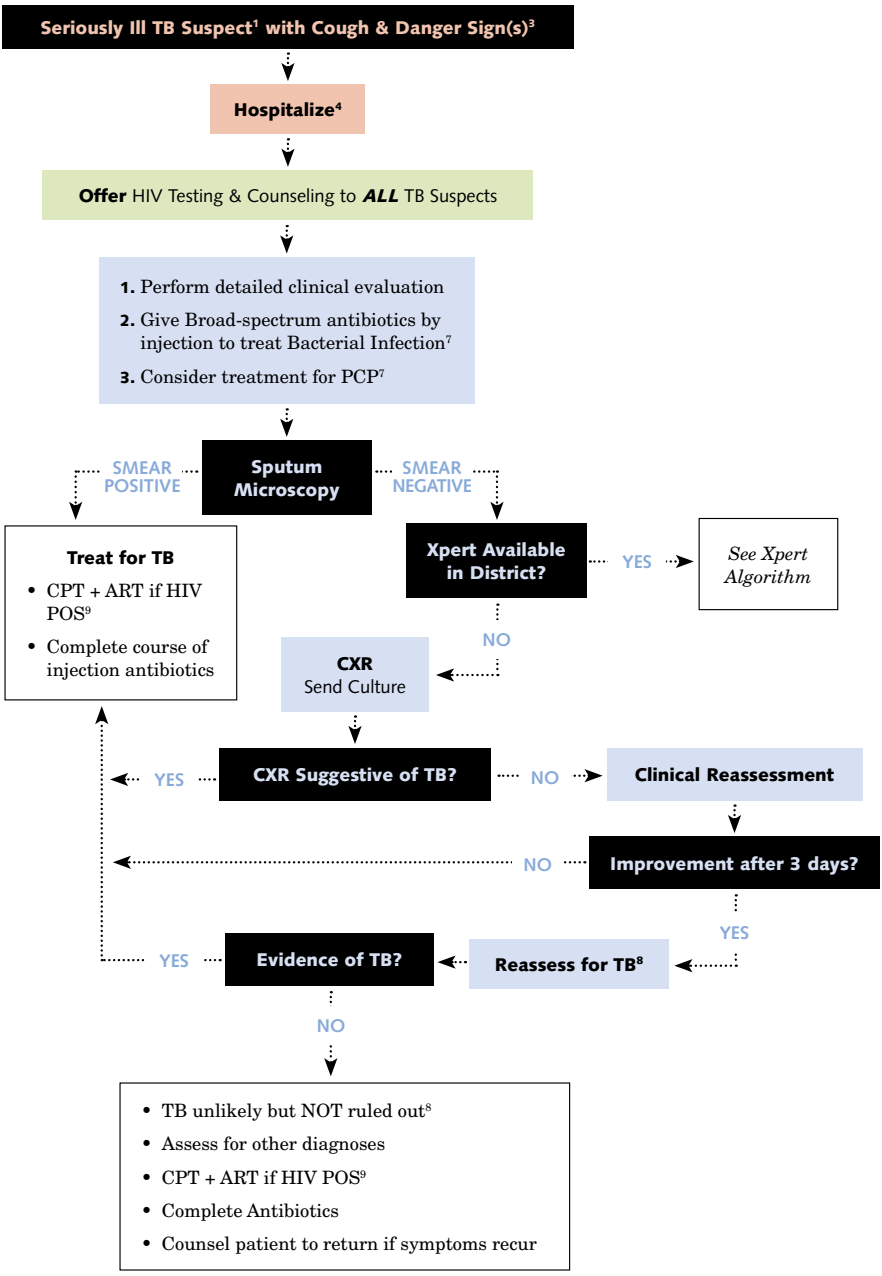


FIGURE 3.7 Approach to TB diagnosis in the severely ill patient



CHAPTER 4

Tuberculosis Control Methods

4.1 Case finding and effective treatment

Rapidly detecting infectious cases and appropriately treating all TB patients are two of the most important ways to prevent TB transmission. While most TB cases continue to be detected through self-referral (e.g. passive case finding), NTP is now intensifying case detection through TB screening of contacts as well as screening in congregate settings and at community sputum collection points, HTC sites and HIV/ART clinics. The programme continues to implement universal access to TB care to extend TB services to communities.

Intensified TB case finding in HIV care settings

Routine TB screening should be done using the standard 4-point screening tool in all HIV care and treatment settings, including HTC sites, ART and PMTCT clinics and STI service delivery areas, etc.

KEY POINTS

- Register the patient in the Chronic Cough Register AND ask the patient to submit sputum if one or more of the following symptoms are present:
  - Cough (of any duration)
  - Fever
  - Night sweats
  - Weight loss or failure to thrive/malnutrition
- These screening questions should be asked to all PLHIVs at every clinic visit.
- If an HIV positive patient answers NO to all the above questions and active TB is ruled out, consider IPT (see Section 4.3).

4.2 Contact tracing

This is a form of active case finding when a health worker actively looks for the contacts of a PTB (index) case or MDR-TB case. All symptomatic contacts should be investigated for TB disease and treated if active TB is present. All symptomatic contacts of confirmed MDR-TB cases should submit sputum for culture and DST in addition to smear microscopy or Xpert MTB/RIF testing.

The following steps should be taken to identify contacts of known index PTB cases:

- Ask the TB patient for the names and ages of their household and workplace contacts,
- Add these names to the TB Contact Tracing Register,
- The health worker should counsel these contacts to report to the nearest health facility for clinical evaluation and TB screening, and
- If the contacts are ill, the health worker should visit the contacts in their homes.

4.3 Isoniazid preventive therapy (IPT)

IPT can prevent TB in people who are at high risk of developing TB disease (such as PLHIV).

4.3.1 ELIGIBILITY FOR IPT

HIV-infected patients are eligible to start IPT if active TB is ruled out. Use the standard TB screening criteria below:

- Cough (of any duration)
- Fever
- Night sweats
- Weight loss

For HIV-positive patients who develop TB while on IPT, stop the IPT and give full TB treatment.

For IPT eligibility guidelines for children, see Chapter 5.

4.3.2 IPT CONTRA-INDICATIONS

Contra-indications for IPT include:

- Suspected or confirmed TB disease
- Active hepatitis
- Severe peripheral neuropathy
- History of alcoholism

Note: For details on IPT for PLHIV, please refer to the 2011 Malawi Integrated PMTCT/ ART Guidelines.

4.4 TB infection control (IC)

TB IC should be implemented within the scope of general infection prevention at each health facility.

4.4.1 MANAGERIAL INTERVENTIONS

- Strengthen the existing infection prevention coordinating body to include TB IC.
- All health facilities should have an infection control committee responsible for developing a written infection control plan, monitoring its implementation and providing effective training for health care workers and other staff. Each health facility should appoint one person to serve as the infection control coordinator. This person should also oversee TB IC.
- Every health care worker should be trained in TB IC.
- HIV-positive health care workers should not work in high-risk areas, including TB wards, general medical wards and TB suspect/patient waiting areas such as TB clinics, MDR-TB clinics, cougher triage areas, etc. Encourage all health care workers to undergo HIV testing and counselling (HTC).

4.4.2 ADMINISTRATIVE INTERVENTIONS

- Recognize TB suspects early and expedite the diagnostic process.
- Separate TB suspects and patients from other patients in congregate areas.
- Collect sputum in designated areas, ideally with ample ambient UV radiation (e.g. sunlight) and ventilation.

- Triage TB suspects to more quickly access diagnostic services (e.g. establish facility-based TB Walk-in Centres).
- Encourage cough etiquette for TB suspects and patients and, where possible, providing surgical masks to all hospitalised TB suspects.

4.4.3 ENVIRONMENTAL INTERVENTIONS

- *Natural ventilation*: ensure that all areas of the working healthcare environment (e.g., OPD, consultation rooms, wards, HTC rooms, clinic, laboratory etc.) are well ventilated. Open windows and doors to ensure maximum natural ventilation.
- *Mechanical ventilation*: ensure that ceiling fans, air-conditioners and exhaust fans are in good working condition.
- *Ultraviolet germicidal irradiation* (UVGI): ensure that the lamps are cleaned and monitored weekly. Install UVGI lamps in open clinical areas to ensure maximal radiation coverage. Lamps should be left switched on continuously for 24 hours per day. UV bulbs should be replaced every 6 months.

4.4.4 PERSONAL PROTECTIVE EQUIPMENT

Certified N95 or greater respirators are recommended for health workers when in close contact with infectious TB patients or working in high risk areas like MDR-TB wards, TB wards, general medical wards, TB reference laboratories or when conducting aerosol-producing procedures (like inducing sputum). The respirator should be properly fitted in order to provide maximum protection. An N95 respirator can be reused several times provided that the mask holds its shape.

4.5 BCG vaccination

BCG vaccination is given to infants at birth to protect them from developing TB, particularly severe forms of the disease such as tuberculous meningitis and miliary tuberculosis. Maintaining a cold chain is of paramount importance in order to preserve the efficacy of the vaccine. For its BCG vaccination policies, the NTP follows the recommendations of the Malawi Expanded Programme for Immunisation (EPI).

Dosage: For children under one year of age, 0.05 ml is the accepted dosage. Children aged one year or more are given 0.1 ml.

In the presence of HIV infection, BCG is safe and effective. BCG should be given to children with asymptomatic HIV infection, but it should not be given to children with advanced HIV disease or AIDS.

CHAPTER 5

Paediatric Tuberculosis

5.1 Investigation and management of children suspected to have TB or who are close contacts of a TB case (sputum smear-positive or -negative)

The recommended approach to diagnosing TB in children includes:

- Gathering a detailed patient history, including history of TB contacts and symptoms consistent with TB;
- Clinical examination including growth assessment;
- HIV testing: provider initiated testing and counselling (PITC);
- Sputum microscopy and culture when possible (especially in children > 8 years of age); and
- Mantoux test (tuberculin skin test) if available.

The presence of any of the following strongly suggests a diagnosis of TB:

- Current cough of any duration (productive or non-productive in nature)
- Unexplained weight loss
- Failure to thrive and/or malnutrition
- History of contact with a TB case
- Fever and/or night sweats

All children with symptoms suggestive of TB should be investigated. Children can present with TB at any age but it is most common in the under-5 age group and during adolescence.

The following symptoms are suggestive of TB meningitis, especially in young children with TB exposure:

- Decreased appetite, often with weight loss;
- Vomiting without diarrhoea, early morning headache, irritability;
- Drowsiness/lethargy and convulsions, especially focal seizures;
- Dehavioural changes (irritability, confusion or agitation).

KEY POINTS

- Children who are close contacts of an infectious TB case are at high risk of becoming infected with *M. tuberculosis* and developing active TB.
- Clinicians should have a low threshold for investigating TB and commencing young children on TB treatment.
- Once an adult contact is confirmed, the main clinical decision is whether the child needs full 4-drug treatment or isoniazid preventive therapy (IPT) chemoprophylaxis.

5.2 Physical findings suggestive of TB in children

Physical findings suggestive of TB in children include:

- Abnormalities detected when listening to the lungs: crackles, coarse breath sounds, etc.;
- Dullness to percussion of the chest may suggest a TB pleural effusion;
- A painless, enlarged mass of lymph nodes in the neck, without response to a course of antibiotics, is highly suggestive of TB cervical adenitis; and
- Other features of EPTB (see Table 3.3).

5.3 Investigations and Management

5.3.1 SPUTUM COLLECTION

TB in children is usually sputum smear-negative. Collection of sputum specimens is difficult since children usually swallow their sputum. Sputum in younger children with TB contains few TB bacilli, but this is not true for older children (> 8 years of age). The sputum smear (and sputum for Xpert MTB/RIF or TB culture, where available) remains a valuable test to perform in any child who is able to produce a sputum specimen.

In children who are unable to expectorate spontaneously, obtaining an aspirate of gastric fluid is a reasonable alternative to obtaining sputum. Gastric aspirates are safe and easy to perform in hospital after a 3-hour fast or early in the morning after an overnight fast.

5.3.2 FINE NEEDLE ASPIRATION (FNA)

In children with large, palpable cervical lymph nodes, collection of an aspirate offers a convenient way of collecting samples for microscopy and culture. The aspirate can be smeared onto a slide and sent for microscopy where culture is not available.

5.3.3 LUMBAR PUNCTURE (LP)

Should be performed on any child in whom TBM is suspected and repeated on a child failing to respond to standard treatment for bacterial meningitis. Suspect TBM if the CSF demonstrates an elevated WBC count with a lymphocytic predominance, a high protein level and/or a low glucose concentration. Absence of bacilli on microscopy does not exclude a diagnosis of TBM. TB

culture is of particular value when there is a concern regarding drug resistance. The probability of obtaining a positive TB culture result increases when more than one sample is taken.

