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MINISTRY OF HEALTH

UGANDA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAMME

MANUAL FOR MANAGEMENT AND CONTROL OF TUBERCULOSIS AND LEPROSY

3RD EDITION

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FOREWORD

Uganda, like other Sub-Saharan countries, continues to identify thousands of tuberculosis (TB) cases (43,858 TB patients of all types were notified in 2015/16), yet these are only half of the estimated TB cases. The recent national TB prevalence survey conducted in 2014/15 found a much higher TB burden (prevalence of 253/100,000 population), than was previously estimated. This highlights the task ahead for Uganda to achieve the new ambitious global target of ending tuberculosis by the year 2035. Uganda has also made significant progress in leprosy control. The country already achieved the target of elimination of leprosy as a public health problem. However, several new cases of leprosy continue to be notified annually. Many of these have established disabilities and a significant proportion are children.

One of the key factors in the success of Uganda in TB and leprosy control is standardization of TB control activities through publication of guidelines for TB and leprosy control. One of these guidelines is the Tuberculosis and Leprosy Manual. The manual contains updated information on the structure and functions of the NTLP, basic biology of the two diseases, diagnostic pathways, management strategies, and monitoring and evaluation. The manual also contains chapters on special issues in TB and leprosy.

This revised manual comes at a time when the world has just changed its approach from stopping TB to ending TB. There is now global commitment to end TB in the new strategy called the "End TB strategy". The Ministry of Health is making plans to adopt this global TB strategy to end TB. This manual comes at a time the NTLP has undertaken to revise the strategic plan 2015/16-2019/20, to incorporate strategies to address the expanded TB burden and incorporate components of the WHO End TB strategy. The manual therefore introduces these global targets concepts along the traditional practices in TB and leprosy control.

Although the manual is written to meet local needs, it is written in line with international guidelines, specifically those of the World Health Organization (WHO). The current 3rd edition of the manual has been improved by including pictures and information boxes to facilitate easy grasp of the key principles and practices in TB and leprosy control.

The Ministry of Health is strongly committed to TB and leprosy control. I congratulate the NTLP and stakeholders on this achievement and strongly recommend this manual to all involved in TB and Leprosy prevention and care in Uganda and beyond.

Professor Anthony Mbonye
Director General of Health Services, Ministry of health

PREFACE

Understanding the operations of the National TB/Leprosy Program is paramount for efficient delivery of services by first line health workers as well as TB/Leprosy focal points at district level and their supervisors.

During the last four years following the dissemination of the 2nd edition of the NTLP Manual significant developments have taken place in the areas of:

- Alignment of the NTLP operations to the mainstream Ministry of Health (MOH) regional structure
- Programmatic management of drug resistant TB
- Use of new diagnostic tools
- Implementation of community based TB care
- Diagnosis and management of pediatric TB
- The management of TB/HIV co-infection
- Monitoring and evaluation of the program

While leprosy control has been sustained, there are challenges in reducing the burden to even lower levels in the context of the scattered high burden sites or "hot spots" in an otherwise low endemic setting and the dwindling knowledge about leprosy in the community as well as the health service providers.

This revised manual provides an update on those and other areas and pays special attention to the key role of the district TB/leprosy supervisors (DTLS). It provides guidance on how the district TB and leprosy supervisor (DTLS) function relates to the health facility staff on the one hand and the health service managers at the district, regional and national levels on the other. The lay out has been modified to enrich the indicated areas.

Effort has been made to align the national TB strategic plan (NSP) to the MOH Health Sector Development Plan and to the relevant World Health Organization (WHO) guidelines.

The manual should be a ready reference for the various service providers but also serve to meet the needs of any other people with a stake in the care of tuberculosis and leprosy patients as well as the provision of preventive services.

Dr. Frank R Mugabe
Program Manager, NTLP

ABBREVIATIONS

AFB	acid-fast bacilli
AIDS	acquired immune deficiency syndrome
ART	antiretroviral treatment
BCG	Bacille Calmette-Guerin
BI	Bacteriological Index
CB-DOT	community-based DOT
CBR	community-based rehabilitation
CME/CPD	continuing medical education/continuous professional development
CPT	cotrimoxazole preventive therapy
DG	disability grading
DOT	directly observed therapy
DST	drug susceptibility testing
DTLS	District TB Leprosy Supervisor
E	Ethambutol
EHF	Eye-hand-foot
ENL	erythema nodosum leprosum
EQA	external quality assurance
FDC	fixed dose combination
FEFO	"first to expire, first out"
H	Isoniazid
HIV	human immunodeficiency virus
HSD	Health Sub-District
IDP	Internally displaced persons
ILEP	International Federation of Anti-Leprosy Associations
IPT	Isoniazid preventive therapy
IRIS	Immune reconstitution syndrome
LAM	Lipoarabinomanon
LC I	Local Council I
MB	Multi bacillary leprosy
MDR	Multi-drug resistant
MDR-TB	Multidrug-resistant tuberculosis
MDT	Multidrug therapy
MGIT	Micro growth indicator tube
NAAT	Nuclear Acid Amplification Test
NTLP	National Tuberculosis and Leprosy Program
NTRL	National TB Reference Laboratory
PB	Pauci bacillary leprosy
PHC	Primary health care

PLHIV	People living with HIV and AIDS
PNFP	Private not for profit
POD	Prevention and management of disability
PPD	Purified protein derivative
PTB	Pulmonary tuberculosis
PWD	Persons with disabilities
QFT-G	QuantiFERON-TB Gold
R	Rifampicin
RR	Rifampicin resistance
S	Streptomycin
SCC	Short-course chemotherapy
SCHW	Sub-county Health Worker
ST	Sensory test
STD	Sexually transmitted disease
TB	Tuberculosis
TB IC	TB infection control
TST	Tuberculin skin test
VHT	Village health team
VMT	Voluntary muscle test
WHO	World Health Organization
XDR	Extensively drug-resistant
XDR-TB	Extensively drug-resistant tuberculosis
Z	Pyrazinamide
RTLP	Regional TB and Leprosy focal Person

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SECTION ONE

INTRODUCTION AND DESCRIPTION OF THE NTLP

1.1 INTRODUCTION

1.1.1 Geography and Demography

Uganda is a land locked country located in East Africa bordered by South Sudan in the north, Kenya in the east, Tanzania and Rwanda in the south and Democratic Republic of Congo in the West. It covers a surface area of 241,038 Km^2. The capital city is Kampala with English as the official language. Uganda's climate is typically tropical with two rainy and two dry seasons.

The 2014 national census estimated the population of Uganda to be 34.9 million people, with about half of the population below 15 years. About 82 percent of the population lives in rural areas, while 18 percent live in urban areas. The life expectancy at birth is 63.3 years (men 62.2, women 64.2, up from 50.4 years in 2002). Infant and under-five mortality rates are 53 and 80 deaths per 1,000 live births respectively (UBOS, 2014). The maternal mortality ratio decreased from 438 maternal deaths per 100,000 live births in 2011(UDHS, 2011) to 360 maternal deaths per 100,000 live births in 2013 (WHO, 2015)

1.1.2 Health Service delivery

Health services are provided by the public and private sectors with each covering about 50% of the population (HSSIP-3). The public sector consists of the Central Government of Uganda and local governments. The private sector consists of Faith based and NGO private not for profit (PNFP) organizations, private for profit providers and traditional and complementary medicine practitioners. The Ministry of Health (MoH) is a government body responsible for policy formulation, resource mobilization and technical guidance on health matters in Uganda.

1.1.3 Burden of Tuberculosis

The National TB prevalence survey conducted in 2015 puts the incidence of TB at 234/100,000 population for all TB cases and prevalence of TB is 253/100,000 population. The survey further showed that about 24% of TB patients are HIV co-infected. Based on the 2015 global TB report, the mortality rate from TB (excluding HIV positive TB) in 2014 was estimated at 12/100,000 population. Multidrug resistant TB is an emerging problem with more than 1,040 estimated cases every year and the actual case finding is around 200 cases per year.

1.1.4 Burden of Leprosy

The elimination of leprosy as a public health problem which was first attained in 2004 has been sustained at national level. Since 2014 elimination has also been achieved at regional and district levels. However, in some districts, there are still leprosy hot spots with unusually high numbers

of new cases. Less than half of districts had at least one patient registered for treatment at the end of 2015. Leprosy has not yet been eradicated. All districts need to maintain a surveillance system. New leprosy case detection rate per 100,000 population has decreased from 1.12 in 2008 to 0.7 in 2015. About 5% of new cases were children under 15 years of age. The proportion of new cases with visible (Grade 2) disabilities at the time of detection was 25% in 2015. There are an estimated 2000 leprosy affected persons living with medical and social rehabilitation needs.

1.2 THE NATIONAL TUBERCULOSIS AND LEPROSY PROGRAM

The NTLP, is a disease control program under the department of National Disease Control of the Ministry of Health (MoH). The NTLP is charged with performing the national core function of TB and Leprosy control through;
1) Establishment of country wide facilities for quality diagnosis and treatment of TB and leprosy;
2) Coordination and supervision of the implementation of TB and leprosy prevention and care
3) Prevention and management of leprosy-related disabilities.

The NTLP follows internationally accepted strategies of TB control. WHO has now designed a new strategy called the End TB strategy. This strategy was adopted by the 67th World Health Assembly on May 19, 2014. The NTLP revised its strategic plan for 2015-16/2019-20, to address the findings of the recent TB prevalence survey that reported a much higher TB burden than was previously estimated. The revision also aimed at incorporating the components of the End TB strategy which provides a unified response to end TB deaths, disease, and suffering. The strategy has three pillars and 10 components, and is based on four principles.

Pillar 1: integrated, patient centred care and prevention

Components

A. Early diagnosis of TB including universal drug susceptibility testing, and systematic screening of contacts and high risk groups
B. Treatment of all people with TB including drug resistant TB, and patient support
C. Collaborative TB/HIV activities; and management of comorbidities
D. Preventive treatment of persons at high risk; and vaccination against TB

Pillar 2: Bold policies and supportive systems

Components

A. Political commitment with adequate resources for TB care and prevention
B. Engagement of communities, civil society and all public and private care providers
C. Universal health coverage policy and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
D. Social protection, poverty alleviation and actions on other determinants of TB

Pillar 3: Intensified research and innovations

Components

A. Discovery, development and rapid uptake of new tools, interventions and strategies
B. Research to optimize implementation and impact and promote innovations

The leprosy control strategy:

A new global leprosy strategy for 2016-2020 has been set. The Global Leprosy Strategy 2016-2020: Accelerating towards a leprosy-free world has the goal to further reduce the burden of leprosy at the global and local level.

The Global Leprosy Strategy 2016-2020 is also based on three pillars:
1. Strengthening government ownership, coordination and partnership
2. Stopping leprosy and its complications
3. Stopping discrimination and promoting inclusion

1.2.1 Organisation structure of the NTLP

NTLP is headed by a Program Manager and several program officers who coordinate the different activities within NTLP. A new structure for NTLP has been proposed. In this structure which is yet to be approved NTLP will have a central unit headed by the Program Manager and supported by a number of officers who coordinate the following units: Prevention and Health promotion, Monitoring and Evaluation, Care and Treatment services, Laboratory Services, and Policy and Regional TB and Leprosy services. Under the above units, there are focal officers for specific program functions (Annex 1).

At the regional level, management and supervision of TB and Leprosy services is performed by the Regional TB and Leprosy focal Person (RTLP). There are currently 12 regions which are aligned to the 12 MoH Regional performance monitoring teams (RPMT) structure. At the district level, the District Health Officer (DHO) is responsible for the management of health service delivery including TB and Leprosy prevention and care. The DHO assigns a district health team member as District TB and Leprosy Supervisor (DTLS) with responsibility of overseeing TB and Leprosy care and prevention services in the district.

At the Health Sub-district level (HSD), the in-charge of the HSD is responsible for the management of health service delivery including TB and Leprosy care and prevention services. A health worker is assigned the responsibility of overseeing TB and Leprosy care and prevention services at the HSD level and this person is referred to as the Health Sub-district Focal Person.

At the district, HSD and health facility level, TB and Leprosy care and prevention services/services are integrated into the general health services. Table 1.1 summarizes the responsibilities in the proposed structure:

Table 1.1: Responsibilities for different levels with regard to TB and Leprosy control

Level of management	Responsibilities
National level (Central Unit) (Programme Manager) including NTRL	Formulating and revising policies and guidelines Planning, including development of strategic and operational plans Resource mobilization Setting standards and quality assurance Advocacy, coordination and networking Training Monitoring and evaluation Surveillance of (DR)-TB (Operational) research
Regional level (Regional TB and Leprosy focal Person)	Assist the Program manager with the above responsibilities Supervision of district TB and Leprosy activities Mentoring of DTLS Advocacy, coordination and networking in the region Dissemination of policies and guidelines Training Monitoring and evaluation Operational research.
District level (District Health Officer)	Plan and prioritize TB and Leprosy care and prevention interventions Ensure compliance to national policy and guidelines Support and supervise the DTLS, District Laboratory focal person (DLFP) and Health sub-district in-charges Identify training needs and support training Monitor and evaluate TB and Leprosy care and prevention interventions. Resource mobilisation Advocacy, coordination and networking in district Operational research
District TB and Leprosy Supervisor	Support/ensure critical activities are included in District plans Supervise health workers implementing TB and Leprosy care and prevention services Ensure compliance to national policies and guidelines Train, support and supervise HSD focal persons and sub-county HWs. Ensure availability of drugs at health facilities Validate data on TB and Leprosy Update district registers.
Health sub district in charge and/ focal person	Support the DTLS to ensure that the above activities are done at HSD level Advocacy, coordination and networking in health sub-district
Community level	Village Health Team and local council III: Suspicion and referral of presumptive TB Treatment support

SECTION TWO

TUBERCULOSIS

2.1 TUBERULOSIS DISEASE

2.1.1 Causative organism

Tuberculosis (TB) is usually caused by a bacterium, ***Mycobacterium tuberculosis (M.tb) complex (such as Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium africanum and Mycobacterium microti)***. In clinical and laboratory settings, these bacteria are also referred to conventionally as tubercle bacilli (because they cause lesions in tissues called tubercles) or acid-fast bacilli (AFB), because they retain a red dye after washing with alcohol following staining. In few cases mycobacterium bovis that causes TB in animals can cause TB among humans. However, the most common cause is *myc. tuberculosis*.

2.1.2 Transmission

Transmission of tubercle bacilli occurs when a patient suffering from pulmonary TB who is not on effective treatment expels into the environment air containing droplets with the bacilli (coughing, singing or sneezing). The liquid in the droplets evaporates leaving the droplet nuclei containing the bacilli. The droplet nuclei are small enough to be inhaled into the lungs and deposited into the alveoli. Transmission is easier in the following situations:

- Closed environment where ventilation is poor.
- High number of TB bacilli in the sputum
- Close contact over a prolonged period with a pulmonary TB sputum smear-positive patient who is not yet on treatment increases the chance of becoming infected with *M.tb*.
- Duration of exposure to the infectious source
- High prevalence of TB in the community

On the other hand, the chance of getting infection is low if the contact is occasional or the patient has extra-pulmonary TB.

2.1.3 Infection and Development of TB Disease

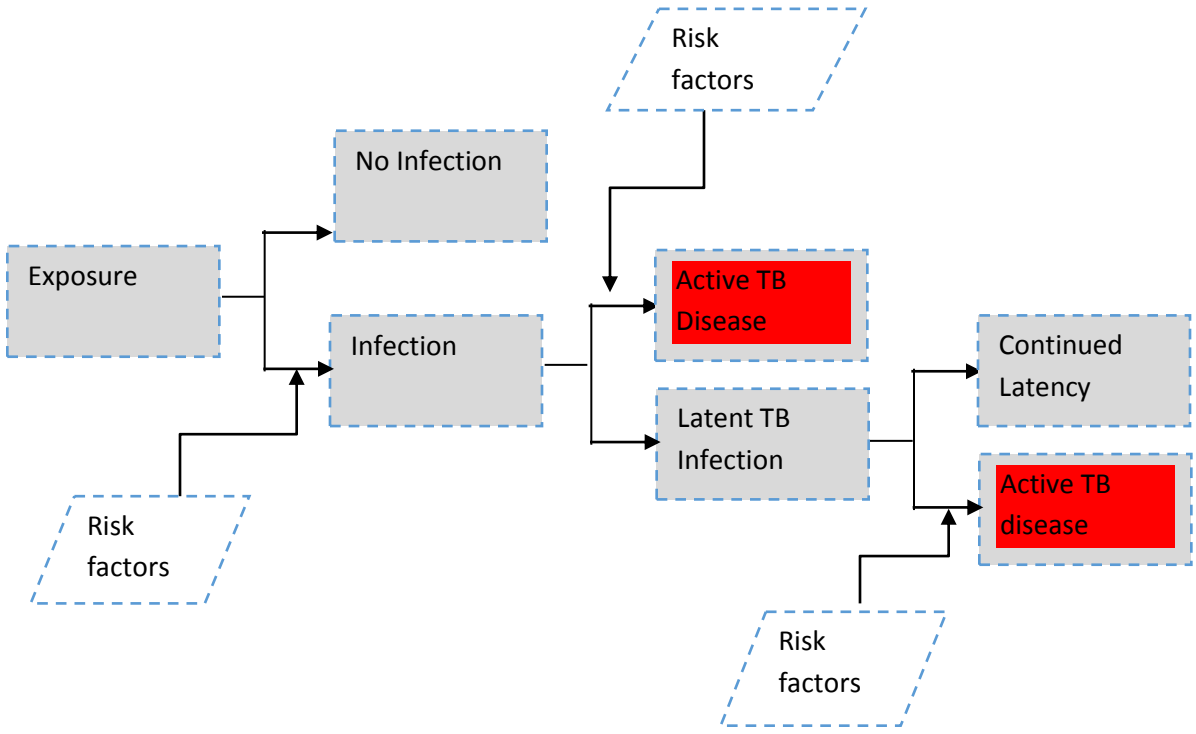
When transmission of tubercle bacilli takes place and the person is infected for the first time ever, it is called **primary infection**. Tubercle bacilli multiply in the lungs and lymphatic organs and causes lymph node enlargement in the chest. The tubercle bacilli may also spread from lymphatic organs through blood to other parts of the body. This process takes 6-8 weeks. At the end of 6-8 weeks, immunity is developed in up to 90 percent of persons who get primary

infection. This immunity then controls the further multiplication and spread of the tubercle bacilli, and the person recovers (figure 2.1).

However, tubercle bacilli have a special ability to remain dormant for long periods. This is the situation in 90 percent of these infected persons. Under normal conditions, these infected persons can be recognized by being tuberculin (Mantoux) positive and the new TB infection tests.

The immunity of about 10 percent of people, however, may be too low to contain infection at the time of primary infection. These persons develop disease as a direct result of primary infection. Such disease is referred to as **primary disease** because it is a direct progression of primary infection. This may occur in conditions like HIV infection, diabetes mellitus, alcoholism, cancer, and use of immunosuppressive drugs, malnutrition, advancing age and many others. When such a situation arises, the previously dormant tubercle bacilli start to multiply and cause tissue damage (commonly in the lungs) and disease in the affected person. This is called **post-primary disease (or adult disease)**, in contrast to **primary disease,** which is also sometimes referred to as **childhood disease**. Most TB patients develop their disease by the post-primary mechanism (approximately 90%).

Figure 2.1: Infection and Development of TB Disease



Clinically TB is divided into two groups, **Pulmonary TB and Extra pulmonary TB**

Pulmonary TB is TB that involves the lungs. It is the most common form of TB and accounts for approximately 80 percent of all the patients with TB. These patients, particularly the sputum smear-positive ones can transmit the bacilli to others. One form of TB of the lungs that deserves special mention is **endobronchial TB**. This form of TB is highly infectious. In this form of TB, TB bacilli invade the airways by direct extension from infection in the lung tissue (parenchyma). This kind of TB presents with a barking cough. It may wheeze and easily misdiagnosed as asthma.

Extra-pulmonary TB is TB that occurs in organs of the body other than the lungs (including the pleura). These patients are unlikely to transmit the bacilli to other people.

NB: In TB program setting, a TB patient with both pulmonary and extra-pulmonary TB is classified as a pulmonary TB patient since this category is of public health importance.

2.2 DIAGNOSIS OF TUBERCULOSIS

Key points

- Health care providers should follow the NTLP diagnostic algorithm for diagnosis of TB.
- Early diagnosis of TB is important for both the individual and the community.
- Bacteriological diagnosis of TB depends on isolation of the M.tb organism or identification of components e.g. DNA in clinical specimen.
- All presumptive and diagnosed TB patients should be offered an HIV test.
- All patients at risk of drug resistance must be screened and investigated for drug resistance.
- A diagnosis of TB must be recorded in the relevant registers and notified irrespective of whether they have started treatment or not.

2.2.1 Approach to diagnosis of TB

Diagnosis of TB is based on a compatible TB history including of contact with TB and positive TB tests; and where tests are not positive a clinician's decision to treat as TB. TB irrespective of body organ affected presents with constitutional symptoms of fevers (especially in the evening), weight loss, and loss of appetite and night sweats. Other symptoms depend of site affected.

For pulmonary TB (PTB), the most common form of TB, presents with one or more of respiratory of symptoms of cough, chest pain, hemoptysis and dyspnea. Specific respiratory symptoms of more than two weeks are most suggestive of TB although among those who are immunosuppressed, such as HIV patients, any of these symptoms for any duration are suggestive of TB.

The procedure(s) for diagnosing tuberculosis are usually carried out on patients who have symptoms and have reported to the health facility on their own. To ease and standardize TB screening the NTLP has designed an intensified TB case finding form (ICF), see below. In all care entry points, TB screening should be carried out using the Intensified Case Finding (ICF) guide (Figure 2.2a). Patients positive on the ICF are termed presumptive TB patients.

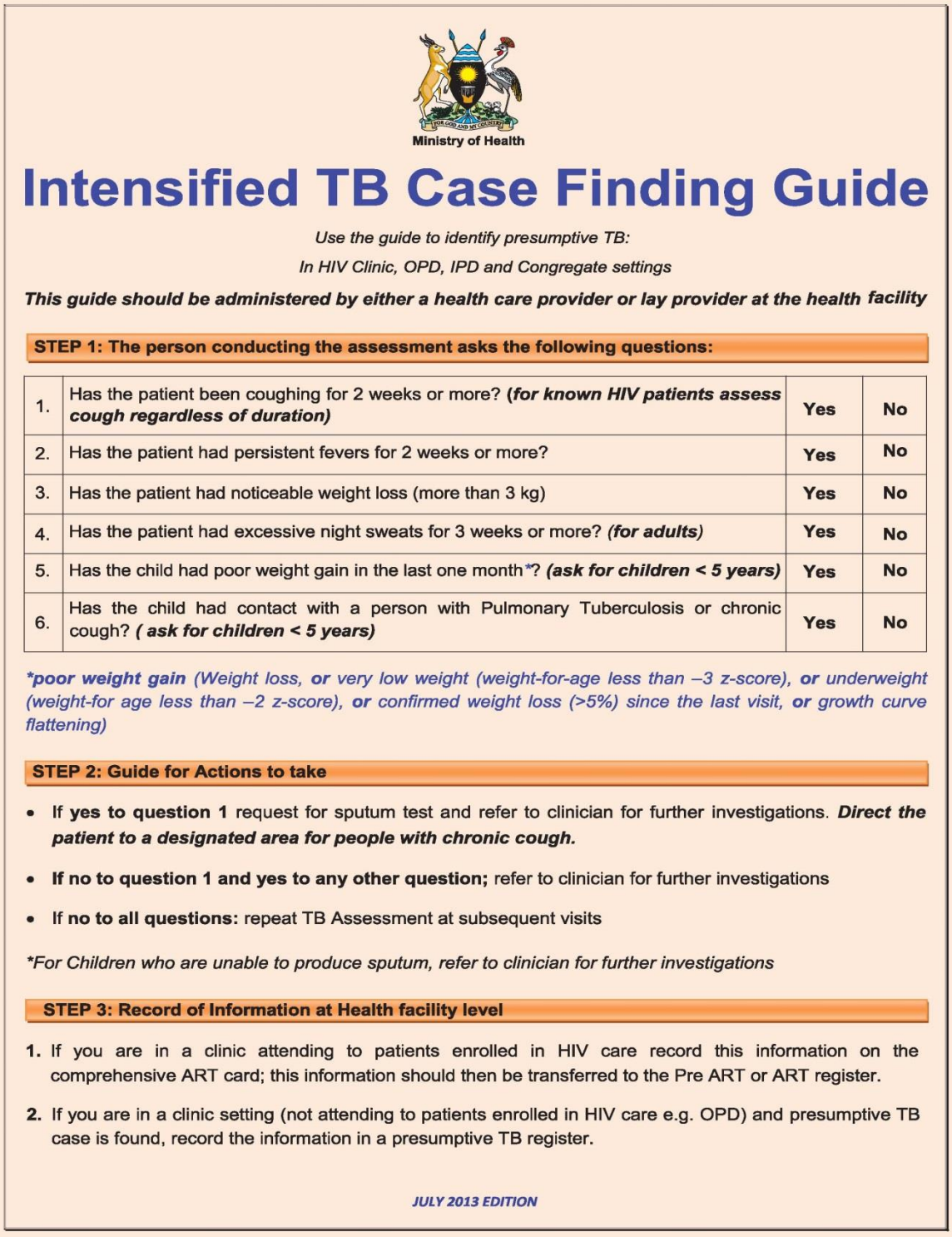
After the patient's history, has been taken and a physical exam has been performed, investigations are carried out depending on availability of the tests and the TB site. In pulmonary TB (PTB) sputum specimens (1 spot and 1 early morning) are examined using microscopy for the TB bacilli or using a new molecular test called Xpert MTB/RIF (GeneXpert) test.

If facilities are available, and the patient is at high risk of multidrug resistance, the sputum sample can also undergo MTB culture and drug susceptibility test (DST). Other tests such as chest x-ray (PTB) and histology (lymph nodes, pleural TB, pleural fluid analysis, cerebral spinal fluid analysis) are conducted for specific organs affected by TB.

For programmatic purposes, TB should be diagnosed following steps presented in the national algorithm for TB screening, diagnosis and management (Figure 2.2b). The algorithm has two arms; one for facilities with GeneXpert machine on site and another for facilities with no machine on site. In facilities with GeneXpert TB test all presumptive TB patients should be tested on this test. In the same visit, HIV, should be tested.

In facilities without GeneXpert testing with smear microscopy is recommended. All presumptive TB patients are bacteriological negative (i.e. no laboratory evidence of TB is found) should undergo further evaluation (clinical and with chest X-ray, CXR). Patients who have likelihood of TB should be treated as TB and those who are not need reassessment. The patient's clinical diagnosis should be treated and reviewed in two weeks' time.

Figure 2.2a: Intensified TB Case Finding guide



Ministry of Health

Intensified TB Case Finding Guide

Use the guide to identify presumptive TB:

In HIV Clinic, OPD, IPD and Congregate settings

This guide should be administered by either a health care provider or lay provider at the health facility

STEP 1: The person conducting the assessment asks the following questions:

1.	Has the patient been coughing for 2 weeks or more? **(*for known HIV patients assess cough regardless of duration)***	**Yes**	**No**
2.	Has the patient had persistent fevers for 2 weeks or more?	**Yes**	**No**
3.	Has the patient had noticeable weight loss (more than 3 kg)	**Yes**	**No**
4.	Has the patient had excessive night sweats for 3 weeks or more? ***(for adults)***	**Yes**	**No**
5.	Has the child had poor weight gain in the last one month*? ***(ask for children < 5 years)***	**Yes**	**No**
6.	Has the child had contact with a person with Pulmonary Tuberculosis or chronic cough? ***(ask for children < 5 years)***	**Yes**	**No**

****poor weight gain** (Weight loss, **or** very low weight (weight-for-age less than –3 z-score), **or** underweight (weight-for age less than –2 z-score), **or** confirmed weight loss (>5%) since the last visit, **or** growth curve flattening)*

STEP 2: Guide for Actions to take

- If **yes to question 1** request for sputum test and refer to clinician for further investigations. ***Direct the patient to a designated area for people with chronic cough.***
- **If no to question 1 and yes to any other question;** refer to clinician for further investigations
- If **no to all questions:** repeat TB Assessment at subsequent visits

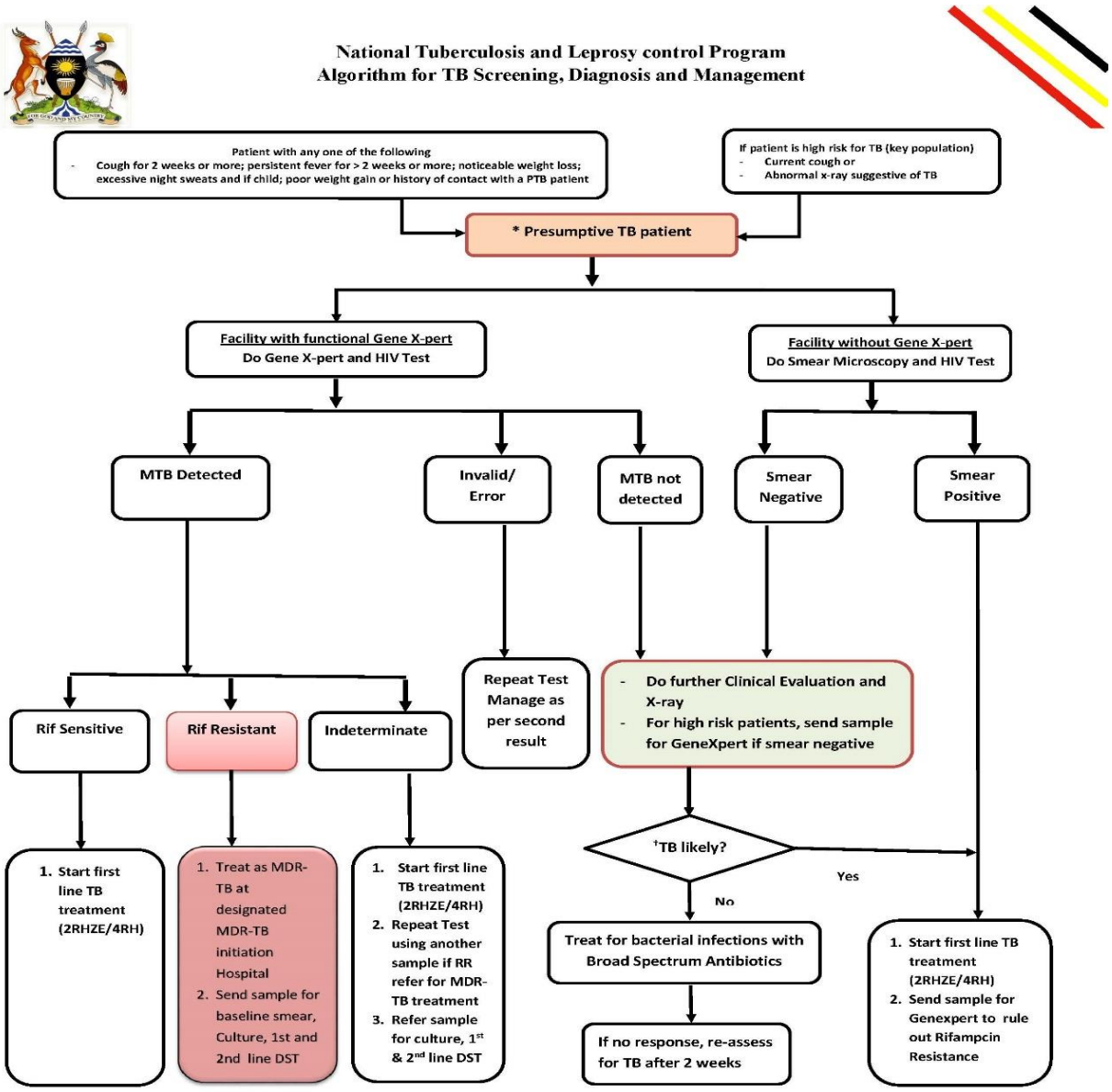
**For Children who are unable to produce sputum, refer to clinician for further investigations*

STEP 3: Record of Information at Health facility level

1. If you are in a clinic attending to patients enrolled in HIV care record this information on the comprehensive ART card; this information should then be transferred to the Pre ART or ART register.
2. If you are in a clinic setting (not attending to patients enrolled in HIV care e.g. OPD) and presumptive TB case is found, record the information in a presumptive TB register.

JULY 2013 EDITION

Figure 2.2b Algorithm for screening, diagnosis and management of tuberculosis



1. ***Presumptive TB** is presence of any or a combination of the following symptoms; cough≥ 2weeks or current cough if high risk patient, fever, night sweats, history of contact with a TB case, weight loss or poor weight gain for children. Also consider abnormal chest x-ray in a high risk patient as presumptive TB
2. **"High risk patients"** include PLHIV, previously treated TB patients, prisoners, contacts of TB patients, diabetic patients, health workers, miners and refugee populations
3. **Smear positive** (AFB positive): is defined as at least one positive smear
4. **Smear negative**: defined as two negative smears. If patient is from high risk category, send a sample for GeneXpert test
5. **†TB likely:** Abnormal Chest X-ray findings suggestive of TB e.g. cavitation, pleural effusion, miliary picture , hilar lymph nodes
6. **HIV positive patients:** Presumptive or diagnosed TB patients who are HIV positive should be offered comprehensive HIV care services. Chest x-ray should be used to screen for active TB for all PLHIV enrolling in care. Those in whom TB has been excluded should be offered IPT as per IPT guidelines. HIV positive adults in whom TB is not picked by microscopy or GeneXpert and are very sick (CD4 less than 100) should be tested for TB using **Urine TB LAM test.** If positive, treat as clinically diagnosed TB.
7. **Treatment monitoring;** Follow up sputum smear microscopy should be done at the end of 2, 5 & 6 months for susceptible TB and monthly smear and culture for DR-TB.
8. **Recording & Reporting**: All diagnosed TB patients (resistant, sensitive, and indeterminate) record in the Unit TB register and included in facility quarterly(HMIS 106a) notification report and all rifampicin resistant(RR) TB patients should be notified in the weekly (HMIS 033b)report by the facility that refer the sample for Gene Xpert test. In addition record RR TB patients in the district line list and the Drug resistant TB register at the treatment initiation facility.

22nd June 2017 version

2.2.2 Laboratory diagnosis

All efforts should be made to make a laboratory confirmation of TB diagnosis in all patients with presumptive TB. This is important for clinical monitoring of treatment response. It is also important for TB reporting and monitoring of TB control efforts. However, a clinician can still make a diagnosis of TB even in the absence of confirmatory laboratory confirmation.

The investigations and tests useful in the diagnosis of TB are described below:

Bacteriological

Microscopy

It is the most commonly available test currently for diagnosis of TB. It can be either ***Ziehl-Neelsen*** **microscopy (Figure 2.2.2a) or** ***Fluorescence microscopy (*****Figure 2.2.2b*****)***. It can be used to examine sputum specimen or gastric aspiration fluid or any other body material suspected to contain the TB bacilli.

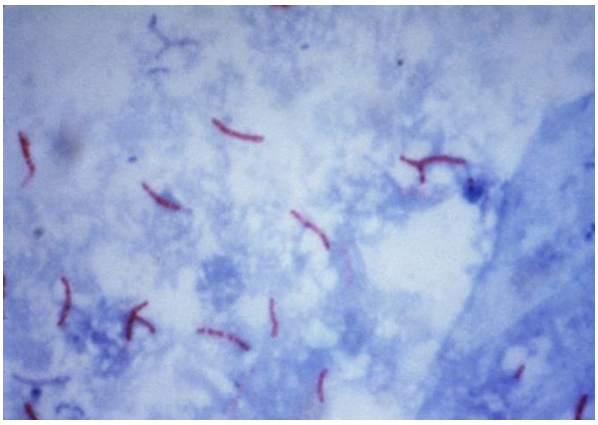


Figure 2.2.2a. Positive Ziehl Neelsen Smear

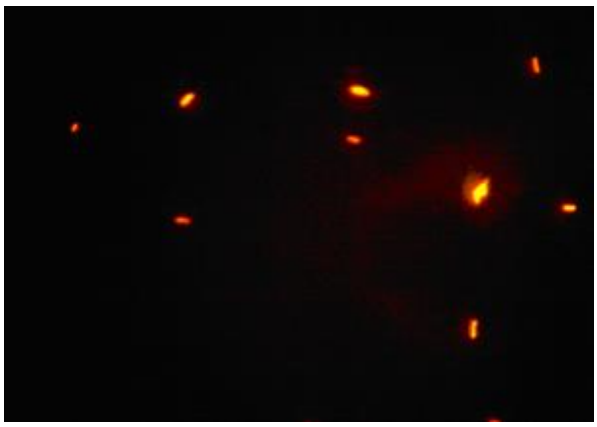


Figure 2.2.2b. Positive fluorescent microscopy

Nuclear Acid Amplification Tests

Nucleic Acid Amplication tests (NAAT) are based on the principle of detecting and amplifying (making more copies of) the M.tb genetic material. In TB diagnosis two tests are now available in the clinic namely the Xpert MTB/Rif test and the line probe assay (LPA).

Xpert MTB/Rif is the most used NAAT in Uganda. ***Xpert*** *MTB/Rif* is an automated DNA test for mycobacteria specific for MTB (IS6110) and for the mutation that causes resistance to Rifampicin (rpoB). The following body fluids or samples can be examined for TB using Xpert MTB/Rif: Sputum, Lymph node tissue and aspirates, Pleural fluid, Cerebrospinal fluid and Gastric aspirates. Results that can be expected from Xpert MTB/Rif test are shown in the table below.

Table 2.2.1: Xpert MTB/Rif results and their meaning

Result	Meaning	Interpretation
Mycobacterium tuberculosis (MTB) complex detected	MTB was isolated from the specimen therefore the patient has bacteriologically confirmed TB	The patient has TB disease and should be treated
Mycobacterium tuberculosis (MTB) complex not detected	MTB was not isolated from the Specimen	This result does not exclude TB in people with pauci bacillary disease i.e. children and HIV positive people and EPTB. The sensitivity of Xpert is low in smear negative, culture positive patients. It means that TB disease could not be confirmed bacteriologically by Xpert MTB/Rif. Further investigations are required to confirm TB in these patients ***HIV positive adults in whom TB is not picked by microscopy or Xpert MTB/Rif and are very sick should be done CXR and Urine LAM test if (CD4 less than 100)***
Rifampicin resistance detected	Means that the MTB strain isolated was resistant to Rifampicin. Therefore, the patient has Rifampicin resistant TB	Rifampicin resistance by Xpert MTB/Rif does not rule out or confirm MDR-TB and XDR-TB hence a full 1st line and 2nd line DST is required
Rifampicin susceptible	The MTB strain isolated was susceptible to Rifampicin therefore, patient has Rifampicin susceptible TB	This does not exclude the possibility of resistance to other first line drugs i.e. H, Z, E

Line Probe Assay test is another molecular test that is designed to identify M. tuberculosis complex and simultaneously detect mutations associated with drug resistance (http://www.who.int/tb/areas-of-work/laboratory/policy_statements/en/. It is recommended for patients in whom a rapid confirmation of MDR status is needed.

Culture

A culture test involves studying bacteria by growing the bacteria on different substances. This is to find out if particular bacteria are present. In the case of the TB culture test the test is to see if the TB bacteria Mycobacterium tuberculosis, are present. - See more at: http://www.tbfacts.org/culture-tb/#sthash.YFcLUfu1.dpuf

The probability of finding AFB in sputum specimens by smear microscopy or molecular tests is directly related to the concentration of bacilli in the sputum. In comparison, mycobacterial culture can detect far lower numbers of TB bacilli. Moreover, the culture makes it possible to identify the mycobacterial species based on biochemical and other properties. Culture using both solid LJ media and liquid MGIT 960 media. It is done in specialized laboratories for example the NTRL. All clinical samples can be cultured.
Culture of *M. tb* bacilli is very sensitive and specific, but is expensive, as it is a complex and sophisticated procedure. It requires a specialized laboratory set-up, and culture results are available only after 6 to 8 weeks. Culture with DST takes even longer. If available, culture can be used for diagnosis or confirmation of the diagnosis of TB in patients with PTB and EPTB. Since it is more sensitive than smear, culture may also have a role in the diagnosis of smear-negative, HIV-positive TB suspects who are likely to be paucibacillary.

Antigen tests

TB LAM test is based on the detection of LAM in urine and has the potential to be point-of-care tests for TB. WHO recommends the test to assist the diagnosis of TB in HIV positive adult in-patients with signs and symptoms of TB (pulmonary and/or extra-pulmonary) with a CD4 cell count less than or equal to 100 cells/μL, and people living with HIV who are deemed "seriously ill". (http://www.who.int/tb/areas-of-work/laboratory/policy_statement_lam_web.pdf).

The NTLP has adopted the use of LAM to assist in the diagnosis of TB in HIV positive adult in-patients based on WHO recommendation. "Seriously ill" is further defined based on 4 danger signs: respiratory rate > 30/min, temperature > 39°C, heart rate > 120/min and unable to walk unaided

2.2.3 Radiology

Radiology investigations such as ***chest X-ray:*** Features of chest X-ray consistent with TB disease include cavitation (Figure 2.3a) milliary picture (Figure 2.3b), pleural effusion and mediastinal lymph gland enlargement with lung infiltration. Although the findings of radiology are nonspecific, abnormalities like any heterogeneous opacities and cavitation, if located in the upper parts of the lung, are more likely to be caused by TB.

All presumptive TB patients who are bacteriologically negative should be offered CXR and if suggestive of TB, treatment should be initiated (Refer to NTLP TB diagnostic algorithm above)

Figure 2.3: Chest X-ray showing a cavitatory and milliary patterns of TB

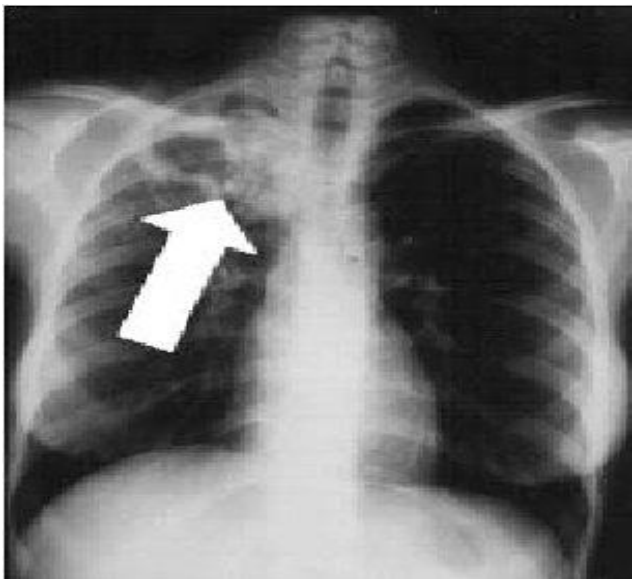


Figure 1.3a: Cavitory pattern of TB

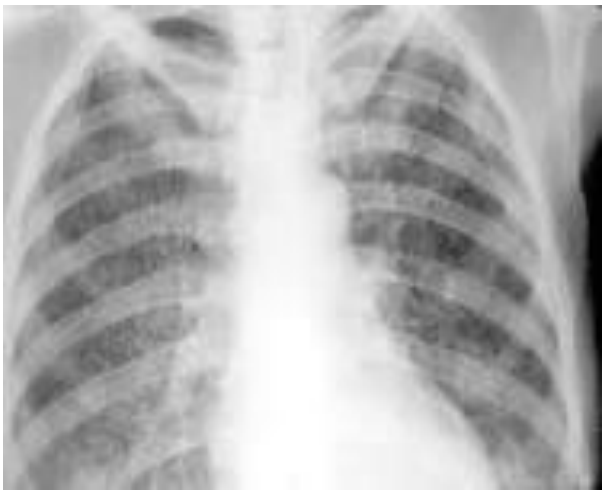


Figure 2.2b: Milliary pattern of TB

Ultrasound

Diagnostic ultrasound is a useful test in the diagnosis of extra pulmonary TB. For example, ultrasound is useful in abdominal TB in which case you can see omental thickening, increase in mesenteric thickness and an increase in the mesenteric echogenicity (due to fat deposition), combined with retroperitoneal and mesenteric lymphadenopathy.

Presence of dilated and matted small bowel loops and ascites further substantiate the diagnosis. Calcifications within granulomas due to TB in the liver and spleen can also be picked by abdominal ultrasound scans.

2.2.4 Histology

Pathology can play a complementary role in confirming the diagnosis of EPTB, such as tuberculosis lymphadenitis. Multiplication of tubercle bacilli in any site of the human body causes a specific type of inflammation, with formation of characteristic granuloma that can be found on histological examination.

Samples can be taken in the following ways:

- Fine needle aspiration of the lymph nodes: affected peripheral lymph nodes, particularly cervical nodes, can be aspirated.
- Tissue biopsy: serous membranes (pleura, pericardium and peritoneum), skin, lymph node, endometrium, bronchial mucosa or liver tissue can be taken, with an appropriate instrument or during surgery. Surgical procedures can be useful in getting tissues for biopsy from deep organs.

2.2.3 Case Definitions

For standardizing the process of data collection (case registration) and TB reporting requirements to permit for cohort analysis of treatment outcomes, case definitions are necessary. Standard TB case definitions are shown in table 2.1

Note:

For a presumptive TB patient to be treated as a TB patient, s/he must first be declared a TB patient and decision is made to treat him/her for TB. A TB patient is what is referred to as a case of TB. However not all TB patients have the same classification. It is this process of classifying the different types of TB patients that is called ***Case definition.***

Table 2.2.2: Standard TB case definitions

Case definition	*Description*
Presumptive TB patient	Any patient who presents with symptoms and signs suggestive of TB (previously called a TB suspect).
Bacteriologically confirmed TB patient	A **bacteriologically confirmed TB patient** is one from whom a biological specimen is positive by smear microscopy, culture, Nucleic Acid Amplification Tests e.g. Xpert MTB/RIF or WHO recommend new diagnostics. All such cases should be recorded in the unit TB register and notified, regardless of whether TB treatment has been started.
Clinically diagnosed TB patient	A **clinically diagnosed TB patient** is one who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and extra-pulmonary cases without laboratory confirmation. Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.

2.2.3 Classification of TB patients?

Four factors determine the classification: the site of the disease (body organ involved), drug resistance, HIV status and the patient's history of previous treatment.

Classification based on Site of the disease

The description below applies to all patients irrespective of HIV status.

A. **Pulmonary tuberculosis (PTB)**; Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extra-pulmonary TB.
B. **Extra-pulmonary tuberculosis (EPTB)**; Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints bones, and meninges.

A patient with both pulmonary and extra-pulmonary TB should be classified as a case of PTB.

Classification based on History of treatment

There are two types of TB patients based on treatment history

1) New patients: These are patients who have never been treated for TB or have taken anti-TB drugs for less than one month.

2) **Previously treated TB patients:** These are patients who have received one month or more of anti TB drugs in the past. They are sub classified as follows:

i) Relapse patients have previously been treated for TB, completed treatment, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection);

ii) Treatment after failure patients: are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment;

iii) Treatment after loss to follow-up patients: have previously been treated for TB and were declared lost to follow-up at the end of their most recent course of treatment. (These were previously known as treatment after default patients).

iv) Other previously treated patients are those who have previously been treated for TB but whose Outcome after their most recent course of treatment is unknown or undocumented.

3) Patients with unknown previous TB treatment history do not fit into any of the categories listed above.

NB: New and relapse cases of TB are **incident TB cases**.

Classification based on HIV infection status

HIV-positive TB patient refers to any bacteriologically confirmed or clinically diagnosed case of TB who has a positive result from HIV testing conducted at the time of TB diagnosis or other documented evidence of enrolment in HIV care, such as enrolment in the pre-antiretroviral therapy (ART) register or in the ART register once ART has been started.

HIV-negative TB patient refers to any bacteriologically confirmed or clinically diagnosed case of TB who has a negative result from HIV testing conducted at the time of TB diagnosis. Any HIV-negative TB patient subsequently found to be HIV-positive should be reclassified accordingly.

HIV status unknown TB patient refers to any bacteriologically confirmed or clinically diagnosed case of TB who has no result of HIV testing and no other documented evidence of enrolment in HIV care. If the patient's HIV status is subsequently determined, he or she should be reclassified accordingly.

Classification based on Drug resistance

Cases are classified in categories based on drug susceptibility testing (DST) of clinical isolates confirmed to *be M. tb*:

Mono resistance: resistance to one first-line anti-TB drug only.

Poly drug resistance: resistance to more than one first-line anti-TB drug (other than both Isoniazid and Rifampicin).

Multidrug resistance: resistance to at least both Isoniazid and Rifampicin.

Extensive drug resistance: resistance to any fluoroquinolone and to at least one of three second-line injectable drugs (Capreomycin, Kanamycin and Amikacin), in addition to multidrug resistance.

Rifampicin resistance: Resistance to Rifampicin detected using phenotypic (usual drug susceptibility testing, DST) or genotypic methods (commonly Xpert MTB/Rif), with or without resistance to other anti-TB drugs. It includes any resistance to Rifampicin, whether mono, poly, multi, or extensively drug resistance. These categories are not all mutually exclusive. When enumerating Rifampicin resistant TB (RR-TB), for instance, multi-drug TB (MDR-TB), and Extensively drug resistance (XDR-TB) are also included.

"Pre-XDR" TB: refers to an isolate that is resistant to either a fluoroquinolone or a second-line injectable, but not both. It is a commonly used designation but not officially accepted terminology by WHO or the global TB community.

2.2.4 Post TB patients

Currently there is no consensus definition of a post TB patient. However these patients commonly present to TB clinicians. A post TB patient is a patient who was successfully treated for TB who presents with respiratory symptoms. Many people who have been treated and cured of TB continue to present with respiratory symptoms long after their TB is cured. The common symptoms are chest pain, cough, shortness of breath and hemoptysis.

The public health importance of these patients is just being recognized. There are no standard guidelines on how they can be evaluated and treated. Health workers should immediately repeat

a TB evaluation according standard TB diagnosis practices (sputum examination and chest x-rays). If the sputum is positive for TB, the patient is then treated as retreatment TB as described elsewhere in this manual. If TB tests are negative the patients should be further re-evaluated for post TB lung diseases namely bronchiectasis, chronic obstructive pulmonary disease (COPD), pulmonary hypertension, and colonization with fungal infections such as aspergillosis.

In most cases these patients will have residual lung damage on chest x-rays from the previous TB episode. This usually prompts the health worker to retreat as bacteriologically negative TB. Indeed, many patients have been treated this way several times exposing them to repeated toxic effects of TB treatment.

2.3 TREATMENT OF TUBERCULOSIS

- Early diagnosis and effective treatment of TB are critical to improving clinical outcomes of TB patients.
- Anti-TB drugs are given in combinations called regimens according to patients' TB category.
- Different standardized TB treatment regimens are recommended for pan susceptible and drug resistant TB.
- Anti-TB drugs have side effects of varied severity and these should be managed appropriately.
- TB treatment monitoring should be done by clinical, sputum and where possible by radiological examination.

Early diagnosis and effective treatment is the key to stop the spread of TB and to improve treatment outcomes of patients suffering from TB. Individuals should start treatment as soon as possible after a diagnosis of TB is made and should be treated according to NTLP recommended regimens under Directly Observed Treatment (DOT).
The aims of treatment are to:

- Cure the TB patient
- Prevent complications and death from TB disease
- Prevent TB relapse
- Reduce TB transmission
- Prevent development of drug-resistant TB

2.3.1 Anti-TB medicines

Anti-TB medicines can be classified into first and second line.
F**irst-line** anti-TB medicines are used for the treatment of susceptible TB while second line medicines are used for treatment of drug resistant TB.

The first-line anti-TB medicines, together with their standard abbreviations, are shown below:

Rifampicin (R)
Isoniazid (H)
Pyrazinamide (Z)
Ethambutol (E)

This section considers details the first-line anti-TB medicines.

Table 2.3.1: First-line anti-tuberculosis drugs and characteristics

Drug	Adult Dose*	Route of admin.	Side-effects	Contraindications	Important drug interactions
Isoniazid	10 mg/kg body wt.-(max.300mg)	Oral	Hepatitis, peripheral neuropathy	Active liver disease, known hypersensitivity	Stavudine, phenytoin, carbamazepine
Rifampicin	10mg/kg body wt.-(max.600mg)	Oral	Flu syndrome, dermatitis, hepatitis, reddish-brown coloration of urine	Hepatic dysfunction, hypersensitivity to rifamycins	Oral contraceptives, Nevirapine, Warfarin, Phenytoin, Glibenclamide
Pyrazinamide	30 – 40 mg/kg daily body wt. (max dose 2500 mg)	Oral	Joint pains, hepatitis	Hepatic impairment known hypersensitivity	None
Ethambutol	15mg/kg body wt.	Oral	Impaired visual acuity and color vision	Pre-existing optic neuritis, established kidney failure	None

***Dose adjustment may be required in special situations**

Fixed-dose combinations

In the table above, anti-TB drugs are presented as single drugs. However, these drugs are usually given as fixed-dose combinations (FDC). The FDCs contain two or more drugs in a single tablet with known strength (mg) of the drugs in each tablet. Examples of FDC TB drugs used in the country include; 2-drug FDC [Rifampicin+ Isoniazid (RH)], 3-drug FDC [Rifampicin+ Isoniazid+ Pyrazinamide (RHZ)] and 4-drug FDC [Rifampicin+ Isoniazid+ Pyrazinamide+ Ethambutol (RHZE)].

FDC tablets have the following advantages:

- Prescription errors are minimized. Dosage recommendations are more accurate and adjustment of the dose according to patient weight is easier.
- The patient has fewer tablets to swallow, which contributes to adherence.
- If the treatment is not supervised, patients cannot be selective about which the drugs to swallow.

2.3.2 TB Treatment Regimens

Anti-TB drugs are given in combinations called ***regimens.*** The regimens have the following characteristics;

- Contain at least one of the most effective anti-TB drugs (Rifampicin or Isoniazid) in both the **initial** and **continuation** phase of treatment
- Must be written in abbreviation that clearly identifies the drugs in the **initial** and **continuation** phases of treatment
- Defines a specific duration of treatment and frequency of giving the drugs
- Duration in months is written in numbers in prefix for which the drugs that follow should be taken.
- The slash (/) separates initial from continuation phase. For examples, 2RHZE/4RH means an initial phase of two months consisting of daily Rifampicin, Isoniazid, Pyrazinamide and Ethambutol, followed by a 4-month continuation phase of Rifampicin and Isoniazid.

There are also **second-line** anti-TB drugs used for treating drug-resistant TB (Section 2.6.5).

2.3.3 Recommended treatment regimen based on disease classification

Type of TB	**Disease category and recommended treatment regimen**		**Comment**
	New patient	Previously treated patient	
Susceptible TB	2RHZE/4HR	2RHZE/4HR	Both new and previously treated TB patients should receive the same regimen provided rifampicin resistance has been excluded
	2RHZE/10RH*		TB Meningitis†, TB of the Bones & joints, Spinal TB *treatment duration may be extended depending patient's response to treatment †Steroids may be added as adjuvant therapy.
Drug resistant TB			
	Short course regimen (9-11 months)		New MDR patients without resistance to injectable and fluoroquinolone receive the short course regimen
	Standard MDR TB regimen (20-24 months)		Patients previously treated for MDR TB receive standard or individualized treatment regimen

Treatment categorization is a system whereby TB patients are grouped according to previous history of treatment: new and previously treated TB patients.

New patients; are TB patients with no prior history of TB treatment or had been treated for less than one month. On the other hand, previously treated patients are those with prior history of TB treatment.

Previously treated patients; are of different types: relapses, treatment failures and loss to follow up. The later needs close follow to address the issues surrounding loss follow up. The risk of drug resistance is also higher in this group and should therefore get an Xpert MTB/Rif test. Previously treated TB patients were treated with a category 2 treatment regimen. This category included drugs used in first line regimen but streptomycin would be added onto the regimen. Streptomycin was added mainly to address drug resistance.

Currently with the availability of rapid methods to identify key drug resistance such as the Xpert MTB/Rif test all patients presenting with a previous history of TB treatment are tested with Xpert MTB/Rif and if they do not have rifampicin resistance they are treated with first line regimen.

This development has therefore necessitated a new categorization of TB patients: Drug sensitive TB (DS TB) and multidrug resistant TB (RR/MDR TB). DS TB patients are treated with first line TB drugs while RR/MDR TB patients are treated with second line TB drugs.

2.3.4 Recommended Standard Regimens in Uganda

I. Susceptible TB

Initial phase: The initial phase is the first two months of treatment. The combination of 4 drugs used during this phase is Isoniazid, Rifampicin, Pyrazinamide and Ethambutol (RHZE). Using these 4 drugs, results in rapid killing of the tubercle bacilli. Patients become non-infectious in about 2 weeks. Symptoms reduce, and most smear-positive cases become smear-negative within the first 2 months.

Continuation phase: The continuation phase is the second part of treatment which lasts 4 months. Here, two drugs are used in combination, usually Rifampicin and Isoniazid (RH).

Table 2.3.2: Recommended anti-TB drug doses for drug susceptible TB cases (>15 years)

Pre-treatment body weight(kg)	**2 month initial phase**	**4 month continuation phase**
	RHZE (150+75+400+275) mg	**RH** (150+75) mg
33-39	2 tablets	2 tablets
40-54	3 tablets	3 tablets
55-70	4 tablets	4 tablets
>70	5 tablets	5 tablets

Note: If an adult is < 33kgs, determine the appropriate dose based on patient's weight using dosage table 2.6

II. Rifampicin resistant TB

These patients should be treated with second line regimen which is used for treatment of RR/MDR-TB according to national RR/MDR-TB treatment guidelines. Current regimens are described in the chapter for RR/MDR-TB.

2.3.5 Adjunctive therapy during TB treatment

Non-anti-TB drugs are usually given to accompany anti-TB treatment. There are two such commonly used drugs, namely pyridoxine (Vitamin B6) and prednisolone.

I. **Pyridoxine**: This drug may be given to all TB patients once they start on treatment. Isoniazid interferes with the metabolism of pyridoxine in the body thus leading to its deficiency and hence peripheral neuropathy. Pyridoxine should thus be given in a dose of 25 mg daily for the entire duration the patient is on Isoniazid containing regimen. In case of peripheral neuropathy, a high dose (up to max dose of 200mg) should be given until symptoms resolve followed by maintenance (25mg) dose up to end of TB therapy

II. **Prednisolone:** This is a high potency anti-inflammatory drug, and is therefore useful in TB patients in whom complications of severe fibrosis are anticipated because of severe inflammation such as TB meningitis. Prednisolone is given in a dose of 1-2mg/kg body weight (not more than 60mg/day) as a single dose for four weeks, and then tapered off over two weeks.

Table 2.3.3: Managing frequent side-effects of anti-TB drugs

Side-effects	Drug(s) likely to cause	Management
Low appetite, nausea, abdominal pain	Pyrazinamide, Rifampicin	Give drugs with small meal or just before going to bed
Joint pains	Pyrazinamide	Give an analgesic e.g. ibuprofen or Paracetamol
Burning sensation in the feet	Isoniazid	Pyridoxine 25-100 mg daily
Orange/red urine	Rifampicin	Reassure the patient that it is not harmful
Skin rash	Any anti-TB drug	Stop anti-TB drugs, wait for patient to recover then reintroduce one drug at a time OR Refer the patient
Deafness (no wax on auroscopy)	Streptomycin	Stop streptomycin. Use Ethambutol
Dizziness, vertigo, and nystagmus	Streptomycin	Stop streptomycin.
Jaundice (other causes excluded)	Pyrazinamide, Rifampicin and Isoniazid	Stop anti-TB drugs till jaundice clears then restart drugs
Mental confusion	Isoniazid, Rifampicin and Pyrazinamide	*1. If jaundiced,* suspect liver failure, treat as liver failure. *2. If no jaundice*, suspect Isoniazid, increase dose of pyridoxine.
Visual impairment (other causes excluded)	Ethambutol	Stop Ethambutol. Refer to a higher level for further management.

Box 2.1 Key messages for TB patients

The health worker should provide this information to the TB patients started on treatment to facilitate adherence.

Key Messages for TB Patients

1. TB is a disease caused by a germ (bacteria) that is very strong and difficult to kill by just one drug.

Because of this:

2. The treatment uses a combination of more than one drug, and takes a long time (6 months). The treatment is divided into two parts. In the **first part,** lasting 2 **months** you will take more drugs than in the **second part** which lasts **4 months**.

During the 6 months of your treatment:

3. You will be requested to give sputum for examination at **2 months, 5 months** and in the 6th **month.** This is a continuous check to see how the drugs are working on the germs that caused your disease.
4. Do not stop taking the drugs even if you feel well **because** TB will not be cured if you stop the drugs before the correct time has passed. You have to be discharged from treatment when you are confirmed cured.

Should you feel the drugs are giving you problems

5. Do not stop taking the drugs by yourself or on someone else's advice. Report your problem immediately to the health worker at the facility where you collect your drugs; you will be helped properly.

Remember
This should be preceded by explanation about how TB spreads and risk to family etc
6. To bring your family members, particularly children under 5 years of age to be checked for TB; particularly if they are suffering from cough.
7. If you came from a village for treatment in town and would like to go back, (or you wish to change your residence) before 6 months of treatment are completed, tell the health worker who gives you your drugs, who will explain how to get drugs from your changed place of residence.
8. When you cough, turn your face away from people. Cover your mouth with a handkerchief or hands.
9. As a TB patient, it is important for you to know your HIV status. You are hereby advised take an HIV test.

2.3.6 Treatment monitoring

Once a TB patient is started on treatment, it is important to find out if the patient is getting better as a result of the treatment. This is called **treatment monitoring**. The following methods are used for treatment monitoring in order of importance:

Laboratory monitoring– Sputum microscopy (or culture) must be used for monitoring all pulmonary TB patients. Sputum smears are performed at the end of the **initial phase** (2 months), at beginning of 5 months and beginning of 6th month of treatment. This should be done for both smear-positive and smear-negative pulmonary TB patients.

If the patient has a sputum smear that is positive at the end of the **initial phase** of treatment, consider the following as possible explanations:

- The treatment was poorly supervised.
- The bacillary load was too high, e.g. in cavitary disease with slow clearance of the bacilli.
- The patient could have RR/MDR-TB.
- Could also be dead bacteria

For patients registered as sputum smear-negative before the anti-TB treatment was started, clinical monitoring is recommended together with sputum monitoring. Sputum examination is important in these patients because:

- An error could have occurred at the time of diagnosis
- The patient may have drug-resistant TB

Box 2.2 shows the action points to be taken during sputum smear monitoring in a new case.
For patients on second line drugs, treatment should be done as for MDR TB patients. GeneXpert should not be used for treatment monitoring. However, it can be used to exclude rifampicin resistance in patients who have positive sputum smears during treatment

Box 2.2. Monitoring treatment for susceptible TB cases

Action points during treatment

At the end of the initial 2 months:

- Sputum smear-negative; start continuation phase
- Sputum smear-positive; do Xpert MTB/Rif, If RR, refer for MDR treatment and if RS, continue with first-line treatment, explore adherence issues but repeat smear at 3 months, if positive, do DST, if smear negative continues with first-line treatment.

At the end of 5 months:

- Sputum smear-negative, continue with continuation treatment
- Sputum smear-positive, diagnose **Treatment Failure**
- Take sputum for GeneXpert to rule out RR.
- If RR, refer for DR treatment.
- If MTB detected but not RR and re start first line regimen but explore adherence issues

At the end of 6thmonths:

- Sputum smear-negative, complete treatment and declare **cured** or **treatment completed**
- Sputum smear-positive, diagnose **treatment failure**
- Take sputum for GeneXpert to rule out RR.
    - If RR, refer for DR treatment.
    - If MTB detected but not R restart first line regimen but explore adherence issues

Clinical monitoring **–**is useful for all patients but is particularly useful for children and extra-pulmonary TB cases. Treatment monitoring is carried out through clinical observation. A patient's weight gain and reduction in symptoms are useful indicators.

Radiological monitoring –is a method that should not be used as the sole monitoring tool.

In cases where radiological monitoring is used, sputum and clinical monitoring should accompany the radiological monitoring.

2.3.7 Monitoring and recording adverse effects

Most TB patients complete their treatment without any significant adverse drug effects. However, a few patients do experience adverse effects. It is therefore important that patients are clinically monitored during treatment so that adverse effects are promptly detected and properly managed. Routine laboratory monitoring is not necessary. Health personnel can monitor adverse drug effects by teaching patients how to recognize the symptoms of common effects, urging them to report if they develop such symptoms, and by asking about symptoms when patients come to collect drugs.

Adverse reactions to drugs should be recorded on the TB Treatment Card under "comments" and treatment register under the remarks section

2.3.8 Defining Treatment Outcome

A conclusion should be made regarding ***treatment outcome*** of every TB patient who has been started on anti-TB treatment within the same year (reporting period). This is called **Cohort Analysis**. In considering treatment outcomes, a distinction is made between two types of patients:

- Patients treated for drug-susceptible TB;
- Patients treated for drug-resistant TB using second-line treatment

The two groups are mutually exclusive. Any patient found to have drug-resistant TB and placed on second line treatment is removed from the drug-susceptible TB outcome cohort. This means that management of the standard TB register and of the second-line TB treatment register needs to be coordinated to ensure proper accounting of the outcomes of treatment.

Box 2.3 presents Treatment outcomes for TB patients (excluding patients treated for RR-TB or MDR-TB), treated outcomes for RR-TB and MDR TB are given in the section for MDR TB.

Box 2.3 Treatment outcomes for TB patients (excluding patients treated for RR-TB or MDR-TB)

Treatment outcome definitions

a) **Cure:** A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion

b) **Treatment completed:** A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable

c) **Treatment failed:** A TB patient whose sputum smear or culture is positive at month 5 or later during treatment. Or was negative at beginning and is smear positive at 2 months

d) **Died:** A TB patient who dies for any reason before starting or during the course of treatment.

e) **Lost to follow-up** A TB patient who did not start treatment or who completed more than 1 month of treatment and was interrupted for 2 consecutive months or more.

f) **Not Evaluated:** A patient for whom no treatment outcome is assigned. This includes cases "transferred out" to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.

g) **Treatment success:** The sum of cured and treatment completed.

Table 2.3.4: Managing anti-TB treatment interruption (1–2 months)

Duration of interruption	Action	Decision
0-2 months	• Trace the patient • Identify and solve the cause, if possible • Adherence counseling	• Re-initiated on treatment

Table 2.3.5: Managing TB treatment interruption (2 or more consecutive months i.e. loss to follow up)

Action	Sputum result	Decision
• Trace the patient • Identify and solve the cause, if possible • Do GeneXpert, • No treatment while waiting for results	GeneXpert negative	Clinical decision on individual basis whether to restart or continue treatment
	GeneXpert positive	• If Rifampicin resistance detected o Initiate treatment as MDR TB and obtain full DST • If Rifampicin resistance not detected o Restart first line TB treatment regimen

2.3.9 Treatment adherence

TB patients must take all their medications in order to ensure that cure is achieved. However, some TB patients do not take all their medications. One of the key strategy to treatment adherence is directly observed therapy (DOT). Patients are observed while taking their medications. There two forms of DOT: Facility DOT and community DOT). In facility based DOT, TB treatment is observed by a health worker at the health facility. Community DOT involves observation of the patient taking medication in the community by a trained community health worker (VHT, CHEWs, expert client etc.) or a family member who serves as a treatment supporter. This person can be a community volunteer or a relative of the patient. Treatment should be patient centered. NTLP will develop a standard strategy for community based TB care to guide implementation of DOT.

2.3.9.1 Implementation of CB-DOTS in a Rural Setting

Community-based DOT implementation is usually linked to a health facility, which is usually located in a sub-county. Each sub county has a person responsible for DOT for all TB patients in that sub county. Until now this person is called a sub county health workers (SCHW) within the NTLP system. The SCHW is a key person in the implementation of community-based DOT. SCHWs have worked closely with village health teams in the delivery of CB-DOTS. The government of Uganda is planning a new cadre of community health workers called the community health extension worker. When this cadre of health worker becomes active, it is hoped that they play a key role in the implementation of CB-DOTS.

TB patients who are diagnosed in the health facilities and do not require hospitalization and who opt for, should be enrolled in community-based DOT. The SCHW is informed by the health facility staff about the patient and contacts the VHT or Local Council (LC) I who will convene a community meeting to identify a treatment supporter to supervise the patient's TB treatment in the community. The SCHW will brief, orient and supervise the treatment supporters. After training is completed, the SCHW provides the treatment supporter with a two-week supply of the anti-TB drugs and a patient treatment card for each patient with TB in the community.

The treatment supporter is responsible for ensuring DOT and recording each dose of anti-TB drugs swallowed on the patient treatment card. The treatment supporter will also be responsible for referring the TB patient to the health facility at end of 2 (3), 5 and 6 months for follow-up sputum checks and to monitor the patient for side-effects. If the treatment supporter identifies TB suspects (i.e. with a cough of two weeks or more duration) in the community, the treatment supporter should refer them to the health facility for evaluation.

The SCHW will visit the treatment supporter every two weeks during the intensive phase and monthly during the continuation phase to replenish drug supplies, review and record information from the patient treatment card and provide additional training as needed. The SCHW liaises with both the VHT and LC I to update records and recommend community action.
Procedures to observe for TB patients who opt for a **family member as a treatment supporter:**

- Upon diagnosis of TB, the health worker must observe the swallowing of the first dose, give a one-week supply of drugs and request the patient to bring the proposed treatment supporter within 1 week, before the drugs are finished.
- If the TB patient has someone who can be a treatment supporter, the health worker then trains this person to carry out the responsibilities of a treatment supporter.
- The health worker should link the treatment supporter to the SCHW.

Note:

TB patients who are too ill to be started on community-based DOT should be admitted or referred to a health facility with admission facilities. The health facility nurse will be responsible for observing the swallowing of drugs and recording the information on the patient treatment card. TB patients who are no longer ill enough to require hospitalization will be referred to the nearest health facility and started on community-based DOT.

2.3.9.2 Implementation of CB-DOTS in an Urban Setting

The management of TB patients in large hospitals and health centers located in urban areas poses special challenges. The advantage of shorter distances from the health facilities is unfortunately counteracted by many factors; i) the de facto lack of coordination between private and public sector and ii) the frequent absence of an extended family who can support the patients and their closest relatives during the time of sickness.