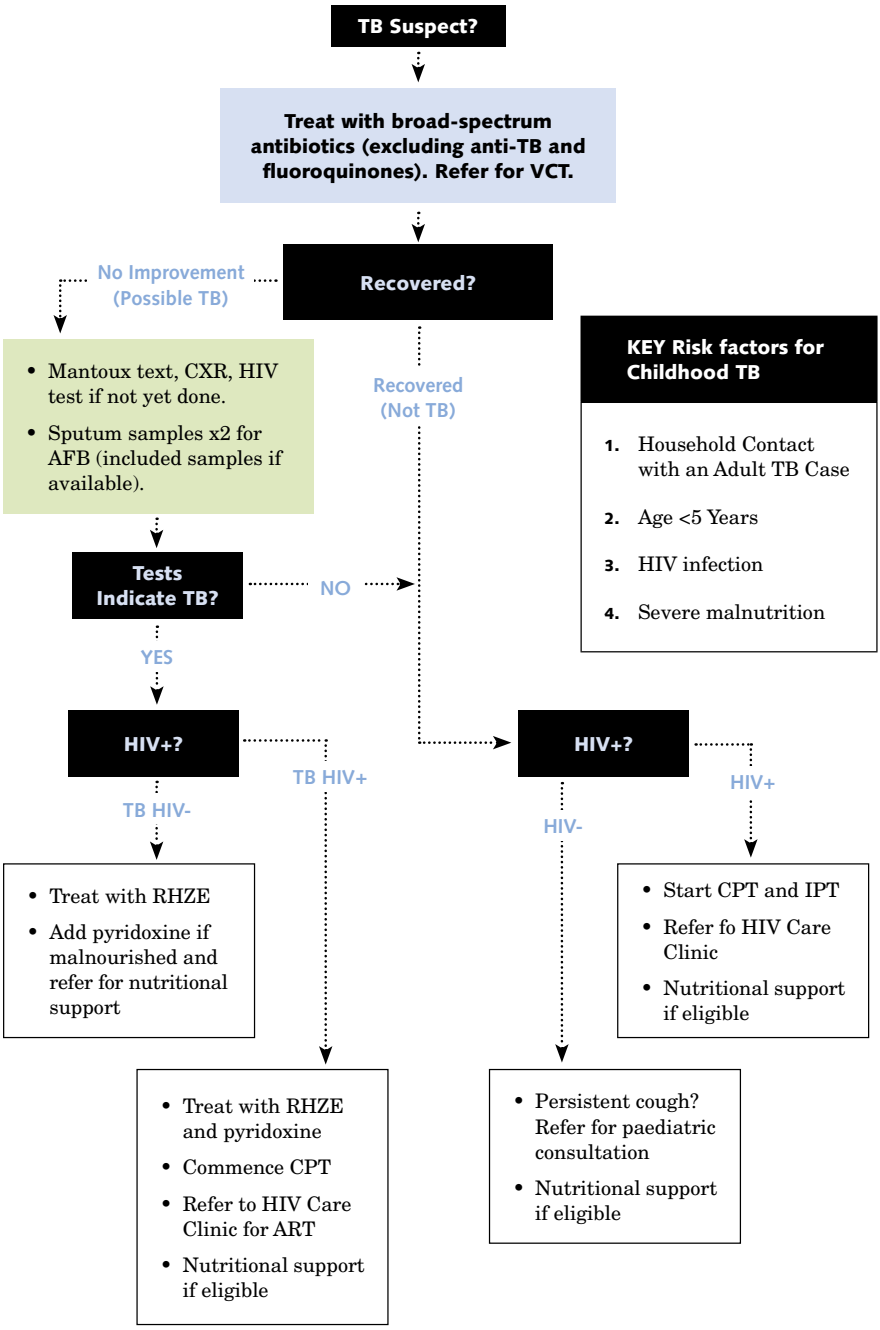
5.4 Chest x-ray

Chest x-rays need to be of good quality and interpretation depends on the expertise of the person reading them. CXR changes are often non-specific and may be completely normal in the HIV-infected or malnourished child. TB disease should not be diagnosed from the CXR alone. The whole clinical picture should be taken into account.

The most common x-ray findings suggesting TB in children are:

- Enlarged hilar lymph nodes as evidenced by splaying of the right and left mainstream bronchi (see Figure 3.3) and/or a widened mediastinum due to enlarged lymph nodes (this is the most common x-ray abnormality in children with TB).
- Unilateral infiltration on x-ray may indicate lobar disease.
- Diffuse uniformly distributed small miliary shadows.
- One-sided pleural effusions usually occur in children > 5 years of age.

FIGURE 5.1 Algorithm for the diagnosis of TB in Children



5.4.2 TUBERCULIN SKIN TEST (TST)—MANTOUX TEST

The Mantoux test measures the delayed-type hypersensitivity response to purified protein derivative (PPD)—a protein precipitate of inactivated tubercle bacilli. PPD is also known as tuberculin. A positive Mantoux does not indicate active TB disease, it only indicates latent infection with *M. tuberculosis* (LTBI). The Mantoux test is positive when the diameter of skin induration (swelling, not redness) is ≥ 10 mm (or ≥ 5 mm in an HIV-infected or malnourished child). A negative TST does not exclude TB infection or disease.

KEY POINTS

The tuberculin skin test may be *falsely negative* in a child with:

- Severe malnutrition
- HIV infection
- Disseminated (miliary) TB and/or TB meningitis
- Very young children (≤ 12 months)

5.5 Treatment of paediatric TB: first-line TB regimen

TABLE 5.1 TB paediatric drug dosages

Drug name	Dosage
Isoniazid (H)	10 mg/kg (range 10 – 15 mg/kg); max. dose 300 mg/day
Rifampicin (R)	15 mg/kg (range 10 – 20 mg/kg); max. dose 600 mg/day
Pyrazinamide (Z)	35 mg/kg (range 30 – 40 mg/kg)
Ethambutol (E)	20 mg/kg (range 15 – 25 mg/kg)

It is important to monitor the child's weight at every clinic visit and to adjust drug doses accordingly. Many children rapidly gain weight after initiation of TB treatment.

TABLE 5.2 Revised treatment guidelines for paediatric TB

Site or type of TB disease	HRZE treatment duration	HR treatment duration	Total length of treatment
TB meningitis Miliary TB Osseous/bone TB (spine, joints)	2 months	10 months	12 months
Pulmonary TB TB lymphadenitis ALL other forms of TB	2 months	4 months	6 months

In TB meningitis and pericardial effusion, steroids have a supportive therapeutic effect. Steroids have been shown to improve survival in patients with TB meningitis and decrease the risk of developing constrictive pericarditis in patients with pericardial effusions.

Prednisolone dosage (first-line): 2-4 mg/kg/day (maximum dose of 40 mg) for three weeks, followed by a reduction regimen over three weeks. See Tables 6.8 and 6.9 for specific steroid regimens in TB meningitis and TB pericarditis.

Pyridoxine (vitamin B6) protects against isoniazid-induced peripheral neuropathy. Pyridoxine is recommended for all children on TB treatment and IPT. The recommended dose is 25 mg/day until treatment is completed.

5.6 Paediatric multidrug-resistant TB

Children with proven or suspected TB caused by multidrug-resistant bacilli should be treated with an appropriate MDR-TB regimen according to the Malawi MDR-TB guidelines, using paediatric doses. The decision to treat should be taken by a clinician experienced in managing paediatric TB or through consultation with the National Tuberculosis Programme. The dosing of second-line TB drugs in children should be determined by a specialist in MDR-TB. Please refer to the National MDR-TB Guidelines for further details.

Suspect MDR-TB in any child:

- Who is a contact of an adult MDR-TB case and has symptoms and signs suggestive of TB disease.
- Who remains symptomatic after completion of first-line TB treatment with good medication adherence.

5.7 Neonates exposed to a mother with TB

If a mother is diagnosed with TB before the third trimester of pregnancy, is taking TB medications with good adherence and is clinically well:

- Examine the newborn for signs of disease. If the baby is well, no action is required.
- Refer all other household children <5 years of age to the TB clinic for clinical assessment.

If a mother is diagnosed with TB in the third trimester of pregnancy or shortly after delivery, examine her baby closely for symptoms and signs of disease. If the baby is well, commence isoniazid (H) prophylaxis at 10 mg/kg/day and continue for 6 months. Do not give BCG vaccine. If the baby is not well and has signs/symptoms suggestive of TB disease, collect gastric aspirates where possible and commence full TB treatment.

Infants need to be reviewed at 1, 3 and 6 months after commencing isoniazid. Infants' weights must be checked regularly and their isoniazid dosages increased as they grow. Refer all other household children to the TB clinic for clinical assessment and screening. As BCG is a live vaccine, isoniazid will kill the vaccine and prevent an effective immune response from developing. If isoniazid is commenced within 12 weeks of receiving BCG vaccination, the infant will need repeat BCG vaccination following the end of treatment. If no BCG vaccine was given at birth, then vaccinate the baby two weeks after completing isoniazid.

KEY POINTS

- A significant number of mothers reactivate latent TB infection in the third trimester of pregnancy or around the time of delivery/immediate post-partum period.
- Any mother in whom TB is suspected should be sent for a CXR and two sputum samples collected for smear microscopy (and Xpert MTB/RIF, where available).

TABLE 5.3 IPT dosages

Baby's weight	Isoniazid dose
<2.5 kg	25 mg (1/4 tablet) every 24 hours
2.5 – 5.0 kg	50 mg (1/2 tablet) every 24 hours
5.0 – 10.0 kg	100 mg (1 tablet) every 24 hours

5.8 BCG vaccine

Bacille Calmette-Guerin (BCG) is a live, attenuated vaccine and is routinely given to neonates in Malawi in the first week of life. BCG may be associated with injection-site abscesses, adenitis, and (very rarely) with disseminated disease. Infants with advanced HIV infection or AIDS are at particular risk of BCG-related complications. The presence of right-sided axillary or regional lymph nodes in a young child or infant indicates

possible BCG disease and an immunocompromised state. This most commonly presents in the two years of life after BCG vaccination. It requires further evaluation. Refer to experienced clinicians if BCG disease is suspected.

5.9 TB and HIV infection in children

The current approach to clinical diagnosis of TB in HIV-infected children is similar to that recommended for HIV-uninfected children (see Figure 5.1). It is recommended that HIV-infected children be treated with the same TB treatment regimens and for the same duration as those for HIV-uninfected children. Children with TB/HIV must be followed up with regularly and have dosages adjusted for changes in weight. HIV-infected children being treated for TB must be started on co-trimoxazole preventive therapy (CPT).

HIV-infected children should also be started on ART within 2 weeks of commencing TB treatment. ART can be started on the same day as TB treatment if the child is stable.

5.9.1 ANTIRETROVIRAL THERAPY IN CHILDREN WITH TB/HIV CO-INFECTION

ART is indicated for all HIV-infected children and infants with any form of TB. Children must be followed up with regularly and drug doses for ART and anti-TB treatment adjusted for changes in weight.

TABLE 5.4 Treatment regimen according to the Malawi National HIV Guidelines (2011)

ART status at time of starting TB therapy	< 3 years of age	> 3 years of age
Not yet started ART	AZT/3TC/ Nevirapine	AZT/3TC/ Efavirenz
On first-line ART	AZT/3TC/ Nevirapine	AZT/3TC/ Nevirapine
On second-line ART	Refer to specialist centre (Note: major drug interactions exist between LPV/r and Rifampicin)	

Note: TB IRIS is more common in severely immunocompromised children and usually occurs within 3 months of starting ART.

KEY POINTS

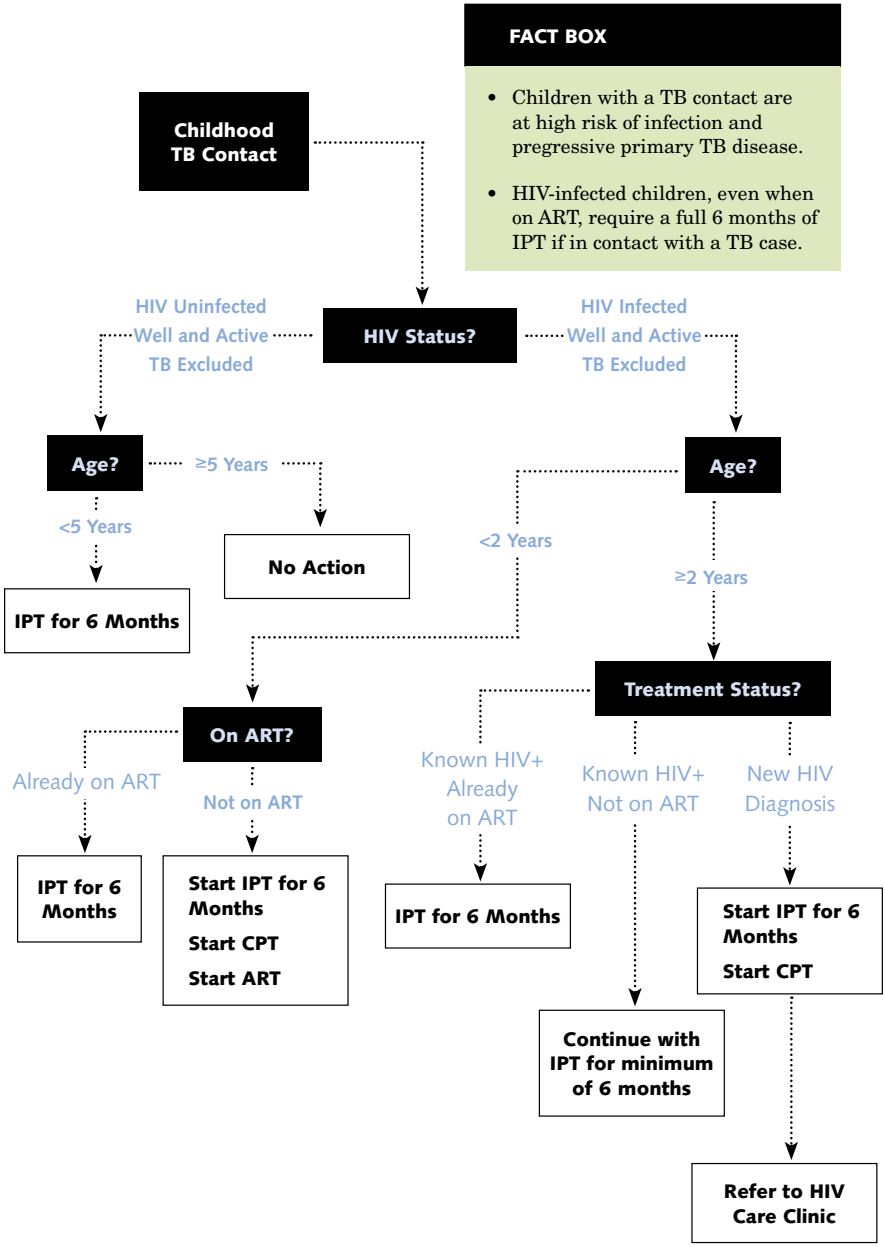
- TB is common in HIV positive children in Malawi.
- HIV-positive children are more likely to be infected with *M. tuberculosis* than HIV-negative children.
- HIV-positive children are at increased risk of TB disease and this risk is related to the degree of immune suppression.