Further, the majority of patients stop the treatment which poses extremely serious immediate threats to the health of the patients and their families and increases the transmission of TB in an environment that is obviously more populated than the rural areas. Despite all these constraints, the anti-TB treatment **must** still be observed, completed and evaluated for the sake of curing the patient and controlling TB. As the social structure and the organization of the health services in large cities are different from that of rural areas, the implementation of DOT must follow different steps outlined below.

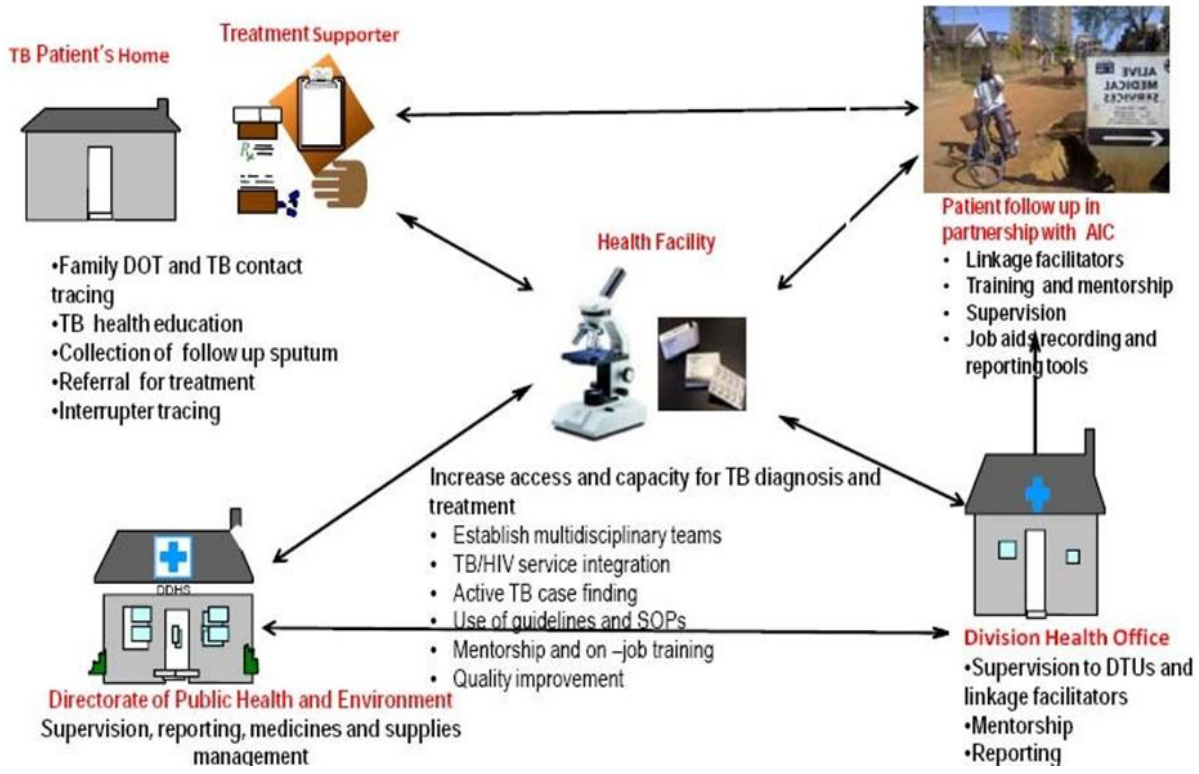
After the diagnosis of tuberculosis is established:

- If the patient's clinical condition requires admission to a health facility, the nurses start DOT and are responsible for the daily administration of drugs and the daily update of the patient treatment card.
- If the patient's clinical condition allows for immediate referral home, the patient is given the essential information about the disease and its treatment, given the first dose of anti-TB drugs to swallow and is told to return along with a treatment supporter to attend a session of health education and training on how to administer DOT at home.
- Patients may receive enough drugs for a few days if they cannot return the following day. They should be told that the drugs are available free of charge.
- On returning with the treatment supporter for the health education session (ideally organized twice a week at the health facility), the patient will receive a 2-week drug supply during the intensive phase and a 4-week drug supply during the continuation phase.
- Every two weeks during the intensive phase, or every four weeks during the continuation phase, either the patient or the treatment supporter will return to the health facility to receive a new drug supply, to report any problem/complication of treatment and to allow transposition of information from the patient treatment card to the Unit TB Register. All TB patients admitted for initial treatment will continue DOT at home with the support of a treatment supporter, after their discharge from the hospital.

Note:
An essential component of the CB-DOTS model is the **referral system** between Diagnostic Unit ⇒ Sub-county Health Worker ⇒ community at LC1, VHT and ⇒ the treatment supporter living close to the patient. This referral system cannot be reproduced in urban areas because of their different social organization and because the primary healthcare (PHC) system is weaker.

In view of the challenges with DOT in urban areas several innovations are being tried in Uganda to find ways to overcome the challenges of DOT in urban settings. One such innovation, called URBAN DOTS model (Figure 2.5), is being implemented in Kampala city. The model consists of the following strategies;

(1) Strengthening the leadership and coordination of TB services in Kampala Capital City Authority through establishing the urban TB control task force.
(2) Increasing access to TB diagnostic, treatment, and follow-up services by increasing the number of DTUs.
(3) Engaging community linkage facilitators (CLFs) to follow-up patients at the community level.
(4) Strengthening the capacity of the existing TB diagnostic and treatment facilities in KCCA to provide improved TB services.
(5) Supporting the integration of TB and HIV services at health facility level through implementation of appropriate TB/HIV integration models and continuous quality improvement.



In a two-year period of implementing the URBAN DOTS model, the proportion of TB patients on DOT increased significantly from 7% to 89%, and cure rate among the pulmonary bacteriologically confirmed TB patients increased from 43% to 75%. HIV testing among TB patients increased from 78% to 99% while ART and CPT coverage among the TB HIV co infected patients increased from 92% to 98% and 56% to 95% respectively.

The key component of the URBAN DOTS model is the deployment of Community Linkage Facilitators (CLFs). Each health facility providing TB services should explore ways of identifying a CLFs. CLFs can be volunteers or health workers already working on community health.

2.3.9.3 Engaging Private Providers in CB-DOTS Implementation

Private providers play a big role in diagnosing and treating TB. Efforts have been made by the NTLP to engage some of the private providers to ensure appropriate delivery of TB services through a coordinated framework. The different categories of private providers who can play a role in managing presumptive and diagnosed TB patients include:

- Private health providers
- Private, not-for-profit hospitals and health centers
- Individual private physicians, nurses, midwives, clinical officers, etc.
- Pharmacies and drug shops
- Practitioners of traditional medical systems

The NTLP can engage the private providers in several ways depending on the capacity and operational level of the private provider. The public-private mix (PPM) DOTS strategy shall include but not be limited to:

- NTLP Training health workers in large hospitals and clinics, on the identification of patients with presumptive TB patients and diagnosis of TB. The health workers in these large hospitals and clinics should also be trained to carry out recording and reporting using the NTLP monitoring and evaluation tools. Quarterly reports from such private health providers are submitted to DTLS to be forwarded to RTLFP.
- The support provided to private providers by NTLP & the District Health Office: NTLP and DHOs' offices do:
    - Conduct training for health workers of the smaller private provider units so that they can recognize and refer patients with presumptive TB to diagnostic facilities and keep a record of such referrals
    - Conduct regular training to update private providers on current TB management recommendations
    - Provide private provider facilities with support supervisory visits to ensure that the private providers carry out their work according to NTLP recommendations.
    - Provide anti-TB drugs to private health providers
    - Monitor private providers to ensure they do not charge TB patients for the anti-TB drugs provided.

2.3.9.4 Facility based DOT

Patients have their anti-TB treatment observed daily by the health worker at the health facility at least during the intensive phase of treatment. Patient that live near the health facility or those admitted should benefit from facility DOT.

2.4 PREVENTIVE TUBERCULOSIS THERAPY

- To prevent the progression of LTBI to active TB, IPT is recommended for all HIV positive persons irrespective of TST results and CD4 cell count.
- IPT is also recommended for under five-year child contacts of persons with active infectious TB.
- Exclusion of active TB using symptom screening algorithms is highly recommended.
- Pregnancy should not be used to exclude women living with HIV/AIDS from symptom based screening and receiving IPT. More still, IPT therapy should be completed even if the woman becomes pregnant while still on IPT treatment.
- IPT treatment monitoring to foster treatment adherence is key in ensuring successful treatment.

TB infection occurs when a susceptible person is exposed to an infectious source case (usually a pulmonary TB patient). In 90-95% of cases, the infected person's immune system halts growth of the bacteria and active disease does not develop, although skin or serological testing for TB will convert to positive. Once positive, a person's TB test will generally remain positive for life. It is this state of positive skin or serological tests that is called latent TB infection (LTBI).

Currently one in three people worldwide are infected with tuberculosis bacilli. It is estimated that up to 90% of the TB that is active develops in people with latent TB as a reactivation.

Preventive therapy of TB is the use of anti-TB drug(s) to prevent the development of active TB disease in an individual who has latent TB infection (LTBI).

For this reason, LTBI therapy t is a key component of TB control. Probably TB elimination will occur once there is wide use of LTBI treatment.

LTBI therapy has been shown to reduce the risk of developing active TB by over 60% in several studies. The efficacy varies according to regimen and duration. For example, the use of Isoniazid (H) for up to 12 months has a protective efficacy of up to 83%.

There have been variable delays in wider use of LTBI therapy for several reasons. Firstly, the protection is short lived (up to 3 years). Re-infection is high and there was fear of development of resistance to the drugs used if active TB is not excluded. Toxicity to the used drug is also a concern. In consideration of these concerns preventive therapy is recommended for groups of patients who are most likely to benefit most.

Uganda NTLP National preventive guidelines recommend preventive therapy using a six -month regimen of only Isoniazid as monotherapy (Isoniazid preventive therapy, IPT) for under 5-year contacts of infectious pan susceptible TB who do not have active TB. It must be noted that other drugs can be used either in combination with Isoniazid or alone. Such drugs include Rifampicin or rifapentine.

Diagnosis of latent TB*:* LTBI is confirmed by a positive tuberculin skin test (TST). The commonest method for the TST is the Mantoux method. For this reason, the TST is loosely called the Mantoux test in clinical settings.

TST is positive when the induration of TST has a diameter of 5 or more mm in an HIV-positive person and 10 or more mm in an HIV- negative person. Other blood tests for LTBI namely Quantiferon TB Gold and TB SPOT have been developed. These tests are generally less accurate and more expensive than the TST but they have some advantages over TST. They do not require a second visit to read the test as is the case with TST, they do not react in non-MTB infections.

2.4.2 Target populations for TB preventive therapy

The highest risk for reactivation of LTBI to active TB disease occurs in the populations below and they are therefore the key target populations for TB preventive therapy

- Persons living with HIV/AIDS
- Child contacts of pulmonary TB patients
- Persons with immunosuppression e.g. Diabetics
- Persons living with HIV/AIDS in congregate settings e.g. Prisoners, Health workers and internally displaced persons

2.4.3 Principles of preventive TB therapy initiation

The following principles guide preventive TB treatment

1. Latent TB infection must be diagnosed. Several studies have shown that the greatest benefit from TB preventive therapy occurs in those with a confirmed TB infection. This is the case even in HIV infected persons

2. Exclude active TB disease. Patients should be screened to exclude active TB disease using standard TB screening methods.

3. In principle, any effective TB chemotherapeutic agent can be used. However, the greatest experience is with Isoniazid as monotherapy or Isoniazid and Rifampicin combination. Commonly Isoniazid monotherapy is used and is called Isoniazid preventive therapy (IPT).

2.4.4 Isoniazid preventive therapy (IPT)

IPT is currently strongly advocated by NTLP for all HIV positive persons and under 5 child contacts of patients with active TB. NTLP has published an IPT health workers guide to assist health workers in initiating IPT. Health workers should consult this guide when considering initiating IPT. It is important that before IPT is initiated that active TB is excluded. This is done to avoid monotherapy for active TB because TB should always be treated with combination therapy.

The following key points from the IPT guidelines need to always be remembered:

1. Adults and adolescents living with HIV should be screened for TB using the four symptom screening tool for TB in PLHIV. Those who do not report any one of the symptoms of current cough, fever, weight loss, or night sweats are unlikely to have active TB. And those unlikely to have active TB upon screening should be offered Isoniazid preventive therapy.
2. Adults and adolescents living with HIV who report any one of the symptoms of current cough, fever, weight loss, or night sweats may have active TB. These individuals should be evaluated for TB and other diseases.
3. Adults and adolescents living with HIV who are unlikely to have active TB should receive at least six months of Isoniazid Preventive Therapy (IPT). This should be irrespective of:
    - The degree of immune suppression,
    - Whether the patient is on antiretroviral therapy or not,
    - Whether the patient is pregnant or not.
4. A Tuberculin Skin Test (TST) is not a requirement for initiating IPT in PLHIV.
5. PLHIV who have a positive TST benefit more from IPT. TST should be used where feasible to identify such individuals.
6. Providing IPT to PLHIV does not increase the risk of developing Isoniazid resistant TB. Therefore, concerns regarding the development of Isoniazid resistance should not be a barrier to providing IPT.
7. Children living with HIV who do not have any one of the following symptoms: poor weight gain, fever, or current cough are unlikely to have active TB.
8. Children living with HIV who have any one of the following symptoms: poor weight gain, fever, current cough or contact history with a TB case may have TB.

    These children should be evaluated for TB and other conditions.

    If the evaluation shows no TB, such children should be offered IPT except if they less than 1 year. Children less than 1 year can be offered IPT if they are active TB contacts.
9. Children living with HIV who are more than 12 months of age:

    For those who are unlikely to have active TB and have no contact with a TB case should receive six months of IPT (10 mg/kg/day).
10. Children living with HIV who less than 12 months are of age (infants):

This group should only receive IPT if there is a history of contact with a TB case and they have no active TB.

11. All children under five years:

    Those who have a history of contact with a TB case should be screened for active TB using the Intensified TB Case Finding Guide.

    Those who have no symptoms and signs suggestive of active TB should receive six months of IPT.

2.4.5 IPT in special situations

a) Pregnancy

IPT is safe in pregnancy and therefore pregnancy should not be used to exclude women living with HIV/AIDS from symptom based screening and receiving IPT. More still, IPT therapy should be completed even if the woman becomes pregnant while still on IPT treatment.

b) Contacts of MDR-TB and XDR-TB

Primary or secondary prophylaxis with IPT is **not applicable** for the case of MDR or XDR-TB contacts or persons previously treated for MDR or XDR-TB irrespective of their HIV status. Strict clinical observation and close monitoring for the development of active TB disease for at least two years and application of TB infection control measures at home as well as instituting effective therapy for the index case are preferred over the provision of MDR-TB or XDR-TB preventive therapy

c) Injecting drug users

Use of IPT among injecting drug users should be undertaken after screening for active TB combined with harm reduction to minimize chances of acquisition of HIV and hepatitis. In this group of patients, HIV and hepatitis screening is always recommended. Referral for specialized care should be done in case of positive results for HIV or hepatitis.

2.4.6 Monitoring IPT therapy for toxicity and adverse events

IPT associated adverse drug reactions are minor and occur rarely. Close monitoring is needed for early detection of these adverse events. The major categories of drug-specific adverse reactions that can occur with IPT are hepatic and peripheral nerve damage. Some hepatic damage is mild presenting as asymptomatic elevation of serum liver enzyme concentrations while others can present with a full blown picture of hepatotoxicity.

The following symptoms should raise suspicion of hepatotoxicity in a patient on IPT: anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-colored urine, pale stools or jaundice. Baseline and periodic laboratory measurements of serum aspartate aminotransferase, alanine aminotransferase, and bilirubin is strongly recommended among

individuals with history of liver disease; regular use of alcohol; chronic liver disease; HIV infection; age more than 35 years; and pregnancy or the immediate postpartum period (i.e., within three months of delivery).

2.4.7 Factors facilitating IPT therapy adherence and completion

Adherence to the full course and completion of therapy are important determinants of clinical benefit to the individual as well as to the success of the program. Therefore, during monthly follow-ups, the provider should encourage adherence, address side effects, provide incentives where possible, educate the patient to minimize stigma and ensure active TB disease is not present. However, initial follow up at two weeks following IPT initiation to check for side effects, patient's understanding and to reinforce adherence is recommended

If an individual on IPT develops active TB, IPT therapy must immediately be stopped and instead, a fully-fledged appropriate TB regimen is provided based on the patient's TB category.

2.5 TREATMENT OF TUBERCULOSIS IN SPECIAL SITUATIONS

2.5.1 Pregnancy

The number of pregnant women with TB has increased because of the current HIV epidemic. The clinical presentation of TB in pregnancy is like non-pregnant women. Therefore, all pregnant women should be screened and tested for TB using the same TB screening tools available. Where possible the chest x-ray should be avoided. If a mother delivers a presumptive TB patient and other diagnostics tests have failed, the placenta should be examined for presence of calcifications. If calcifications are present, endometrial tissue should be obtained and sent for histology for TB. It has been shown to grow MTB and may have histological features of TB.

Undiagnosed TB in pregnancy is associated with poorer perinatal infant outcomes. Particularly disseminated TB, military TB and TB meningitis have been associated with worse peri-natal outcomes. Once a diagnosis of TB is made, treatment should be promptly started because untreated TB presents a much greater risk than toxic effects to the baby. On the other hand, after diagnosing TB in a woman, it is recommended to inquire about pregnancy. This is to ensure that she is not given any drug(s) that may be considered unsafe in pregnancy. Fortunately, the first-line anti-TB drugs – Rifampicin, Isoniazid, Pyrazinamide and Ethambutol – are safe in pregnancy.

The NTLP-recommended regimen of **2RHZE/4RH** for susceptible TB is safe for use in pregnancy. In case of drug resistant TB, the clinician should evaluate the patients to assess the clinical condition of the patient. In patients in who the clinical condition is not life threatening drug resistant TB treatment should be started preferably in the second trimester. Aminoglycosides injectable drugs and Ethionamide should be avoided as much as possible. Aminoglycoside cause ototoxicity in the foetus. Ethionamide causes severe nausea and has been associated with teratogenic effects.

All pregnant women diagnosed with TB should be screened for HIV and if positive managed according to national TB-HIV management guidelines.

2.5.2 Breastfeeding

A breastfeeding woman who has TB should be treated with a full course of a standard regimen recommended by the NTLP. The concern here is to find out if the child already has TB disease or is just a contact likely to be infected by the mother. Concentrations of anti-TB drugs in breast milk are too low to prevent or treat TB in infants. The child should therefore be investigated for TB disease and, if found to have TB disease, must be given full course of anti-TB treatment. If the child does not have TB disease, give Isoniazid preventive therapy (10mg/kg body weight) for 6 months. Mother and child should stay together and breastfeeding should continue normally but standard TB infection prevention measures are recommended. BCG vaccination of the child should then be postponed until the end of Isoniazid preventive therapy.

2.5.3 Treatment in Patients with Liver Disease

Patient can have pre-existing liver disease or develop it as a toxicity of TB drugs.

In patients with liver failure, a regimen without Rifampicin may be used. Streptomycin and Ethambutol may be used if treatment is necessary for patients with severe liver disease. These patients should be referred to higher level of care for specialised management.

2.5.4 Treatment of patients with drug induced liver injury

Suspect liver damage when a patient on anti-TB drugs has developed jaundice plus or minus other symptoms of liver injury such as abdominal pain, nausea and vomiting. If patients develop signs of liver damage during TB treatment, it is advisable to check liver function in the laboratory if facilities are available. If the liver enzymes (ALT/AST) are elevated more than three times the normal upper limit, all medications including non-TB medications should be discontinued and the patient monitored until the enzymes normalise. Then the drugs can be reinitiated. There are different algorithms for reinitiating drugs. However, the principal is to avoid or titrate the introduction of the most hepatotoxic drugs- Pyrazinamide and Isoniazid.

Table 2.5.1: Drug induced liver injury (DILI) management algorithms based on existing guidelines

Authority	Stopping TB drugs if clinical or symptomatic hepatitis	When to restart, TB drugs	What TB drugs to start	Recommended LFT monitoring on re-challenge	If DILI recurs
ATS	Yes	ALT <80IU/I	• R +/- E full dose • After 3-7 days INH (full dose) • Z only if mild DILI	Check ALT 3-7 days after H re-challenge	Stop last drug added
BTS	Yes	ALT within normal limits	• S + E (if unwell or sputum is smear positive within 2 weeks of commencing treatment) • H (dose titration, every 2-3 days) • RIF (Dose titration, every 2-3 days) • Z (Dose titration, every 2-3 days)	Daily monitoring of LFT	Stop offending drug, alternative regimen advised by fully trained physician
ERS, WHO, IUATLD	Yes	LFT within normal limits	• Start all drugs at full dosage	LFT monitoring (no recommendation on frequency)	Stop all drugs, start STR + EMB and start other drugs one at a time
HKTBS	Yes	-	-	-	-

DILI: Drug induced liver injury, ATS: American Thoracic Society, BTS: British Thoracic Society, ERS: European Respiratory Society, WHO: World Health Organisation, IUATLD: International Union against Tuberculosis and Lung Disease, HKTBS: Hong Kong Tuberculosis Service, ALT: Alanine transaminase, LFT: Liver function test, S = streptomycin, H = Isoniazid, Z = Pyrazinamide, R = Rifampicin, E = Ethambutol.

2.5.5 Treatment of Patients with Renal Failure

Isoniazid, Rifampicin, and Pyrazinamide may be given in normal dosage to patients with renal failure, since these drugs are eliminated almost entirely by biliary excretion or are metabolised into non-toxic compounds. Patients with severe renal failure who are receiving Isoniazid should also receive pyridoxine to prevent peripheral neuropathy. These patients should be referred to a higher level of care for further management.

2.5.6 Use of Contraceptives

Rifampicin interacts with estrogen-containing contraceptives and reduces the blood levels of estrogen. This leads to the reduced protective efficacy of the contraceptives and may result in unplanned pregnancy. Therefore, contraceptive pills with higher doses of estrogen, such as NewFem or Ovral, are recommended. Avoid use of contraceptive medications with low amount of estrogen (e.g., Lo-femenal, SoftSure). Alternatively, another method of form of barrier contraception should be used or added.

2.5.7 Bone, Joint, and Spinal Tuberculosis

TB can virtually affect any tissue in the body. TB infects bone, joint tissues and the spine. TB of these tissues requires extended TB treatment durations longer than the standard six months. Although the duration varies from country to country, it is believed that treatment durations of 6-9 months are as effective as longer duration of up to 18 months. Therefore a 9-months regimen is preferred. There is additional benefit of surgical debridement in combination with chemotherapy compared with chemotherapy alone for spinal tuberculosis. As such, uncomplicated cases of spinal tuberculosis are managed with medical rather than surgical treatment. However, based on expert opinion, surgery can be considered in situations in which (1) there is poor response to chemotherapy with evidence of ongoing infection or ongoing deterioration; (2) relief of cord compression is needed in patients with persistence or recurrence of neurologic deficits; or (3) there is instability of the spine. Spinal tuberculosis with evidence of meningitis is managed as tuberculous meningitis, including consideration of adjunctive corticosteroids (Refer to table 2.3.3)

2.5.8 TB Meningitis

TB meningitis requires longer duration of treatment than TB in pulmonary site. The range of duration is 9-12 months. The usual regimens of TB treatment are used. However, a choice can be made between ethambutol and an injectable aminoglycoside. In adults, ethambutol is usually sufficient. In children, there is preference for an aminoglycoside. Adjunctive corticosteroid therapy recommended in the treatment of TB meningitis with dexamethasone or prednisolone tapered over 6–8 weeks for patients.

- Drug resistant-TB (DR-TB) is a more complicated form of TB to manage and poses an obstacle to effective TB care and prevention.
- Four different forms of DR-TB are recognized depending on their pattern of resistance.
- Non-adherence and inadequate TB treatment are the most important factors causing DR-TB.
- DR-TB is confirmed by drug susceptibility testing or by using WHO endorsed molecular tests.
- Treatment of DR-TB is using standardized MDR treatment regimen.
- Groups of first-line and second-line drugs are used for DR-TB treatment in ambulatory or health facility setting.

2.6 DRUG-RESISTANT TUBERCULOSIS

2.6.1 Magnitude of Drug Resistant-Tuberculosis

According to the Uganda Drug resistance survey 2010, the prevalence of MDR-TB among newly diagnosed TB (Primary MDR-TB) patients was 1.4 %. Among previously treated patients Isoniazid resistance occurred in 21.1%, Rifampicin resistance was detected in 12.1%.

2.6.2 Definition of Drug Resistant TB (DR-TB)

Drug resistance is said to occur when TB organisms continue to grow in the presence of one or more anti-TB drugs.

Forms of drug-resistant tuberculosis

- **Mono-resistance:** resistance to one first line anti-tuberculosis drug
- **Poly-resistance:** resistance to more than one than one first line anti-tuberculosis drug, other than both Isoniazid and Rifampicin
- **Multidrug-resistance:** resistance to at least Rifampicin and Isoniazid.
- **Pre- Extensive drug-resistance:** Multi drug-resistance plus resistance to any fluoroquinolone or any one injectable second-line drug (Amikacin, Capreomycin, Kanamycin).
- **Extensively drug-resistance:** Multi drug-resistance plus resistance to any fluoroquinolone and any one injectable second-line drug (Amikacin, Capreomycin, Kanamycin).

2.6.3 Risk Factors for Drug-Resistant Tuberculosis

Although several factors can contribute to the development of drug-resistant TB, inadequate anti-TB treatment is probably the most important. Inadequate anti-TB treatment leads to mutation in drug-susceptibility bacilli making them drug resistant. Overgrowth of initially drug-resistant bacilli also occurs when inadequate anti-TB treatment is used. Below are situations of inadequate anti-TB treatment:

- Inadequate drug regimen
- Inadequate duration of treatment
- Drugs not taken regularly by the patient
- Use of poor quality drugs

Factors causing inadequate anti-TB treatment can be grouped into health provider factors, drug factors and patient factors.

Table 2.6.1: Factors contributing to an inadequate anti-TB regimen

Categories	Factors
Health care providers: **Inadequate regimens**	Inadequate DOT Non-compliance with guidelines Absence of guidelines Poor training No monitoring of treatment Wrong dose or combination Poorly organized or under-funded programs Poor patient education Poor patient support Poor management of adverse events
Drugs: **Inadequate supply/quality**	Poor quality medicines Unavailability of certain drugs (stock-outs or delivery disruptions) Poor storage conditions Poor regulation of medicines
Patients: **Inadequate intake**	Poor adherence Lack of money (no free treatment available) Lack of transportation Adverse effects Social barriers Malabsorption Diabetes Mellitus Alcohol and substance abuse

2.6.4 Diagnosis of Drug-Resistant Tuberculosis

When to suspect drug resistance; Suspect drug-resistant TB under the following circumstances (Risk groups):

- Contact with known drug-resistant tuberculosis
- Relapses
- Treatment after failures
- Return after loss to follow up
- History of frequent interruption of drug treatment
- HIV-positive patient presumed to have TB
- Patients who remain sputum smear-positive at month 2 or 3 months of first-line anti-TB treatment
- Health care workers
- Patients from prisons or other congregate settings
- Chronic cases (still sputum smear-positive after completing a supervised retreatment regimen)

Table 2.6.2: Risk groups for drug-resistant tuberculosis

Risk factors for drug-resistant TB	Comments
Failure of retreatment regimen	Failures of retreatment regimen are defined as patients who remain sputum smear-positive at the end of a supervised retreatment regimen. These patients have the highest MDR-TB rates of any group, often approaching 90%.
Exposure to a known DR-TB case	Most studies have shown that close contacts of MDR-TB patients have very high rates of MDR-TB.
Failure of Category 1	Failures of Category 1 are patients who while on treatment are sputum smear-positive at month 5 or later during the course of treatment. Category 1 failures where Rifampicin was used in the continuation phase and DOT was not used throughout treatment are at higher risk for MDR-TB.
Patients who remain sputum smear-positive at month 2 or 3 of first-line anti-TB treatment	This group of patients is at risk for DR-TB, rates can vary considerably.
Relapse or return after loss to follow-up, without recent treatment failure	Cases of relapse or return after loss to follow-up with a history of erratic anti-TB drug use may be more strongly associated with risk for DR-TB. Early relapses are also associated with DR-TB.

Exposure in institutions that have DR-TB outbreaks or a high DR-TB prevalence (includes health-care workers)	Prisoners and health-care workers in health facilities can have high rates of DR-TB.
HIV-positive patient presumed to have TB	It is strongly recommended that all individuals with HIV-associated TB have DST to rule out DR-TB to avoid high rates of mortality due to unrecognized DR-TB in these patients.

Laboratory testing for DR-TB

Patients presumed to have DR-TB should be screened using a nucleic acid amplification test (NAAT) such as Xpert MTB/Rif or the Line Probe Assay (LPA) which detects genetic determinants of resistance. Definitive diagnosis of drug resistance is made microbiologically after culture and DST has been done in the laboratory. All patients who are presumed to have drug-resistant TB should therefore have sputum/other specimens taken for culture and DST in vivo.

2.6.5 Treatment of Drug-Resistant Tuberculosis

Initiation of MDR TB Treatment and any modification of such treatment should be done by DR TB Expert Review Panels in DR-TB treatment initiation centers. Treatment of DR-TB depends on the resistance pattern; whether it is mono- or poly- resistance or whether it is multi- or extensively resistance. Treatment of patients with mono- or poly resistance using short course chemotherapy has been associated with increased treatment failure and further acquisition of drug resistance. Treatment regimens should be constructed for these patients based on DST patterns. The most effective treatment regimens shall be reviewed by specialists and approved by Expert Review Panels in the DR-TB treatment initiation centers.

For patients with a diagnosis of MDR-TB or XDR-TB, treatment should be started as soon as possible.

Treatment regimen for DR TB

Standardized treatment: This is when DR-TB regimens are designed based on DST data from representative patient populations, and all patients in a defined group or category receive the same regimen. This is usually done in the absence of individualized DST and may be changed once individual results are available. Standard regimen should be used if susceptibility to fluoroquinolones and injectable agents is documented (or almost certain)

Empirical treatment: Is when each regimen is individually designed based on the patient's past history of TB treatment and DST data from the representative patient population. Commonly, an empirical regimen is adjusted when DST on the individual patient becomes available. Practically,

each regimen is designed based on the patient's previous history of anti-tuberculosis treatment and individual index case's DST results.

Individualized Treatment: Is when each regimen is designed based on the patient's past history of TB treatment and individual DST results.

Duration of MDR-TB treatment

Treatment of MDR TB requires long periods than susceptible TB. The treatment duration ranges from 9-20 months depending on the regimen and response to treatment. Based on duration MDR TB regimens can be classified as shorter MDR TB regimens or Conventional MDR TB regimens

Shorter MDR-TB regimens: These regimens are for patients with rifampicin-resistant or multidrug-resistant TB who have not been previously treated with second-line drugs and in whom resistance to fluoroquinolones and second-line injectable agents has been excluded or is considered highly unlikely, the shorter MDR-TB regimen is 9-12 months.

Conventional MDR-TB regimens: These regimens last up to 20 months and the ones that have been used for the longest time until the shorter regimens were developed.

Treatment phases

The treatment of MDR TB like drug susceptible TB is divided into two phases: intensive phase and continuation phase. Characteristic of intensive phase is the injectable drug and the continuation phase has only oral medication.

RR/MDR-TB: Intensive phase duration

- The intensive phase (duration of injectable anti-TB drug use) should be **at least 6 months and at least 4months post-culture conversion*** (whichever is longer).
- For standardized regimen, this injectable phase includes an injectable given six days a week and four oral drugs given seven days a week.
- For short course regimen, the intensive phase is for 4-6 months

RR/MDR-TB: continuation phase duration

- For standardized regimen, the continuation phase is 14 months and includes four oral drugs given seven days a week.
- For short course regimen, continuation is 5 months

*Culture conversion is defined as the first month of two consecutive negative cultures taken at least 30 days apart.

2.6.6 Classes and Groups of anti-tuberculosis drugs

Anti-TB drugs have traditionally been divided into first- and second-line agents with isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin being the primary first-line anti-TB drugs.

A new classification system for second line drugs using an A-D-group system based on efficacy, experience of use, safety, and drug class (but not all medications in the same group come from the same drug class or have the same efficacy or safety). In this new group system streptomycin, has been added to the second line injectable agents. Not all medications listed below are available for use in Uganda, but are provided as a thorough listing for general reference and potential future application.

Table 6.1 Medicines recommended for the treatment of rifampicin-resistant and multidrug-resistant TB[1]

Adapted from the WHO treatment guidelines for drug-resistant tuberculosis, 2016 Update

Group name		Anti-TB drug	Abbreviation
A. Fluoroquinolones[2]		Levofloxacin	Lfx
		Moxifloxacin	Mfx
		Gatifloxacin	Gfx
B. Second-line injectable agents		Amikacin	Am
		Capreomycin	Cm
		Kanamycin	Km
		(Streptomycin)[3]	(S)
C. Other core second-line agents[2]		Ethionamide / Prothionamide	Eto / Pto
		Cycloserine / Terizidone	Cs / Trd
		Linezolid	Lzd
		Clofazimine	Cfz
D. Add-on agents (not part of the core MDR-TB regimen)	D1	Pyrazinamide	Z
		Ethambutol	E
		High-dose isoniazid	H^h
	D2	Bedaquiline	Bdq
		Delamanid	Dlm
	D3	*p*-aminosalicylic acid	PAS
		Imipenem-cilastatin[4]	Ipm
		Meropenem[4]	Mpm
		Amoxicillin-clavulanate[4]	Amx-Clv
		(Thioacetazone)[5]	(T)

1 *This regrouping is intended to guide the design of conventional regimens; for shorter regimens lasting 9-12 months the composition is usually standardised*

2 Medicines in Groups A and C are shown by decreasing order of usual preference for use (subject to other considerations; see text)

3 Refer to the text for the conditions under which streptomycin may substitute other injectable agents. Resistance to streptomycin alone does not qualify for the definition of extensively drug-resistant TB (XDR-TB)

4 Carbapenems and clavulanate are meant to be used together; clavulanate is only available in formulations combined with amoxicillin

5 HIV-status must be tested and confirmed to be negative before thioacetazone is started

Anti-TB drugs listed above that are *not currently available in Uganda* include:, gatifloxacin, prothionamide, terizidone, delamanid, , imipenem/cilastatin, meropenem, and thioacetazone. Bedaquiline is now available.

Group A: Fluoroquinolones

Fluoroquinolones are often the most effective anti-TB drugs in a MDR-TB regimen. Important recommendations include:

- A fluoroquinolone should be used for all MDR-TB cases if susceptible (or felt likely to have efficacy). Recent meta-analyses have found a significant association with cure for MDR-TB treatment when fluoroquinolones are included in the regimen.
- A later-generation fluoroquinolone (levofloxacin or moxifloxacin) rather than an earlier-generation fluoroquinolone (Ofloxacin) should be used if available. Recent meta-analyses also supports a stronger association with cure using later-generation (moxifloxacin and levofloxacin) over early-generation (Ofloxacin) fluoroquinolones. Levofloxacin is included in the standardized MDR-TB regimen.
- Ciprofloxacin has weaker efficacy against TB than other fluoroquinolones and <u>is not recommended</u> to be used as an anti-TB drug.
- Gatifloxacin is associated with serious cases of hypoglycemia, hyperglycemia and new onset diabetes, and due to these safety issues is not recommended for use.
- The fluoroquinolones are known to prolong the QT interval. QT interval prolongation predisposes to Torsades de Pointes, which may result in sudden death. There is variability between the fluoroquinolones in this effect; however, the prolongation is considered minimal. Additional cardiac monitoring is required when used with other medications that prolong the QT interval (e.g. bedaquiline, clofazimine or clarithromycin). Moxifloxacin has more effect on QT prolongation than levofloxacin and ofloxacin.