5.10 Isoniazid preventive therapy (IPT)

A contact is a person who has a history of a close and prolonged exposure to pulmonary TB (sputum smear-positive or smear-negative). Contacts are eligible for IPT. See Figure 5.2 for recommendations on administering IPT to paediatric contacts.

Active TB should be ruled out before starting IPT. For any child with contact history, 6 months of IPT is indicated, even if he or she is on ART. For HIV-infected children not on ART, IPT is to be given for the entire time period until ART is initiated, regardless of contact history. A CXR is recommended, but not required, to rule out active TB in HIV-infected and -exposed children with a positive contact history.

FIGURE 5.2 Algorithm for Isoniazid Preventive Therapy (IPT) in Children



If children have NONE of the following signs or symptoms, then active TB can be ruled-out without TST or CXR:

- Poor weight gain
- Current cough
- Fever

For all paediatric age groups, the recommended dosing of IPT is 10 mg/kg once daily for 6 months. Patients should not be given a 6-month supply to take home. Patients should be monitored every two months at a minimum to check for medication toxicity or development of active TB. Children < 1 year of age should be weighed monthly and the dose of isoniazid adjusted for changes in weight. If a child develops signs and symptoms of active TB while on IPT, then isoniazid should be stopped and the patient should be re-assessed and started on full TB treatment. All HIV-infected children must receive pyridoxine (25 mg/day) for the duration of IPT.

KEY POINTS

- IPT is intended to prevent recent TB infection from progressing to active TB disease and to prevent latent TB infection (LTBI) from reactivating.
- IPT is given for six months after a TB contact.
- If a patient is diagnosed with active TB they need full TB treatment and not isoniazid monotherapy.

TABLE 5.5 IPT durations and recommendations

Contact history?	Age	HIV status	How to rule out active TB	IPT (active TB ruled out)
Yes	0 - 60 months	Negative	History, exam, and available investigations	6 months
Yes	≥ 6 years	Negative	No work-up needed if asymptomatic	Not required
Yes	0 - 2 years	Exposed	History, exam, and available investigations, CXR recommended	6 months
Yes	0 - 2 years	Positive, on ART*	History, exam, and available investigations, CXR recommended	6 months
Yes	> 2 years	Positive, not on ART	History, exam, and available investigations, CXR recommended	IPT until ART is started, minimum 6 months

CONTINUED >

TABLE 5.5 IPT durations and recommendations (CONTINUED)

Contact history?	Age	HIV status	How to rule out active TB	IPT (active TB ruled out)
Yes	> 2 years	Positive, on ART	History, exam, and available investigations, CXR recommended	6 months
No	< 6 years	Negative	No work-up needed if asymptomatic	Not required
No	0 – 2 years	Exposed	No work-up needed if asymptomatic	Not required
No	0 – 2 years	Positive, on ART*	No work-up needed if asymptomatic	Not required
No	> 2 years	Positive, not on ART	No work-up needed if asymptomatic	IPT until ART is started
No	> 2 years	Positive, on ART	No work-up needed if asymptomatic	Not required

*All infected children < 2 years should be on ART per Universal Treatment Guidelines

CHAPTER 6

Tuberculosis Management & Monitoring

6.1 Treatment of TB

The goals of TB treatment are to cure the patient and restore their quality of life, to prevent death from TB, to reduce transmission of TB in the community and to prevent the development and spread of drug-resistant tuberculosis.

KEY POINTS

- Delayed diagnosis and treatment is an important cause of excess mortality particularly among PLHIVs.
- All TB patients should be registered in the district TB register.
- Effective treatment is the most important tool for TB control and depends on:
  - Use of at least three drugs in the initial intensive phase of treatment,
  - Use of two drugs in the continuation phase, and
  - Supporting the patient throughout treatment to achieve good adherence.
- All drugs should be given in the correct dosage (based on regular weight monitoring), taken regularly and for the required length of time.

6.2 Directly observed treatment (DOT)

The treatment supervisor watches the patient swallow the tablets throughout the whole course to treatment. DOT ensures that the TB patient takes the right drugs, in the right doses at the right times. Supervisors or "treatment supporters," can be health workers, volunteers, trained members of the community or guardians.

KEY POINTS

- A patient-centred approach with proper communication between the patient and treatment supporter promotes patient education, good adherence and early identification of challenges with treatment (including side effects and clinical worsening).
- All treatment supporters should be chosen together with and should be acceptable to the patient.
- The need for good adherence and follow-up should be reinforced at all times.
- Patients should be reminded about the duration of treatment and common side effects.

6.3 Treatment of susceptible tuberculosis

Susceptible TB is treated with first-line drugs: Rifampicin (R), Isoniazid (H), Ethambutol (E), Pyrazinamide (Z) and Streptomycin (S). The first four oral drugs (RHZE) come in a fixed dose combination (FDC) tablet. Streptomycin (S) is a first-line injectable drug used in the retreatment regimen and for TB meningitis**.**

TABLE 6.1 Standard regimen for new TB patients (except TB meningitis)

Intensive Phase	Continuation Phase
RHZE daily for 2 months	RH daily for 4 months

Patients should not be admitted in the ward or hospital for administration of TB drugs except where they are too sick or unable to walk. TB drugs should be provided on ambulatory basis in all facilities.

TABLE 6.2 Dosages of Fixed Dose Combination (FDC) Formulations

Adults		
	Initial phase 2 months	**Continuation phase 4 months**
Body weight in kg	[RHZE] [R150/H75/Z400/E275] Number of tablets	[RH] [R150/H75] Number of tablets
30-37	2	2
38-54	3	3
55-74	4	4
75 and over	5	5

CONTINUED >

TABLE 6.2 Dosages of Fixed Dose Combination (FDC) Formulations (CONTINUED)

Children			
	Initial phase 2 months		**Continuation phase 4 months**
Body weight in kg	[RHZ] (R60/H30/ Z150) Number of tablets or sachets	E100 Number of tablets or sachets	[RH] [R60/H60] Number of tablets or sachets
< 7	1	1	1
8-9	1.5	1.5	1.5
10-14	2	2	2
15-19	3	3	3
20-24	4	4	4
25-29	5	5	5

KEY POINTS

- Patient weight should be monitored each month, and doses adjusted if weight changes.
- If the patient continues to lose weight while on treatment, they should undergo a detailed review by a clinician.
- New smear-positive PTB patients treated with first-line drugs should submit a sputum sample for smear microscopy at completion of the intensive phase.
- Xpert MTB/RIF should not be used to monitor response to treatment in TB patients.

6.4 Sputum monitoring by smear microscopy in new PTB patients

New smear-positive cases should submit sputum at 2 months, 5 months and 6 months.

TABLE 6.3 Sputum monitoring in new PTB patients

Month of Treatment					
1	2	3	4	5	6
Intensive phase		Continuation phase			
	♦ If smear-positive, repeat in month 3	♦ If smear positive, obtain culture and DST		♦[a] If smear-positive, obtain culture and DST[b]	♦[a] If smear-positive, obtain culture and DST[b]

Key: ♦ Sputum smear examination

[a] Not necessary if the patient was smear-negative at the start of treatment

[b] Smear- or culture-positive at month 5 or later is defined as treatment failure and requires: (a) re-registration of the patient as a "Treatment Failure"; (b) change to retreatment regimen and (c) sending sputum for Xpert MTB/RIF.

Note: Patients who have a diagnosis of rifampicin-susceptible TB made by Xpert MTB/RIF should be monitored by sputum smear microscopy at 2, 5 and 6 months into treatment.

A positive sputum smear at the end of the intensive phase may indicate one of the following problems:

- The initial phase was poorly supervised;
- Patient adherence to treatment is inadequate;
- The anti-TB drugs are being under-dosed (as may happen if a patient gains weight during the intensive phase);
- There are co-morbid conditions that interfere with treatment response or adherence (e.g., mental illness, ART treatment failure, substance abuse etc.);
- The patient may have drug-resistant TB that is not responding to first-line treatment.

KEY POINTS

- At the end of month 2:
  - Sputum smear-negative: Start continuation phase.
  - Sputum smear-positive: Start continuation phase and repeat sputum smear at the end of month 3.
- At the end of month 3:
  - Sputum smear-negative; keep on with continuation phase.
  - Sputum smear-positive: do Xpert MTB/RIF, culture & DST, consider empirical MDR-TB treatment for a seriously ill patient.
- At the end of month 5:
  - Sputum smear-negative: keep on with continuation phase.
  - Sputum smear-positive: do Xpert MTB/RIF, culture & DST, re-register as Treatment Failure and start on retreatment regimen while awaiting DST results (consider empirical MDR-TB treatment for a seriously ill patient).

6.5 Tuberculous meningitis (TBM)

The regimen for TBM is 2SRHZE/7RH; that is, two months of streptomycin plus FDC RHZE given daily under close supervision followed by seven months of daily RH.

TABLE 6.4 Regimen for tuberculous meningitis

Intensive phase	Continuation phase
SRHZE daily for 2 months	RH daily for 7 months

Corticosteroids should be given along with anti-TB drugs as they have been shown to significantly reduce the risk of death in patients with TB meningitis (see Section 6.8).

6.6 Treatment regimens for patients previously treated for tuberculosis

Previous TB treatment is a strong determinant of drug resistance. It is critical in previously treated patients to detect drug resistance, especially MDR-TB so that an effective drug regimen can be employed. First-line drug regimens are not effective against MDR TB strains and can result in mortality and morbidity, amplification of resistance, and further spread of MDR-TB. The following strategy in previously treated patients in Malawi should be employed:

- The presence of drug-resistance should be determined in all previously treated TB patients at or before the start of treatment.

- Xpert MTB/RIF is the preferred screening method for MDR-TB because of its sensitivity and quick turnaround time. A positive Xpert MTB/RIF in a patient with high risk of MDR-TB (e.g. "failure" of a previous regimen) should lead to empiric MDR-TB regimen. All previously treated patients should submit specimen for culture and DST without necessarily waiting for confirmation of conventional DST.

- When Xpert MTB/RIF results will be delayed (because of transport delays or backlogs):

  – TB patients whose treatment has failed or other patients with high likelihood of MDR-TB should be started on an empirical regimen against MDR-TB. The designing of empirical regimens for MDR-TB is described in Chapter 8.

  – Patients returning after defaulting or relapsing from their first treatment course may receive a retreatment regimen with first-line drugs, **2(HREZ) S/1(HREZ)/5(HRE),** while awaiting DST results (culture or Xpert MTB/RIF). When DST becomes available the regimen should be adjusted if resistance is found. If no resistance is found continue **2(HREZ) S/1(HREZ)/5(HRE).**

TABLE 6.5 Retreatment regimen with first-line drugs for patients previously treated for tuberculosis and low-risk for MDR-TB

Intensive Phase	Continuation Phase
SRHZE daily for 2 months, then RHZE for 1 month	RHE daily for 5 months

Note: All medicines should be given under directly observed treatment (DOT) throughout the whole course of treatment.

KEY POINTS

- The National TB Strategic Plan sets a target of all previously treated patients having access to Xpert MTB/RIF before beginning treatment. The purpose is to identify MDR-TB as early as possible so that appropriate treatment can be given.
- Specimens for culture and drug susceptibility testing (DST) should be obtained from all previously treated TB patients at or before the start of treatment and sent to the Central Reference Laboratory.
- In districts with access to Xpert MTB/RIF, sputum samples should be sent for Xpert MTB/RIF at or immediately before the start of treatment.
- Obtaining specimens for culture and DST or Xpert should NOT delay the start of therapy.

6.7 Sputum monitoring by smear microscopy for retreatment patients receiving the 8-month regimen

Retreatment patients should submit sputum at 3 months, 5 months and 7 months. If the sputum smear is positive at 3 months, send two sputum specimens for culture and DST. In consultation with the NTP, consider starting empiric MDR-TB treatment with second-line drugs for any retreatment case who remains smear-positive at month 5 or 7 while awaiting results of culture and DST/Xpert MTB/RIF or for any seriously ill TB patient suspected of having MDR-TB.

TABLE 6.6 Sputum monitoring of PTB patients receiving the 8-month retreatment regimen with first-line drugs

Month of Treatment							
1	2	3	4	5	6	7	8
Intensive Phase 2SRHZE/1RHZE			Continuation Phase 5RHZE				
		♦ If smear positive, obtain culture and DST		♦ If smear positive, obtain culture and DST[a]			♦ If smear positive, obtain culture and DST[a]

Key ♦ Sputum smear examination

[a] A positive smear- or culture at month 5 or later (or detection of MDR-TB at any point) is defined as treatment failure and necessitates re-registration. MDR-TB should be strongly suspected in any patient who fails a retreatment regimen.

6.8 Use of anti-tuberculosis drugs in special situations

The following special situations require an adjustment of standardised TB regimens.

Pregnancy

- Streptomycin is potentially ototoxic and may cause deafness in babies.
- Streptomycin should not be given in pregnancy.
- Isoniazid, rifampicin, pyrazinamide and ethambutol are safe in pregnancy.
- Pyridoxine supplementation is recommended for all pregnant and breastfeeding women receiving isoniazid.