Group B: Injectable anti-TB drugs

All patients should receive a second-line Group B injectable agent in the intensive phase of MDR-TB treatment unless resistance is documented or highly suspected.

- Either kanamycin, amikacin, or capreomycin can be used as a first choice if all meet the criteria of likely to be effective.
- Kanamycin and amikacin have lower costs than capreomycin, have less ototoxicity than streptomycin and have been used extensively for the treatment of DR-TB throughout the world. Limited evidence suggests capreomycin has less ototoxicity than the aminoglycosides.

- If an isolate is resistant to both streptomycin and kanamycin, or if DST data show high rates of resistance to amikacin and kanamycin, then capreomycin is suggested as the injectable of choice or bedaquiline may be considered as a substitute.
- Given the high rates of streptomycin resistance in patients with MDR-TB (greater than 50% is some countries) and extensive use as a first-line agent in many countries, streptomycin is not often used in MDR regimens. The exception would be if strain is resistant to all the second-line anti-TB injectable agents (amikacin, kanamycin, and capreomycin), but it is susceptible to streptomycin and there are alternative drugs to build an effective regimen.

All of the Group B medications are given intramuscularly (IM). Most commonly, the medications are deeply injected into the upper outer quadrant of the gluteal muscle. Additionally, they can be given intravenously (IV), however, they must be given slowly (over 60 minute period).

Group C: Other core second-line agents

Ethionamide compared to prothionamide are similar in efficacy and side-effects. Of the Group C medications, ethionamide/prothionamide performed the best in the meta-analysis of MDR-TB treatment (2011 WHO guidelines).

- Cycloserine should be included in MDR regimens. Cycloserine shares no cross-resistance to other anti-TB drugs.
- Since the combination of ethionamide/prothionamide and PAS often causes a high incidence of gastrointestinal side effects and hypothyroidism, these agents are usually not used together. PAS is now an Add-on agent in Group D3.
- Group C medications may be started at a low dose and escalated over 3 to 10 days to reduce frequency or severity of side effects (dose-ramping, see section 6.4.1).

D. Add-on agents (not part of the core MDR-TB regimen)

Group D1:

Consists of pyrazinamide, ethambutol and high-dose isoniazid. These agents are usually added to the core second-line medications, unless the risks from confirmed resistance, pill burden and intolerance or drug-drug interaction outweigh potential benefits.

- Pyrazinamide is routinely added to MDR-TB regimens unless there is a reasonable clinical contraindication for its use (hepatotoxicity or other serious adverse effect). DST to pyrazinamide is not reliable and for this reason it is considered an acceptable practice to use pyrazinamide in a regimen even when a laboratory result demonstrates resistance.
- Many DR-TB patients have chronically inflamed lungs, which theoretically produce the acidic environment in which pyrazinamide is more effective. For these reasons, pyrazinamide is included for the entire duration of treatment in the standard MDR-TB regimen.

- Due to difficulties in testing, Ethambutol is often not considered a key medication in a MDR-TB regimen, even if results suggest susceptibility. It is not routinely added to MDR-TB regimens, however, it can be added if the criteria of it being a likely effective medication are met (see Box 6.1 for criteria of a likely effective medications)
- For patients with strains resistant to low concentrations of isoniazid but susceptible to higher concentrations, the use of high-dose isoniazid may have some benefit.

Group D2:
Made up of bedaquiline and delamanid, two new drugs which have been released in recent years. The NTLP has accessed bedaquiline and hopes to introduce delamanid in the future.

Group D3:
Consists of p-aminosalicylic acid (PAS), imipenem-cilastatin, meropenem, clavulanate and thioacetazone. These drugs are only to be used when a MDR-TB regimen with at least 5 effective drugs (i.e. primarily 4 core second-line medicines plus pyrazinamide) cannot be otherwise composed.

2.6.7 How to build an MDR TB and XDR-TB regimen

The treatment regimens for MDR-TB or XDR-TB are built based on first line drugs the patient is susceptible to drugs from different groups of second line drugs. At least a minimum of 5 drugs must be in the regimen

The intensive phase of MDR-TB treatment is at least 6 months and the continuation phase is at least 14 months. Based on the recent drug resistance survey, the recommended standardized regimens for MDR-TB and XDR-TB treatment in Uganda are displayed in table 2.16.

A health worker should directly observe all doses of MDR-TB/XDR-TB treatment. In a health facility where treatment is not possible, the patients should be referred to a health facility or DR-TB treatment initiation center where treatment can be initiated. Follow up treatment can be offered in an ambulatory setting at a health facility near the patient's home or under home based care.

Table 2.6.4: Stepwise approach to building an MDR-TB regimen

STEP 1	**Choose an injectable medication (Group B)**	Kanamycin Amikacin Capreomycin
	Choose a medication based on DST and treatment history. Streptomycin is generally not used because of high rates of resistance in patients with MDR-TB.	
STEP 2	**Choose a higher generation fluoroquinolone (Group A)**	Levofloxacin Moxifloxacin

	Use a later generation fluoroquinolone. If Levofloxacin (or Ofloxacin) resistance is documented, use Moxifloxacin. Avoid Moxifloxacin if possible when using Bedaquiline.	
STEP 3	**Add Group C medications**	Cycloserine/Terizidone Para-aminosalicylic acid (PAS) Ethionamide/Prothionamide
Add two or more Group C medications until you have at least 4 second-line anti-TB drugs likely to be effective. Ethionamide/Prothionamide is considered the most effective Group 4 medication. Consider treatment history, side-effect profile, and cost. DST is not considered reliable for the medications in this group. Ethionamide and Cycloserine are preferred for use in Uganda.		
STEP 4	**Add Group D1 medications**	Pyrazinamide Ethambutol
	Pyrazinamide is routinely added in most regimens; Ethambutol can be added if the criteria for an effective medication are met. If susceptibility to Isoniazid is unknown or pending it can be added to the regimen until DST results become available.	
STEP 5	**Add Group D2/3 medications**	Bedaquiline Linezolid Delamanid Clofazimine Amoxicillin/ clavulanate Imipenem/cilastatin plus clavulanate Meropenem plus clavulanate High-dose Isoniazid Clarithromycin Thioacetazone
	Consider adding Group 5 medications if there are not four second-line anti-TB drugs that are likely to be effective from Groups 2-4. If medications are needed from this group, it is recommended to add two or more. DST is not standardized for the medications in this group.	

(Adapted from WHO Companion handbook to the WHO guidelines for the programmatic management of DR-TB, 2014)

Table 2.6.5: Recommended dosages of for MDR-TB and XDR-TB treatment

	Weight class			
Medication (drug abbreviation), (common presentation)	<33 kg	33-50 kg	51-70 kg	>70 kg (maximum dose)
Isoniazid (H) (100, 300 mg)	4-6 mg/kg daily	200-300 mg daily	600 mg	300 mg daily
Rifampicin (R) (150, 300 mg)	10-20 mg/kg daily	450-600 mg	600 mg	600 mg
Ethambutol (E) (100, 400 mg)	25 mg/kg daily	800-1200 mg	1200-1600mg	1600-2000mg
Pyrazinamide (Z) (500mg)	30-40 mg/kg daily	1000-1750 mg	1750-200mg	2000-2500mg
Streptomycin (S) (1 g vial)	15-20 mg/kg daily	500-750 mg	1000 mg	1000 mg
Kanamycin (Km) (1 g vial)	15-20 mg/kg daily	500-750 mg	1000 mg	1000 mg
Amikacin (Am) (1 g vial)	15-20 mg/kg daily	500-750 mg	1000 mg	1000 mg
Capreomycin (Cm) (1 g vial)	15-20 mg/kg daily	500-750 mg	1000 mg	1000 mg
Ofloxacin (Ofx) (200, 300, 400 mg)	15-20 mg/kg daily	800 mg	800 mg	800-1000 mg
Levofloxacin (Lfx)(200, 500 mg)	7.5-10 mg/kg daily	750 mg	750 mg	750-1000 mg
Moxifloxacin (Mfx)(400 mg)	7.5-10 mg/kg daily	400 mg	400 mg	400 mg
Ethionamide (Eto) (250 mg)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Protionamide (Pto) (250 mg)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg

Cycloserine (Cs) (250 mg)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Terizidone (Trd) (250 mg)	15-20 mg/kg daily	600 mg	600 mg	900 mg
P-aminosalicylic acid (PASER®) (4-g sachets)	150 mg/kg daily	8 g	8 g	8-12 g
Sodium PAS: Dosing can vary with manufacturer and preparation. Check dose recommended by the manufacturer in the drug insert.				
Bedaquiline (Bdq) The dosage in adult is 400 mg once daily for 2 weeks, followed by 200 mg 3 times per week for 22 weeks.				
Clofazimine (Cfz): Usual adult dose is 100 mg to 300 mg daily. Some clinicians begin at 300 mg daily and decrease to 100 mg after 4 to 6 weeks .				
Linezolid (Lzd): Usual adult dose is 600 mg twice daily. Most reduce the dose to 600 mg once a day after 4 to 6 weeks to decrease adverse effects.				
Amoxicillin / Clavulanate (Amx/Clv): Dosages for DR-TB not well defined. Normal adult dose875/125 mg twice a day or 500/125 mg three times a day. Dosages of 1000/250 have been used but adverse side effects may limit this dosing.				
Thioacetazone (Thz) Usual adult dose is 150 mg daily. Its role in treatment of MDR-TB not clear; generally, not used. Contraindicated in patients with HIV.				
Imipenem/cilastatin (Ipm/Cln): Usual adult dose is 500-1000 mg IV every 6 hours.				
Meropenem (Mpm) Usual adult dose is 1,000 mg IV every eight hours.				
Clarithromycin (Clr): Usual adult dose is 500 mg twice daily				
High-dose isoniazid (High-dose H) 16-20 mg/kg daily.				

Monitoring MDR TB treatment response

Patients should be monitored closely for signs of treatment failure. Standard monitoring should be performed following the recommended MDR TB treatment guidelines.

Clinically, the most important way to monitor response to treatment is through regular history-taking and physical examination. The classic symptoms of TB – cough, sputum production, fever and weight loss – generally improve within the first few months of treatment and should be monitored frequently by health-care providers. The recurrence of TB symptoms after sputum conversion, for example, may be the first sign of treatment failure. For children, height and weight should be measured regularly to ensure that they are growing normally. A normal growth rate should resume after a few months of successful treatment.

The most important objective evidence of improvement is conversion of the sputum smear and culture to negative. The use of sputum smear microscopy and culture rather than sputum smear microscopy alone is recommended for the monitoring of patients with MDRTB during treatment

Sputum conversion is slower in DR-TB than in drug-susceptible TB. Paucibacillary culture results should not be automatically regarded as negative when treating DR-TB. Acquired drug resistance and treatment failure often begin with the growth of one or two colonies on a sputum culture. Culture conversion should not be considered to be equivalent to cure. A certain proportion of patients may initially convert and later revert to positive sputum culture. Tests should be performed monthly before smear and culture conversion, with conversion defined as two consecutive negative smears and cultures taken 30 days apart. After conversion, the minimum period recommended for bacteriological monitoring is monthly for smears and bimonthly for cultures
Specimens for monitoring do not need to be examined in duplicate, but doing so can increase the sensitivity of the monitoring.

For patients who remain smear- and culture-positive during treatment or who are suspects for treatment failure, DST can be repeated. It is usually not necessary to repeat DST within less than three months of completion of treatment. Objective laboratory evidence of improvement often lags behind clinical improvement.

The chest radiograph may be unchanged or show only slight improvement, especially in re-treatment patients with chronic pulmonary lesions. Chest radiographs should be taken at least every six months, when a surgical intervention is being considered, or whenever clinically indicated.

2.7 TUBERCULOSIS IN CHILDREN

2.7.1 Introduction

It is estimated that there were 1 million new cases of TB among children accounting for 6.5% of the total new TB cases worldwide in 2014. Children accounted for 7% of global deaths due to TB in the same year. In Uganda, 3316 (7.5% of the total new and relapse TB cases of all forms) in children were notified to the TB program in 2014. However, this proportion falls short of the estimated 15% - 20%. Of all the new cases, 2570 (78%) were pulmonary TB (PTB), and 746 (22%) were Extra Pulmonary TB (EPTB). Children accounted for 2% of the total 211 Multi Drug Resistant (MDR) TB cases notified in 2014.

TB may present at any age in children though the risk is highest below the age of 2 years. When compared to adults, children are more prone to TB infection, TB disease, and severe forms of TB disease. This is because their immune system is not fully developed. The disease in children is mainly airborne and acquired from older children or adults most especially those that are smear positive and not on effective treatment with whom they are in close contact. In rare cases, children may be born with TB (congenital TB) or acquire TB by drinking unpasteurized milk (Bovine TB).

TB disease in children is mainly primary and is associated with a low bacillary load. Older children and adolescents commonly have the adult type of disease which is secondary TB and is due to reactivation. The commonest type of TB disease in children is pulmonary TB (75%).

2.7.2 Risk factors for TB in children

Risk factors for TB infection

The risk factors for TB infection include: -

a) *Contact with an infectious TB case (source case).* The risk of infection is greater with;
   - close contact
   - prolonged duration of contact.
   - bacterial load of source case
   - poor ventilation

b) *Increased exposure in community*
   Children who live in high TB endemic communities are more likely to have TB infection than those in low TB endemic communities.

Risk factors for TB disease

Once exposed to a person with PTB disease, the following are risk factors for developing TB disease in children:

a) *Age less than 5 years*
   Younger children especially those aged less than 2 years have an increased risk of developing TB disease upon exposure and also severe forms of TB disease

b) HIV infection

c) Severe malnutrition particularly undernutrition

Severe malnutrition is associated with impaired cell mediated immunity thereby predisposing to TB disease.

d) Recent episode of measles, pertussis

Measles is associated with weakened immune system that puts a child at risk for developing TB disease.

e) *Other immune suppressive conditions* e.g. diabetes, children on chemotherapy, prolonged steroid use

Risk factors for severe TB disease

a) Young age mainly under one year

Children especially those under the age of 1 year are at a higher risk for severe forms of TB disease such as TB meningitis.

b) Lack of BCG vaccination

BCG vaccination is more effective against severe forms of TB particularly TBM

2.7.3 Presentation of TB in children

The following are the commonest symptoms of TB in children and therefore if any child presents with any, s/he has presumptive TB. The child should be evaluated for such.

(i) Persistent Cough for two weeks or more

(ii) Prolonged Fever for 2 weeks or more

(iii) Poor weight gain for 1 month or more: defined as weight loss, or very low weight (weight-for-age less than -3 z-score), or underweight (weight-for age less than -2 z-score), or confirmed weight loss (>5%) since the last visit, or growth curve flattening, or Mid Upper Arm Circumference (MUAC) measurement in the red color code.

(iv) History of a close or household contact with an individual who has PTB.

(v) Reduced playfulness, poor feeding or decreased activity in the presence of any of the above symptoms

These symptoms are included on the ICF tool which is used to screen for TB in Uganda (figure 2.2a).

Other symptoms of TB include painless enlarged cervical lymph nodes, Gibbus, haemoptysis in older children and adolescents. All children meeting the criteria for presumptive TB, should be evaluated for TB irrespective of any duration of treatment for cough; treatment for fever or response to nutritional rehabilitation.

2.7.4 Diagnosis of TB in children

Although bacteriological confirmation of TB in children is not always possible, it should be sought for whenever possible. The main challenges are the pauci bacillary nature of TB in children and the difficulties of obtaining a good sputum or other specimen sample. Once a sample is obtained, order for the same TB tests as in adults. Complete Blood Count (CBC) and Erythrocyte Sedimentation Rate (ESR) are nonspecific and are NO LONGER recommended as part of routine investigations used in the diagnosis of TB. The diagnosis of TB in children is dependent on conducting a detailed clinical assessment of TB including screening with the ICF tool, history taking including history of contact, clinical examination, and relevant TB tests. The approach to diagnose TB in HIV infected children is similar to that in HIV uninfected children.

Tuberculin Skin Test (TST)

Unlike in adults where the diagnostic value of the TST for active TB is extremely limited, TST is a good supportive test for TB diagnosis in children. In a symptomatic child, with no documented evidence of TB contact, the finding of a positive TST strengthens the possibility of recent TB exposure. Consider TST positive as below:

- 5 mm or more is positive if the child is:
    - HIV positive
    - Severely malnourished
    - Immunosuppressed
    - Having a recent measles or whooping cough episode
- 10 mm or more is positive in all children except the above listed category.

2.7.5 Treatment of TB in Children

The principles and objectives of TB treatment are similar to those of adults (see section 2.3). In addition, effective treatment of TB in children promotes growth and development.

All children diagnosed with TB will be treated with four medicines. The duration of treatment will be guided by the site of disease. TB medicines in children are administered per kg body weight and therefore the weight should be measured at each time of TB medicines refill.

Table 2.7.1: Recommended dosage of first-line anti-TB drugs for children

Drug (Abbreviation*)*	**Daily doses in mg /kg/body weight (Range)**
Isoniazid (H)	10 mg/kg (range 7–15 mg/kg)
Rifampicin (R)	15 mg/kg (range 10–20 mg/kg)
Pyrazinamide (Z)	35 mg/kg (range 30–40 mg/kg)
Ethambutol (E)	20 mg/kg (range 15–25 mg/kg)
As children approach a body weight of 25 kg, adult dosages can be used	

Streptomycin is NOT recommended for use in the management of TB in children because of the associated side effects. Ethambutol is safe for use in children provided the recommended doses are adhered to.

The following is the new recommended treatment regimen for children diagnosed with new TB disease.

Table: 2.7.2: Recommended treatment regimen for children diagnosed with new TB disease

Type of TB disease	**Regimen for a New case**	
	Intensive phase	**Continuation phase**
All forms of TB (excluding TB meningitis and Bone TB)	2RHZE	4RH
TB meningitis Bone (Osteoarticular) TB	2RHZE	10RH

Table 2.7.3: Management of children previously treated for TB

	What to do	**Comments**
Children previously treated for TB (Re-treatment cases e.g. relapse, lost to follow up, treatment failure)	• Do GeneXpert to screen for Rifampicin resistance • Send sample for Drug Susceptibility Testing	• If GeneXpert reveals Rifampicin sensitivity treat as new patient under DOT • If GeneXpert reveals Rifampicin resistance, refer child to MDR treatment site • If unable to obtain a sample or GeneXpert is negative refer to District or Regional Hospital for further evaluation

Table 2.7.4: Recommended doses of anti-TB drugs by weight band based on current FDCs

Weight Bands	**Intensive Phase**		**Continuation Phase**
	RHZ	**E**	**RH**
	75/ 50/150	**100mg**	**75/ 50**
4-7 kg	1	1	1
8-11 kg	2	2	2
12-15 kg	3	3	3
16-24 kg	4	4	4
25kg and above	Use adult dosages and formulations		

Adjunct therapy

1. Pyridoxine is routinely given to children with severe malnutrition and HIV infected children at a dose of 12.5mg -25mg/ day during the anti TB medicines (INH) to prevent peripheral neuropathy.
2. Prednisolone is used in TB meningitis, and for complications of airway obstruction due TB lymph node enlargement. The dose is 2mg/kg/day as a single dose for 4weeks, and then reduced over a period of 1- 2weeks.

2.7.6 Follow up of children on TB treatment

Children on TB treatment should be followed up every 2 weeks in the first month of treatment and thereafter every month until treatment completion. It is important to measure the weight of the child at each clinic visit in order to make dose adjustments. Monitoring of TB treatment in children is summarized in the box 2.5 below.

Box 2.4 Monitoring TB treatment in children

Monitoring TB treatment in children

- Follow up the child every 2 weeks in first month of intensive phase and then monthly up to end of continuation phase
- Weigh the child at each follow-up, document and adjust dosage if necessary
- Check with caretaker regarding treatment adherence.
    - Explain and emphasize to care-giver and child why they must take the full course of treatment even if they are feeling better
    - Note risk factors for poor adherence such as distance/transport; orphan (especially if mother has died) or primary care-giver unwell; adolescents' education and adherence support especially if has TB/HIV
    - Explain that anti-TB drugs in children are well tolerated and safe.
    - CXR is not required in follow-up if the child is responding well to anti-TB treatment

- Most children with TB will start to show signs of improvement after 2 to 4 weeks of anti-TB
    - Treatment. Therefore, assessment at 1-2 months after for treatment failure. If no, poor adherence, consider treatment failure if a child has:
        - No symptom resolution or if symptoms are getting worse
        - Continued weight loss
        - Smear-positive at 2-month follow-up sputum
- On every follow up visit, monitor for hepatitis; the most important adverse effect, which usually presents with abdominal pain, jaundice, nausea, vomiting and tender, enlarged liver.
- Monitor for opportunistic infections if TB-HIV infected on every visit

Indications for referral or hospitalization of children with Tuberculosis

i. Severe forms of TB including TB meningitis, TB pericarditis, milliary TB with respiratory distress and TB spine with neurological complications
ii. Severe malnutrition - for nutritional rehabilitation
iii. Severe pneumonia (i.e. chest in-drawing)
iv. Other co-morbidities e.g. severe anemia, liver disease, renal disease Severe adverse reactions such as hepatotoxicity
v. Retreatment/relapses where bacteriological confirmation is not determined

2.7.7 Prevention of TB in children

The following are approaches used to prevent TB in children.

2.7.7.1 BCG

The BCG vaccine is a live attenuated vaccine and is administered to all new born babies according to the national Program of Immunizations (EPI) guidelines. The vaccine is only effective in protecting against severe forms of TB with an overall efficacy against TB of 50% and 80% efficacy in preventing TB meningitis. BCG should not be administered to children with confirmed HIV infection because of the associated BCG disease and its related mortality in that population.

2.7.7.2 IPT

Isoniazid is effective in preventing TB disease among child contacts of individuals with PTB and people living with HIV. It is important to note that contacts of MDR PTB patients should NOT receive IPT. IPT is recommended for the following categories of patients for 6 months at a dose of 10mg/kg concurrently with pyridoxine upon exclusion of active TB.

a) All children under the age of 5 years with a positive history of contact with a patient with active TB
b) All HIV positive children and adults in whom TB signs and symptoms have been excluded. HIV positive children under 12 months of age with a positive history of contact with a patient with active TB.

2.7.7.3 CONTACT SCREENING AND MANAGEMENT

Contact screening (contact tracing) is a systematic process for identifying TB contacts that have TB or are at risk of developing TB.

Contact screening comprises of contact identification and prioritization is a process that includes: -

a) Interviewing the index TB case to obtain contact information (e.g. name, age)
b) Assessment of contacts' risk of having TB or developing TB.

The following are the categories of TB cases that should be prioritized for contact screening.

i. Bacteriologically confirmed PTB
ii. MDR-TB or XDR-TB (proven or suspected)
iii. Person living with HIV
iv. Child <5 years of age

2.7.8 Children with TB and HIV

The principles and approach to diagnosis, treatment, and follow up of TB in children mentioned above apply to HIV infected children. Cough of any duration in an HIV positive child should trigger evaluation for TB. Once a diagnosis of TB is made, TB treatment should be initiated irrespective of Anti-retroviral Therapy (ART) status. In addition to TB treatment, all children who are co-infected with TB and HIV should receive the comprehensive HIV care package including Anti-Retroviral Therapy (ART) and Co-trimoxazole Preventive Therapy (CPT). In addition, it is important to schedule the TB and HIV clinic appointments on the same day to enhance adherence and minimize loss to follow up. A child on TB-ART co-treatment requires close monitoring for side effects of both anti-TB medicines and ART. The tables below summarize the ART regimen for children with TB/HIV co-infection

Table 2.7.5: Recommended ART Regimen for TB/HIV co-infected children Not on ART

RECOMMENDED REGIMENS FOR TB/HIV CO-INFECTED PATIENTS NOT ON ART **Start TB treatment immediately and initiate ART within 2-8 weeks after starting TB treatment.**	
Younger than 3 years	**Preferred:** AZT+3TC+ABC **Alternative:** ABC + 3TC+ NVP, ensuring that NVP dose is 200 mg/m^2
3 years to 9.9 years **10 years to 14.9 years and < 35kg**	**Preferred:** ABC + 3TC + EFV **Alternative:** AZT + 3TC + EFV
10 to 14.9 years and ≥ 35 kg **Adults & adolescents ≥15 years**	**Preferred:** TDF + 3TC + EFV **Alternative:** AZT + 3TC + EFV

2.7.9 TB-ART co-treatment in HIV infected children on ART

If the child is already on ART, initiate TB treatment immediately and make necessary adjustments to the ART regimen as shown in table below.

Table 2.7.6: Recommended ART Regimen for TB/HIV co-infected patients on ART

Recommended ART regimen for TB/HIV co-infected children on ART Start TB treatment immediately and modify ART regimens as below		
Age	**Current regimen**	**Substitution regimen**
Younger than 3 years	ABC+3TC+NVP OR AZT+3TC+ NVP OR PI based regimen	ABC/3TC/AZT
3 years or older	ABC+3TC+EFV AZT+3TC+EFV TDF+3TC+EFV	Continue the same regimen
	ABC+3TC+NVP AZT+3TC+ NVP TDF+3TC+NVP	Substitute NVP with EFV
	PI based regimen	If the child has a history of failure of NNRTI-based regimen or failure status is unknown: AZT + 3TC + ABC If the child has no history of failure of an NNRTI-based regimen: Substitute with EFV
***For children on triple NRTI, switch back to initial / preferred regimen once TB medication is completed**		

2.7.10 TB Immune Reconstitution Inflammatory Syndrome

Immune Reconstitution Inflammatory Syndrome (IRIS) is an inflammatory process characterized by transient worsening of clinical disease following initiation of treatment due to restoration of the body's immunity. Onset is usually within the first 3 months after starting ART.

Risk factors for TB IRIS include; low baseline CD4 count, extensive TB disease, early initiation of ART, and rapid immunological and virological responses to ART. Symptoms of TB IRIS include worsening TB symptoms and CXR features, new and persistent fevers after starting ART, and evidence of local and/or systemic infection or inflammation (e.g. enlarging lymph nodes and the development of fistulae and cold abscesses).

When IRIS is detected; the following actions should be taken:

Rule out TB/HIV treatment failure, side effects of TB and HIV treatment, and preexisting untreated opportunistic infections.

(i) Continue both ART and anti-TB treatment unless severe toxicity is suspected or confirmed (e.g., elevated LFTs). Give prednisolone at a dose of 1-2mg/kg for 1 to2 weeks; and thereafter, gradually decrease the dose.

(ii) Provide other supportive measures as needed.

2.8 TB/HIV CO-INFECTION

2.8.1 Introduction

HIV is the strongest risk factor for developing tuberculosis (TB) disease in those with latent or new Mycobacterium tuberculosis infection. The risk of developing TB disease is between 20 and 37 times greater in people living with HIV (PLHIV) than among those who do not have HIV infection. TB is the leading cause of HIV-related hospitalization and mortality-accounting for around one quarter (27%, with range of 20-34%) of deaths among hospitalized HIV-positive adults, and almost a third (30%, with range of 11-49%) of deaths among HIV-positive children (WHO HIV/TB update, 2015). At present in Uganda, an estimated 45% of TB patients are also infected with HIV. While less than 1% of HIV patients in care are diagnosed with TB- far below the expected range of 4-25%.

In response to the above situation, the Uganda National TB and AIDS Control Programs work together to implement a set of collaborative TB/HIV activities to reduce the burden of TB in PLHV and reduce the burden of HIV in patients with presumptive and diagnosed TB.

The Uganda MOH recommends TB and HIV services to be provided at a single facility at the same time and location (one-stop shop service). A patient receives all the services they require during one consultation. It includes TB clinic providing HIV treatment and HIV clinic providing TB treatment.

Table 2.8.1: TB / HIV collaborative activities

Strengthen the mechanisms for collaboration between TB and HIV control programs for delivering integrated TB and HIV services
Strengthen coordinating mechanisms for TB and HIV collaborative activities at all levels.
Determine TB prevalence among people living with HIV (PLHIV) and HIV prevalence among patients with presumed and diagnosed TB
Carry out joint TB/HIV planning to integrate the delivery of TB and HIV services
Monitor and Evaluate collaborative TB/HIV activities
Decrease the burden of tuberculosis in people living with HIV and initiate early ART
Intensify TB case finding and ensure high quality anti-TB treatment
Initiate TB Prevention with isoniazid preventive therapy and early ART
Implement tuberculosis infection control practices in health care and congregate settings
Decrease the burden of HIV in patients with presumptive & diagnosed TB
Provide HIV testing and counselling to patients with presumptive and diagnosed TB
Provide HIV prevention interventions for patients with presumptive and diagnosed TB
Provide Co-trimozaxole preventive therapy for TB patients living with HIV
Provide HIV prevention interventions, treatment care and support for TB patients living with HIV
Provide antiretroviral therapy to all TB patients living with HIV

Adapted from National Policy Guidelines for TB/HIV collaborative activities 2nd Edition, 2013

2.8.2 TB prevention in HIV

Intensified TB case-finding

All people living with HIV (children, adolescents & adults), wherever they receive care should be regularly screened for TB using the Intensified TB Case Finding tool (Appendix 8.11) at every visit to the health facility or contact with a health worker. Intensified TB Case Finding (ICF) means regular screening of all people with or at high risk of TB in health facilities and congregate settings (prisons, military barracks, slums) for symptoms and signs of TB, followed promptly with diagnosis and treatment, and then doing the same for household contacts. ICF is important, regardless of whether the HIV patient is receiving IPT or ART.

ICF facilitates rapid identification of presumptive TB patients allowing for triage and other steps to reduce TB transmission.

Isoniazid preventive therapy (IPT)

In Uganda, IPT is offered to the following groups of people: HIV-positive children, adolescents and adults. Before IPT is given active TB disease should be excluded. Furthermore, the combined use of Isoniazid preventive therapy and antiretroviral therapy among people living with HIV significantly reduces the incidence of TB. IPT is therefore recommended irrespective of immune status and whether or not a person is on ART.

However, when PLHIV have any one of the four symptoms (current cough, fever, weight loss or night sweats), they may have active TB and should be evaluated for TB and other diseases prior to IPT initiation. IPT initiation should only be undertaken after active TB disease has been ruled out.

Infection Control

People living with HIV are at high risk of acquiring TB in health care facilities and congregate settings. Therefore, TB infection control practices should be implemented in these settings to reduce the risk of TB transmission.

Each health care facility should have a facility TB infection control plan that includes managerial, administrative, environmental, personal protection measures. And should have a TB IC focal person.

2.8.3 HIV/AIDS Care and Support in TB Clinics

The provision of HIV/AIDS care in TB clinics is part of a continuum of a comprehensive AIDS care package. The package includes clinical management and laboratory support (prophylaxis, early diagnosis of TB or HIV/AIDS, rational treatment and follow-up care for non-TB opportunistic infections). Those who have completed their TB treatment should continue with HIV care service or be referred where such service can be offered.

TB/HIV collaborative care aims to provide comprehensive care to the TB/HIV co-infected patient. As part of TB/HIV collaborative activities, the following should be planned and carried out in TB clinics:

Provider Initiated HIV testing and counselling

HIV testing of patients with presumptive and diagnosed TB should be provider initiated. Provider-initiated testing and counselling (PITC) is HIV testing and counselling offered by a health-care provider in a clinical setting. PITC is recommended to everyone (all adults and children) with presumptive and diagnosed TB [9]. Provider-initiated testing and counselling should be voluntary and should be provided according to the national HIV counselling guidelines.

HIV prevention methods in the TB clinics

Health workers should provide HIV prevention messages to all TB patients. Positive living among those already infected and safe sex practices, including provision and correct use of condoms should be emphasized in order to prevent spread within the community. All clients attending the TB clinics should be screened for sexually transmitted diseases using recommended approaches. Those with symptoms of sexually transmitted infections should be treated or referred to an STD clinic. A referral linkage should be established within and between TB and HIV service provision points.

Co-trimoxazole preventive therapy (CPT)

Routine Co-trimoxazole preventive therapy should be administered to all HIV-infected patients (including children and pregnant women) with active TB disease regardless of CD4 cell count. Co-trimoxazole preventive therapy should be implemented as an integral component of the TB-HIV care package because it is effective in reducing new WHO stage 3 or 4 clinical events, severe bacterial infections, malaria and hospitalization.

Provision of antiretroviral treatment

All TB patients co-infected with HIV should be given antiretroviral drugs. Antiretroviral therapy should be started immediately the diagnosis of HIV is made in a TB patient. If the drugs cannot be obtained at the facility, the patient should be referred to a facility where they can obtain the drugs.

2.8.4 Community Involvement in TB/HIV Activities

Through support groups for people living with HIV/AIDS, village health teams (VHTs) and community-based organizations, TB prevention and care should be integrated with HIV/AIDS prevention, care and support. Communities should be effectively mobilized to advocate for resources and opportunities to implement collaborative TB/HIV activities. Community-based organizations, CB-DOTS treatment supporters and workplace managers or staff associations should also be involved in identifying people with symptoms and signs of TB or HIV/AIDS, referring them to health facilities for diagnosis and treatment and ensuring directly observed treatment. Innovative mechanisms for delivery of ART could be designed along these same lines.

2.8.5 Monitoring and Evaluation of Collaborative TB/HIV Activities

Monitoring and evaluation provide the means to assess quality, effectiveness of delivery and coverage of collaborative TB/HIV activities. Monitoring and evaluation involve collection and analysis of data for indicators of TB/HIV collaborative activities. These data are collected from the level of provision of service.

2.8.6 Presentation of TB in HIV infected persons

EPTB and clinically diagnosed TB commoner among HIV + than HIV – persons. Also, the more advanced the immunosuppression the more TB tends towards clinically diagnosed, EPTB and disseminated forms.

The clinical presentation of TB in early HIV infection is similar to that in HIV-negative persons. However, as HIV infection progresses, CD4+ T lymphocytes will decline in number and function. These cells play an important role in the body's defense against tubercle bacilli. Thus, the immune system becomes less able to prevent growth and local spread of *Mycobacterium tuberculosis*. Disseminated and extra pulmonary TB diseases become more common.

I. Pulmonary TB in HIV-infected patients

Even in HIV-infected patients, PTB is still the commonest form of TB. The presentation depends on the severity of immunosuppression. Table 2.8.2 below shows how the clinical picture, sputum result and chest x-ray appearance often differ in early and late HIV infection. You could copy a figure 55 from UNION book "Epidemiologic Basis of Tuberculosis Control". It demonstrates this better.

Table 2.8.2: Comparison of pulmonary TB in early and late HIV infection among adolescents and adults

Features of PTB	Stage of HIV infection	
	Early	Late
Clinical picture	Often resembles post-primary PTB	Often resembles primary PTB
Sputum smear result	Often positive	Often negative
Chest X-ray appearance	Often cavities	Often infiltrates with no cavities

II. Extra pulmonary TB in HIV-infected patients

The usual forms of extra pulmonary TB; pleural effusion, lymph node, pericarditis, miliary, meningitis and disseminated TB (with myco-bacteremia) can occur in patients who are HIV positive. Occurrence of extra pulmonary TB (except TB lymph node only) implies severe HIV disease (WHO disease classification stage 4).