Oral contraceptives

- Rifampicin reduces the effectiveness of the oral contraceptive pill.
- Health workers should advise patients on TB treatment to use barrier contraception like male or female condoms while on rifampicin.

Renal impairment and renal failure

- Ethambutol and pyrazinamide are cleared by the kidneys and should be reduced to three times per week.
- Streptomycin should be avoided in patients with renal failure or if it must be used, the frequency should be reduced.

TABLE 6.7 Recommended dosages in patients with renal failure

Drug	Dose	Normal frequency	Frequency in renal failure
Pyrazinamide (Z)	25 mg/kg	Daily	3x/week
Ethambutol (E)	15 mg/kg	Daily	3x/week
Streptomycin (S)	15 mg/kg	Daily	2 – 3x/week

Liver impairment and liver failure

- Isoniazid, rifampicin and pyrazinamide are recognised to be hepatotoxic.
- TB patients with active liver disease (i.e., those with jaundice or ascites) should not receive pyrazinamide or rifampicin.
- They should be given 2 months of streptomycin, isoniazid and ethambutol during the intensive phase of treatment, followed by 10 months of isoniazid and ethambutol.
- If the jaundice is acute and severe, then treat initially with only streptomycin and ethambutol.

Epilepsy

- Rifampicin induces liver enzymes that reduce levels of anticonvulsant medications (phenobarbital and phenytoin) in the blood.
- Increase the dose of the anticonvulsant and monitor the patient closely for increasing seizure frequency.

TB/HIV and taking ART

- Rifampicin induces liver enzymes that reduce levels of nevirapine in the blood.
- All HIV-positive TB patients should initiate an efavirenz-based regimen to minimise drug interactions with rifampicin.
- Refer to Chapter 7 for more details on the treatment of TB/HIV.

Corticosteroids and tuberculosis

- Corticosteroids, in conjunction with anti-TB drugs, reduce the risk of death in TB meningitis and TB pericarditis.
- Patients with TB meningitis or TB pericarditis should be given corticosteroids for an initial period of 21 days followed by tapering off by 25% per week over four weeks.
- Either prednisolone or dexamethasone may be used.

TABLE 6.8 Corticosteroid dosing in TB meningitis

Patient category	Corticosteroid	Initial phase dose	Initial phase duration
Children	Prednisolone	2 mg/kg (max 40 mg)	21 days
Adults	Dexamethasone	12 mg per day	21 days
	Prednisolone	60 mg per day	21 days

TABLE 6.9 Prednisolone dosing in tuberculous pericarditis

Patient Category	Days 0 – 28	Days 29 – 56	Days 57 – 70	Days 71 – 77
Adults	60 mg	30 mg	15 mg	5 mg
Children	1 mg/kg	0.5 mg/kg	0.25 mg/kg	0.1 mg/kg

6.9 Management of hospitalised TB patients

Hospitalised TB patients merit a **DAILY** ward round like any other patient. Daily ward rounds should assess for patient symptoms, vital signs, response to therapy, side effects and complications of TB (including anaemia, pleural effusion, respiratory failure, renal failure, hearing loss, cachexia/malnutrition, IRIS, etc.). Patients with tachypnea (respiratory rate > 20 breaths per minute) and hypoxemia (oxygen saturation < 90%) due to PTB, TB pericarditis or pleural TB may require prolonged oxygen therapy until improvement in respiratory status is achieved.

6.10 Default tracking action

During each visit, the health worker should record and confirm the patient's address, other relevant addresses (such as those of family members) and, if possible, the patient's or a family member's mobile phone number in case the need to contact or track the patient arises. Should a TB patient miss a scheduled appointment, action must be taken within three days of the date the patient was due for his or her scheduled appointment or drug collection. It is the responsibility of the District TB Officer (DTO) to ensure a sound default-tracking plan is in place and implemented at district level. The DTO may call upon HSAs, community volunteers and/or other health workers to locate a patient who has defaulted.

6.11 Managing transfer-out and transfer-in patients

When a patient transfers out to another treatment facility, it should be indicated in the district TB register. The date of transfer-out and the new treatment facility must be indicated. Transfer-out forms must accompany the patient and must be sent to the new treatment facility.

A copy of each transfer-out form must be sent to the DTO of the receiving district. A copy of each transfer-out form must be kept at the original treatment unit in a special transfer-out folder. TB patients being transferred out MUST carry their drugs for the remaining period of treatment.

When patients transfer in from another facility, they should be registered in the transfer-in register. The patient's treatment outcome must be entered in the transfer-in register; and results must be communicated to the original treatment unit. Transfer-in registers must be properly filled in. Just like the main register, TB officers must indicate when quarters start and finish. All transfer-in forms must be kept in a special transfer-in folder.

6.12 Recording results of treatment

It is vital for assessing programme performance that accurate recording of treatment outcome results are entered in the TB registers and treatment cards for ALL patients. Treatment cards for patients who have completed treatment, died or defaulted must be collected from health centres. These treatment cards must be kept safely and in chronological order in the TB office.

At the end of treatment, results of chemotherapy should be recorded according to treatment outcome (see Table 6.10).

TABLE 6.10 Definitions of treatment outcomes

Outcome	Definition
Cured	A patient whose sputum smear or culture was positive at the beginning of treatment but is smear- or culture- negative in the last month of treatment and on at least one prior occasion.
Treatment completed	A patient who has completed treatment (with a full course of TB treatment) but does not have a negative smear or culture result from the last month of treatment and at least one prior occasion.
Treatment Failure	A patient whose sputum smear or culture is positive at 5 months or later during chemotherapy. (Of note, also included in this definition are patients found to have MDR-TB at any point during treatment, regardless of whether they were initially smear-negative or -positive.)
Died	A patient who dies for any reason during the course of their chemotherapy.
Defaulted	A patient whose treatment was interrupted for two consecutive months or more.
Transferred out	Patient who has been transferred to another treatment centre and in whom the treatment outcome is not known.
Treatment success	A patient who has been cured or completed treatment, according to the above definitions.

CHAPTER 7

Tuberculosis and HIV

7.1 HIV infection

Infection with HIV leads to destruction of the body's immune system. Persons who are infected with HIV are therefore more prone to TB disease than those without HIV infection. When recognised opportunistic diseases accompany HIV infection, the affected person is said to have AIDS.

7.1.1 THE INTERACTION BETWEEN TB AND HIV

A strong immune system usually prevents the development of TB disease following infection with TB bacilli. HIV reduces the protection provided by the immune system and enables TB bacilli to multiply unchecked, facilitating rapid progression to active TB disease. In Africa, HIV prevalence among tuberculosis patients is approximately 38%, while in Malawi about 64% of TB patients are HIV-positive. HIV-related tuberculosis is associated with poor TB treatment outcomes. It is therefore imperative to rapidly identify and treat TB cases among PLHIV.

7.1.2 IMPACT OF HIV ON TB

High HIV prevalence is associated with an increase in the number of new TB cases. HIV infection increases susceptibility to new TB infections and accelerates the progression from LTBI to active TB disease. In particular, HIV is associated with an increase in smear-negative and EPTB cases.

Smear-negative TB and EPTB are more common in HIV-infected TB patients. Most HIV patients with TB do not have typical TB symptoms (productive, chronic cough etc.). In Malawi, about 41% of all TB cases are smear-negative and 22% are EPTB. HIV-positive TB patients are more likely to develop TB outside of the lungs (EPTB) than similar patients who are HIV-negative. When HIV-positive patients do develop TB in the lungs, the number of bacilli secreted into the sputum is fewer than in HIV-negative patients. This makes diagnosis by conventional microscopy difficult. Studies show that up to 17% of new TB cases are acquired from smear-negative cases. It is important to identify and treat smear-negative cases early in order to break the cycle of TB transmission in the community and health facilities.

HIV infection increases TB-associated morbidity and mortality. HIV-positive TB patients have a higher case-fatality during TB treatment compared with HIV-negative patients. HIV-positive, smear-negative patients and EPTB patients have worse treatment outcomes than in smear-positive TB patients. Adverse reactions to anti-TB drugs are also more frequent in PLHIV compared to the general population, leading to interruptions of treatment and poor outcomes.

TB recurrence rates are higher in HIV-positive patients than in HIV-negative patients. Recurrence of TB may be from reactivation of persistent organisms not killed by previous anti-TB treatment or re-infection due to re-exposure to another infectious person.

MDR-TB has been reported amongst patients with HIV in Malawi. HIV does not itself cause MDR-TB, but it can increase the spread of this condition by increasing susceptibility to infection and accelerating the progression from infection to disease.

7.2 Collaboration and coordination between the TB and HIV programmes

Controlling TB/HIV requires collaboration and coordination between the TB and HIV programmes at all levels. Service integration can include referral of patients and suspects between TB and HIV services, partial provision of joint TB/HIV services, or full integration of the TB and HIV/AIDS clinics (so-called "one-stop shop" or "all services under one roof").

Examples of integrated TB/HIV services include:

- Provider-initiated HIV testing and counselling (PITC) of TB patients,
- Provision of co-trimoxazole preventive therapy (CPT),
- Early initiation of ART in HIV-infected patients with TB,

- Offering of anti-TB drugs and ART in the same room by the same person ("one-stop shop"),
- Screening of all HIV-positive persons for active TB, and
- Provision of isoniazid preventive therapy (IPT) to PLHIV who do not have evidence of active TB.

Please refer to the National TB/HIV Operational Manual for further details.

7.2.1 PROVIDER-INITIATED HIV TESTING AND COUNSELLING (PITC) FOR TB PATIENTS

All TB suspects and patients should be offered HIV testing and counselling by health workers. HIV testing should be carried out if HIV status is unknown, was previously reported as negative in the past 3 months or was refused or opted out of during the patient's previous visit. If a patient reports having been previously tested for HIV but has no documented evidence of this fact, the test should be repeated. All HIV-positive TB patients are entitled to quality HIV treatment, care and support services.

KEY POINTS

- It is important to note that HIV testing in TB patients and suspects is provider-initiated (PITC).
- Health workers should encourage HIV-positive TB patients to bring their partners and small children for HIV testing.

7.2.2 PROVISION OF ANTIRETROVIRAL THERAPY IN HIV-INFECTED TB PATIENTS

Regardless of CD4 count, all TB/HIV co-infected patients should be started on ART **within the first 2 weeks of TB treatment**. If the TB/HIV co-infected patient is clinically stable, ART and TB treatment may be started concurrently on the same day. The ART regimen for TB patients initiating antiretroviral therapy is a combination of tenofovir/lamivudine/efavirenz [TDF/3TC/EFV (Regimen 5A)]. Refer to the 2011 Integrated National PMTCT/ART Guidelines for additional details.

KEY POINTS

- Patients who develop TB while on d4T/3TC/NVP should continue on the same regimen and should be referred to the integrated ART/TB clinic.
- Provision of ART in TB patients co-infected with HIV should be given in an ART/TB integrated approach as stipulated in the National ART/TB SOPs.

7.2.3 PROVISION OF CO-TRIMOXAZOLE PREVENTIVE THERAPY (CPT)

All HIV-positive TB patients should be started on CPT to reduce the risk of death and the occurrence of opportunistic infections. If possible, CPT should be started on the same day that the patient's HIV-positive status is determined. Once CPT is started, it should be given for life.

The following are contraindications to cotrimoxazole:

- Known severe drug reaction to sulphur-containing drugs,
- Severe megaloblastic anaemia or pancytopenia,
- End-stage renal disease.

7.3 Management of HIV-positive patients with active TB

Management of TB in HIV co-infected patients may present challenges related to TB diagnosis, drug-drug interactions, medication side effects and IRIS. The response to treatment may be slow in HIV-positive TB patients, especially when the patients are severely immunocompromised.

7.3.1 IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

An HIV-positive patient's condition could worsen within the first 6 months of starting ART because of IRIS. IRIS is a result of recovery of the body's immune system. There are two common IRIS scenarios:

- An unmasking of an occult OI,
- A paradoxical symptomatic relapse or worsening of a prior infection that was seemingly diagnosed and treated successfully.

Before starting ART, counsel TB patients about the possibility of a temporary worsening of symptoms.

If a patient develops IRIS while on anti-TB treatment and ART, seek the advice of a senior ART provider or medical specialist. There is no need to stop or change TB or ARV treatment. Confirm that the patient is adhering to his or her medication regimen as prescribed. Admit severe cases to hospital.

If treatment with steroids is indicated, give dexamethasone 8 – 16 mg/day (divided into twice daily dosing) or prednisolone 1 mg/kg body weight (once daily) for 14 – 21 days. After 14 – 21 days, rapidly taper the steroids over a 10 – 14 day period while monitoring for recurrence and/or worsening of symptoms.

Consider TB treatment failure or MDR-TB if the patient worsens despite having received one or more months of anti-TB treatment.

KEY POINTS

- Occasionally an HIV/TB co-infected patient may experience a temporary worsening of TB symptoms soon after beginning ART and TB treatment. IRIS should be considered as a potential cause of such clinical worsening.
- Signs and symptoms include: high fever, lymphadenopathy, and worsening CXR findings.
- Other causes of clinical worsening should be ruled out before making a diagnosis of IRIS; these include undiagnosed TB disease, cryptococcal meningitis and Kaposi Sarcoma.
- Patients with advanced AIDS who start ART late are at the greatest risk of developing IRIS.

7.3.2 OVERLAPPING ARV AND TB DRUG SIDE EFFECTS

Concurrent use of ARVs and TB drugs has potential for added toxicity. The most common causes of skin rashes are pyrazinamide, isoniazid and rifampicin. ARVs such as nevirapine and efavirenz are also known to cause skin rashes. These overlapping side effects make it difficult to identify the causative drug when a patient is receiving treatment for both TB and HIV concurrently. Patients on both treatments need a thorough history and clinical assessment to establish which drug is responsible for the side effects.

TABLE 7.1 Drug interactions between ARVs and TB drugs

Drug	Isoniazid	Rifampin	Streptomycin	Ethambutol	Pyrazinamide
TDF	--	--	Renal Toxicity*	--	--
AZT	--	--	--	--	--
3TC	--	--	--	--	--
D4T	Neuropathy*	--	--	--	--
ddI	Neuropathy*	--	--	--	--
EFV	--	--	Skin Rash*	--	Hepatitis*
NVP	Skin Rash*	Hepatitis*	Skin Rash*	--	Hepatitis*
ABC	--	--	--	--	--
LPV/r	--	Increased metabolism of BOTH drugs—major dose adjustment required⋆	--	--	--

Adapted from the *2011 Malawi Integrated Guidelines for the Clinical Management of HIV in Children and Adults.*

* Combination usually does not cause a problem, but vigilant monitoring for increased toxicity required

⋆ Do not combine without seeking specialist advice

CHAPTER 8

Drug Resistant Tuberculosis

This chapter provides the basics in the management of drug-resistant TB (DR-TB). For more information the reader should refer to two national manuals: *Guidelines for the Programmatic Management of Drug Resistant Tuberculosis in Malawi* (revision planned for 2012) and *A Guide for Community-based and Outpatient Care for Drug Resistant Tuberculosis* (1st edition planned for 2012). The former is a clinical care guide and the latter is an implementers guide on caring for the patient at home.

8.1 Definitions

In general, strains of TB can either be susceptible or resistant to anti-TB drugs:

- **Susceptible TB** refers to a tuberculosis strain that is not resistant to any anti-TB drugs.
- **Drug-resistant TB** is confirmed through laboratory tests that show that the infecting isolates of *M. tuberculosis* grow *in vitro* in the presence of one or more anti-TB drugs.

The types of different drug resistance are defined as follows:

- **Mono- or poly-drug resistant TB:** in this guideline we consider mono- or poly-drug resistant TB patients presenting with active TB due to an *Mtb* strain that is resistant to at least H or R but not both at the same time.
- **Multidrug-resistant TB (MDR-TB)** is a form of tuberculosis in which the TB bacilli demonstrates resistance to, at a minimum, the two most powerful drugs used in first-line TB treatment, rifampicin and isoniazid.
- **Extensively drug-resistant TB (XDR-TB)** is MDR-TB plus resistance to any fluoroquinolone, and at least one of the three injectable second line anti-TB drugs (capreomycin, kanamycin or amikacin).

Currently, Malawi does not have the laboratory capacity to diagnose XDR-TB. However, there is an agreement with the Medical Research Council of South Africa to analyse all confirmed MDR-TB samples from Malawi for XDR-TB.

8.2 Extent of drug resistance in Malawi

A nationwide drug resistance survey (DRS) completed in 2011 indicated MDR-TB prevalence of 0.4% among new smear-positive TB patients and of 4.8% among retreatment patients. The NTP has set a target of providing access to DST for ALL previously treated TB patients before beginning retreatment. The purpose is to identify MDR-TB as early as possible so that appropriate treatment can be given.

8.3 Causes of drug resistance

TB drug resistance is a man-made problem arising mainly from inadequate TB therapy caused by some of the factors listed in Table 8.1.

TABLE 8.1 Possible causes of drug resistance

Health care providers *inadequate regimens*	**Drugs** *inadequate supply or poor quality*	**Patients** *inadequate drug intake*
• Inadequate guidelines • Inappropriate guidelines • Poor compliance with guidelines • Poor training • Absence of guidelines • No monitoring of treatment	• Poor quality of drugs • Stock outs of certain drugs • Poor storage conditions • Wrong dosage(s) or combination(s)	• Poor adherence (poor DOT) • Lack of information • Lack of transportation • Adverse or unpleasant side effects • Social barriers

8.4 MDR-TB suspects/risk groups

According to the National DRS, previously treated patients are 12 times more likely to have MDR-TB than new patients.

An MDR-TB suspect is defined as a patient from one of the following risk groups:

- Patients who have had contact with a known MDR-TB patient;
- Contacts of a patient who died while on directly observed TB treatment;
- All patients, including retreatment cases, who remain smear-positive after 3 months of therapy with first-line drugs;
- All patients, including retreatment cases, who remain smear-positive after 5 months of therapy;
- New patients coming from areas with high prevalence of MDR-TB (certain parts of South Africa, Lesotho etc.);
- Patients previously successfully treated for TB;
- Health care workers in hospital/ health facility setting;
- Patients returning after default;
- Any patients in whom there is significant clinical concern for acquired resistance.

When encountering MDR-TB suspects, request the patient to submit sputum for microscopy, Xpert MTB/RIF, culture and DST. Manage patients according to results: All confirmed DRTB patients should be treated according to national guidelines (refer to the *Guidelines for the Programmatic Management of Drug-Resistant TB in Malawi* and the Xpert MTB/RIF Algorithms included in the Annexes).

8.5 Testing for drug resistance

The initial screening test for DR-TB is the Xpert MTB/RIF. If the specimen is RIF resistance positive, culture and DST should be sent to confirm resistance. Treatment of MDR-TB should be started while waiting for confirmation. Sputum specimens should be submitted for Xpert MTB/RIF for all smear-positive and smear-negative MDR-TB suspects in Section 8.4.

Culture and DST should be performed for any sputum sample found to be RIF resistance positive. Culture and DST can also be done when the sputum sample is RIF resistance negative but RIF resistance or other resistance is highly suspected clinically.

8.6 Collecting a sputum specimen for screening with Xpert MTB/RIF and for confirmation of resistance with culture and DST

The following outlines the roles and responsibilities for each member of the team.

Responsibilities of the clinician

- It is the responsibility of the clinician to arrange a screening test for MDR-TB with Xpert MTB/RIF under the indications described above and to follow up on the results with the patient. Screening tests requests with Xpert for DR-TB do not need to go through the DTO.
- For confirmation culture and DST, a sputum specimen requisition form must be completed by the ordering clinician and submitted to the DTO. The form asks for the patient's identifying and clinical information. A copy of the form will accompany the sample to the culture laboratory to link the sample to the patient and to provide a means of reporting the results of culture and DST back to the ordering clinician.

Responsibilities of the DTO

- The DTO should be aware of all Xpert MTB positive/RIF positive specimens and assure that a confirmation culture and DST is sent.
- For culture and DST confirmation, the patient's name, registration number and other vital information must

be entered into the MDR-TB Suspect/ culture and DST Confirmation Register prior to sample transportation.

- Two sputum specimens for culture and DST should be collected in two separate specimen bottles for each patient. Instructions for the collection of a quality sputum specimen apply equally to culture samples as they do samples for smear microscopy (see Section 3.3.1).
- Ideally, specimens should be collected before TB treatment starts or as soon as possible thereafter.
- For culture and DST, the DTO should liaise with the reference laboratory one week after sample collection to confirm successful receipt of the sample by the reference laboratory and again after 8 weeks to request the results of culture and DST if they have not already been communicated.
- It is the responsibility of the DTO and focal TB clinician to follow-up with all patients to communicate culture and DST results and to start patients with positive results on appropriate anti-TB therapy determined by the drug susceptibility pattern.

Responsibilities of the nurse

- In the cases of hospitalised patients or where a DTO is not available, the ward nurse or TB focal nurse should distribute sputum collection bottles and collect sputum specimens from the patients (see Section 3.3.1).

Responsibilities of laboratory personnel for culture and DST confirmation

- Ensure that screw caps are fixed tightly to prevent leakage of sputum during transportation.
- Ensure the specimen bottles are properly labelled with the patient's name, date and suspect/culture registration number.
- Store sputum awaiting culture securely under refrigerated conditions (between 2 – 8° C—do NOT freeze) and away from sunlight while awaiting transportation to the referral laboratory.
- Pack sputum specimens in an NTP/CRL-approved cooler box along with the corresponding specimen request forms. The transport/cooler box must be leak-proof and durable and have space to hold culture and DST laboratory request forms. Laboratory personnel should ensure that specimens for culture and DST reach the TB Reference Laboratory within 4 days of collection. To do so, laboratory personnel should deliver sputum specimens to the approved specimen courier service, e.g. AXA.

8.7 Treatment of multidrug-resistant TB.

Multidrug-resistant TB in Malawi is treated with second-line TB drugs for a minimum period of 24 months. The standardised treatment regimen comprises 6Cm (or Km)-Lfx-Eto-Cs-Z/18Lfx-Eto-Cs. Drugs used in the standardized treatment of drug-resistant TB are summarised in Table 8.2. Alternatives whose indications are mentioned in the Malawi DR-TB guidelines are also mentioned in Table 8.2.

TABLE 8.2 Drugs used in the standardized treatment of MDR-TB

First-line oral agents	Pyrazinamide (Z)
Injectable agents	Capreomycin (Cm) *Alternatives:* Kanamycin (Km), Amikacin (Amk)
Fluoroquinolones	Levofloxacin (Lfx) *Alternatives:* Moxifloxacin (Mfx)
Second-line oral bacteriostatic drugs	Ethionamide (Eto), Cycloserine (Cs) *Alternatives:* Prothionamide (Pto), P-aminosalicylic acid (PAS)

Where standardised treatment has failed or the drugs in the standardized regimen are not indicated (due to resistance or adverse effects), the reader should refer to the Malawi DR-TB

guidelines. Other drugs including p-aminosalicylic acid (PAS), Linezolid (Lzd), clofazimine (Cfz), Amoxycilin/Clavulanate (Amx/Clv) or others may be needed.

MDR-TB is managed under a community- and outpatient-based strategy where patients receive treatment from health workers/treatment supporters in their homes and undergo longitudinal clinical follow-up at zonal DR-TB Referral Clinics.

For more information on the management of MDR-TB, please refer to the *Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis in Malawi* and the accompanying *Guidelines for the Community-based and Outpatient Care of MDR-TB*.

The following IC measures are recommended in the care of all patients with MDR-TB:

- Isolation for all hospitalized patients with MDR-TB;
- Use of surgical masks by the patients in the presence of others;
- Use of N95 masks by health workers and visitors, where possible;
- Allowance of adequate ventilation in the patient or clinical encounter room and, where possible, placement of patients in rooms with abundant sunlight; and
- Restriction of patient movement—until the patient is documented to be doing well on treatment the patient should voluntarily refrain from visiting indoor spaces where others could be newly exposed to the resistant TB.

8.8 Actions of the National TB Programme to combat drug resistance

The NTP has endeavoured to control the spread of MDR-TB in Malawi through the following actions summarised below:

- Training both government health workers and private practitioners;
- Educating the public on TB treatment adherence;
- Monitoring first- and second-line drug consumption and conducting drug audits;
- Conducting surveillance of drug resistance;
- Taking serious disciplinary action regarding anti-TB drug theft;
- Preventing vendors, shopkeepers and health personnel from selling anti-TB drugs;
- Restricting use of anti-TB drugs; and
- Finding cases of MDR-TB and promptly putting them on effective therapy, one of the most effective ways to prevent MDR-TB from spreading.

CHAPTER 9

Management of Complications

9.1 Management of complications

The management of common TB-related complications are outlined in Table 9.1.

TABLE 9.1 TB-related complications

PTB	
Complication	**Management**
Haemoptysis (coughing up blood)	Admit patient to hospital for oxygen, blood transfusion and intubation if bleeding is severe. Protect the non-bleeding lung by placing the side of the suspected site of bleeding in a dependent position. Order chest x-ray to rule out potentially treatable conditions such as invasive aspergillosis or bronchiectasis.

CONTINUED >

TABLE 9.1 TB-related complications (CONTINUED)

PTB (CONTINUED)	
Complication	**Management**
Pleural effusion or empyema	This may subside with TB treatment alone but sometimes drainage is necessary to relieve symptoms of dyspnoea. All empyema should be drained.
Spontaneous pneumothorax	Admit patient to hospital for placement of a chest tube and drainage with an underwater seal.
EPTB (complications vary depending on the site of the disease)	
Complication	**Management**
Paraplegia (may be due to spinal TB)	Refer the patient to the hospital Surgery may be needed
Cranial nerve damage (due to TB meningitis)	High doses of steroids (see Table 6.8)
Cold abscesses and suppurating fistulae	Drainage of abscesses

CONTINUED >

TABLE 9.1 TB-related complications (CONTINUED)

EPTB (CONTINUED) **(complications vary depending on the site of the disease)**	
Complication	**Management**
Heart failure (due to pericardial effusion)	High doses of steroids (see Table 6.8) Cardiac tamponade (i.e. distress associated with shock) may necessitate pericardial aspiration by an experienced clinician.
Respiratory failure (due to pleural effusion)	Drainage (if difficulties in breathing)

9.2 Side effects of anti-TB drugs

Side effects of anti-TB drugs should be looked for and treated. Some side effects can be hazardous for the patient's health or may force the patient to stop treatment. In general, a patient who develops a minor adverse side effect should continue the TB treatment and be given symptomatic treatment. If a patient develops a severe side effect, the responsible drug (or the entire regimen if the culprit drug cannot be identified) should be stopped and the patient should be referred to the district hospital. Common side effects are listed in Table 9.2.