2.8.7 Diagnosis of TB in HIV-Infected Patients

Diagnosis of TB among people infected with HIV follows the same principles as in HIV negative individuals. There are however some differences that must be noted. HIV infected persons tend to have smear negative TB, they have atypical radiological presentations of TB and they present more

with disseminated TB. There are newer tests that have better accuracy in HIV infected persons such as Xpert MTB/Rif test. The NTLP TB diagnostic algorithm recommends that this test be used as the first test to diagnose TB among HIV infected persons. Another test called LAM is especially useful among HIV patients with low CD4 cell counts.

2.8.8 TB Treatment in HIV-Infected Patients

All patients diagnosed with TB, including those who are HIV infected should be treated with anti-TB drugs according to the NTLP recommendations. All patients on TB treatment should be supported to adhere and complete their medications under directly observed treatment (DOT).

Antiretroviral therapy should be offered to all HIV-positive TB patients, according to the National ART and care guidelines for all adults and children. If the patient is not on ART at the time TB diagnosis ART should be initiated within 8 weeks of starting anti tuberculosis treatment. It is a lifelong treatment requiring a high adherence rate to achieve long-term benefits and minimize the development of drug resistance. Availability of antiretroviral therapy can serve as an incentive for people to be tested for HIV.

The table below gives guidance on when to start ART in a TB patient who is HIV infected.

2.8.9 Common TB-ART Co-Treatment Regimens

A trained staff or medical officer needs to decide when to start ART and the ART regimen. For patients being considered for, or already on TB-ART co-treatment, the attending health worker should note the following:

A patient on TB-ART co-treatment will have many tablets to swallow and may experience more side-effects. Educate the patient on how to manage mild to moderate side-effects and report to the health worker immediately for severe ones. The patient continues receiving Cotrimoxazole. There are many tablets and several changes may take place in the regimen during the course of treatment. This requires careful education of the patient and treatment supporter at each change. The TB treatment is not necessarily in the morning.

The following examples are based on a Rifampicin-based regimen during the initial and continuation phases of TB treatment. The patient is put on an Efavirenz-based ART regimen if it is started during TB treatment.

Table 2.8.3: Recommended antiretroviral therapy regimens for adult patients on anti-TB treatment

Patient group	First-choice regimen	Alternative regimen
Children younger than 3 years or weighing 10kgs or less	AZT +3TC +ABC	NRTIs +NVP
Adults	AZT +3TC + EFV	AZT or d4T + 3TC + NVP or TDF+3TC+EFV

EFV=efavirenz, NVP = nevirapine, TDF=tenofovir, D4T=stavudine
NRTIs, e.g., zidovudine (AZT), didanosine (ddI), lamivudine (3TC), abacavir (ABC), emtricitabine (FTC), zalcitabine (ddC)

Table 2.8.4: Recommended ARV regimen for children and adolescents initiating ART while on anti-TB treatment

<table>
<tr><td colspan="2">Younger than 3 years</td><td>Two NRTIs + NVP, ensuring that dose is 200mg/m^2 or
Triple NTRI (AZT + 3TC + ABC)</td></tr>
<tr><td colspan="2">3 years and older</td><td>Two NRTIs + EFV or
Triple NRTI (AZT + 3TC + ABC)</td></tr>
<tr><td colspan="3">Recommended regimen for children and infants initiating TB treatment while receiving ART</td></tr>
<tr><td rowspan="2">Child on standard NNRTI based regimen

(Two NRTIs + EFV or NVP</td><td>Younger than 3 years</td><td>Continue NVP, ensuring that dose is 200mg/m^2 or Triple NRTI (AZT + 3TC + ABC)</td></tr>
<tr><td>3 years and older</td><td>If the child is receiving EFV, continue the same regimen or
If the child is receiving NVP, substitute with EFV or Triple NRTI (AZT + 3TC + ABC)</td></tr>
</table>

Box: 2.5 Immune reconstitution syndrome (IRIS)

Immune reconstitution syndrome (IRIS)

Occasionally a patient's condition becomes worse after starting antiretroviral treatment. The patient develops fever, lymph nodes increase in size, worsening radiological signs and increasing pleural effusions. This is called immune reconstitution syndrome (or paradoxical reaction). However, the diagnosis should only be made after thorough investigations have excluded other causes of failure to respond to treatment. The treatment is prednisolone at a dose of 1mg/kg body weight for two weeks, then gradually reduced over another two weeks. ART and anti-TB treatment should be continued.

2.9 TUBERCULOSIS INFECTION CONTROL

Box 2.9.1: Highlights of the Uganda TB infection control guidelines

Instituting TB Infection Control (TB IC) measures is recommended to minimize TB transmission in congregate settings. To achieve this, four elements of TB IC are recommended:

a) Managerial measures - These measures constitute the basis for setting up TB IC and implementing them to ensure effective and smooth implementation of TB IC measures at a health facility level.

b) **Administrative measures -** This is the most important level, which attempts to stop/prevent the release of droplet nuclei into the air thereby reducing the exposure of the HCWs, patients and visitors to M. tuberculosis. Ensures that all patients with presumptive TB are promptly identified, separated, educated and started on effective TB treatment while minimizing stigma.

a) **Environmental measures –** Opening of windows and use of mechanical ventilation through use of fans reduces the concentration of droplet nuclei in the air in high risk areas and complements the administrative measures.

b) Personal measures- Wearing of N95 respirators is recommended for health workers, patient attendants and visitors while in TB facilities or attending to patients with or suspected to have DR-TB. For N95 masks to be effective a fitting test is required. Face mask for patients.

2.9.1 Introduction

Pulmonary Tuberculosis is an airborne disease transmitted when a patient with infectious pulmonary or Laryngeal TB coughs, sneezes, talks and sings. These situations release droplet nuclei in the air. The droplet particles that are approximately <5 μm quickly dry up and therefore stay suspended in air for long and thus can circulate throughout a room or building while droplets that are >5 μm in diameter settle faster within about a meter of their source and therefore will not reach the alveoli where TB infection occurs. Large droplet particles > 5 μm impact the nose, throat and large airways where they are normally ingested by macrophages and fail to cause infection. Therefore, it's the < 5 μm droplet nuclei that can be inhaled by a close contact (person living in the same household, or spending many hours a day together with the infectious TB patient in the same indoor living or working space) of this infectious TB patient thereby resulting into TB infection and subsequently into TB disease. The TB patients who are most likely to release these infectious droplet nuclei are the ones who are pulmonary TB (PTB) bacteriologically confirmed and not on effective treatment, although infectious droplets may also be produced by PTB AFB sputum smear-negative. Pulmonary TB patients are most likely to transmit tuberculosis when they are not yet on effective anti-TB treatment.

Although inhalation of infectious droplet nuclei is the most common route of acquiring TB infection, infection can also be acquired by drinking unpasteurized milk or milk products containing M. bovis (bovine TB, a different species).

2.9.2 Tuberculosis Infection Control (TB IC) measures

TB IC is a combination of measures and work practices aimed at minimizing the risk of TB transmission within populations or congregate setting. TB Infection Control measures should complement general infection control efforts and airborne infection control efforts.

The Set of TB infection control Measures that should be implemented at Health facility level is outlined below:

a) Managerial activities at health facility level.

To have effective and smooth implementation of TB IC measures at a health facility, there is need have managerial activities in place. These measures constitute the basis for setting up and implementing the other controls at facility level. They thus ensure administrative commitment and leadership at facility level. These managerial activities include:

- Identification or strengthening a TB IC coordinating team
- Conduct of TB IC facility assessment to inform TB IC plans. The assessment should consider type of clinical services offered by the facility (e.g. TB, HIV, general services, etc.), the number of beds, the number of employees, location of facility and the different clinics, disease prevalence in the community, volume of patients and the risks of exposure to employees and patients prior to the creation of the action plan.
- Development of a facility specific TB IC plan (based on the above assessment) that is time bound with a budget (that includes human and material resources, policies and procedures that ensure sustained and effective implementation of the TB IC measures outlined below. The plan should cover Radiology, Sputum induction and cough inducing procedures, surgical autopsy suites, Intensive case areas and other high risk areas/ procedures.
- Organization of TB IC at a facility level
- Consideration of usage of available space, needed renovation/remodeling or construction to optimize implementation of TB IC
- Conduction of onsite surveillance of TB among Health Care Workers (HCWs). HCWs are all people engaged in actions whose primary intent is to enhance health and these include only paid workers and cleaners working in a health facility.
- Conduction of Advocacy, Communication and Social Mobilization for HCWs, patients and visitors.
- Conduct of monitoring and evaluation of the set of TB IC measures at this facility
- Participation in TB IC operational research

2.9.3 Administrative TB-IC in General Health Facilities

The staff in the general clinics should take the following steps to ensure infection control:

i) Develop a "triage" system whereby known TB patients or persons likely to be presumptive TB patients and their accompanying contacts are promptly identified, isolated in a well-ventilated place upon arrival at a health facility clinic and are fast tracked to diagnosis and treatment follow up. Fast tracking of these patients, reduces the time they spend in a health facility thereby minimizing TB transmission. The health workers do this by asking the patients questions such as: Who among you has a cough that has lasted for two or more weeks? Is there anyone among you who has ever been treated for TB? To minimize stigma, explain to patients that safety without stigma is the goal of IC and that screening for, and prevention of TB transmission is part of providing quality health care.

ii) Educate patients about cough hygiene: When you cough, cover your mouth and nose with a handkerchief or paper tissue. If you do not have a handkerchief or paper tissue, turn to the inside of your arm, and cover your nose and mouth with it (See Figure 2.6). This figure should hang on the wall in the clinic. If a face mask is available, give to known or presumptive TB patients to wear over their mouth and nose.

iii) Even if the mouth is covered, tell the patients always to turn away from facing other people when coughing, whether the mouth is covered by a handkerchief, tissue, face mask or an arm.

iv) Identify an area of the ward or isolation room that is separated from the main ward and designate it for diagnosed and presumptive TB patients. This area should be a well-ventilated area of the ward.

v) Develop written instructions on keeping windows and doors open for ample circulation of air. This instruction should clearly indicate time to open windows and doors, and the patients should be informed about this when first admitted and constantly reminded about it.

vi) Transport known and presumptive TB patients with window open or patients seated in a separate cabin

vii) Designate TB IC responsibilities clearly and correctly and at same time communicate with all relevant partners and stakeholders.

2.9.4 Administrative TB-IC Measures in Tuberculosis clinics and wards

The staff in the TB clinics should:

i) Regularly educate TB patients about the importance of preventing transmission of TB in the wards and at all outpatient clinics.

ii) Ask the patients to identify anyone with two or more weeks of cough in their family or community so that they can be examined for TB disease.

iii) Educate the patients about cough hygiene. Instruct patients to cover their mouths and noses with a handkerchief (Figure 2.9.1). This is to prevent further transmission between patients, attendants and staff. Explain to them that this is for the benefit of everybody and should not make them feel bad or discriminated against.

iv) Sputum produced after coughing should be placed in a screw capped container, disinfected after use and place in a highly infectious waste bin before final disposal.

v) Identify known or suspected drug-resistant TB patients and separate them from other TB patients.

vi) Develop and hang health education messages on the ward and clinic walls.

vii) Develop written instructions on keeping windows and doors open for free circulation. This instruction should clearly indicate time to open windows and doors, and inpatients should be informed about this when they are first admitted and constantly reminded about it.

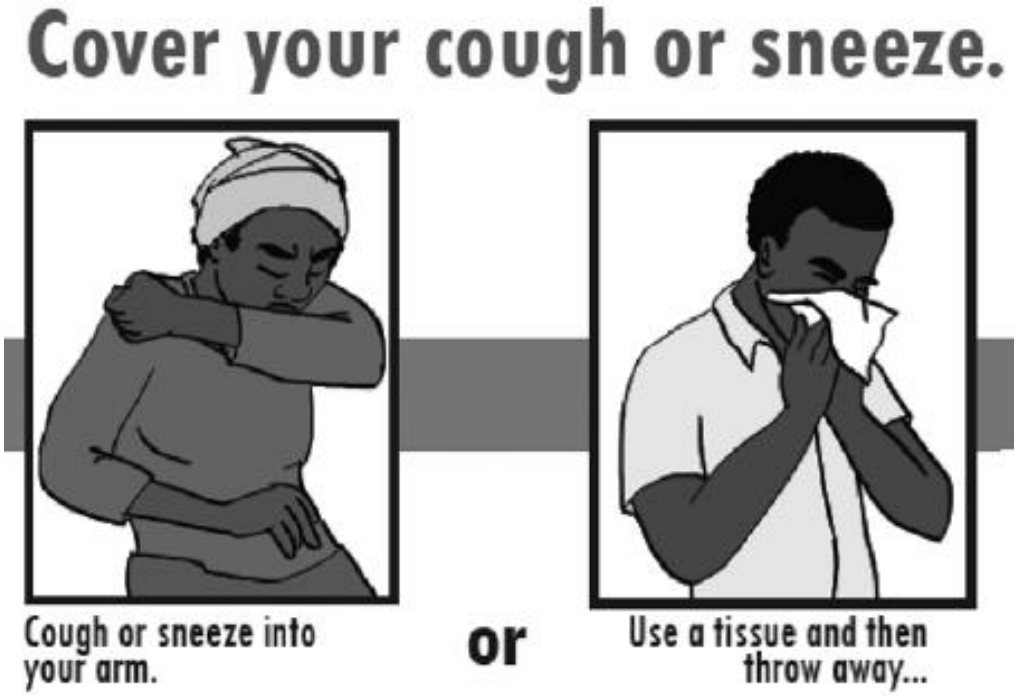
viii) All staff should periodically be screened for symptoms of active TB disease. Schedule TB testing for all staff at least once a year using Xpert MTB/Rif for those symptomatic and or CXR.

ix) Offer staff voluntary, confidential HIV counseling/testing, and annual repeat testing if HIV negative on previous occasions.

x) Document both TB and HIV results in staff member's occupational file. HIV positive staff should be offered Anti-retroviral therapy and Isoniazid preventive therapy (IPT) and should not be deployed high-prevalent TB settings. Offer HIV preventive services to HIV negative health care workers.

Figure 2.9.1 Illustration showing cough hygiene

Adapted from WHO



2.9.5 Environmental Controls at facility level

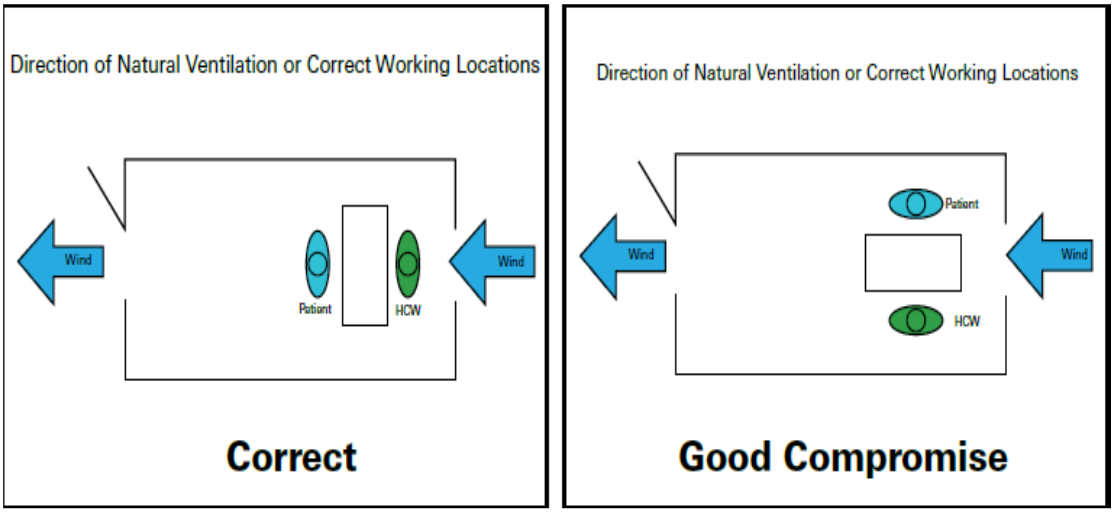
The objective of environmental control measures is to ensure sufficient air exchange and to control direction of airflow to reduce the risk of TB exposure. Sufficient air exchange of about ≥ 8-12 air changes per hour (ACH) reduces the concentration of droplet nuclei in the room air.

The forms of environmental control measures include; Ventilation (Natural ventilation like opening of windows and Mechanical Ventilation through use of fans – ceiling, floor and wall exhaust fans which force air exchanges and to drive air flow by generating negative pressure in the room thereby driving bad air out and fresh air in), Mixed-mode Ventilation (uses both mechanical and natural ventilation), HEPA filtration, Air flow by negative pressure mechanism and Ultraviolet Germicidal Irradiation (UVGI).

They all have both advantages and disadvantages therefore, the choice of any of the above environmental measures is based of available technology, building design, local climatic factors, specialty of the health facility and technical capacity to install these devices as well as resources to procure and maintain them. In our settings and in most health care facilities, use of natural ventilation that achieves ≥ 8-12 air changes per hour (ACH) is adequate and cost effective.

Natural air movement should be monitored to determine the sitting arrangement in consultation rooms between patients and HCWs as illustrated in figure 2.7 below.

Figure 2.9.2: Clinic sitting arrangement



In addition to paying attention to sitting arrangement to reduce the risk of exposure, the inter-bed distances in TB risk areas like TB wards and medical wards etc. have to be kept at 2.5 meters (measured from the center of one bed to the center of the next bed to prevent overcrowding thereby allowing improved air circulation within facility wards. The bed arrangement should be with head-to-foot, instead of head-to-head (Figure 2.9.3). Furniture should be positioned in a way that does not interfere with the free flow of fresh air within a clinic or facility ward.

Figure 2.9.3: Bed arrangement in a TB ward

2.9.6 Personal TB-IC Measures for Health Workers

In order to control TB infection among health care workers, they should:

i) Learn the symptoms of presumptive TB. Should any health worker have a cough that lasts for 2 or more weeks that is associated with fevers, loss of weight and reduced appetite, such a health worker should report for examination to diagnose TB.

ii) Be encouraged to know their HIV status and, if positive, must not be assigned to work in TB wards or clinics.

iii) Whenever possible, health workers should be examined to exclude TB twice a year.

iv) Use personal protection exposures (PPE) such as N95 mask whenever possible during work within TB wards or clinics. Wearing of N95 respirators is a must while working in drug resistant TB (DR-TB) facilities or attending to patients with or suspected to have DR-TB. Those working in areas such as x-ray rooms and the mortuary should be prioritized for N95 masks. For N95 masks to be effective a fitting test is required.

2.9.7 Disinfection and Disposal of Sputum

i) Health workers must ensure that, after instructing the patients how to obtain a sputum specimen, the patient goes to perform the act of producing the specimen in an open place away from the laboratory and other people. When a designated area for taking sputum, specimen is available, the patient is sent to the area.

ii) Sputum of inpatients that is collected for disposal should be in a sputum mug or a plastic screw cap container. This container should have disinfectant liquid (5% Lysol) poured into it before the sputum material is put in it. Sputum from all the inpatients wards should be collected into one big container, further disinfected, and then disposed of according to standard guidelines for disposal of biological waste.

2.9.8 TB-IC in Congregated Populations

A congregated population is a group of people staying close in proximity to each other – for example, school children, refugees, soldiers and prisoners. The measures described below are useful for controlling TB infection in such a population:

i) Plan for and develop TB and HIV/AIDS collaborative activities for the institution with a congregated population.

ii) Establish TB diagnostic and treatment services.

iii) Educate population and staff on relationship between TB and HIV infection, so that they can recognize TB suspects.

iv) Advocate for an isolation unit for patients diagnosed with TB or suspected to have TB.

v) Consider "active screening" of the immediate group members for TB, when a new pulmonary TB sputum smear-positive is diagnosed.

2.9.9 TB-IC in Households

TB-IC activities and measures used in health care facilities also apply to households (HHs). All stakeholders must be involved. Policy makers, community leaders, patients and their families have to appreciate the importance of TB-IC in HHs. TB-IC in households begins with ensuring early diagnosis of TB. Patients and their family members are the first to notice TB symptoms. They should immediate ensure that care is sought. Once a diagnosis is made, adherence to treatment is key to TB-IC. Furthermore, practices to reduce the spread of TB should be implemented. These practices include:

- Houses should be adequately ventilated, particularly rooms where people with infectious TB spend considerable time (natural ventilation may be sufficient to provide adequate ventilation).
- Anyone who coughs should be educated on cough etiquette and should follow such practices always.
- While smear positive, TB patients should spend as much time as possible outdoors, sleep alone in a separate, adequately ventilated room and spend as little time as possible in public places or in public transport.
- While smear or culture positive, MDR-TB patients who cough should always practice cough etiquette (including use of face masks) when in contact with people.

- Ideally, health service providers should wear respirators when attending patients in enclosed spaces.
- Ideally, family members living with HIV, or family members with strong clinical evidence of HIV infection, should not provide care for infectious MDR-TB patients. If there is no alternative, HIV positive family members should wear respirators.
- Children below five years of age should spend as little time as possible in the same living spaces as culture-positive MDR-TB patients. Such children should be followed up regularly with TB screening for two years and, if positive, drug-susceptibility testing must be done.
- When conditions do not exist to minimize risk of TB infection in a household, XDR-TB patients should be admitted to a specialized healthcare facility.
- Household members of any TB patients should be encouraged to get screened for HIV and TB and be given appropriate (preventive) therapy.
- If possible, HIV-positive family members, or family members with a strong clinical evidence of HIV infection, should not share a household with culture positive XDR-TB patients.
- If possible, renovation of the patient's home should be considered, to improve ventilation (e.g. building of a separate bedroom, or installation of a window or wind catcher – "Whirly bird"– or both).

2.9.10 Hierarchy of Infection control measures

Infection control measures can also be looked at as being in a form of hierarchy. This hierarchy highlights the relative importance of infection control measures. The hierarchy is:

a) ***1st priority: Administrative controls (workplace)***
   This is the most important level, which aims to stop/prevent the release of droplet nuclei into the air thereby reducing the exposure of the HCWs, patients and visitors to M. tuberculosis.
b) ***2nd priority: Environmental Engineering) controls***
   These actions complement the administrative measures. They reduce the concentration of droplet nuclei in the air in high risk areas.
c) ***3rd priority: Personal protective measures***
   These measures protect individual persons especially HCWs from releasing or inhaling the droplet nuclei.

2.10 TUBERCULOSIS LABORATORY SERVICES

2.10.1 Diagnostic Methods

The End TB Strategy calls for the early diagnosis of TB and universal drug susceptibility testing (DST), highlighting the critical role of laboratories for rapidly and accurately detecting TB and drug resistance. Laboratory confirmation of TB and drug resistance is essential to ensure that individuals with TB are correctly diagnosed and have access to the appropriate treatment as soon as possible. All presumptive TB patients should be examined per the standardized procedures and national algorithms. In Uganda, the commonly used diagnostic tests used to confirm/exclude TB are:

- Microscopy
- Xpert MTB/Rif test
- Culture
- Histopathology

2.10.2 Microscopic Examination of Sputum Smears

Although newer genotypic TB testing methods such as Xpert MTB/Rif have now been rolled out in most clinics in the country, sputum microscopy is still the most widely used method of identifying patients with infectious forms of pulmonary TB. Microscopy is easy to perform at the peripheral laboratories, cheap and accurate. It can be used for diagnosis, monitoring response to treatment and defining cure. It is a key tool for case detection and monitoring. The light microscope and Ziehl–Neelsen staining (and its modifications) have been in use for more than a century. Light microscopy has a good specificity but variable and low sensitivity which is worse in HIV- infected TB patients. To improve sensitivity of light microscopy, concentration methods have been developed. Concentration methods improve ZN yield by 13% and should be encouraged where appropriate. However, this approach can only be performed at relatively well equipped laboratories; where there is electricity and centrifuge- limiting its usefulness in peripheral clinics where the need is highest.

Fluorescent Microscopy (FM) is an improvement on the light microscope. FM has been demonstrated to be superior to light microscopy (ZN). In the developed world, this has virtually replaced the light microscope. However, the cost and need for electricity has led to limited application of fluorescent microscopy. Because of this the Foundation for Innovation of New Diagnostics (FIND) has been supporting the developments of newer diagnostics for TB. It has supported the development of a new fluorescent microscopy using Light Emitting Diodes (LED) which can use ordinary batteries and do not need the use of a dark room (WHO, 2010). The LED has a sensitivity comparable to that of standard FM and it is also cheaper. This technology has been rolled out in Uganda. Sputum microscopy is kept reliable if laboratories participate in external quality assurance (EQA) such as blinded rechecking. In blinded rechecking, randomly selected slides examined at the laboratory are re-examined at another laboratory usually a higher-level laboratory. However, one S+ is sufficient to clinch a diagnosis of TB, provided the DTU is EQA certified. A maximum of two sputum specimens should be collected and examined on two consecutive days **(spot** and **early morning).**

The laboratory should keep all positive and negative slides in the same slide box in sequence to facilitate quality assurance procedures. The sputum specimen collection procedures are provided in the annex.

2.10.3a Xpert MTB/ RIF test (GeneXpert)

Xpert MTB/Rif is a new molecular test that has been designed to test for a part of the TB DNA that is highly specific for MTB. This part is biologically referred to as IS6110. The test also tests for a mutation that confers to the MTB organism resistance to the most effective TB drug, Rifampicin. The mutation occurs in the rpoB gene. Xpert MTB/Rif is an automated test that can be used in peripheral laboratories directly on sputum samples as they are collected from patients to test for the IS6110 and rpoB gene. When the test is done on fresh sputum it called direct Xpert MTB/Rif. The test requires minimal sample processing and returns a result within 4 hours. Xpert MTB/Rif is recommended as the first test for all presumptive TB patients

Table 2.10.1: Xpert MTB/Rif results and their meaning

Result	Meaning	Interpretation
Mycobacterium tuberculosis (MTB) complex detected	MTB was isolated from the specimen therefore the patient has bacteriologically confirmed TB	The patient has TB disease and should be treated
Mycobacterium tuberculosis (MTB) complex not detected	MTB was not isolated from the Specimen	This result does not exclude TB in patients with pauci bacillary disease i.e. children and HIV positive people and EPTB. The sensitivity of Xpert MTB/Rif is low in smear negative, culture positive patients. It means that TB disease could not be confirmed bacteriologically. Further investigations are required to confirm TB in these patients
Rifampicin resistance detected	Means that the MTB strain isolated was resistant to Rifampicin. Therefore, the patient has Rifampicin resistant TB	Rifampicin resistance by Xpert MTB/Rif does not rule out or confirm MDR-TB and XDR-TB hence a full 1st line and 2nd line DST is required
Rifampicin susceptible	The MTB strain isolated was susceptible to Rifampicin therefore, patient has Rifampicin susceptible TB	This does not exclude the possibility of resistance to other first line drugs i.e. H, Z, E

2.10.3b Line probe assay (LPA)

The LPA test is another molecular test that tests for mutations that confers to the MTB organism Rifampicin resistance as well as H resistance hence allowing a full diagnosis of MDR TB. It is recommended for patients in whom a rapid confirmation of MDR status is needed.
One spot sputum specimen should be collected for smear microscopy, if AFB positive then another specimen must be collected for LPA. If smear microscopy is AFB negative, another sample for culture and LPA must be collected. Like Xpert MTB/Rif, LPA returns the following results: MTB detected or MTB not detected. MTB not detected does not completely rule out TB. Then it returns MTB detected, Rifampicin and H susceptible. It can also return the result MTB detected, Rifampicin resistant and H susceptible. This result, does not completely rule out MDR TB because the gene test for H resistance is not as perfected as the Rifampicin resistance test. MTB detected Rifampicin and H resistant means the patient has MDR TB. MTB detected INH resistant; Rifampicin susceptible is also a possible test result. This result means that the patient has H mono resistance.

2.10.4 Culture

The probability of finding AFB in sputum specimens by smear microscopy or molecular tests is directly related to the concentration of bacilli in the sputum. In comparison, mycobacterial culture can detect far lower numbers of TB bacilli. Moreover, the culture makes it possible to identify the mycobacterial species based on biochemical and other properties.

Culture of *M. tb* bacilli is very sensitive and specific, but is expensive, as it is a complex and sophisticated procedure. It requires a specialized laboratory set-up, and culture results are available only after 6 to 8 weeks. Culture with DST takes even longer. If available, culture can be used for diagnosis or confirmation of the diagnosis of TB in patients with PTB and EPTB. Since it is more sensitive than smear, culture may also have a role in the diagnosis of smear-negative, HIV-positive TB suspects who are likely to be paucibacillary.

In addition to its use in surveillance, culture with DST is valuable for diagnosis and management of drug-resistant TB. It is mainly used to screen patients who have a poor response to correct treatment, as well as those that have been previously treated – a group of patients likely to have drug-resistant TB.

2.10.6 Network of TB laboratory services in Uganda

Microscopy sites: Health facilities with laboratories performing TB microscopy, referred to as diagnostic TB units (DTU), in Uganda have increased from 303 in 2006 to about 1,336 by the end of 2015. At parish level, there are only 85 HCII DTU because the national health policy targets HCIII and above for laboratories, 953 DTU HC III at sub-county level, 163 DTU HCIV at county level and 133 DTU hospitals that include the 2 National Referral Hospitals, 17 Regional referral (13 government of Uganda (GoU) and 4 PNFP) and 9 private hospitals. The rest of the hospitals are General hospitals (64 GoU and 52 PNFP).

Nucleic Acid Amplification Test (NAAT): Genotypic methods have considerable advantages when the programmatic management of drug-resistant TB is being scaled up, in particular with regard to their speed, the standardization of testing, their potentially high output and the reduced requirements for biosafety. The most commonly used NAAT in Uganda is the Xpert MTB/RIF. The Line Probe Assay (LPA) at the National TB Reference Laboratory is mainly for research purposes.

As of 2016, the country installed 111 Xpert MTB/Rif machines in 105 sites/health facilities through the support of Government and its partners, that is in 87 public facilities and these are Mulago National Referral Hospital, 13 Regional referral hospitals, 43 general hospitals, 21 HC IV, six HC III, one HC II and the NTRL, 13 PNFP i.e. 10 hospitals and three HIV care facilities, two private clinics and three research institutions.

Culture and Drug susceptibility testing: WHO and other international technical agencies advocate-one TB culture laboratory for every 5 million population, and one DST laboratory for every 10 million population supporting the TB control program. Thus, Uganda with approximately 35 million populations, would be requiring seven culture laboratories as well as four DST laboratories at the minimum. As of date, nine TB culture laboratories are functional in the country, in both public and NGO/Private sector.

National TB Reference Laboratory (NTRL)

The National TB Reference Laboratory (NTRL) is under the NTLP central Unit. The mission of the NTRL is to provide quality laboratory services and to strengthen the national tuberculosis laboratory diagnostic network through leadership and expert guidance in support of the NTLP to reduce the burden of tuberculosis and leprosy in Uganda. NTRL provides referral laboratory services for TB diagnosis, surveillance and monitoring through laboratory testing and provision of professional and technical advice. The NTRL is not yet providing similar services for leprosy.

In 2013, the NTRL received international accreditation under the ISO 15189 and was elevated to a Supra-national TB Reference Laboratory (SRL), the second SRL in the WHO AFRO region. Through the SRL status, the NTRL supports over 18 countries in East and Central Africa.

System for sample transport and transmission of results

The country has established a hub network for sample referral to diagnostic laboratories and returning results to referring health facilities. Each hub has a motorcycle rider who transports samples and results to and from the DTUs. Samples from RR patients are referred to NTRL through Posta Uganda.

The country currently has 100 hubs in the lab network and has strategically placed Xpert MTB/RIF in 62% of the hubs (Annex 11). The country has plans to cover all the hubs with Xpert MTB/RIF and implement online monitoring tools such as GxAlert and Xpert MTB/RIF Laboratory Information Management System (GxLIMS) to help in real-time transmission of results to the health facilities.

2.10.7 External Quality Assessment (EQA)

To be reliable, laboratories performing microscopy, culture and molecular tests must participate in external quality assurance (EQA) programs. The process involves the examination of previously prepared slides to see if:

- Slides were prepared properly
- Slides were examined, and the reported results (positive or negative) are correct
- Recommended laboratory procedures are followed
- Safety measures are adhered to

2.11 TB MONITORING AND EVALUATION

2.11.1 Introduction

What is monitoring?

Monitoring is continuous process of data collection to track how a program/activity is being implemented in relation to activity plan. Routine tracking of the key elements of program/project performance, usually inputs and outputs is achieved through record keeping, regular reporting and surveillance systems. Therefore, monitoring is useful to:

- Track progress toward the set performance standards (targets)
- Determine whether activities are proceeding according to plan or need adjustment during the intervention or implementation is order to realize desired outputs or outcomes

What is evaluation?

Evaluation is the systematic assessment of an on-going or completed service, project, program or policy, involving its design, implementation and results to determine its worth or merit; determine how well the project or program has met set objectives and/or the extent to which changes in outcomes can be attributed to the interventions, project or program.

Impact evaluation is the process of measuring of how much things have changed because of the intervention(s) implemented. Because there are many factors that cause things to change, a formal evaluation tries to demonstrate how much a specific intervention contributed to the change.

2.11.2 Importance of monitoring & evaluation

Monitoring and evaluation (M&E) plays an important role in the management of the TB program at all levels. It is important for National TB programs to follow epidemiological trends in TB, identify strengths and weaknesses in program design or implementation and informs program priorities and advocacy among policy makers. M&E ensures that the resources going into the program including human and financial resources are being efficiently utilized; services are being optimally accessed; activities are occurring in a sustainable timely manner; and expected results are being achieved.

Table 2.11.1: Monitoring and evaluation activities by operational level

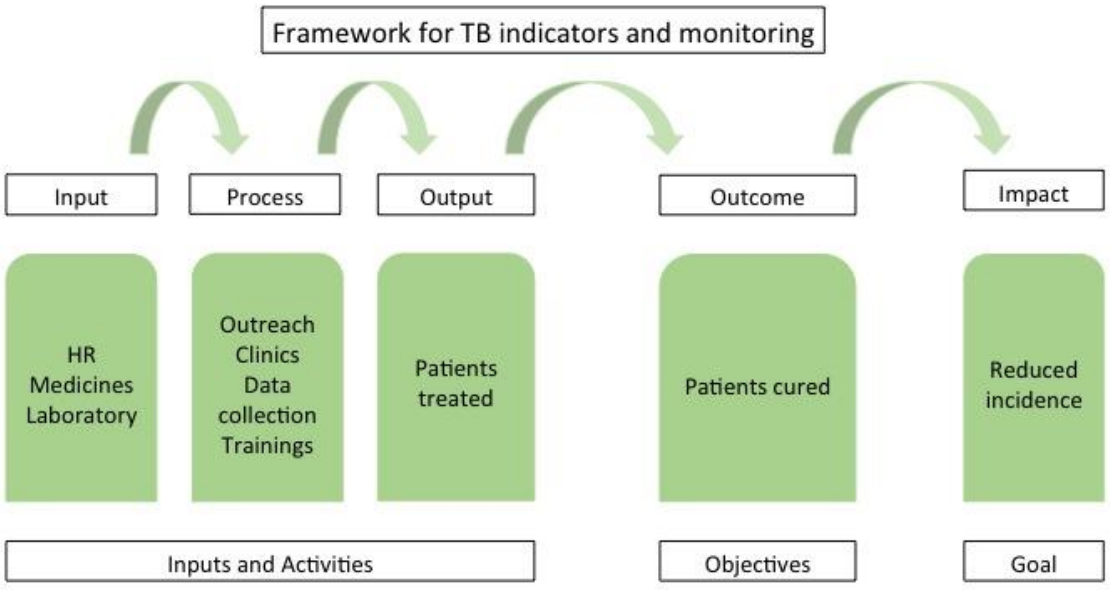
Level	Monitoring activities	Evaluation activities
Facility	• Keeping accurate and complete records monitoring tools • Reviewing and updating the collected records regularly • Compiling and analyzing data on TB indicators such as: TB case finding, case holding, DOT, TB-HIV collaboratives and other activities of the TB program	• Measurement of facility performance against set targets on TB case finding, case holding, DOT and TB-HIV collaboratives (e.g. IPT, ART, CPT, TBIC coverage)
district	• Carrying out support supervision • Reviewing and updating the collected records regularly • Compiling data on key TB indicators: TB case finding, case holding, DOT, TB-HIV collaboratives, and other activities of the TB program	• Measurement of district performance against district set targets on TB case finding, case holding, DOT, and TB-HIV collaboratives (IPT, ART, CPT, TBIC coverage)
National	• Carrying out support supervision • Compiling data on key TB indicators: TB case finding, case holding, DOT, TB-HIV collaboratives and other activities of the TB programme	• Measurement of national performance against set targets on TB case finding and case holding, DOT, TB-HIV collaboratives (IPT, ART, CPT, TBIC coverage) • Conduction of TB surveys to determine prevalence, and incidence, community awareness

2.11.3 How does M&E work?

- It has elements of data collection, reporting, analysis and supervision
- It is systematically done
- It promotes data demand and information use
- It generates data that informs policy decisions, design and implementation of TB control activities by the National TB program.
- It works in an established framework for tracking progress and demonstrating Program results.
- It is based on indicators that measure changes in service delivery for instance, TB case detection, treatment outcomes, etc. as outlined in the NTLP national strategic plan

The NTLP has developed a monitoring and evaluation (M&E) plan to measure the performance of NTLP strategic plan. The M&E plan uses the following monitoring framework to track progress of TB control in Uganda and implementation of the National Strategic Plan. It can be seen from figure 2.11.1 that TB indicators can be derived from inputs, processes and outputs. Furthermore, more indicators are derived from outcomes and impacts. Altogether these form the backbone of indicators that are used to measure the performance of the NTLP.

Figure 2.11.1: Framework for TB indicator and monitoring



2.11.4 Data reporting system

The routine reporting system is from Diagnostic and Treatment Unit (DTU) to district, from district to the central NTLP office. Standard operating procedures (SOPs) have been developed to guide health facility, district, regional and national level officers in data completeness, quality and utilization for performance improvement at different levels.

TB service data is currently reported through two systems;

- By facilities through HMIS to the MOH/Resource center.
- By the district, TB and leprosy supervisors (DTLS) through the Regional TB and Leprosy focal persons, to the NTLP using the TB quarterly report form.

2.11.5 TB monitoring tools.

Monitoring requires that there should be "monitoring tools." The NTLP uses the following forms and registers as tools to monitor program activities.

Facility level recording tools

- TB laboratory request form
- Xpert MTB/Rif request form
- Request for culture and sensitivity
- TB Laboratory Register
- TB Patient Treatment Card
- TB Unit Register
- Isoniazid Preventive Therapy Register
- Sub-county Health Worker Register
- Presumptive TB Register
- HMIS 105 & 106A
- Quality Improvement Documentation Journal

District level recording and reporting tools

- District TB Register
- Quarterly Report Forms (Case finding (notification form) and treatment outcome)
- TB performance assessment & mentorship tool

National level recording and reporting tools

- TB performance assessment & mentorship tool

2.11.6 TB indicators

i) **Case finding:** This is an activity that measures the detection of TB patients in the population. The indicator is case detection rate and can be disaggregated by age: Case detection rate

a. TB Case Detection Rate
b. Case notification rate
c. Proportion of childhood TB cases

ii) **Case holding:** This is the measurement of how well TB patients adhere to the anti-TB drugs prescribed for them. The indicators used to monitor case holding are:

i. Cure rate
ii. Treatment completion rate
iii. Treatment success rate for incident TB cases
iv. Lost to follow up rate
v. Death rate
vi. Treatment failure rate

iii) **Program management:** The indicators used to measure TB management aspects:

a. Proportion of supervisory visits carried out
b. Proportion of TB treatment facilities reporting stock-outs of anti-TB drugs
c. Proportion of TB patients on DOT
d. Completeness of reporting to NTLP
e. Accuracy of reporting to NTLP
f. Timeliness of reporting

iv) **TB/HIV collaborative activities:** The indicators listed under this category cover only TB/HIV collaborative activities that are carried out or can be carried out in a TB treatment health facility:

a) TB patients with documented HIV status
b) Proportion of HIV testing among TB patients
c) Proportion of positive HIV tests among TB patients
d) Proportion of HIV-positive TB patients started or are receiving CPT
e) Proportion of HIV-positive TB patients started or are receiving ART
f) Proportion of PLHIV who are eligible for IPT and are receiving it

Data source: Unit TB register, IPT register, HIV care card, pre-ART and ART registers

v) **TB in children:** Here the indicator is:

a) Proportion of all incident (new and relapse TB) cases notified to/by the program, who are children
b) Proportion of children under five years of age who are contacts of TB patients on treatment that are screened for active TB.
c) Proportion of under five years contacts of TB patients who are eligible for IPT and received it.

Data source: Unit TB register, IPT register

vi) **Laboratory services:**

a) Proportion of TB microscopy units submitting slides for rechecking
b) Proportion of TB suspects who are sputum smear positive
c) Proportion of sputum smear-positive PTB registered for treatment
d) Proportion of MDR-TB identified out of cultured specimen

vii) **Programmatic Management of Drug Resistant TB**

a) Percentage of close contacts of DR-TB patients traced and screened for TB
b) Number of confirmed DR-TB cases started on DR-TB treatment
c) Treatment success rate for confirmed DR-TB cases

The indicators, calculation, data source, level and frequency the indicators should be calculated for each of the above categories are shown in the tables that follow.

Table 2.11.2: Monitoring TB program performance

	Facility	**District**	**National**
Case detection	Yes	Yes	Yes
Case holding	Cure rate Treatment completion rate Treatment success rate Lost to follow up rate Death rate Treatment failure rate TSR TB in children	Cure rate Treatment completion rate Default rate Death rate Treatment failure rate Not evaluated rate TSR TB in children	Cure rate Treatment completion rate Default rate Death rate Treatment failure rate Not evaluated rate TSR TB in children
Program management	Proportion of TB patients on DOT Accuracy and completeness of recording	Proportion of supervisory visits carried out Proportion of TB treatment facilities reporting stock-outs of anti-TB drugs Proportion of TB patients on DOT Completeness of reporting to district Accuracy of reporting to NTLP Timeliness of reporting	Proportion of supervisory visits carried out Proportion of TB treatment facilities reporting stock-outs of anti-TB drugs Proportion of TB patients on DOT Completeness of reporting to NTLP Accuracy of reporting to NTLP Timeliness of reporting
TB/HIV collaborative activities	# & % incident TB cases with documented HIV test result Proportion of positive HIV tests among incident TB patients Proportion of HIV testing among TB patients Proportion of HIV-positive	Proportion of positive HIV tests among TB patients Proportion of HIV testing among TB patients Proportion of HIV-positive TB patients who received at least 1 month of CPT	Proportion of positive HIV tests among TB patients Proportion of HIV testing among TB patients Proportion of HIV-positive TB patients who received at least 1 month of CPT Proportion of HIV-positive TB patients who are receiving of ART

	incident TB patients who were started and/or continued on CPT Proportion of HIV-positive TB patients who are receiving of ART (same as above) Proportion of PLHIV eligible for IPT and are receiving it	Proportion of HIV-positive TB patients who are receiving of ART Proportion of PLHIV who are eligible for IPT and are receiving it	Proportion of PLHIV who are eligible for IPT and are receiving it
TB in children	Proportion of all incident (new and relapse) TB cases notified who are children Proportion of children under 5 years of age who are contacts of registered new pan susceptible TB patients who are screened for active TB. Proportion of children under 5 years of age who are contacts of TB patients that received IPT	Proportion of all new TB case notification who are children Proportion of children under 5 years of age who are contacts of TB patients on treatment that are screened for active TB. Proportion of children under 5 years of age who are contacts of TB patients that are eligible for IPT and are receiving it.	Proportion of all new TB case notification who are children Proportion of children under 5 years of age who are contacts of TB patients on treatment that are screened for active TB. Proportion of children under 5 years of age who are contacts of TB patients that are eligible for IPT and are receiving it.
Laboratory services	Proportion of TB suspects who are sputum smear positive Proportion of sputum smear-positive PTB registered for treatment Proportion of MDR-TB identified out of cultured specimen Cumulative number of MDR-TB reported	Proportion of TB microscopy units submitting slides for rechecking Proportion of TB suspects who are sputum smear positive Proportion of sputum smear-positive PTB registered for treatment Proportion of MDR-TB identified out of cultured specimen Cumulative number of MDR-TB reported	Proportion of TB microscopy units submitting slides for rechecking Proportion of TB suspects who are sputum smear positive Proportion of sputum smear-positive PTB registered for treatment Proportion of MDR-TB identified out of cultured specimen Cumulative number of MDR-TB reported

PMDT	Percentage of close contacts of DR-TB patients traced and screened for TB (at least once) Number of confirmed DR-TB cases started on DR-TB treatment Treatment success rate for confirmed DR-TB cases	Percentage of close contacts of DR-TB patients traced and screened for TB (at least once) Number of confirmed DR-TB cases started on DR-TB treatment Treatment success rate for confirmed DR-TB cases	Percentage of close contacts of DR-TB patients traced and screened for TB (at least once) Number of confirmed DR-TB cases started on DR-TB treatment Treatment success rate for confirmed DR-TB cases

Table 2.11.4: Monitoring TB case holding

Indicator	Calculation	Data source	Level	Frequency
1) Cure rate among new PBC	***Numerator:*** Number of new Pulmonary Bacteriologically Confirmed (PBC) TB cases with cured treatment outcome ***Denominator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in that quarter	Unit TB register Quarterly reports on treatment outcomes	Health facility District Central	Quarterly Annually
2) Treatment completion rate	***Numerator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases with treatment completed outcome ***Denominator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in that quarter	Unit TB register Quarterly report on treatment outcomes	Health facility District Central	Quarterly Annually
3) Treatment success rate for incident TB cases	***Numerator:*** Number of notified new and relapse TB patients who are cured plus those who completed treatment ***Denominator:*** All notified new and relapse TB patients in a given period	Unit TB register Quarterly report on treatment outcomes	Health facility District Central	Quarterly Annually
4) Death rate	***Numerator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in a quarter who died irrespective of cause ***Denominator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases e registered in that quarter	Unit TB register Quarterly report on treatment outcomes	Health facility District Central	Quarterly Annually
5) Loss to follow u rate	***Numerator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in a quarter that get lost to follow up ***Denominator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in that quarter	Unit TB register Quarterly report on treatment outcomes	Health facility District Central	Quarterly Annually
6) Treatment failure rate	***Numerator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in a quarter who remained sputum smear-positive 5 months or later after starting treatment ***Denominator:*** Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in that quarter	Unit TB register Quarterly report on treatment outcomes	Health facility District Central	Quarterly Annually

Table 2.11.5: Monitoring TB program management

Indicator	Calculation	Data source	Level	Frequency
1) Proportion of support supervision visits	***Numerator:*** Total number of supervisory support visits made in a quarter for region or district ***Denominator*:** Total number of planned supervisory support visits for region or district	Quarterly report on program management	District Region Central	Quarterly Annually
2) Proportion of TB treatment health facilities reporting stock-outs	***Numerator:*** Total number of TB treatment health facilities that reported stock-out of TB medicines s in each quarter or year ***Denominator:*** Total number of TB treatment health facilities	Reports on support supervision visits	District Region Central	Quarterly Annually
3) Proportion of TB patients on DOT	***Numerator:*** Total number of TB patients receiving treatment under DOT during a given quarter or year ***Denominator:*** Total number of TB patients registered in the specified quarter/year	Quarterly reports on case-finding	District Region/ District	Quarterly Annually
4) Completeness of reporting to NTLP	***Numerator:*** Total number of districts that submitted TB case-finding and treatment outcomes report to NTLP in each quarter or year ***Denominator:*** Number of districts expected to submit TB case-finding and treatment outcomes reports to NTLP in each quarter or	Regional and NTLP reports	Region Central	Quarterly Annually
5) Accuracy of reporting to NTLP	***Numerator:*** Number of TB case-finding and treatment outcome reports submitted that were recorded completely and accurately ***Denominator:*** Total number of case-finding and treatment outcome reports examined for completeness and accuracy	Regional Unit and district TB registers	District Region Central	Quarterly Annually

Table 2.11.6: Monitoring TB/ HIV collaborative activities

Indicator	Calculation	Data source	Level	Frequency
1) Proportion of registered TB patients tested for HIV	***Numerator:*** Number of registered TB patients in a given quarter or year tested for HIV during TB treatment ***Denominator:*** Total number of registered TB patients in the same quarter or year	TB unit and district registers Quarterly report on case-finding	Health facility District Central	Quarterly Annually
2) Proportion of TB patients who are HIV- positive	***Numerator:*** Number of registered TB patients in a given quarter or year who tested HIV-positive ***Denominator*****:** Total number of TB patients registered in the same quarter and tested for HIV	TB unit and district registers Quarterly report on case-finding	Health facility District Central	Quarterly Annually
3) Proportion of registered TB patients co-infected with HIV who get at least 1 month of CPT during TB treatment	***Numerator*****:** Number of registered TB patients co-infected with HIV who received at least one month of CPT in a given quarter ***Denominator:*** Total number of registered TB patients co-infected with HIV over the same quarter	TB and HIV service delivery health facilities Quarterly reports on TB case-finding and treatment outcomes	Health facility District Central	Quarterly Annually
4) Proportion of registered TB patients co-infected with HIV who started or continued ART during TB treatment	***Numerator:*** Number of registered TB patients in a given quarter co-infected with HIV who started or continued ART ***Denominator:*** Total number of registered TB patients in the same quarter co-infected with HIV	TB unit/district registers Quarterly reports on TB case-finding and treatment outcomes	Health facility District Central	Quarterly Annually

Table 2.11.7: Monitoring TB in children

Indicator	Calculation	Data Source	Level	Frequency
1)Proportion of childhood TB cases among all new case notifications	***Numerator:*** Number of childhood TB cases (new and relapses) ***Denominator:*** Total number of registered TB cases in the same quarter; number of all new cases of all forms of TB (new and relapses)	Unit and district TB registers Quarterly report on program management	Health facility District Central	Quarterly Annually
2) Number of under-five contacts who are initiated on IPT	Not Applicable	Not applicable		
3) Proportion of childhood TB cases that received HCT	*Numerator*: Number of childhood TB cases that received HCT *Denominator*: Number of all childhood TB cases			

Table 2.11.8: Monitoring TB laboratory services

Indicator	Calculation	Data source	Level	Frequency
1) Proportion of TB microscopy units submitting slides for rechecking	***Numerator:*** Number of TB microscopy units for which slide rechecking results are available during a quarter ***Denominator:*** Total number of TB microscopy units performing TB smear during the same specified quarter	NTRL	Central	Quarterly
2) Proportion of presumptive TB cases who are Pulmonary bacteriologically confirmed	***Numerator:*** Number of presumptive TB cases found to be Pulmonary bacteriologically confirmed TB cases during a quarter/year ***Denominator:*** The number of Presumptive TB cases identified e in the same quarter/year	Laboratory and/or TB presumptive register	Health facility District Central	Quarterly Annually
3) Proportion of pulmonary bacteriologically confirmed PTB registered for treatment	***Numerator:*** Number of new pulmonary bacteriologically confirmed TB cases who have initiated treatment during a quarter/year ***Denominator:*** Total number of new pulmonary bacteriologically confirmed TB cases detected in same quarter	Laboratory Unit and District TB registers	Health facility District	Quarterly Annually
4) Proportion of MDR-TB identified out of cultured specimen	***Numerator:*** Number of MDR-TB cases diagnosed in a quarter/ year ***Denominator:*** Number of cultures performed in the same quarter/year	NTRL	Central	Quarterly Annually
5) Cumulative number of MDR-TB reported	Count Total number of MDR-TB cases diagnosed in a quarter/year	NTRL	Central	Quarterly Annually
6) Proportion of health facilities with high false negatives AFB smear microscopy result	***Numerator:*** Number of health units sampled having at least two high false negative AFB smear microscopy results ***Denominator:*** Total number of health units sampled	NTRL	Central	Quarterly Annually

Table 2.11.9: Programmatic Management of Drug Resistant TB

Indicator	Calculation	Data Source	Level	Frequency
1) Percentage of close contacts of DR-TB patients traced and screened for TB (at least once)	***Numerator:*** Number of contacts of MDR TB cases screened for TB ***Denominator:*** Total number of contacts of MDR-TB patients	Contact tracing register for Susceptible and Resistant TB	Treatment Initiation Health facility District Central	Quarterly Annually
2) Number of confirmed DR-TB cases started on DR-TB treatment	*Numerator*: Number of laboratory-confirmed MDR-TB cases registered and started on a prescribed second-line anti-TB treatment regimen during the specified period of assessment	MDR Register		
3) Treatment success rate for confirmed DR-TB cases	*Numerator*: Number of laboratory-confirmed MDR-TB cases enrolled on second-line anti-TB treatment during the year of assessment who are successfully treated (cured plus completed treatment) *Denominator*: Total number of laboratory-confirmed MDR-TB cases enrolled on second-line anti-TB treatment during the year of assessment	MDR Register		

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SECTION THREE

LEPROSY

3.1 GENERAL INFORMATION ABOUT LEPROSY

- Leprosy is a chronic infectious disease.
- It has a very long incubation period.
- Its different clinical manifestations are determined by the level of immunological defense of the body.
- It affects people of all races, ages and sexes.
- The main sources of infection are untreated patients with the infectious forms of the diseasen

3.1.1 Definition of Leprosy

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* that affects the skin, peripheral nerves and the mucous membranes. The disease affects people of all races and ages and both sexes.
In this context, a case of leprosy is a person with clinical signs of leprosy who requires chemotherapy (MDT); this excludes people with residual signs of leprosy after completion of a full course of treatment.

3.1.2 Source of Infection and Mode of Transmission

The mode of transmission is uncertain, but it is believed that M. *leprae* is spread from person to person primarily as nasal droplet infection. Untreated leprosy patients discharging bacilli are considered the main source of infection. Persons living in the same household or who otherwise are in frequent contact with an infectious person have the greatest risk of being exposed to the bacilli.

The incubation period is usually long, ranging from 3 to 5 years but it may vary from 6 months to more than 20 years. The peak age of onset is young adulthood, usually 20 to 30 years of age. Whereas there are published reports of people co-infected with leprosy and HIV, there is no conclusive evidence suggesting an association between HIV infection and leprosy.

3.1.3 Natural History

While most individuals exposed to an infectious case of leprosy become infected, only a very small proportion (less than 5 percent) of those infected develop the disease. In the majority of cases, specific immunological defences kill the bacilli.
The different manifestations of leprosy (multibacillary and paucibacillary) are due to differences in the degree of immunological defence of the human body and not due to different kinds of bacilli. Individuals with a partially impaired immunity have a higher chance to develop paucibacillary leprosy (the form with

few bacilli) while those with a low natural immunity to *M. leprae* a higher chance to develop multibacillary disease.

Patients carrying many leprosy bacilli are called multibacillary. They are considered the main source of infection.

Untreated multibacillary leprosy patients continue spreading the infection. When left untreated, leprosy can cause progressive and permanent damage to the skin, nerves and eyes.

3.2 CASE FINDING AND DIAGNOSIS OF LEPROSY

- Early diagnosis and prompt treatment reduces disabilities due to leprosy and stops transmission to others.
- Early detection of new patients is a joint effort of communities and health service providers
- Persons with suspect signs should be referred to the nearest diagnostic facility
- Diagnosis of leprosy must be based on careful clinical examination
- Leprosy is diagnosed after finding at least one of the three cardinal signs.
- Leprosy patients are classified into PB and MB for purposes of determining the treatment regimen
- Newly diagnosed patients should receive sufficient explanation to ensure prompt and proper treatment

A case of leprosy is a person with clinical signs of leprosy who requires chemotherapy.

The clinical signs which are referred to as the "cardinal signs" of leprosy are:

i) Hypopigmented patches with definite loss of sensation in them

ii) Thickened or enlarged peripheral nerves at sites where nerves are often affected with loss of sensation and/or weakness of the muscles supplied by those nerves

iii) The presence of acid-fast bacilli in a slit skin smear

3.2.2 Case-finding

The NTLP aims at early diagnosis of most cases occurring in the community by:

- Training health workers to recognize symptoms and signs of the disease
- Providing health education to communities aimed at increasing awareness of the disease
- Engaging Village Health Teams in leprosy case finding initiatives.
- Delivering good treatment services to known leprosy patients, so that other persons with suspect signs and symptoms may also have confidence in the good treatment and thus come forward to be examined and treated (self-reporting)
- Establishing a clear referral system to deal with difficult diagnoses
- Proper examination of all persons presenting themselves at health facilities with different skin conditions
- Carrying out systematic examination of house-hold contacts of all newly detected leprosy cases.

3.2.2.1 When to suspect leprosy

Leprosy should be suspected in people with any of the following symptoms and signs:

- Pale or reddish patches on the skin (the most common sign of leprosy)
- Loss or decrease of feeling in the skin patch
- Numbness or tingling of the hands or feet
- Weakness of the hands, feet or eyelids
- Painful or tender nerves
- Swellings or lumps in the face or earlobes; and
- Painless wounds or burns on the hands or feet

If one is not sure of the diagnosis, the patient with suspect signs and symptoms should be referred to the next level. Such a person should not be registered as a case of leprosy.

3.2.3 How leprosy is diagnosed

Diagnosis of leprosy must be based on careful **clinical examination** of the patient and, when necessary, backed by bacteriological examination. Leprosy is diagnosed when at least one of the following **cardinal signs** is present:

i) Hypopigmented patches with definite loss of sensation in them

ii) Thickened or enlarged peripheral nerves at sites where nerves are often affected (see diagram) with loss of sensation and/or weakness of the muscles supplied by those nerves

iii) The presence of acid-fast bacilli in a slit skin smear

A patient not having at least one of those signs should **not** be registered as a case of leprosy

3.2.3.1 Diagnostic and treatment units for leprosy

One or more health facilities in every district will be designated as a **diagnostic and treatment unit** for leprosy. The number of such units will be determined according to the level of endemicity of leprosy in the district.

Staff at diagnostic units will be expected to diagnose, register and treat leprosy patients as described in 3.2.2.4 below.

At undesignated facilities, specific treatment must be given only after the diagnosis has been confirmed by the District TB/Leprosy Supervisor (DTLS) or appropriate staff of the nearest leprosy diagnostic/treatment center. If the DTLS in not expected to visit the facility soon, the patient should be referred to the unit where the DTLS is based or to the nearest leprosy diagnostic and treatment unit.

3.2.3.2 Responsibilities of health workers in leprosy diagnostic and treatment units

The health workers at the diagnostic and treatment unit for leprosy are expected to:

- Carry out a complete physical examination (according to guidelines outlined in this manual)
- Confirm the diagnosis of leprosy
- Explain to the patient what the disease is, what might be expected of treatment and possible complications
- Prescribe the appropriate treatment and inform the patient where and when the treatment can be accessed.

- Enter the patient's particulars in the Unit Leprosy Register. The unit in-charge should notify the patients through the HMIS
- Write out the patient's Clinic Appointment Card
- Carry out systematic assessment of the close contacts of the newly detected patient within the first one month of establishing the diagnosis.

3.2.3.3 Leprosy related responsibilities of the DTLS on visiting a health unit

The **DTLS or other designated Focal Person** on visiting a health facility does the following:

- Carries out complete physical examination on known leprosy patients and those with suspect symptoms and signs
- Validates the information recorded by the health facility staff on the Leprosy Record Card and the Unit Leprosy Register
- Organises the taking of skin smears
- Explains to the patient about the disease and its treatment
- Enters patient data in the District Leprosy Register
- Enter the District Registration number in the Unit Leprosy Register, Leprosy Record Card

3.2.3.4 Clinical examination

Information that must be asked for and recorded on the Leprosy Record Card:

- *General information on the patient:* complete name, sex, place, date of birth, full address (village. Parish and sub-county), mobile telephone number, distance from home to health unit, occupation
- *Contact information:* Other people in the same household and family (including children) and indicating if any of them were ever diagnosed or treated for leprosy.

History taking

- *Main complaints*: date of onset, sites of the lesions, subsequent changes and development of the disease, treatment received

Physical examination

It is recommended that the physical examination be carried out with:

- adequate light (preferably daylight) available, because it is difficult to see the lesions in poor light
- enough privacy for the person to feel at ease

To ensure that no important sign is missed, the clinical examination should include the entire skin surface, back and front, in the following sequence:

- Head and neck
- Front of chest and abdomen
- Arms
- Back of chest and buttocks
- External genitalia in male patients
- Legs

I. Examination of the skin

The skin should be examined for:

- Presence of skin lesions (patches or nodules)
- Number of skin lesions
- Loss of sensation on the skin lesions (patches)

Instructions for sensory testing

Test the sensation of skin lesions with a wisp of cotton wool as follows:

- Roll the end of a wisp of cotton wool into a fine point.
- Explain to patients the purpose of the test and what is expected of them.
- After the explanation, conduct a trial test by touching the patients on normal skin with their eyes open so that they can exactly see what is done. Continue until they show that they understand the purpose of the test.
- Then do the testing with the patients' eyes closed. First test on normal skin. When they point correctly, test in the skin patches while touching normal skin now and then. Watch at every touch that the patients keep their eyes closed.
- Touch the skin with this point so that the cotton wool bends.
- Patients should be asked to indicate accurately with the tip of a finger, every spot you have touched with the cotton wool.*
- Failure of the patient to indicate tested areas accurately implies loss of sensation.

Sometimes patients point accurately to areas of normal skin but point more than 2 cm away from where the skin patch is tested. This is called **mis-reference, and shows diminished sensation in the patch. If this is consistent during repeated testing of a patch, it is a cardinal sign and thus diagnosis of leprosy is made. For thickened skin areas such as the palms and soles use the tip of a ballpoint pen for testing sensation.*

II. Examination of peripheral nerves

The peripheral nerves are examined for*:*

- Size (enlargement or thickening)
- Tenderness (pain on palpation)
- Nerve function assessment

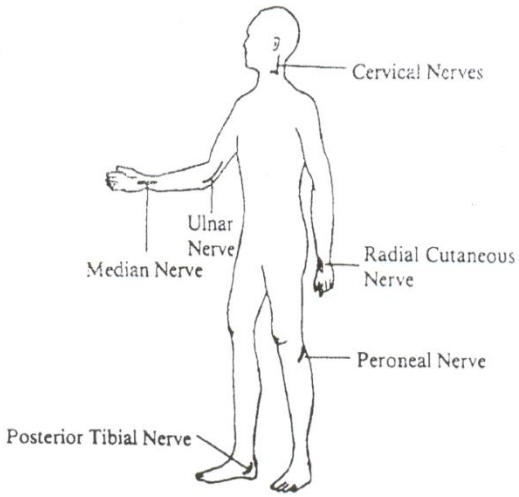


Figure 3.1 Names of superficial nerve trunks and sites where they can be palpated

How to palpate nerves for size and tenderness

- To assess the thickness of a nerve, compare the size of your nerve to that of the patient
- Always compare the patient's left side with the right side nerve(s).
- Palpate the nerve with 2 or 3 fingers by rolling the nerve on the surface of the underlying bone and determine the thickness and tenderness (pain on pressure) at the sites indicated in Fig 3.1 above.
- Finding thick nerves, especially in combination with other signs and symptoms of leprosy, is diagnostic of leprosy.

How to carry out nerve function assessment

Peripheral nerve trunks carry 3 types of nerve fibers – ***autonomic, sensory and motor.*** *It is recommended to assess each nerve function separately. Any loss of function will indicate possible damage to the relevant nerve fibers*.

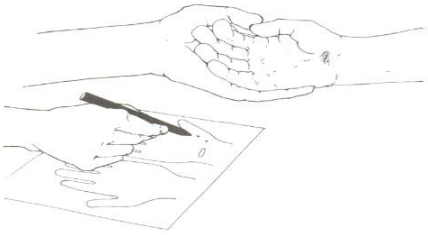
- **Autonomic nerve function** is assessed by looking for dry skin especially on the palms of the hands or the soles of the feet. Finding dry palms and soles of feet implies loss of autonomic nerve function.
- **Sensory nerve function is assessed by carrying out sensory testing (ST) of the eyes, hands and feet as follows:**
    - **Eyes**: Observe the eyelids for blinking. If the patient is blinking, assume that the corneal sensation is normal. If the patient does not blink, record "spontaneous blink absent" and refer the patient to the eye clinic.

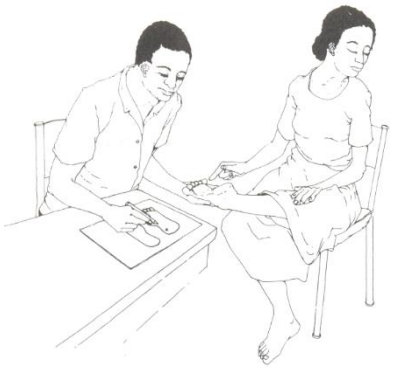
- **Hands and feet:** Sensory testing on palms and soles should be done with a ballpoint pen on 10 standard points as indicated on the Leprosy Record Card. The procedure for sensory testing is described in Figure 3.2 below.

Figure 3.2 Procedure for sensory testing (ST) of hands and feet

1. Mark any wounds, open cracks, clawing of digits and bone loss or absorption on the Leprosy Record Card.

2. Support the patient's hand or foot to prevent any joint movements in fingers/toes during the test.





3. Then touch the skin very gently denting it as little as possible, about 1 mm. The dots on the hand and foot maps on the Leprosy Record Card show you where to touch.
First test while patients are watching and ask them to point with one finger wherever they feel a touch, to the exact place touched. When patients understand the test well and are pointing clearly, ask someone to screen off their eyes or ask them to close their eyes and turn away.

Each time that you dent the skin **record on the hand or foot map** on the Patient Record Card. Record √ **(tick)** at the place if the patients feel and point within 3 cm and **X** if they do not feel anything or point somewhere else.

- **Motor nerve function:** The motor function of peripheral nerves is assessed through **voluntary muscle testing (VMT)**. All muscle movements should be assessed for

range and the **strength** against the resistance of your hand. Muscle strength should be graded as Strong (S), Weak (W) or Paralyzed (P). Test the muscle strength of eyes, hands and feet as follows:

Procedure for Voluntary muscle testing (VMT) of eye

Eye closure: [Facial nerve function]
Ask patients to close their eyes lightly as in sleep. Observe whether or not the closure is complete. Inability to fully close the eye is termed **lagophthalmos**. If there is lagophthalmos, measure the lid gap. The lid gap is recorded in millimetres. A lid gap of more than 5 mm necessitates immediate action to prevent damage. If closure is normal, record "0 mm". Then ask patients to close their eyes firmly while you gently check for strength. Is the closure S, W or P?

Procedure for VMT of hands and feet
Little finger out: [Ulnar nerve function]
Ask patients to move their little finger all the way in (touching the side of the ring finger) and all the way out. Is the movement full?
If the movement is full, ask patients to hold their **little finger out** fully while you apply resistance to the outward movement at the base of the finger by pushing it in. Record the findings as S, W or P.
Thumb up*:* [Median nerve function]
Ask patients to bring the **thumb up and** in front of the index finger but as far away from it as possible. Focus attention on the movements at the base of the thumb rather than the tip. Can they achieve this testing position? Is the movement full?
To test the strength of this movement, instruct patients to maintain the starting position while you push downwards towards the index finger. Record the findings as S, W or P
Foot up; [Peroneal nerve function]
Ask patients to fully lift their foot up towards the shin (dorsiflexion). Check if the movement is full (no more movement possible at the ankle joint).
To test the strength in the testing position, apply resistance to the top of the foot by pushing down.
Record the findings as S, W or P.

III. Examination of other organs

Examination of other organs is important in cases of MB leprosy.
i) Examination of the eye
The eyes should be examined carefully under good light, preferably daylight. Besides the changes examined under VMT above, other aspects to be checked include:

- Loss of eyebrows
- Corneas for clearness, ulcers or scars
- Conjunctiva for redness indicating infection, such as conjunctivitis (peripheral redness) or iridocyclitis (redness around the cornea)

- Pupils for regular and round shape. Also check reaction to light and look for signs of cataracts
- Eyeball pressure for glaucoma
- Vision by asking the patient to count fingers as in Figure 3.3

Stand 6 meters from the patient. The vision of each eye is tested separately. Ask the patient to **cover** one eye. **Raise your hand** against a light background and show the patient 4 times, different numbers of fingers and **ask the patient to count** aloud.
If he can count fingers at 6 meters, record 6/60 for that eye.

Then test the other eye.

Figure 3.3 Vision testing
A patient who cannot count fingers at 6 meters has severe visual impairment.

ii) Examination of the nose, tongue and gums, throat, breasts and testes
These organs can also be affected. They should be examined and, in case of doubt, the patients should be referred to leprosy referral centers.

IV. Examination of the skin smear
A skin smear is a test in which a sample of material is collected from a tiny cut in the skin and stained for *Mycobacterium leprae.*
The purpose of taking a skin smear is usually to:

- Confirm the diagnosis of skin smear-positive MB leprosy in a suspect
- Help to diagnose MB relapse in a patient who has been previously treated
- Help with the classification of new patients

Only 1 slide, with smears taken from 2 sites must be collected and examined. The basic field guidelines for selection of skin smear sites and steps for taking skin smears are included in Annex 7. The technique for collecting and examining skin smears is described in the ILEP Learning Guide Three: How to do a skin smear for leprosy. Skin smear services are available in the National TB Reference Laboratory (NTRL), Lira Regional Referral Hospital, and Buluba, Kagando, Kuluva and Kumi hospitals. One positive smear result is diagnostic for MB leprosy.

V. Main messages

When the diagnosis of leprosy is certain*:*

- Carefully record all information on skin, nerves, hands, feet and other organs on the Leprosy Record Card.
- Fill in all of the information asked for at the start of treatment as baseline information.
- After each review examination, record every change in findings on the same card.

If leprosy is suspected, but the diagnosis is not certain:

- Patients should be labeled as "suspects"
- Educate them about symptoms and signs of leprosy and either:
    - Refer to the next level facility;
    - Consider the possibility of another skin disease and treat appropriately; or
    - Wait three months and review the skin lesions again.

If it is leprosy, loss of sensation may now be observed. If there is no loss of sensation in the skin lesions and no enlarged nerves, but there are suspicious signs such as nodules or swellings on the face or earlobes, or infiltration of the skin, it is important to try and get a **skin smear** examination done. A positive skin smear confirms the diagnosis of leprosy while a negative result (in the absence of other cardinal sign) would rule out leprosy.