TABLE 9.2 Symptom-based approach to managing side effects of anti-TB drugs

Side effects	Drug(s) responsible	Management
Major: Stop responsible drug(s) and refer to clinician urgently		
Skin rash with or without itching	S, H, R, Z	Stop anti-TB drugs and refer to hospital
Deafness (no wax on otoscopy)	S	Stop streptomycin and refer to hospital
Dizziness (vertigo and nystagmus)	S	Stop streptomycin and refer to hospital
Jaundice (other causes excluded), hepatitis	H, Z, R	Stop anti-TB drugs and refer to hospital
Confusion (suspect drug-induced acute liver failure if there is jaundice)	Most anti-TB drugs	Stop anti-TB drugs and refer to hospital
Visual impairment (other causes excluded)	E	Stop ethambutol and refer to hospital
Shock, purpura, acute renal failure	R	Stop rifampicin and refer to hospital
Decreased urine output	S	Stop streptomycin and refer to hospital

CONTINUED >

TABLE 9.2 Symptom-based approach to managing side effects of anti-TB drugs (CONTINUED)

Side effects	Drug(s) responsible	Management
Minor: Continue anti-TB drugs, check doses		
Anorexia, nausea, abdominal pain	Z, R, H	Give drugs with small meals or just before bedtime; Advise patient to swallow pills slowly with small sips of water; If symptoms persist or worsen, refer to hospital.
Joint pains	Z	Non-steroidal anti-inflammatory (e.g. brufen) or paracetamol
Burning/numbness in the hands/ feet	H	Pyridoxine 50–75 mg daily
Orange/red urine	R	Reassure, counsel patients before starting treatment

Further details about common adverse effects associated with the first-line anti-TB drugs and their respective management are provided below.

STREPTOMYCIN (S)

Minor side effects include:

- Local reaction at injection site, including sterile abscess;
- Numbness around the mouth;
- Tingling sensation soon after the injection.

Major side effects include:

- Cutaneous hypersensitivity;
- Anaemia, thrombocytopenia and agranulocytosis;
- Vestibular and auditory nerve damage, including that to the foetus;
- Renal damage.

Adverse effect management:

Damage to the vestibular and auditory nerves usually occurs in the first 2 months and is manifested by ringing in the ears, giddiness, ataxia and/or deafness. Vestibular and auditory nerve damage are dose and age related. Persons weighing less than 55 kg and those aged ≥ 45 years should have the dose reduced to 0.75 g. The condition is reversible if the drug dosage is reduced by 0.25 g. If the above reactions are severe, the drug should be stopped.

ISONIAZID (H)

Major side effects include:

- Skin rash
- Hepatitis
- Peripheral neuropathy (paraesthesia, numbness and limb pains)

Rare side effects include:

- Convulsions
- Optic neuritis
- Pellagra
- Arthralgia
- Anaemia
- Agranulocytosis
- Lupoid reactions

Adverse effect management:

Vitamin B6 (pyridoxine) 10 mg/day or vitamin B complex functions to prevent peripheral neuropathy. Pyridoxine 10 mg/day is especially useful in HIV-infected patients because of their added risk of HIV-related peripheral neuropathy. For established peripheral neuropathy, pyridoxine should be given at larger doses of 50 – 75 mg/day.

RIFAMPICIN (R)

Major side effects include:

- Gastrointestinal reactions
- Hepatitis
- Generalised cutaneous reactions
- Thrombocytopaenic purpura (TTP)

The gastrointestinal symptoms such as anorexia, nausea, abdominal pain and vomiting occur soon after administration and can last several hours. Patients should be warned that rifampicin colours urine, tears and sweat red or orange.

Rare side effects include:

- Osteomalacia
- Pseudomembranous colitis
- Pseudoadrenal crisis
- Acute renal failure
- Shock

Adverse effect management:

For serious side effects such as TTP, shock, acute renal failure, or haemolytic anaemia, the drug must be stopped immediately and never administered to the patient again.

PYRAZINAMIDE (Z)

Major side effects include:

- Arthralgia
- Hyperuricaemia
- Hepatitis

Rare side effects include:

- Gastrointestinal reactions
- Cutaneous reactions
- Sideroblastic anaemia

Adverse effect management:

Pyrazinamide may cause high concentrations of uric acid (i.e. hyperuricaemia), which can lead to gout (swollen and tender joints). For joint involvement, simple treatment with ibuprofen usually minimises the symptoms. For more severe joint involvement, indomethacin may be used. If frank gout occurs, then treatment with allopurinol may be required after the acute episode resolves.

ETHAMBUTOL (E)

Major side effects include:

- Visual impairment, including blindness, from optic (retrobulbar) neuritis
- Peripheral neuritis

Rare side effects include:

- Generalised cutaneous reactions
- Arthralgia

Adverse effect management:

Ethambutol may produce impairment of vision, a decrease in visual acuity and red-green colour blindness; however, the toxicity is dose dependent and rarely occurs when 15 mg/kg body weight is given or 25 mg/kg body weight is given three times weekly. All patients should be warned that if visual symptoms occur, they should go to the nearest health facility for clinical evaluation.

For visual problems, an ocular examination should be undertaken. If in doubt, the drug should be stopped. Impaired vision usually returns to normal within a few weeks of stopping the drug.

9.3 Cutaneous and generalised hypersensitivity reaction skin eruptions

If a patient complains of itching without a rash, give anti-histamines. If a rash develops, then all treatment should be stopped because of the risk of precipitating a severe reaction. If the rash is severe, or there is evidence of mucosal involvement or hypotension, corticosteroid treatment (1 mg/kg prednisolone) should be instituted. The amount of prednisolone is gradually reduced in the following days according to the patient's response. In patients with severe reactions, anti-TB treatment sometimes has to be stopped for 3-4 weeks.

Re-introduction of anti-TB drugs

Once the reaction has subsided, anti-TB drugs are reintroduced sequentially according to Girling's standard guidelines using increasing challenge doses (see Table 9.3). First, see if the patient tolerates a full dose of isoniazid before adding rifampicin, then evaluate if the patient tolerates a full dose of rifampicin before introducing pyrazinamide, and so on.

TABLE 9.3 Challenge doses

Drug	Day	Dose 1	Dose 2	Dose 3
Isoniazid (H)	1	50 mg		
	2		300 mg	
	3			300 mg
Rifampicin (R)	4	75 mg		
	5		300 mg	
	6			Full dose
Pyrazinamide (Z)	7	200 mg		
	8		800 mg	
	9			Full dose
Ethambutol (E)	10	100 mg		
	11		400 mg	
	12			Full dose
Streptomycin (S)	13	125 mg		
	14		500 mg	
	15			Full dose

The drugs at the top of the table are the least likely to cause a reaction, and should be reintroduced first. Those at the bottom of the table are most likely to cause a reaction. If the initial cutaneous reaction was severe, smaller initial challenge doses should be given, approximately 1/10 of the doses shown for Day 1. If a patient is recommenced on an adequate anti-tuberculosis treatment regimen (e.g. isoniazid, rifampicin and pyrazinamide), then re-challenging with the implicated drug (e.g. streptomycin) is not advisable.

9.4. Drug-induced hepatitis

Mild, symptomless increases in serum liver transaminases occur during the early weeks of treatment. There is no need to interrupt or change treatment unless there is anorexia, malaise or vomiting or clinically evident jaundice with hepatic enlargement. Clinical features of concern include protracted vomiting, mental status changes and signs of bleeding—these all suggest impending acute liver failure.

If jaundice or any of the clinical features suggestive of acute liver failure develops, all drugs must be stopped until the jaundice or hepatic symptoms have resolved and the liver function tests have reverted to normal. If liver function tests cannot be measured, then it is advisable to wait an extra two weeks after the jaundice has disappeared before recommencing anti-TB therapy.

Once the drug-induced hepatitis has resolved, the drug regimen can be re-introduced, although it is safer to avoid pyrazinamide. Therefore, in the initial phase, a regimen of isoniazid, rifampicin and ethambutol could be used, followed by rifampicin and isoniazid in the continuation phase. If there has been severe hepatitis; however, it is probably safer to use the previous standard regimen of streptomycin, isoniazid and ethambutol.

Severely ill patients with TB who develop drug-induced hepatitis should have the drug regimen stopped. If it is felt that anti-TB treatment should continue, then interim therapy may be started with streptomycin and ethambutol.

CHAPTER 10

Health Promotion

10.1 TB health promotion and communication

Health promotion and communication are key contributors to the NTP's goals. These tools are used across all aspects of TB control, from case finding to treatment. Advocacy is used to make sure that TB services are a consistent priority at every level and that resources are available and allocated accordingly. Case finding requires that health workers and the community be aware of the signs and symptoms of TB and that TB suspects be able to easily access TB diagnostic services. Health promotion enhances early case detection and treatment with all the benefits these confer to improving treatment outcomes.

Health workers attending to patients at outpatient departments in every health delivery setting should be very familiar with TB as a disease as well as common TB diagnostic procedures. Health workers should ensure that frequent health education sessions are conducted in all OPD departments by the District TB Officer, focal clinician, focal nurse or the Health Education Officer.

Communication devices such as TVs and radios can supplement the information provided during health education sessions. Health education drama groups, available at the hospitals, can also be used to provide TB information whilst the patients are waiting for a diagnosis.

The Information, Education, and Communication (IEC) Officer, in coordination with the TB Officers, is charged with the responsibility to develop a list of topics or themes for the routine health education sessions performed at the hospital.

TB education should start immediately after a suspect is diagnosed with TB. The TB Officers, the TB focal nurse, the TB focal clinician and the DTOs are responsible for educating patients about TB. Each health worker should exhibit exemplary interpersonal skills and form a strong patient-provider relationship in order to promote patients' adhering to anti-TB treatment and following medical advice.

10.2 Key TB and TB/HIV messages

- TB is a disease caused by germs.
- TB is spread to others through the air when someone with TB coughs or sneezes.
- People with TB have many different symptoms. The major symptom of TB in the lungs is cough.
- It is important for TB patients to take all the prescribed TB drugs as scheduled for the whole duration of treatment to

avoid the disease becoming resistant to anti-TB medicines.

- To prevent the spread of TB, it is important for patients
  - to seek out TB services as soon as they notice symptoms,
  - take all medicines as prescribed for the entire duration of treatment in order to be cured of TB, and
  - always cover their mouths when coughing or sneezing.
- Each patient has a choice for their DOT provider and may receive DOT through the nearest hospital or health centre or through a guardian after hospital treatment.
- All smear-positive patients must have follow-up sputum smear examinations after 2 and 5 months of anti-TB treatment.
- Apart from ensuring the best chance of treatment success, adhering to therapy for the entire treatment period prevents the development of drug-resistant TB strains, which are much more difficult to treat than the usual form of TB.
- TB patients on TB treatment should report any adverse drug reactions to a health worker at the nearest health facility.
- It is important for TB patients to eat a well balanced diet and to avoid alcohol and tobacco.
- TB patients can have sex if they so wish while on TB treatment.

In addition to the above key messages, TB patients must be given information about and be tested for HIV:

- Some people with TB have HIV as well. It is important to get tested for HIV.
- TB is curable even when the patient is co-infected with HIV. Benefits of testing for HIV include ART and co-trimoxazole preventive therapy for those TB patients found to be HIV positive.

All HIV-positive TB patients should be referred to the ART clinic immediately after diagnosis of HIV infection. The DTO should discuss HIV testing with all TB patients who have not been tested for HIV in the last 3 months. All HIV-positive patients at the HTC, ART and HIV care clinics should be screened for TB through the use of a 4-symptom questionnaire. Apart from at the TB ward and TB office waiting area, IEC on TB should also be given at the OPD, HTC, ART and maternal and child health (MCH) clinics.

Having adequate and correct information about TB is important since health workers are the primary sources of TB information for TB suspects, patients and the community. Provision of TB information to TB patients should be done regularly. IEC materials should supplement facility-based health talks.

After the one-on-one interaction with a newly-diagnosed TB patient, the DTO should make sure that TB education continues through sessions done on all the TB wards twice weekly. To supplement information dissemination, the DTO should routinely invite different ex-TB patients to provide moral support to current patients. Former patients may serve as an important source of information for current patients by sharing their

experiences living with and overcoming the disease.

The TB ward chairperson should be provided with information on TB and should be counselled on how to provide this information to fellow patients and their guardians on a daily basis.

The DTOs should make sure that they always coordinate with the district IEC officers when conducting health education sessions with all the target groups.