3.2.3.5 Differential diagnosis of leprosy

Leprosy can be easily mistaken for a number of skin diseases. If patients are examined carefully, mistakes in diagnosis should not occur as none of the cardinal signs of leprosy are found in the common skin diseases such as:

- **Birthmarks:** Lightly or deeply pigmented areas of different sizes that have been present since birth or soon after birth and do not change.
- **Post-inflammatory hypopigmentation**: The skin may become temporarily or permanently hypopigmented at the end of treatment of several inflammatory skin conditions. It also can follow the deliberate application of skin-lightening products for cosmetic reasons. This can be ruled out through appropriate history taking.
- **Tinea versicolor:** These lesions often itch. They are hypopigmented, but with no loss of sensation. Usually they clear up within six weeks with application of antifungal ointment or cream.
- **Tinea corporis (ringworm):** Lesions are well-defined areas of hypopigmentation with white scales and without loss of sensation. Usually, they clear within six weeks of application of antifungal ointment.
- **Vitiligo:** a chronic skin condition characterized by portions of the skin losing their pigment causing whitish patches of different sizes and shapes often with no clear cause.
- **Pityriasis alba:** Present most commonly on the face, but the upper trunk may be affected. Hypopigmented rounded or oval patches, variable in size and with the margin sharply demarcated, covered with fine adherent scales. Often patients only present with the final hypopigmentation.

- **Psoriasis:** Raised areas with white fatty scales that bleed easily on scratching (test for pin point bleeding).
- **Molluscum contagiosum:** Nodular lesions with a depression in the center. Firm squeezing results in the appearance of a creamy substance.
- **Onchocerciasis (in endemic areas):** Previous complaints of intense itching. There are itchy nodules and scratch marks. Hypopigmented macules may be one of the manifestations. There is loss of sensation. In a later stage, there are mottled lesions particularly on the loins and shins. Skin smears are negative for AFB.
- **Neurofibromatosis:** Multiple deeply pigmented **soft** nodules that do not itch. Skin smears are negative for AFB.
- **Syphilis:** Secondary syphilis presents with a considerable variety of lesions, e.g. papular and nodular lesions. Skin smears are negative for AFB. Serological tests for syphilis will be positive.
- **Kaposi sarcoma:** In HIV-positive patients and others, Kaposi's sarcoma often presents with nodules on the face and ear lobes. There are often lesions within the mouth and the throat, which may bleed. Skin smears are negative for AFB.

3.2.4 Classification of Leprosy

It is important to classify the type of leprosy the patient has because it determines the treatment regimen and the appropriate messages to give to the patient before administration of treatment.

In relation to this, there are two treatment groups:

I. Paucibacillary (PB) leprosy

These are patients who have up to five skin lesions in total. These patients should also be skin smear-negative. This group of patients is likely to have high body resistance to leprosy bacilli.

II. Multibacillary (MB) leprosy

These patients have six or more skin lesions. All leprosy patients with a positive skin smear must be classified as **MB,** irrespective of the number of skin lesions. The bacilli infecting an individual with very low body resistance will multiply freely in the body, and the person will develop MB leprosy, the more severe form of the disease.

If there is doubt about the classification, the patient should be classified and treated as MB leprosy

When patients are newly diagnosed with leprosy, they should receive help and counseling so that the disease can be treated quickly and in the best possible way. The following categories of messages should be given to patients (not necessarily at the same sitting):

- General information
  - People affected by leprosy should continue to live a normal life.
  - Leprosy is caused by a germ and is curable.
  - Explain where to get answers to any questions regarding leprosy.
  - Consultation and treatment are free of charge.
  - Discuss how frequently the person should attend the clinic.
  - Persons who have been in close contact with patients, particularly those living in the same household, need to be examined at the earliest opportunity.
- Information about treatment
  - Leprosy is curable.
  - Leprosy is no longer infectious once treatment has begun.
  - The treatment lasts 6-12 months depending on the leprosy type.
  - Tablets must be taken every day at home.
  - A new blister pack is needed every 28 days.
  - Common side-effects include reddening of the urine and darkening of the skin.
  - The skin patches may take time to disappear.
- Complications called "reactions" may occur and can be treated. These can present as follows:
  - Patches can suddenly become red, swollen, and more clearly visible.
  - There may be:
    - Pain or numbness in the limbs
    - Weakness of the hands or feet
    - Swelling of hands and feet
    - Eye problems such as redness, pain, or impairment of vision
- Disabilities
  - New disabilities can occur at any time, but they can be managed.
  - Existing disabilities may or may not improve with treatment.
  - When problems occur, treatment may be available locally, or the patient may have to be referred to another clinic for specialist care.
  - Various new skills will have to be learnt to prevent and manage disability.

3.3 TREATMENT OF LEPROSY

The aims of leprosy treatment are to:

- Cure the leprosy.
- Prevent the occurrence of disabilities.
- Prevent relapse and the development of drug-resistant leprosy.

- MDT is a safe and effective oral treatment of leprosy.
- It is provided as 28-day blister packs.
- The intake of the monthly treatment containing rifampicin should be supervised.
- There are different blister packs by age category for PB and MB leprosy patients.
- The total duration of treatment is six months for PB leprosy and 12 months for MB leprosy.
- Relapses after MDT are very rare.

3.3.1 Multidrug Therapy

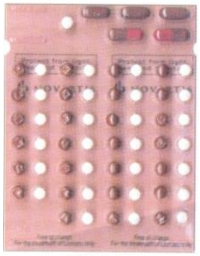
MDT is a combination of drugs that is very safe and effective in treating leprosy to prevent the emergence of drug resistance. Leprosy patients should never be treated with a single drug.

Important information:

- MDT is distributed free of charge to all those who need it.
- The drugs are all taken orally. The daily drugs should be taken in a single dose on an empty stomach.
- The drugs are given out in blister packs that provide four weeks of treatment (1 month).
- There are different packs with the same drugs but in smaller doses for children.
- MDT is safe for women and their babies during pregnancy and breastfeeding.
- MDT can be given to HIV-positive patients, those on antiretroviral treatment, and to patients on treatment for TB. If a leprosy patient is on treatment for TB, the MDT regimen should omit rifampicin as long as the TB regimen contains rifampicin.

3.3.2 MDT regimens

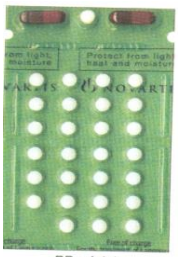
The standard **adult** treatment regimen for **MB** leprosy is:


MB - Adult

Rifampicin: 600 mg once a month
Clofazimine 300 mg once a month and 50 mg daily
Dapsone: 100 mg daily.

Duration: 12 months (12 blister packs)

The standard **adult** treatment regimen for **PB** leprosy is:


PB - Adult

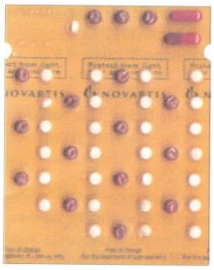
Rifampicin: 600 mg once a month
Dapsone: 100 mg daily

Duration: 6 months (6 blister packs)

The standard **child** (10–14 years old) treatment regimen for **MB** leprosy is:

Rifampicin: 450 mg once a month
Clofazimine: 150 mg once a month and 50 mg every other day
Dapsone: 50 mg daily

Duration 12 months (12 blister packs)

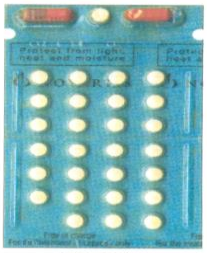


MB - Child

The standard **child** (10–14 years old) treatment regimen for **PB** leprosy is:

Rifampicin: 450 mg once a month
Dapsone: 50 mg daily

Duration: 6 months (6 blister packs)



PB - Child

PB patients are given two drugs for six months, while **MB** patients are given three drugs for 12 months. Every effort must be taken to ensure regularity of drug intake, so that PB patients complete their treatment in six months and MB cases in 12 months.

Specific blister packs are available for MB and PB leprosy, for adults and children.

The health worker or other accompanying person (if the health worker is not available) should see the patient take the monthly dose of treatment. This helps to guarantee that the treatment is taken properly as a measure to prevent drug resistance. It also gives the health worker an opportunity to check the patient for any complications of leprosy.

3.3.3 MDT for children under 10 years of age

The appropriate dose for children under 10 years of age can be decided on the basis of body weight. [Rifampicin: 10mg/kg body weight; clofazimine: 1 mg/kg body weight daily and 6 mg/kg body weight monthly; dapsone: 2mg/kg body weight daily].

The standard child blister pack may be broken up so that the appropriate dose is given to children under 10 years of age. Clofazimine can be spaced out as required in consultation with the DTLS.

3.3.4 MDT for MB patients with a very high bacterial index

Rarely, it may be considered advisable to treat a patient with an average bacterial index (BI) of four or more for more than 12 months. This decision may only be taken by the Regional TB/Leprosy Focal Person or specialists at referral units, after careful consideration of the clinical and bacteriological evidence.

3.3.5 MDT for leprosy patients who are co-infected with HIV

For any leprosy patients who are co-infected with HIV **and are receiving cotrimoxazole preventive treatment (CPT)**, dapsone should be stopped. In PB patients, dapsone should be substituted with clofazimine for six months in the same dosage as used in the standard MDT for MB leprosy. For MB patients, no further modification of the MDT regimen is required.

3.3.6 Procedure for administering MDT

For patients to be treated with MDT, carry out the following steps:

- Determine which type of MDT is required, PB or MB.
- Fill in the Patient Record Card, the Leprosy Unit Register and the Patient's Identity Card.
- Counsel the patient (and the caregiver, if patient is a child).
- Directly observe first dose of treatment and explain how to continue the treatment at home.

The drugs administered once a month should be directly observed, the health worker should make sure that the drugs have actually been swallowed. The taking of the supervised dose is most conveniently arranged by having the patient attend the clinic each month. This monthly visit is also useful for monitoring the regularity of treatment and for identifying complications at an early stage. The other drugs are taken at home.

MDT is safe, and serious side-effects are very rare. Common side-effects are summarized in table 3.1

Table 3.1 Side-effects of MDT drugs and their management

Side-effects of MDT	Drug responsible	Management
Red urine	Rifampicin	Reassurance
Darkening of the skin	Clofazimine	Counseling
Gastrointestinal irritation e.g., abdominal pain, diarrhea, nausea	All 3 drugs. Increased with high-dose clofazimine	Give drugs with food
Anaemia	Dapsone	Give iron and folic acid
Itchy skin rash	Dapsone	Stop dapsone and refer
Allergy, urticaria	Dapsone or rifampicin	Stop both and refer
Jaundice	Rifampicin	Stop rifampicin and refer
Shock, purpura, renal failure	Rifampicin	Stop rifampicin and refer

Note: Other drugs e.g. Minocycline, Ofloxacin and Moxifloxacin can be used if one or more of the standard drugs have been stopped, however, the determination of appropriate regimens and supervision of treatment should be undertaken by specialists.

3.3.6 How to ensure that treatment is taken regularly

- Patients should be treated with respect.
- Take time to explain the illness and its treatment to each patient.
- Make sure patients understand how to take the treatment and the date of their next clinic visit.
- Make sure there is a good supply of medicines ready for your patients to take.
- Listen to patients' concerns and answer their questions.
- With the consent of the patient, identify and engage another person (family member or other) as treatment supporter.
- Record the treatment given on the Patient's Identity Card, the Leprosy Record Card, and the Unit Leprosy Register.
- The DTLS should check those documents regularly to make sure that all patients are taking their treatment regularly.

3.3.7 Management of patients who miss scheduled clinic visits

As soon as patients miss an MDT appointment, action should be taken by the treatment facility staff to find out the reason and to remind them to attend the clinic regularly. This is facilitated by recording mobile telephone contacts for patients at the start of treatment. If this proves insufficient, a home visit by a local community worker should be arranged (preferably within the first month following the date of the missed visit).

If patients have difficulty attending the clinic, it is possible to give them two blister packs at once, but in such cases a treatment supporter (community volunteer, family member, or neighbor) should be involved in helping the patients to continue the treatment at home and reporting to the clinic in case of any problem.
Patients may miss scheduled clinic visits for reasons such as:

- Poor accessibility of the clinic (long distance, difficult terrain, or inconvenient timing).
- Difficulty in getting time off at work.
- Being overwhelmed with demands or effects of other health problems.
- Nomadic life style.
- Lack of understanding of the disease and the need for regular treatment.
- Stigma.
- A poor relationship with the health worker.

3.3.8 How to care for patient at follow up visits

Every time patients come to take their drugs they should:

- Be asked if there have been any problems since the last visit
- Be re-examined including carrying out nerve function assessment.
- Have the attendance recorded in the patient's card and the unit leprosy register.
- Be informed about the remaining MDT doses and the date of their next visit.
- Have the date of the next clinic visit recorded in the patients' identity card.

3.3.9 Management of patients who have completed MDT

When the patient has completed six months of treatment for PB leprosy or 12 months for MB leprosy, document in the unit register that the patient has **completed the treatment** under the heading "Treatment Outcome." Record any residual signs in the patient's record card and issue certificate for treatment completion.

Although patients who have completed MDT are cured, some signs of leprosy may remain:

- Skin patches caused by leprosy may not disappear immediately or may remain permanently.
- Loss of feeling, muscle weakness, and other nerve damage may also remain.

These residual signs should be recorded on the Leprosy Record Card at the time of stopping MDT.

The patient should be counseled on the following issues and asked to return to the clinic for review at least once a year or at any time when any of the previous symptoms recur.

- Significance of the remaining patches.
- Essential actions to take in order to prevent further damage.
- Signs and symptoms of reactions that can occur after MDT.

When patients return with a leprosy reaction after completing a full dose of MDT, only the reaction should be treated. This is not a reason to re-start MDT.

3.3.10 Loss to follow up

Every effort must be made to ensure that PB patients complete their treatment in six months and MB patients in 12 months. When that is not possible, the treatment regimen for PB leprosy must be completed within a **maximum** period of nine months. The treatment regimen for MB leprosy must be completed within a **maximum** period of 18 months.

Whenever a PB patient has missed more than three months of treatment, or an MB patient has missed more than six months, it is not possible for them to complete the regimen in the maximum time allowed, and they should be declared **lost to follow up.** This should be indicated in the Unit Leprosy Register under the heading "Treatment Outcome."

A patient who fails to complete treatment within the maximum allowed timeframe is regarded as lost to follow up.

Patients returning after loss to follow up should be examined and the findings recorded in the same way as for new cases. Returning patients should be managed as follows:

- Count the number of lesions to confirm the original classification.
- Reclassify as PB or MB according to the number of lesions, register the patient under category "Treatment after Default" and treat with a full course of MDT.
- If there are signs of reaction, manage appropriately.
- Remember that a reaction can be mistaken for a return of the disease.

A patient who either remains very irregular on treatment or is repeatedly lost to follow up should be referred to the district leprosy diagnostic/treatment facility.

3.3.11 Relapse

Relapse in leprosy is defined as the re-occurrence of the disease at any time after the completion of a full course of treatment with WHO-recommended MDT. Relapse after MDT is rare. It is important to continue vigilance because some sporadic cases of relapse due to drug resistance have been reported.

Signs of a relapse

- The appearance of definite new lesions.
- An increase in the skin smear BI of two or more units at any single site compared to BI taken from the same site at the previous examination. Care should be taken to exclude patients suffering from leprosy reactions.
- MB patients who start MDT with an average BI of four or more are more likely to suffer a relapse later; most relapses occur long after the treatment was given (sometimes more than 10 years later).

It can be difficult to distinguish relapses from reactions. Table 3.2 provides guidelines for distinguishing.

Table 3.2 Differentiating a leprosy relapse from a reaction

Criteria	Relapse	Reaction
Time since completion of treatment	More than 3 years	Less than 3 years
Progression of symptoms and signs	Slow	Fast
Site of skin lesions	In new places	Over old patches
Pain, tenderness, or swelling	No	Yes, skin and nerves
Damage	Occurs slowly	Sudden onset
General condition	Not affected	Inflammation

Investigation of suspected relapse

The options for investigating a suspected relapse include:

- Skin smears, at regional referral centers.
- Skin biopsy for histopathological examination, not routinely available outside teaching hospitals.
- Drug sensitivity testing using recently standardized molecular (DNA sequencing) techniques, though these are not yet available for Uganda.

Management of relapse cases

Suspected relapse cases should be referred to the Regional TB/Leprosy Focal Person or one of the leprosy referral centers. Skin smear examinations should be performed on all such cases. Relapse cases should be retreated with the same MDT regimen.

3.3.12 Prevention of leprosy

- At the moment the most important preventive measure against leprosy is **early diagnosis of cases and treatment.**
- **Screening of contacts of known patients** provides the opportunity for early diagnosis of cases among them. The programmatic implementation of chemoprophylaxis of contacts without leprosy disease is under investigation.

- **BCG vaccination**: Several studies have demonstrated protection against both PB and MB leprosy by BCG even though the observed protection has varied between study populations from 20% to 80%. In Uganda BCG is routinely given to newborns for its protection against severe forms of TB.

3.4 COMPLICATIONS OF LEPROSY AND THEIR MANAGEMENT

- Complications of leprosy include leprosy reactions, effects of nerve damage, complications of advanced disease, and psychosocial problems.
- Leprosy reactions due to associated inflammation can lead to severe nerve injury, impairments, and disabilities.
- The main-stay of treatment of severe leprosy reactions is corticosteroids.
- Leprosy can cause impairment of vision or even blindness due to damage to the cornea or internal structures of the eye.

3.4.1 Leprosy reactions

A reaction is the sudden appearance of symptoms and signs of inflammation in the skin lesions and /or nerves of a person with leprosy. There is pain, redness, swelling, and sometimes tenderness of the skin lesions. New skin lesions may appear. There may also be swelling, pain, and tenderness of nerves often accompanied by loss of function.

Please note:
Sometimes impairment of nerve function occurs without other signs of inflammation, making it less obvious. This is called “silent neuritis.”

Any type of leprosy may show a reaction, but the nature of the reaction differs according to the leprosy type. Reactions can occur before, during, or after completion of MDT.

There are two types of reactions:

- Reversal reaction or type 1 reaction
- Erythema Nodosum Leprosum (ENL) or type 2 reaction

Apart from PB patients with single lesions, most other patients have some risk of experiencing reversal reactions. Only a small group of MB patients with a high load of bacilli are at risk of developing ENL reaction.

Both types can be divided into mild or severe; severe reactions require treatment with corticosteroids.

Signs of severe reversal reaction

If any of the following signs is found, the reaction should be treated as severe:

- Loss of nerve function, that is, loss of sensation or muscle weakness.
- Pain or tenderness in one or more nerves.
- Silent neuritis.
- A red, swollen skin patch on the face, or overlying another major nerve trunk.
- A skin lesion anywhere that becomes ulcerated.
- Marked edema of the hands, feet, or face.

Signs of severe ENL reaction

If any of the following signs is found, the reaction should be treated as severe:

- Pain or tenderness in one or more nerves, with or without loss of function.
- Ulceration of ENL nodules.
- Pain and/or redness of the eyes, with or without loss of visual acuity.
- Painful swelling of the testes (orchitis) or of the fingers (dactylitis).
- Marked arthritis or lymphadenitis.

3.4.2 Management of reactions

All patients who develop reactions while on MDT should have continue MDT without alteration of dosage.

Both types of reactions can be precipitated or their response to treatment adversely affected by other concurrent conditions, including malaria, intestinal worms, or tuberculosis. Patients should be carefully screened for these and appropriate treatment should be given.

Mild reactions

Patients not showing any of the signs of severity listed in the box above may be managed at the treatment center symptomatically with aspirin. If, after 1 week's treatment, there is no apparent improvement, patients should be managed as having severe reaction.

Severe reactions

Patients with severe reactions must be referred to the regional referral level where they can be treated and monitored effectively. Recent loss of function (within the last six months) in one or more peripheral nerves is the main reason for steroids to be prescribed in leprosy. Nerve function should be monitored on a regular basis following the recommendations in section 3.2.2.4.

Severe reversal reactions

Those should be treated with a course of prednisolone usually lasting 12 -24 weeks. Prednisolone should be prescribed by a person properly trained in using it.

Table 3.3a Recommended prednisolone regimen for severe reversal reactions in PB patients

Weeks of prednisolone treatment	Daily dose of prednisolone
1-2	40 mg
3-4	30 mg
5-6	20 mg
7-8	15 mg
9-10	10 mg
11-12	5 mg

Table 3.3b Recommended prednisolone regimen for severe reversal reactions in MB patients

Weeks of prednisolone treatment	Daily dose of prednisolone
1-4	40 mg *
5-8	30 mg
9-12	20 mg
13-16	15 mg
17-20	10 mg
21-24	5 mg

* Up to 60 mg of prednisolone may be prescribed at the start, depending on the decision of the clinician.

Because of the prolonged treatment with the prednisolone, patients must be monitored for potential side-effects such as peptic ulceration, osteoporosis, diabetes mellitus, cataracts, and exacerbation of latent infections like TB.

As soon as nerve tenderness decreases, patients with muscle weakness or paralysis should be taught exercises to strengthen the affected muscles and prevent joint stiffness.

Management of severe ENL reactions

ENL reactions are complex medical problems requiring careful management by experienced clinicians. Short courses of prednisolone are often used.

Patients should be treated with prednisolone starting with 60 mg as a single daily dose. After a few days the dose can be lowered and, in general, the prednisolone can be stopped after a period not exceeding four weeks. The patient's condition should be assessed before the dose of prednisolone is decreased.

In patients with recurrent attacks of ENL or those on prolonged treatment of corticosteroids, clofazimine should be started and prednisolone gradually withdrawn. It is important to ensure that the patient has no worm infestation, especially strongyloides, before giving high doses of prednisolone. Immune suppression can cause dissemination of strongyloides.

3.4.3 Complications of advanced disease

3.4.3.1 Eye complications

Leprosy can lead to blindness following damage to the cornea or due to damage to the internal structures of the eye. Patients who report decreased vision or who have red or painful eyes should be referred to the Ophthalmology Clinical Officer or other eye specialist.

- **Lagophthalmos**

  Patients with blink inefficiency should:
  - Inspect their eyes daily for redness and foreign bodies by looking through a mirror or asking a neighbor to look.
  - Learn to blink with effort so that their eyeballs roll up, even if their lids do not close.
  - If possible, use sunglasses to help to protect them from dust.
  - Apply artificial tears or ointment without injuring the eye.
  - Keep dirty fingers and flies away.

  In cases of severe lagophthalmos, where part of the cornea remains exposed even on forced closure, patients need surgical treatment and should be referred to the nearest unit where such services are available.
- **Eye infections and corneal ulcer**

  These should be treated with antibiotic eye drops or ointment (e.g. chloramphenicol or tetracycline) to be applied four times a day. Those with corneal ulcer should be referred to hospital.
- **Iridocyclitis (Uveitis)**

  Signs of iridocyclitis include red painful eyes, photophobia, diminished vision, and flood of tears. Patients with these symptoms should be referred to hospital immediately.

  Chronic iridocyclitis is identified from an irregular pupil that does not dilate fully. This can lead to secondary glaucoma and blindness. These patients should also be referred to hospital.

3.4.3.2 Facial and other deformities

The sunken nose, loss of eyebrows (madarosis) and the so called "leonine" face which used to be characteristic of untreated MB leprosy are disfigurements that can be associated with severe stigma and discrimination. These instances are now rare. They can be corrected with plastic surgery.

3.4.3.3 Other medical problems

Longstanding untreated leprosy and chronic ENL reactions lead to medical complications. These patients should be referred to appropriate specialists.

3.4.3.4 Psychosocial problems

Disabilities, as well as beliefs and prejudices concerning leprosy and its causes, are the main sources of psychosocial problems in leprosy patients. People with leprosy often develop low self-esteem and depression as a result of the negative attitudes of their family and community. Such negative attitudes are also observed among some religious leaders and health service providers, including doctors. People suffering from psychosocial problems may need to be referred for counseling or other help.

3.5 PREVENTION OF DISABILITY (POD) AND SELF-CARE

- Early diagnosis and prompt treatment of leprosy prevents occurrence of disabilities.
- The extent of disability at the time of diagnosis should be assessed for every patient.
- Recent nerve damage can be reversed with corticosteroid treatment.
- Grading of leprosy-related disability on a scale from 0-2 guides programmatic decisions on prevention and management of disabilities.
- Prevention and management of disabilities among individual patients includes aspects to be managed at home, in the nearest health facility, or at higher levels of the referral system.

3.5.1 Patients at greater risk of nerve damage

Patients experiencing long delays between the appearance of the first symptoms of leprosy and the start of treatment are at greater risk of nerve damage. Early diagnosis and treatment of leprosy prevents the occurrence of long-term complications.

MB patients with impaired nerve function at diagnosis should be monitored more closely. Nerve damage can occur during MDT and after the patient has completed MDT. The risk declines steadily over the following three years.

3.5.2 The effects of nerve damage in leprosy

Recent nerve damage (present for less than six months) can usually be reversed with the use of steroids. Many patients present with nerve damage of very long duration, from which no further recovery is expected.
The common physical problems resulting from nerve damage that affect people with leprosy are described in table 3.4.

Table 3.4 Common physical problems and aims of appropriate POD action

Problem	**Signs**	**Secondary effects**	**Aims of POD action**
Weakness of eye closure	Dryness, ulceration of cornea, and scarring	Impairment of vision Blindness	Preservation of sight
Loss of sensation in the hand	Dryness, cracking, and ulceration	Loss of tissue, joint stiffness	Keeping the skin in good condition and avoiding injury
Weakness and deformity of the hand	Visible deformity	Contracture and fixed deformities	Preservation of muscle strength and prevention of contractures and deformities
Loss of sensation and ulceration of the foot	Dryness, cracking, and ulceration	Chronic infection	Keeping the skin in good condition Provision of protective footwear Prevention of injury
Weakness and deformity of the foot	Foot drop	Ulceration and permanent deformity	Preservation of muscle strength and prevention of deformity

3.5.3 Assessment and recording of disabilities

Disability is a broad term covering any impairment, activity limitation, or participation restriction affecting a person.

3.5.3.1 Disability grading in leprosy

Every new case of leprosy must be assigned a disability grade that depicts the condition of the patient at diagnosis. The grade is on a scale from 0-2. Each eye, hand, and foot is given its own grade, totaling 6 grade measurements per person. The highest grade is used as the disability grade of that patient.
Grade 0 means **no disability found**.
Grade 1 means that **loss of sensation** has been noted in the hand or foot.

This should not be confused with the loss of sensation in a skin patch, which is caused by local damage to the small nerves in the skin, and not to the main nerve trunks. For the eye, grade 1 means loss of blinking reflex and/or inability to hold the eyelids closed against moderate force to open them.
Measuring and recording grade 1 disability is an essential step in preventing damage to the hands and feet of people affected by leprosy. It is therefore a key component of quality leprosy services.

Grade 2 means **that visible damage or disability** is noted**.**
For the eyes, this includes the inability to close the eye fully or obvious redness of the eye. In leprosy, this is typically caused by either a corneal ulcer or by iridocyclitis. Visual impairment or blindness is also measured as a disability grade of 2.

For the hands and feet, visible damage includes wounds, ulcers, shortening of fingers and/or toes, as well as deformity due to muscle weakness, such as a foot drop or a claw hand.

The Eye-Hand-Foot (EHF) score
The EHF score is the sum of all the individual disability grades for the eyes, hands, and feet. Since the disability grade can be scored as 0, 1, or 2, it follows that the EHF score ranges from 0 to 12. A score of 12 would indicate grade 2 disability in both eyes, both hands, and both feet.

Health workers at the health facility should be able to:

- Determine at minimum grade 1 disability by asking patients about loss of sensation in their hands and feet.
- Look for signs of visible disability (grade 2), including wounds or ulcers on the hands or feet, or redness of the eye.
- Record the visible disability.
- Refer patients to the facility where POD services are provided.

Health workers at the referral level should be able to:

- Re-examine the disability status more accurately (refer back to guidelines for nerve function assessment).
- Record the findings accurately in the Leprosy Record Card.
- Institute appropriate POD action (**Table 3.6**)

3.5.3.2 Care for people with disabilities due to leprosy
Interventions for disabilities are carried out at the following levels:

- Home-based care, including those activities that can be done by the person at home.
- Local health facility.
- Referral services (requiring the input of specialists).

3.5.3.3 Home-based care for patients
Patients should be taught how to carry out these self-care activities.

a) Problems with eye closure

- Inspect the eye in a mirror to check for redness (if no mirror, ask a neighbor to check).
- Learn to blink frequently to keep the eyes moist and exercise the lids.
- Wear a hat with a large brim and/or sunglasses to prevent dust from getting into the eyes.
- Use a sheet or mosquito net to cover the head at night.

b) Problems with hands and/or feet

- Inspect daily for signs of injury.
- Soak the hand/foot in water for about 30 minutes every day.
- Use a rough stone to smoothen the dead skin.
- Apply oil or petroleum jelly when the skin is still wet to prevent the skin from drying out.
- Use a clean cloth to cover any open wound.
- Walk as little as possible, and walk slowly. Take frequent rests (foot care).
- If foot ulcers are present, rest is essential.
- If there is any muscle weakness, such as foot drop, passive stretching and active exercises help to prevent contracture and may assist muscle strengthening.
- Use protective footwear (e.g., microcellular rubber sandals) all the time for insensitive feet and protective appliances (e.g., gloves) for insensitive hands.

3.5.3.4 Local health facility interventions

The next level of interventions can be carried out in a H/Center III or IV. The health workers should

- Discuss the management of their patients' disability problems with the district supervisor, but eventually take over the responsibility for implementing the interventions.
- Instruct and assist the patient in carrying out the relevant home-care activities above.

a) Problems with eye closure

- Provide artificial tears or any eye ointment (not containing steroids) if the eyes are very dry.
- Treat conjunctivitis with antibiotics.
- Refer more serious eye problems to an Ophthalmology Clinical Officer, Ophthalmologist or the nearest specialist eye clinic.

b) Problems with the hand

- Review to assess the implementation of expected home-care activities and advise as necessary.
- Refer, if required.

c) Problem with the foot

- Review to assess the implementation of expected home-care activities and advise as necessary.
- Take foot maps for protective footwear or arrange for these to be taken by the DTLS or trained community-based rehabilitation worker.
- Refer, if required.

3.5.4 Interventions conducted at a regional referral centre

a) Problems with the eyes

- Management of acute eye problems at eye clinic.
- Corrective surgery in severe cases of lagophthalmos (with cornea exposed).
- Cataract surgery (leprosy is not a contraindication to cataract surgery).

b) Problems with the hand

- Instruction and assistance with adaptation of tools to avoid injury to insensitive hands.
- Removal of thick callus and trim ulcers with a scalpel blade.
- Splinting of joints in the presence of weakness or contractures.
- Management of severe infection of hand ulcers.
- Reconstructive surgery to correct some cases of weakness or claw-hand (as long as the joints remain mobile).

c) Problems of the foot

- Removal of thick calluses and trimming of ulcers with a scalpel blade.
- Management of severe infections of foot ulcers.
- Surgical management of chronic ulcers.
- Provision of orthopedic appliances, including those for foot drop.
- Surgical correction of foot drop.

3.5.4.1 Encouraging people to practice self-care at home

It is important that individual patients be given self-care instructions that are relevant to their particular situation and that they are supported to practice self-care at home.

Such support may be provided by:

- Health workers
- Family members
- Local community based organizations
- Community development extension workers
- Self-care groups for people affected by leprosy or living with disabilities from other causes

3.5.4.2 The value of appropriate footwear for people affected by leprosy

The use of appropriate footwear is important for preventing ulceration among people with loss of feeling in their feet. The shoes should be locally available**,** socially acceptable and used whenever patients walk. The NTLP-recommended footwear for people with loss of sensation in their feet is microcellular rubber (MCR) sandals, with a firm under-sole, a soft insole, and heel straps. Velcro straps are preferred to other kinds of fastenings. Other shoes meeting the basic criteria can be used.

- People affected by leprosy ,especially those with disability, have physical, functional and social economic rehabilitation needs
- Health service providers are responsible for identifying such needs and assuring access to the appropriate rehabilitation services.
- The rehabilitation needs of people affected by leprosy should be addressed in by services available for all other people using the CBR approach

3.6 REHABILITATION

3.6.1 What is rehabilitation?

Rehabilitation is the process of helping an individual achieve the highest level of function, independence, and quality of life possible.

"Rehabilitation includes all measures aimed at reducing the impact of disability on an individual, enabling him or her to achieve independence, social integration, a better quality of life, and self-actualization." UN Standard Rules for Equalization of Opportunities for Persons with Disabilities (PWD).

3.6.2 The role of health workers in rehabilitation

Whereas health workers and some district supervisors may not have the time or expertise to be involved in rehabilitation activities, they are expected to:

- Be able to identify physical, functional, or socioeconomic problems resulting from disability among patients under their care.
- Know about available services for rehabilitation including those providing assistive devices.
- Know how to refer people to make use of those services.
- Be an advocate for ensuring that people affected by leprosy have access to health care and rehabilitation services in the same way as other people do.
- Discourage restrictive thoughts and ideas of other health workers.

Table 3.5 Examples of services to which people with disability can be referred

Problem	**Rehabilitation service required**
Deformity of the hand	Exercises, reconstructive surgery, peer support
Foot drop	Ankle-foot appliance, reconstructive surgery
Amputee	Artificial limb, wheelchair
Depression	Counseling
Mobility limitation	Crutches, walking stick, wheelchair, white cane
Stigma in the family	Counseling
Exclusion from community activities	Education, advocacy, and promotion of inclusion
Poverty	Microcredit for self-employment or income generation

3.6.3 Community-Based Rehabilitation

Community-based rehabilitation (CBR) is defined as a strategy within general community development for the rehabilitation, equalization of opportunities, and social inclusion of all people with disabilities.

Leprosy may lead to variety of physical, functional, and social and/or economic problems needing different types of physical and social economic rehabilitation. To address these, comprehensive approaches that maximize benefits for the individual, family and society at large are needed.

CBR is one such approach. It emphasizes community participation and empowerment of the individuals involved. CBR requires the full participation of **the clients, their families, and the communities** in the rehabilitation process. While people with disabilities may need temporary referral to specialized services (e.g., for provision of assistive devices or appliances), these should be linked to CBR programs.

Organizations of people with disabilities need to be involved in the planning and management of rehabilitation services.

Persons affected by leprosy who are in need of rehabilitation should have access to existing general rehabilitation services. Similarly, any existing leprosy-specific rehabilitation services should be extended to people with other disabilities.

3.6.4 Promoting inclusion of persons affected by leprosy in CBR

The following actions may assist in formulating a CBR strategy at district level:

- Develop a district plan for community-based rehabilitation that conforms to the national policy/plan.
- Prepare guidelines for mobilizing local resources to provide special services from government and non-governmental organizations.
- Establish a network of services.
- Develop the capacity of service providers and mechanisms to create awareness about leprosy-related disabilities among people with disabilities.
- Promote a team approach for service provision.
- Introduce locally-specific techniques to train and develop skills and knowledge of people with disabilities and their families.
- Promote opportunities for educational, functional, and vocational training and job-placements.
- Involve people with disabilities and their families in the decision-making process.

3.7 MONITORING OF LEPROSY CONTROL

- A focused monitoring and evaluation system is required for the continuous assessment of the leprosy control status in the district, region, and country.
- Leprosy control services are monitored based on two main sets of indicators.
- In order to gather monitoring information for the leprosy control program, it is essential to use additional tools than those of the mainstream HMIS.
- The quality of monitoring information is determined by the accuracy, completeness, and timeliness of data collection especially in the treatment facility.