Annexes

ANNEX 1 Core TB programme indicators

Indicator		Target
DOTS expansion and enhancement		
1. Percentage of laboratory diagnosed smear-positive cases started on TB treatment		95%
2. Treatment success rate among smear positive TB cases		92%
3. Treatment completion rates among smear negative PTB and EPTB		75%
4. Cure rate among sputum smear positive TB cases		75%
5. Smear Conversion Rate	at 2 months	> 80%
	at 3 months	> 80%
6. Death rates among smear positive TB cases to below		< 15%
7. Default rate and transfer out rate		1%

CONTINUED >

Indicator	Target
TB/HIV	
8. Percentage of TB patients who know their HIV status	100%
9. Percentage of HIV positive TB patients treated with ART	85%
10. Percentage of HIV positive TB patients started on ART within 2 weeks of starting TB treatment	70%
11. Proportion of HIV positive TB patients enrolled on CPT	100%
12. Percentage of TB patients who are HIV positive starting cotrimoxazole preventive therapy within 2 weeks of starting TB treatment	> 95%
13. Percentage of PLHIV attending HIV care services who were enrolled on IPT, among those eligible	100%

CONTINUED >

ANNEX 1 Core TB programme indicators (CONTINUED)

Indicator	Target
PMDT	
14. Percentage of AFB microscopy laboratories using LED fluorescent microscopes	40%
15. Percentage of laboratories with Xpert MTB/RIF machines	20%
16. Patients on retreatment who have sputum examined for culture and drug sensitivity	80%
17. Number of confirmed cases of MDR-TB enrolled on treatment according to international guidelines	96%
18. Percentage of previously treated TB patients tested for resistance to first-line drugs	100%
19. Percentage of cases with confirmed MDR-TB started on appropriate treatment in accordance with national guidelines	100%
20. MDR-TB cases on MDR-TB treatment regimen cured	75%

CONTINUED >

Indicator	Target
Health system strengthening	
21. Bacteriological coverage	100%
22. Sputum result turnaround time (TAT): 80% of facilities with a TAT	< 48 hours
23. Percentage of smear-positive PTB cases start treatment within 2 months of onset of cough	70%
24. Percentage of PTB suspects with the recommended number of sputum specimens submitted	90%
25. Percentage of smear-positive PTB patients with follow-up smears done by the end of treatment	95%

Form 1: Sputum Examination Request Form

Sputum Smear Examination Request Form

Requesting facility: _____ Date: _____

Name of patient: _____ Age _____ Sex: ☐ M ☐ F

Complete address: _____

_____

Date Sputum collected: _____

Reason for sputum smear microscopy examination: ☐ Diagnosis **OR**

☐ Follow-up: ☐ 2 months; ☐ 5 months; ☐ 6 months

TB Registration No.: _____

Name and signature of person requesting examination: _____

_____

Results (to be completed in the laboratory)

Laboratory Serial No.:_____ Date received in lab: _____

Date collected[1]	Sputum specimen	Visual appearance[2]	RESULTS				
			NEG	POSITIVE			
				1-9 (scanty)	(+)	(++)	(+++)
	1						
	2						

[1] *To be completed by the person receiving the sample*

[2] *Blood-stained, muco-purulent, saliva*

Examined by (Name): _____ Signature _____ Date _____

Tuberculosis Laboratory Register

Lab Serial No.	Date			Name (in full)	Sex (M/F)	Age	Complete Address	Name of Requesting Facility	Reason for Examination		Results of Smear Microscopy Examination*		TB Registration No.	Remarks
	Collected	Received	Examined						Diagnosis	Follow Up	1	2		

* Indicate the result for each specimen. (NEG): 0 AFB/100 fields; (1-9): exact number if 1 to 9 AFB/100 fields; (+): 10-99 AFB/100 fields; (++): 1-10 AFB/field; (+++): > 10 AFB/field

Form 3: Request for Culture and Sensitivity Tests

Request for Culture and Sensitivity Tests

Facility: _____ District: _____
Address: _____
Name:_____ Age (yrs):_____ Sex:_____
Patient TB Register Number: _____ Date treatment started: _____
Date specimen collected: _____ Date specimen sent to CRL: _____
Date specimen received by CRL: _____
District and laboratory serial number: _____
Sputum taken at: ☐ Month 0 ☐ Month 2 ☐ Month 5 ☐ Month 8
☐ Other (specify):_____
Type of Patient: ☐ New ☐ Relapse ☐ Failure ☐ Return after default ☐ Chronic excretor
Site: ☐ Pulmonary ☐ Extra-pulmonary (specify):_____
Specimen: ☐ Sputum ☐ Other (specify: _____
Local laboratory smear result: 1st:_____ 2nd:_____ Specimen: _____

Chemotherapy	Date from	To	Chemotherapy	Date from	To
Isoniazid			Cycloserine		
Streptomycin			Ethionamide		
Rifampicin			Ofloxacin		
Pyrazinamide			Levofloxacin		
Ethambutol			Para-aminosalicylic acid		
Capreomycin			Other:		

Person (officer) requesting examination (name):_____

Reference laboratory results
Reference laboratory serial number: _____

Microscopic Examination

Specimen	Neg	1-9 (scanty)	1+	2+	3+
1					
2					

Culture Results

Specimen	Neg	≤ 50 colonies actual count	> 50 – 100 col 1+	> 100 – 200 col 2+	> 200 col 3+
1					
2					

Comments: _____

Sensitivity Testing Results

Drug	Date	Sensitive	Resistant	Drug	Date	Sensitive	Resistant
Isoniazid				Kanamycin			
Streptomycin				Cycloserine			
Rifampicin				Ethionamide			
Pyrazinamide							
Ethambutol							

Name: _____ Signature:_____ Date:_____
The Central Unit will send the blue copy with result of culture and sensitivity tests to the treating physician, and the pink copy with result of culture and sensitivity tests to the Zonal TB Officer

Form 4: Laboratory Request Form for Xpert MTB/RIF Test

Laboratory Request Form for Xpert MTB/RIF

Health Facility: _____ Department: _____

Name of Patient: _____ Address: _____

Age: _____ Sex: M / F

Date Collected: _____/_____/ 20_____

Reason for Xpert MTB/RIF (Please mark "X" in the appropriate box):

New suspect—Outpatient	
New suspect—Hospitalised	
Relapse	
Failure	
Return after default	
MDR-TB suspect	

HIV Status (Please mark "X" in the appropriate box):

Pos	Neg	Unknown

Results of smear examination (if any): (Please mark "X" in the appropriate box)

Smear-pos	Smear-neg	Not Done

Name of person requesting Xpert_____ Signature: _____

RESULTS (section to be completed by laboratory)

Laboratory register number: _____

Xpert MTB/RIF results (please mark "X" next to the reported result):

MTB:	MTB detected	MTB not detected
RIF Resistance:	RIF Resistance detected	RIF Resistance not detected

Date _____ Examined by (Name) _____

(Signature)_____

Form 5: Laboratory Register for Xpert MTB/RIF Test

Laboratory Register for Xpert MTB/RIF

Lab serial No	Date specimen tested	Name (Full)	Age	Complete Address	Requesting Facility	M	F	Indication for Xpert MTB/RIF Please tick one box below (√)				Xpert MTB/RIF Result Please tick one box below (√)				
								Retreatment case/MDR suspect	TB Suspect-Hospital	TB Suspect-New	Other	MTB Pos	MTB Neg	RIF Resistance Detected	RIF Resistance NOT Detected	Remarks
TOTALS																

Chronic Cough Register

Date	Serial No	Name	Age	Sex		Complete Address	Date Sputum collected	Date sputum sent to Lab	Date result received	Microscopy result		Xpert sample collected		Xpert Result		HIV Result*		
				M	F					1st	2nd	Y	N	MTB Detected	MTB Not Detected	Pos	Neg	ND

* Pos = Positive; Neg = Negative; ND = Not done. Documented evidence of HIV test performed during or before TB treatment is reported here.

Form 7: Contact Tracing Register

Year_____ **Register of TB Contacts** **Name of facility_____**

Name of index case	MDR TB? (Yes/No)[1]	TB Register No.	Name of contact[2]	Age	Sex	Address of contact	Date of screening	Method of screening[3]	Result of screening[4]	Remarks

[1] Contacts of MDR TB cases should submit sputum for culture and DST in addition to smear microscopy or GeneXpert

[2] List all contacts under the name of the index case. Definition of contact: child 5 years or less with pulmonary tuberculosis and symptomatic adult in close proximity, e.g. household or workplace (index case).

[3] Method of screening: PE = Physical Examination; R = Radiological, S = Sputum, O = Other

[4] TB positive or TB negative

Form 8: TB Patient Identity Card (FRONT)

TB Patient Identity Card

Name: _____ TB Registration No.:_____

Address:_____ Date of registration: _____

Sex: ☐ M ☐ F Age: _____ Date treatment start: _____

Health facility: _____

Supporter (name and address):_____

Sputum smear microscopy				Weight (kg)
Month	Date	Lab No.	Result	
0				
2/3				
5				
6/8				
Xpert				

Disease site (check one)
☐ Pulmonary ☐ Extra-pulmonary (specify) _____

Type of patient (check one)
☐ New ☐ Treatment after default
☐ Relapse ☐ Treatment after failure
☐ Transfer in ☐ Other (specify) _____

CPT ☐ Y ☐ N **ART** ☐ Y ☐ N **ART Reg. No**._____

I. INITIAL PHASE

CAT (I, II): ☐

(RHZE)	S	Other

Drugs and dosage:

II. CONTINUATION PHASE

(RH)	(RHE)	Other

Drugs and dosage:

Form 8: TB Patient Identity Card (BACK)

Appointment dates: _____

_____

_____

_____

_____

_____

Kumbukirani izi

1. Samalani kadi yanu.

2. Mungathe kuchira ngati mumwa mankhwala mwa ndondomeko.

3.TB itha kufalikira kwa anthu ena ngati simumwa mankhwala anu mwandondomeko.

Form 9: IPT Identification Card (FRONT & BACK)

IPT IDENTITY CARD

District_____ Health Unit_____

IPT Registration No _____

Name of IPT Client_____ Age_____ Sex _____

Address _____

_____

_____

Reason for IPT (tick one): ☐ Contact with PTB

☐ Other

Date IPT started _____

Date IPT to be completed_____

IPT Identity Card (reverse)

Date IPT given	Number of tablets	Date of next appointment

IPT Monitoring and Evaluation Register

Reg. No.	Date IPT started	Name of IPT client	Age	Sex	Physical address (in full)	District TB No. (index case)	HIV status (tick)*		
							Pos	Neg	ND

* **Pos** = Positive; **Neg** = Negative; **ND** = Not done.

IPT Monitoring and Evaluation Register

Number of month IPT given/received (tick)						IPT Outcome*				Remarks
1	2	3	4	5	6	T/C	Def	D	T/O	

* **T/C** = IPT completed (i.e. taken for at least 6 months); **Def** = Defaulted; **D** = Died; **T/O** = Transferred Out

MDR-TB Suspect Register

District: _____ **Facility:** _____ **Zone:** _____ **Quarter:** _____ **Year:** _____

Date	TB Reg No.	Name	Age	Sex (M/F)	Address/Phone	Type of suspect*	HIV status	Culture and DST (results)	Comments

* Type of suspect: **R**= Retreatment; **F1**= Failure of Category I; **F2**= Failure of Category II; **RAD**= Return after default; **C**= MDR-TB Contact; **O**=Other

Total number of suspects (in quarter):_____ Total DST done (in quarter):_____

Form 12: Category IV Register (LEFT)

MDR-TB Register

Unique MDR-TB Reg. No.	Date	Patient name	Age	Sex	Address	District TB Reg. No.	Site of disease	Type of case[1]	Results of drug susceptibility testing (DST)[2]								Date of DST report
									H	R	E	S	Other	Other	Other	other	

[1] **N** = New, **R** = Retreatment, **F1** = Failure Category I, **F2** = Failure Category II, **RAD** = Return after default, **O** = Other, [2] **R** = Resistant, **S** = Sensitive

Form 12: Category IV Register (RIGHT)

MDR-TB Register

19		20		21		22		23		24		25		26		27		28		29		30		31		32		33		34		35		36		Outcome
S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	

S = Smear (**NEG**: 0 AFB/100 fields; **1-9**: 1 to 9 AFB/100 fields; **+**: 10-99 AFB/100 fields; **++**: 1-10 AFB/field; **+++**: > 10 AFB/field)
C = Culture (**P** = Positive; **N** = Negative; **Co** = Contaminated; **L** = Leaked specimen)

District Quarterly Report on TB Case Registration (All Cases)

Name of Reg. Centre: _____ Facility:_____	Patients registered during _____ quarter of year_____
Name of TB Coordinator:_____ Signature: _____	Date of completion of this form: _____

Pulmonary Tuberculosis									Others						Total		
Age category (in years)	Smear-positive pulmonary TB				Smear-negative pulmonary TB		Extra-pulmonary TB		Treatment after default		Treatment failure		Recurrent				
	New cases		Relapses														
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	All
0-4																	
5-14																	
15-24																	
25-34																	
35-44																	
45-54																	
55-64																	
65+																	
Total																	

District Quarterly Report on TB/HIV Case Finding

DISTRICT _____ FACILITY _____

ZONE _____ PATIENTS REGISTERED DURING

NAME OF TB OFFICER _____ _____ QUARTER OF THE YEAR _____

SIGNATURE _____

AGE BREAK DOWN	NEW CASES		RETREATMENT		SMEAR NEGATIVE		EXTRA PULMONARY		OTHER					
									Treatment after default		Treatment after failure		Recurrent	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
0-4														
05-14														
15-24														
25-34														
35-44														
45-54														
55-64														
65+														

Monthly Anti-TB Drug Balance Record Book

Health Unit: _____ Name of Drug: _____ Year: _____

No.	Name of Patient	Reg No.	Days Regimen	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Total Monthly Consumption:															
Drug Received:															
Balance at the end of month:															
Pot Pill Count (PPC):															
Differences:															

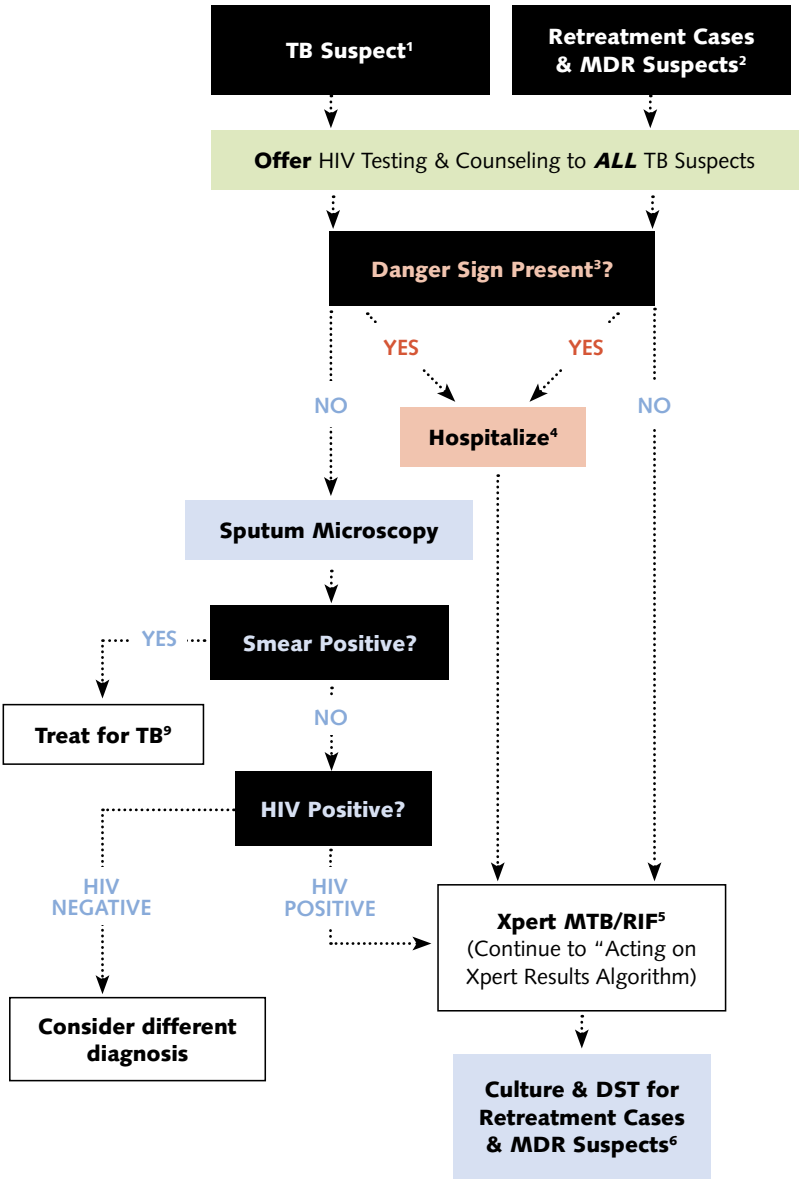
Form 16: Anti-TB Drug Order Book

Anti-TB Drug Order Book

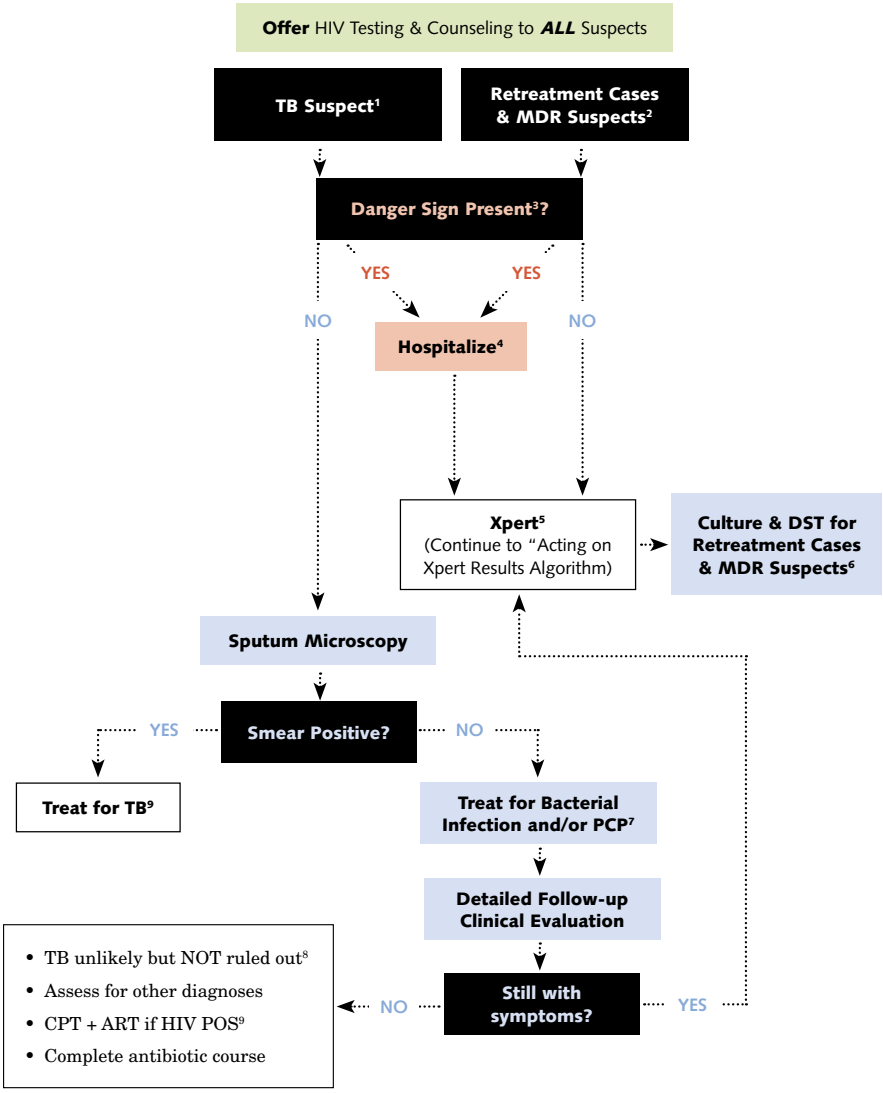
Name of Unit: _____ Date: _____

Name of Drug	Drugs on Hand	Drugs Ordered	Drugs Issued	Total	Name & Signature (Ordering Officer)	Name & Signature (Issuing Officer)
First-line Anti-TB Drugs						
$RHZE_{150/75/400/275}$						
$RH_{150/75}$						
$RHE_{150/75/275}$						
$RHZ_{60/30/150}$						
$RH_{60/60}$						
E_{100}						
H_{100}						
H_{300}						
Z_{400}						
E_{400}						
S_{1g}						
Second-line Anti-TB Drugs						
Capreomycin $_{1g}$						
Cycloserine $_{250}$						
Ethionamide $_{250}$						
Levofloxacin $_{250}$						
$Linezolid_{250}$						
$Clarithromycin_{250}$						
Para-aminosalicylic acid (PAS) $_{50g}$						
$Kanamycin_{1g}$						

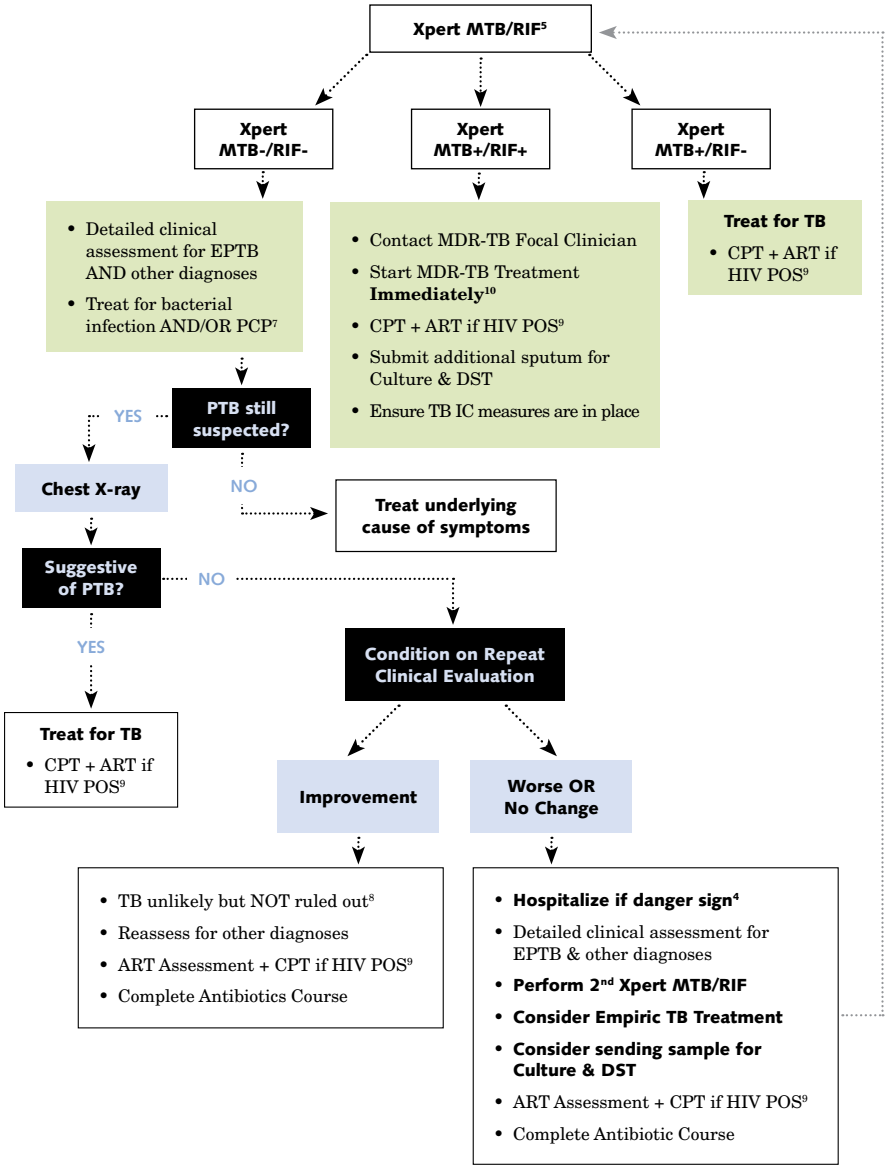
ANNEX 3 Facility with Xpert MTB/RIF—Central & District Hospital Level



ANNEX 4 Facility without Xpert MTB/RIF—but in an Xpert MTB/RIF district



ANNEX 5 Acting on Xpert MTB/RIF results



Footnotes for Algorithms

(Figures 3.5, 3.6, 5.1 & Annex)

1. A TB Suspect is defined as a person who reports any one of the following current symptoms of any duration:

   - Cough
   - Fever
   - Weight loss
   - Night sweats

   If a person has a negative HIV test documented within the last 3 months, the following alternative definition applies:

   - Productive cough OR fever for more than 2 weeks with or without respiratory symptoms (shortness of breath, chest pains, hemoptysis) and/or constitutional symptoms (loss of appetite, weight loss > 5%, night sweats).

Among children, a TB suspect is defined as a person who reports one of the following symptoms:

- Poor weight gain
- Fever
- Current cough
- History of contact with a known or suspected TB case

2. A retreatment TB case is defined as a person who has received TB treatment at any time in the past and has started the 8 month standard regimen (Category II), being diagnosed with TB relapse or returning after default.

An MDR suspect is defined as a patient from one of the following risk groups:

a. Persons who develop active TB after known exposure to a patient with documented MDR-TB or thought to have MDR-TB;

b. All patients who remain smear-positive after 2 months of therapy with first-line drugs;

c. New patients coming from areas with high prevalence of MDR-TB (certain parts of South Africa, Lesotho etc.);

d. Any patient in whom there is significant clinical concern for acquired resistance.

3. Danger Signs include:

   - Respiratory rate > 30 per min
   - Temperature > 39°C
   - Heart rate > 120 beats per minute
   - Patient confused or agitated
   - Respiratory distress
   - Systolic blood pressure < 90 mmHg
   - Inability to walk unassisted

4. For seriously ill patients with danger signs, the most critical treatment is life-saving supportive therapy with oxygen, IV antibiotics and IV fluids (if the patient is in septic shock). The patient should be hospitalised immediately at the nearest facility that can provide this treatment. If such services are not available at the initial point of care, the patient should be transferred to the next highest-level facility, preferably one with Xpert MTB/RIF to accelerate the TB diagnostic process.

5. The first ("spot") sputum specimen should undergo smear microscopy the same day that the sample is received by the laboratory. The second ("morning") sample should also undergo microscopy on the day of receipt. Residual sputum from the "morning" sample should be set aside by the lab worker for Xpert MTB/RIF. If both the "spot" and "morning" smears are negative, the residual sputum should be automatically sent for testing by Xpert MTB/

RIF without having to seek clinician authorisation. The patient does not need to submit a second set of samples.

6. All retreatment cases and MDR-TB suspects should submit sputum specimens simultaneously for Xpert MTB/RIF AND for culture and first-line drug susceptibility testing before starting treatment.

7. Treat with antibiotics (except fluoroquinolones) to cover respiratory pathogen bacteria and/or high-dose trimethoprim-sulfamethoxazole to treat PCP according to the Malawi Standard Treatment Guidelines (MSTG). Patients should be re-evaluated for TB, particularly if symptoms persist after treatment.

8. A TB diagnosis is not ruled out by a negative sputum smear examination and negative chest x-ray. Clinical response to treatment for bacterial pneumonia or PCP does not exclude a diagnosis of TB as both may occur concurrently in patients with underlying TB disease. Advise the patient to return to the health facility if symptoms recur.

9. All TB patients should have a documented HIV sero-status; those with HIV co-infection are eligible for ART and co-trimoxazole prophylactic therapy (CPT) irrespective of CD4 count. Start TB treatment and CPT first, followed by ART as soon as possible within the first 2 weeks of TB treatment. Refer to the National ART guidelines.

10. While there is a risk of a false-positive test result for rifampicin resistance, given the low background prevalence of MDR-TB in Malawi, immediate initiation of treatment is

recommended due to the benefits of preventing death, not delaying treatment in true positive cases and preventing transmission of MDR-TB. Health workers should request an additional sputum specimen from patients for culture and DST to confirm the diagnosis of MDR-TB. However, if a patient tests positive for rifampicin resistance without a prior history of TB treatment, discuss the case with the MDR-TB focal clinician before initiating treatment with second-line drugs.

USAID
FROM THE AMERICAN PEOPLE

TB CARE II