3.7.1 Leprosy Control Indicators

Leprosy control indicators include the following categories:

- Those for monitoring progress in leprosy control
- Those for assessing quality of leprosy services

3.7.1.1 Indicators for measuring progress in leprosy control

Indicators for measuring progress include general (core) indicators and those intended for evaluating case-finding activities in particular. They are summarized in Table 3.8.

- The number of new cases in the district is used to estimate the amount of MDT required for that district during the following year. Depending on the methods used for case detection, the annual figures over a period of several years will show if there is an increase or decrease, which in turn indicates whether leprosy control activities are effective. Calculating the case detection rate makes it possible to compare one area with another.
- The number of cases with Grade 2 disabilities detected in a population gives an indication of under-detection.
- The proportion of new cases with Grade 2 disabilities among all new cases detected during the year is used to assess the delay in diagnosis as an indicator for quality of case detection activities.
- The proportion of new cases with Grade 2 disabilities per 100,000 population at national level is used to indicate the contribution by leprosy to disability in the general population.
- If transmission of leprosy is being reduced in an area, it is expected that the number of child leprosy cases (below the age of 15) will decrease. This trend should be monitored over several years. It is also used for estimating the required stock of child MDT blister packs.

- The proportion of new child cases with Grade 2 disabilities is a further indicator of the quality of case detection activities.
- Some districts diagnose leprosy more frequently in men than women, but there is concern that women may have less access to health care in some districts. If a male-to-female ratio of higher than 2 is observed, steps should be taken to ensure that women have adequate access to diagnostic services.
- The number and proportion of MB cases among new cases is a useful guide to the cases at risk of complications and is used for estimating the required quantities of MDT drugs.

Table 3.6 Indicators for measuring progress in leprosy control

Indicator	Calculation	Source of data	Level	Frequency
1) Number of new leprosy cases	Count absolute number	Leprosy registers	District National	Quarterly Annually
2) Case detection rate	Number of new leprosy cases ---------- x 100,000 Total population	District quarterly reports on leprosy control	National	Annually
3) Number of new cases with Grade 2 disability	Count absolute number of new cases with Grade 2 disability	District quarterly reports on leprosy control	District National	Quarterly Annually
4) Proportion of new cases with Grade 2 disability	Number of new cases with Grade 2 disability ---------- x 100 Total number of new cases	District quarterly reports on case-finding	District National	Annually
5) Proportion of new cases with Grade 2 disability per 100,000 population	Number of new cases with Grade 2 disability ---------- x100,000 Total population	District quarterly reports on case finding	National	Annually
6) Proportion of new PB cases who complete MDT *	Number of new PB cases who complete MDT ---------- x 100 Total number of new PB cases who started MDT 1 year ago	District quarterly reports on treatment outcomes	District National	Annually

Indicator	Calculation	Source of data	Level	Frequency
7) Proportion of new MB cases who complete MDT*	Number of new MB cases who complete MDT ---------- x 100 Total number of MB cases who started MDT 2 years ago	District quarterly reports on treatment outcomes	District National	Annually
8) Proportion of new child cases	Total number of new child cases ---------- x 100 Total number of new cases	Leprosy registers and district quarterly reports	District National	Annually
9) Number of new child cases with Grade 2 disability	Calculate absolute number of new child cases with Grade 2 disabilities at diagnosis	District quarterly reports on case finding	District National	Annually
10) Proportion of new female cases	Total number of new female cases ---------- x 100 Total number of new cases	Registers and quarterly reports	National	Annually
11) Proportion MB cases	Total number of new MB cases ---------- x 100 Total number of new cases (PB + MB)	Registers and quarterly reports on case-finding	National	Annually

***S**ee box 3.4 How to calculate MDT completion rates

3.7.1.2 Indicators for assessing the quality of leprosy services

The indicators for quality of leprosy services, summarized in the table below, will be collected at regional level:

- The proportion of new cases that are correctly diagnosed is an indication of the capacity of the health system to detect new cases. The Regional TB/Leprosy Focal Person will validate the diagnosis of at least 50 percent of the new cases reported in the region or make arrangements with a suitable other person to do so. In regions with less than 10 new cases, all new cases should be validated. Validation should be performed within three months of starting the patient on MDT.
- This exercise will help to identify areas where additional training and/or supervision is required.
- The proportion of new patients who complete their treatment on time is an indication of how well the leprosy patients are being served by the health services. The rate is calculated separately for PB and MB patients in a cohort analysis. A cohort is a group of

patients who all started treatment in the same batch (in the same quarter). The total of the figures from the four quarters in a year will give the annual report.

- The NTLP Central Unit will be responsible for organizing confirmation of reported suspected relapse cases and their management.
- The proportion of patients who develop new or additional disability during MDT is an indicator to measure how well new nerve damage is detected and treated. Information for calculating this indicator will be collected using the EHF (eye-hand-foot) score. In order
- The NTLP Central Unit will be responsible for organizing confirmation of reported suspected relapse cases and their management
- The proportion of patients who develop new or additional disability during MDT is an indicator of how well new nerve damage is detected and treated. Information for calculating this indicator will be collected using the Eye-Hand-Foot (EHF) score which should be calculated and recorded at diagnosis and then repeated at the time when treatment is completed.

Box 3.4 How to calculate leprosy treatment (MDT) completion rate

How to calculate the MDT completion rate

For PB completion rate, the cohort will be from the same quarter 1 (one) year ago.

- Identify all the PB patients who are new cases in the district register and who started MDT in the reporting quarter 1 (one) year back. Note this number.
- From the cohort, count the number who completed treatment within 9 (nine) months of registration
- The PB treatment completion rate is calculated as follows:

  Number of new PB cases who completed MDT x 100

  Number of new PB cases who started MDT

For MB completion rate, the cohort will be from the same quarter 2 (two) years ago:

- Identify all the MB patients who were new cases in the register and who started MDT in the reporting quarter 2 (two) years back. Note this number.
- From this cohort, count the number who completed treatment within 18 months of registration.
- The MB treatment completion rate is calculated as follows:

  Number of new MB cases who completed MDT x 100

  Number of new MB cases who started MDT

Table 3.9 Indicators for quality of leprosy services

Indicator	Calculation	Source of data	Level	Frequency
1) Proportion of new cases correctly diagnosed	Number of new cases validated as correctly diagnosed (within 3 months of registration) ---------- x 100 Total number of new cases validated	Activity reports	Regional National	Quarterly Annually
2) Proportion of new PB cases who complete MDT *	Number of new PB cases who complete MDT ---------- x 100 Total number of new PB cases who started MDT 1 year ago	District quarterly reports on treatment outcomes	District National	Quarterly Annually
3) Proportion of new MB cases who complete MDT*	Number of new MB cases who complete MDT ---------- x 100 Total number of MB cases who started MDT 2 years ago	District quarterly reports on treatment outcomes	District National	Quarterly Annually
4) Number of relapses	Record absolute number of relapses after MDT	Leprosy registers District quarterly reports on leprosy control	National	Quarterly Annual
5) Proportion of patients who develop new or additional impairments/disabilities during MDT	Number of cases with increased EHF score ----------x100 Total number of cases started on MDT 1or 2 years earlier	District leprosy register	Regional National	Quarterly Annual

*See Box 3.4 How to calculate leprosy treatment completion rates.

3.7.2 Monitoring tools for recording and collecting information about leprosy cases

- LEPROSY RECORD CARD
  Individual patients' details and those of the household contacts are recorded on these cards. The cards are kept in the treatment unit.
- UNIT LEPROSY REGISTER
  Data about leprosy patients in each treatment unit is recorded. The data is useful for planning and for calculation of indicators. Instructions for completing the register are printed in the inside covers of the register. The DTLS is responsible for ensuring that the register is properly completed. One unit leprosy register may be used for several years.
- PATIENT'S CLINIC APPOINTMENT CARD
  Kept by every patient on MDT, this card indicates the treatment category, the MDT doses received, and the date of the next supervised MDT dose.
- DISTRICT LEPROSY REGISTER
  The register lists every patient receiving MDT in the district. For each patient, it contains a summary of the information in the Unit Leprosy Register apart from details of the monthly clinic attendance. The information in this register forms the basis for compiling the quarterly reports on case-finding and the outcome of leprosy treatment.
- DISTRICT DISABILITY REGISTER
  Maintained by the DTLS, this register is a summary of individual information about people living with disabilities during and after MDT.
- QUARTERLY REPORT ON LEPROSY CONTROL
  Completed quarterly by the DTLS, this report is a summary of information in the District Leprosy Register. It is important to continue reporting even when there are no patients on MDT (zero reporting).
- QUARTERLY REPORT ON TREATMENT OUTCOMES
  Completed by the DTLS, this report summarizes treatment outcomes of patients started on MDT 12 and 24 months earlier for PB and MB cohorts respectively.
- CERTIFICATE OF MDT COMPLETION
  Kept by the patient, this certificate indicates the date when MDT was completed. It is useful for making decisions regarding relapse or other complications occurring after MDT.

3.8 ORGANIZATIONAL ISSUES FOR THE DISTRICT MANAGER

- The greatest expectation of leprosy-affected people and their communities is to receive quality services.
- District-, regional-, and national-level managers must assure availability of such quality services through staff capacity-building, mentoring, and supportive supervision.

3.8.1 Quality Leprosy Services

Quality is based on:

- Appropriate training of staff at every level
- Regular technical support supervision
- Monitoring of key indicators (see under Table 3.8 above)

Characteristics of quality leprosy services

- Accessible to all who need them.
  - MDT can be provided at the nearest health unit.
  - There are no geographical, economic, or gender barriers.
- Patient-centered and observe patients' rights, including the rights to timely and appropriate treatment and to privacy and confidentiality.
- Address each aspect of case management based on solid scientific evidence regarding:
  - Diagnosis (timely and accurate with supportive counseling)
  - Treatment with MDT (available free of charge and user-friendly)
  - Prevention of disability
  - Referral for complications
  - Maintenance of records

3.8.2 Content of Training for General Health Facility Staff

Leprosy should be included in the core curriculum of all institutions training health workers in Uganda. Training of general health workers should aim at enabling them to do the following:

- Suspect leprosy and refer to a facility where diagnosis can be made.
- Correctly diagnose and classify a case of leprosy (clinical staff).
- Treat a leprosy patient with the appropriate MDT regimen.
- Manage or refer cases with complications.
- Maintain a patient's leprosy record card and unit leprosy register.
- Keep adequate stocks of drugs for MDT.
- Provide appropriate information about leprosy to the patients, their families, and other community members, including importance of contact surveillance.
- Recognize patients in need of rehabilitation and refer them to appropriate services for medical rehabilitation and community-based rehabilitation.

3.8.3 Organization of Support Supervision and Mentorship

The aim of support supervision is to ensure the following:

- Technical skills required for leprosy control activities are present.
- Any obstacles faced by the health facility staff are identified and removed.
- Plans for future work and improved performance are made.
- Health workers are supported and motivated in their work.
- Additional information not available under the routine reporting system is collected and analyzed.

RECOMMENDED FURTHER READING

The following resources are available online at no charge.

- Common Skin Diseases in Africa. An illustrated guide. Colette van Hees and Ben Naafs, 2001.
- How to Diagnose and Treat Leprosy (ILEP Learning Guide One, 2001)
- How to Recognize and Manage Leprosy Reactions (ILEP Learning Guide Two, 2002)
- How to do a Skin smear Examination (ILEP Learning Guide Three, 2003)
- How to Prevent Disability in Leprosy (ILEP Learning Guide Four, 2006)
- WHO/ILEP technical guide on community-based rehabilitation and leprosy (WHO/ILEP, 2009)
- WHO. Enhanced global strategy for further reducing the disease burden due to leprosy. Questions and Answers
- WHO. Global leprosy strategy 2016-2020. Accelerating towards a leprosy free world.
- WHO. Global Leprosy Strategy 2016-2020. Accelerating towards a leprosy free world: Operational Manual
- WHO. Global Leprosy Strategy 2016-2020. Accelerating towards a leprosy free world: Monitoring and Evaluation Guide
- International Textbook of Leprosy

GLOSSARY

Acid-fast bacilli Bacilli that hold colour even after washing with acid. Tubercle bacilli are acid-fast bacilli.

Bacilli Rod-shaped bacteria.

Bacteriological Index (BI) An index of the bacillary load in the patient. This is expressed on a semi-logarithmic scale as given below.

BI Interpretation

1+ 1 to 10 bacilli per 100 high power (oil immersion) fields

2+ 1 to 10 bacilli per 10 high power fields

3+ 1 to 10 bacilli per high power field

4+ 10 to 100 bacilli per high power field

5+ 100 to 1000 bacilli per high power field

6+ >1000 bacilli per high power field

Morphological Index (MI) An index of viability of the bacilli.

MI Interpretation

Solid bacilli are deemed to be viable while fragmented or granular bacilli are considered to be non-viable. Two hundred discrete bacilli are evaluated if possible. The MI is equal to the percentage of viable bacilli. Paucibacillary lesions may not be assessable for the MI. The MI in untreated multibacillary leprosy usually ranges between 25 and 75 and should decline to 0 after 4–6 months of effective chemotherapy.

CD4 Specific lymphocytes that are destroyed by HIV. The number of CD4 lymphocytes is reduced in severe HIV infection.

Chronic case A TB patient who is sputum smear-positive after a retreatment regimen.

Continuation phase The phase of TB treatment after initial phase. The continuation phase lasts 4–6 months during which the patient takes fewer drugs to eliminate remaining bacilli and prevent relapse. For

	MDR/XDR-TB, the continuation phase is 12 months and includes four oral drugs given seven days a week for the same reason.
Contact/household contact	Someone who lives in the same dwelling with the TB patient (sleeps and eats at least one meal a day there).
Convert	To change from sputum smear-positive to sputum smear-negative.
Conversion	Changing from sputum smear-positive to sputum smear-negative. It is the best indicator that the initial phase of TB treatment has been effective.
Conversion rate	The proportion of new sputum smear-positive cases that are sputum smear-negative at the end of 2–3 months of treatment.
Culture	A method of diagnosis involving growing bacteria in a special medium that promotes their growth.
Denominator	In a fraction, th**e** number below the line.
Diagnostic sputum smear examination	Sputum smear examination is done using a microscope to identify tubercle bacilli and thus diagnose pulmonary TB.
Directly observed treatment (DOT)	Treatment in which a health worker watches the TB patient swallow the anti-TB drugs and the monthly supervised dose of leprosy MDT.
Disability	A broad term covering any impairment, activity limitation, or participation restriction affecting a person.
Drug resistance	Failure of drugs to kill microorganisms.
Expired drugs	Drugs in stock past the date recommended for use. The safety and effectiveness of such drugs may be reduced.
Expiry date	The date on which a drug expires, or becomes possibly less safe and effective.
Focal person	A health worker assigned specific responsibilities for a specific disease.
Follow-up sputum smear	

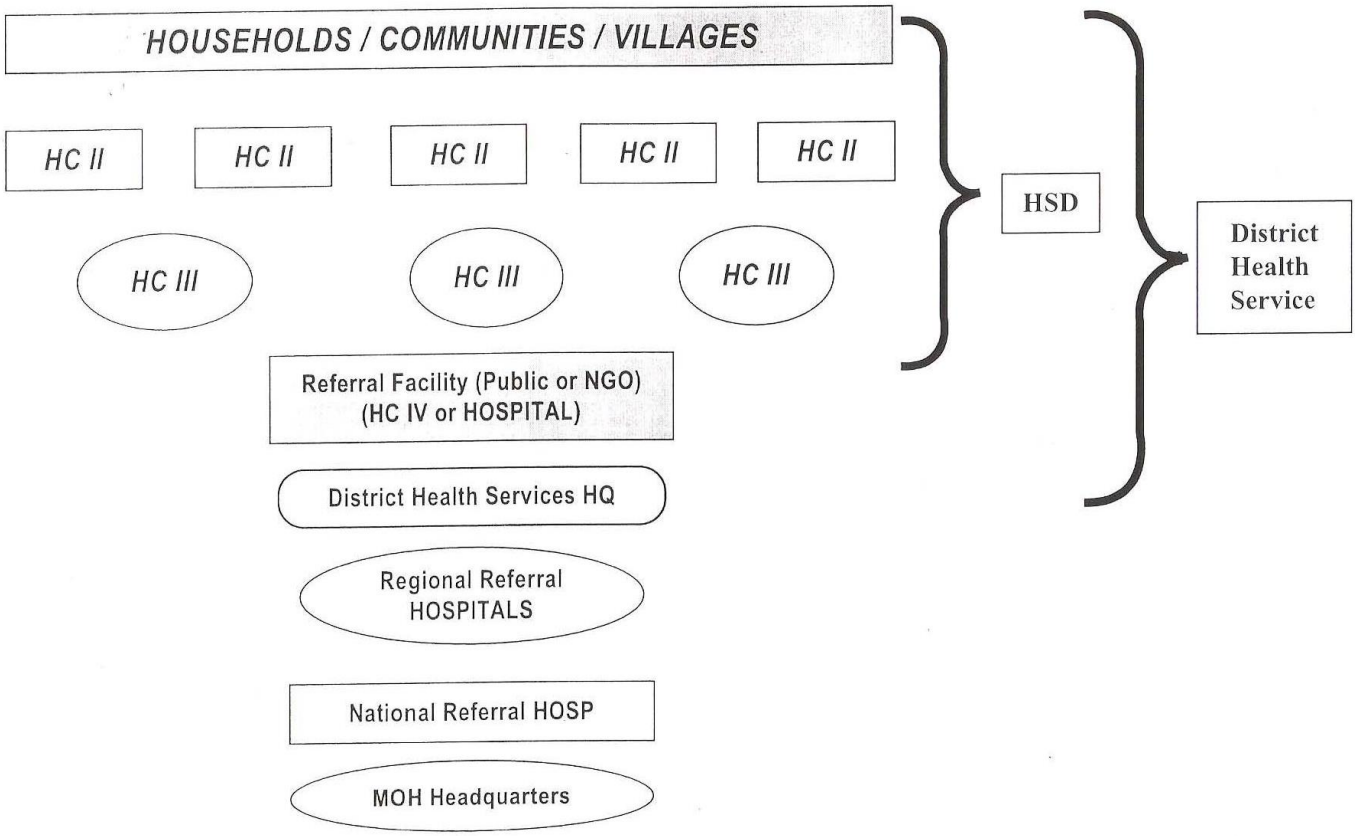
examination	Sputum smear examination done by microscope to assess the progress of TB treatment or prove cure.
Health facility (unit)	Any location where health care is provided. Health facilities range from small clinics and doctor's offices to urgent care centers and large hospitals with elaborate emergency rooms and trauma centers.
Diagnostic health unit	The unit where sputum microscopy for diagnosis is done and the diagnosed TB patients are referred to another treatment unit for provision of TB treatment.
Diagnostic and treatment health unit	The unit where both sputum microscopy for diagnosis and treatment services for TB are offered.
Incidence	The number of new cases of a disease occurring in a defined population during a given time period.
Indicator	A measureable number, proportion, percentage or rate that suggests or indicates the extent of a programme's achievement or the level of some condition among the population.
Initial phase	The first phase of TB treatment, usually lasting two (3) months during which the patient takes an intensive drug regimen (4–5 drugs). For MDR/XDR-TB, the intensive phase (duration of injectable anti-TB drug use) is eight months and is at least four months post-culture conversion* (whichever is longer). This injectable phase includes an injectable given six days a week and four oral drugs given seven days a week. Culture conversion is defined as the first month of two consecutive negative cultures taken at least 30 days apart.
Jaundice	Yellow coloration of the eyes or tongue
Drug-resistant TB	**A** type of TB where the TB bacilli (resistant) continue to grow in the presence of one or more anti-TB drugs. There are several forms of drug resistance. Mono resistance: resistance to one first-line anti-TB drug only. Poly drug resistance: resistance to more than one first-line anti-TB drug (other than both Isoniazid and Rifampicin). Multidrug resistance: resistance to at least both Isoniazid and Rifampicin. Extensive drug resistance: resistance to

	any fluoroquinolone and to at least one of three second-line injectable drugs (Capreomycin, Kanamycin, and Amikacin), in addition to multidrug resistance. Primary drug resistance occurs naturally without prior exposure to anti-TB drugs (due to mutations) while secondary drug resistance follows drug exposure.
Mentor	A person who is perceived to have greater relevant knowledge, wisdom, or experience who informally transmits knowledge, social capital, and the psychosocial support relevant to work, career, or professional development through face-to-face interaction with a person who is perceived to have less.
Microscopy	Examination by means of a microscope.
Monitor	To watch closely or check on a routine basis.
Mucopurulent	Containing both mucus and pus.
Multibacillary (MB) leprosy	Diagnosis for a leprosy patient with six or more skin patches. Includes any patient with positive skin smear.
Paucibacillary (PB) leprosy	Diagnosis for a leprosy patient with up to five skin patches.
Pleura	The membrane covering the lung and the wall of the chest cavity containing the lungs.
Prevalence	The number of all cases of a disease (new and old) existing in a defined population at a specific point in time or during a given time period.
Proportion	The relationship of a part to a whole, often written as a decimal fraction (0.5) or percentage (50 percent).
Radiographic abnormalities	Abnormalities seen on chest X-rays.
Referral	Sending a patient to another health facility or clinician. Patients may be referred for diagnosis, specialized treatment, or admission.
Reserve stock	Extra stock kept by the health facility to ensure adequate supplies even if there is increased use or a delay in drug delivery.
Scanty	Result of examination of a sputum sample when fewer than 10 acid-fast bacilli are observed.

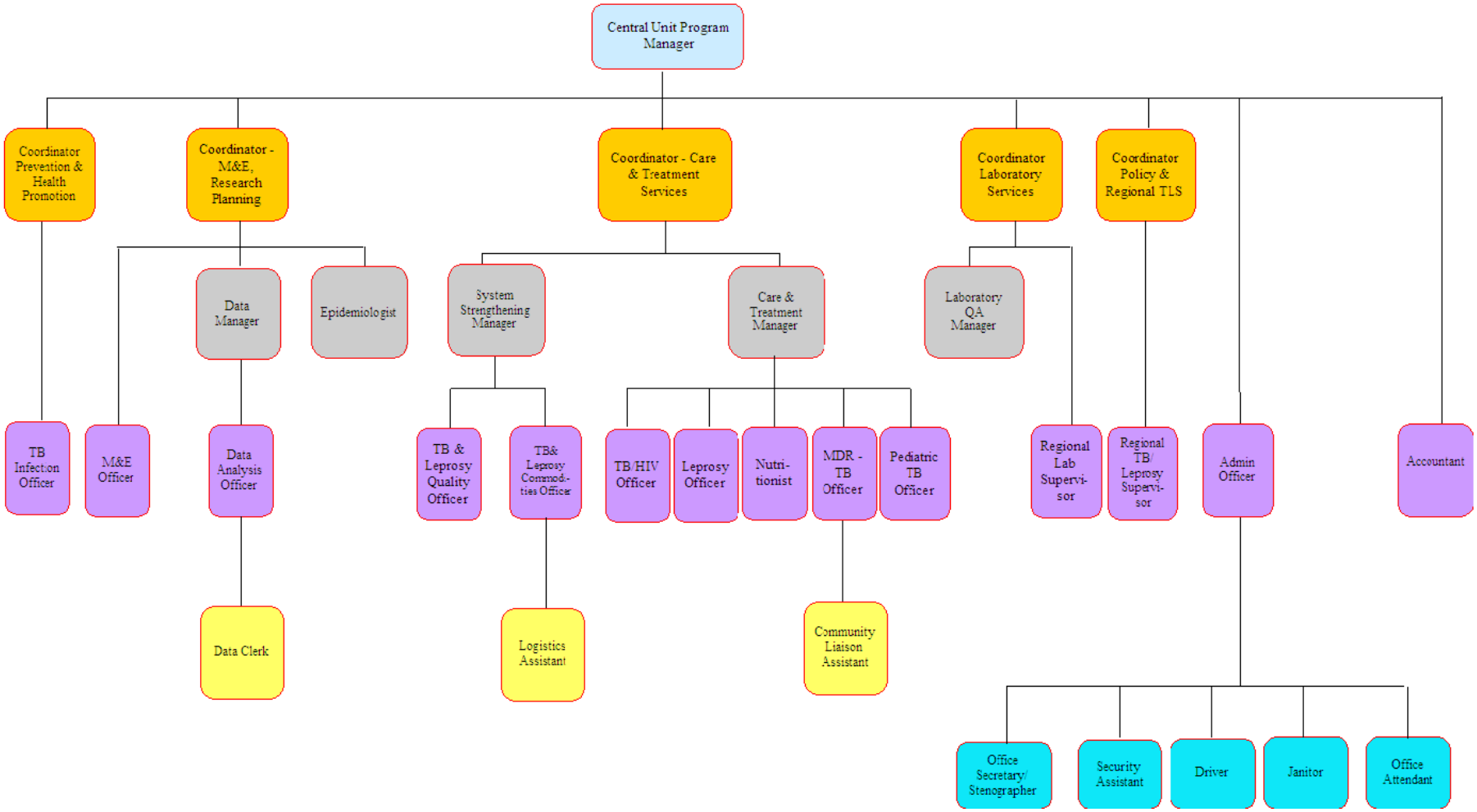
Side-effect	A secondary and usually discomforting or harmful effect of a treatment or drug.
Skin smear examination	Means of estimating the number of acid-fast bacteria present, reported as the BI, and is important in determining the type and severity of leprosy disease as well as assessing the response to treatment.
Skin smear positive	When rod-shaped, red-stained leprosy bacilli, which are diagnostic of the leprosy disease, are seen in skin smear under a microscope.
Specimen	Sample or a small amount to be tested (e.g., stool, urine, sputum).
Sputum	Matter ejected from the lungs through the mouth.
Sputum smear microscopy	Examination of sputum with a microscope to determine whether acid-fast bacilli are present.
Sputum smear-negative	Sputum smear microscopy result showing absence of AFB bacilli.
Sputum smear-positive	Sputum smear microscopy showing presence of AFB bacilli.
Transfer	Changing a TB or leprosy patient's treatment facility when that patient moves.
Transfer in	A TB patient who has been transferred to another TB register to continue treatment.
Transferred out	A TB or leprosy patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known.
Treatment success	An indicator calculated by adding the number or proportion of patients cured to those who completed treatment.
Treatment supporter	A person who observes (watches) as a TB or leprosy patient swallows anti-TB / anti-leprosy drugs and records that the patient has taken the drugs. This person may be a trained community member, family member, or a health worker.
Tuberculin test	Intradermal injection of 0.1ml of PPD/ tuberculin (protein extracted from TB bacilli). The test indicates TB infection, not disease. In a person infected with TB, a hardening of the skin can be observed at the injection site in 48–72 hours.

ANNEXES

Annex 1a: Organizational Structure of Ministry of Health



Annex 1b: NTLP Organogram



Annex 2: Technique for Collecting Sputum

General Principles

- ✓ Sputum specimen collected under instruction of a trained medical worker is likely to be of a better quality.
- ✓ Sputum collection should be done in an open air space. If not, the collection should be done in a well-ventilated designated sputum collection room. Patients are more likely to collaborate and cooperate if they are out of sight of other patients.
- ✓ Patients who have been chewing food shortly before the sputum collection should rinse their mouths with water before collecting the sputum.
- ✓ For early morning specimen, the patients should collect the sputum before brushing teeth.

Before instructing patients to collect sputum specimen, the health worker should:

- ✓ Fill in the *Sputum Request Form* for each patient with all of their identification features, as shown in the form.
- ✓ Enter the patient's record in the *Laboratory Register*.
- ✓ Write on the side of the sputum container the same number as is written on the forms.
- ✓ Give the patient the specimen bottle.

Instructing patients to collect sputum specimen

- ✓ Explain to patients the reasons for sputum collection and demonstrate how to open and close the sputum container.
- ✓ Tell patients that no one should be standing in front of them while they are producing sputum.
- ✓ The patient opens the sputum collection container.
- ✓ Before collecting sputum, the patient should breathe in deeply and rapidly. This starts the coughing.
- ✓ The patient then carefully puts the coughed out material (sputum) into the sputum container without contaminating the outside of the container. The amount of sputum specimen put in the sputum container should be about 5 mls. *If the outside of the sputum container is soiled, the container should be discarded and collect a fresh sample*
- ✓ The patient closes the sputum container and returns it to the laboratory.

Schedule for collecting two sputum samples

Day 1:

- Collect the "on-the-spot" sample as described above
- Instruct the patient how to collect early morning sample (first sputum after waking)

Day 2:

- Receive early morning sample from the TB suspect

Instructions for handling sputum samples in the health facility

The health worker:

- ✓ Receives the sputum specimen and examines it in the laboratory OR
- ✓ Isolates each sputum container in a plastic bag and stores it in a cool place, ready for transportation to where it can be examined
- ✓ Washes hands
- ✓ Ensures that the duration of time between sputum collection and examination in the laboratory does not exceed four days

Annex 3: Logistics

Estimating anti-TB drug quantity

The quantity of anti-TB drugs required for a health facility, district, or region needs to be calculated accurately. This will ensure that the patients receive their drugs without interruption.

Regarding anti-TB drugs, the following terms are important:

> ***Shelf life:*** Shelf life is the length of time anti-TB drugs may be stored in adequate conditions without affecting their usability, safety, purity, or potency.

Pipeline: Pipeline is defined as the entire chain of transportation links through which supplies move from manufacturer to consumer.

Table: Shelf life of anti-TB drugs

Product	**Shelf life**
(RHZ) + E blister strip 225 mg/150 mg/750 mg + 800 mg	3 years
RHZE blister strip 75 mg/150 mg/275 mg/400 mg	3 years
HE blister strip 400 mg/150 mg	5 years
RH (adult) tablet 150 mg/100 mg	4 years
RH (pediatric) tablet 60 mg/30 mg	2 years
Ethambutol tablet 400 mg	5 years
Ethambutol blister strip 400 mg	3 years
Pyrazinamide (pediatric) tablet 150 mg	3 years
Streptomycin vial 1 mg	3 years

Storage conditions

Storage conditions are important in order to maintain the potency of the drugs. The following conditions should be adhered to:

- Store space/room should be clean, well lit, ventilated, and free of insects and rodents.
- Store should be protected from floods, pools of water, or damp conditions.
- Keep fire extinguisher at the main entrance of the store, and train staff to use it in order to protect the store from fire.
- Maintain cold storage or cold chain, where applicable for TB supplies.
- Limit access of control area to store staff only.
- Arrange cartons at least 10 cm. (4 in.) off the floor with identification labels visible.
- Cartons marked (↑) should be stored likewise.
- Separate and remove expired drugs from usable stock.
- Arrange drugs to facilitate "first-to-expire, first-out" (FEFO).

Dispensing

Anti-TB drugs should be dispensed according to the regimen shown on the patient treatment card. After dispensing anti-TB drugs, the quantity of drugs dispensed is recorded on the TB drug dispensing log form.

At the end of the month, the quantity of the drugs dispensed by the unit for each day of the month is added up to give the quantity dispensed for the whole month – in blister strips, tablets, or vials.

Stock-taking

Stock-taking is the process of preparing a balance sheet for drug consumption for a specific period. This process requires the following steps:

- **Stock card review:** In this step the stock balance is counted and quantified by writing down the quantity of drugs received, issued, and lost during the period of stock-taking.

- **Physical count:** Next a physical count of all the anti-TB drugs available in the store is carried out. A date is set for this purpose, and the exercise is conducted by a physical count team. After setting the date for the physical count:

    - ✓ Update stock cards and ledgers
    - ✓ Prepare the store by arranging expiry dates, damages/losses
    - ✓ Suspend issuing drugs during the time of the physical count
    - ✓ Include receipts of drugs issued that day

Compiling facility report and request for anti-TB drug supply

i) Facility Reports

To complete the facility report, the following parameters need to be filled in:

- Beginning balance (A)
- Received during review period (B)
- Dispensed (C)
- Losses/adjustments (D)
- Ending balance from physical count (E)

Calculated balance (E) =A+B–C+ (–D). This equation should balance.

ii) Request for anti-TB drug supply

Request anti-TB drug supply for four months, by adding the quantity consumed over the previous four months (total quantity dispensed in this report plus previous report) subtracted from ending balance from physical count (E), four months' consumption (F), quantity needed = (F–E).

iii) Patient statistics

Count the number and type of patients treated and recorded in the register and write it in the corresponding section in the form.

No. of New Cases_____

No. of Retreatment Cases_____

No. of Transfer-in Cases_____

The facility report and request for drugs should be submitted to the NTLP Central Unit within seven days following the end of the reporting period.

Distribution/Storage

An efficient system for distributing anti-TB drugs must be put in place to ensure that the drugs reach the health facilities and thus the patients. This requires a reliable transport system, preferably managed by the NTLP Central Unit. The anti-TB drugs must be stored in a safe place. The criteria for a good storage place are:

- Accessible by road throughout the year
- Water and electricity
- Telephone or radio call communication
- Safe from flooding
- Security protection

Annex 4: Support Supervision

Supervision is helping people improve their own work performance. Supervisory visits are an opportunity to provide feedback on the reports received on the indicators of monitoring and evaluation. Acknowledge areas of good performance and thank the health workers for a job well done. Areas where performance is lacking should be pointed out and discussed freely with the health workers at the facility. In particular, the focus of discussion should be directed towards learning why the undesirable events occurred and finding solutions.

Schedule of supervisory visits

The NTLP manager should supervise zonal supervisors in their respective zones at least once a year. The ZTLS should make supervisory visits to districts within their zones at least twice a year. DTLS should visit hospitals and health center IVs at least monthly and lower-level facilities at least once a quarter.

Ways of collecting information during a supervisory visit

- Interview health workers
- Observe interactions between patients and health workers
- Interview TB/leprosy patients
- Review TB/leprosy treatment cards and registers
- Visit the laboratory and check working condition of microscopes and availability of supplies
- Check the drug store, inventory, storage, and records of TB/leprosy drugs and

Preparation for supervisory visit

I. Review the quarterly recording and reporting forms submitted. Note which of the monitoring and evaluation indicators have insufficiencies (refer to indicators for monitoring and evaluation).
II. Prioritize the insufficiencies in order of importance.
III. Arrange and obtain requirements – transport, accommodation, meals, per diem, stationery, and schedule date and health facility for the supervisory visit.
IV. Usual items to check in supervisory visits:
    - The quality and completeness of data on quarterly reports
    - The completeness of smear conversion rates at two (3) months
    - The reported incidence rate and case detection rate for smear-positive cases in the health facility, district, or region

- The proportion of PTB sputum smear-positive out of all the PTB patients registered in the health facility, district, or region
- The proportion of PTB sputum smear-positive, PTB sputum smear-negative and extra-pulmonary TB out of all TB patients registered in the health facility, district, or region
- Treatment outcome for new and retreatment PTB sputum smear-positive cases in health facility, district, or region
- Any scheduled training in TB for health facility and laboratory staff of district or region
- Supervisory visits to the health facilities by DTLS
- Record of referral between diagnostic units and treatment units – whether the referred patients reached the laboratory, their sputum specimens were examined, and results recorded.
- Anti-TB and leprosy drugs – quantity, expiry dates, stock cards, dispensing logs, facility report, and request for drugs and buffer stock for health facility, district, or region.
- Check laboratory for reagents, staff, and safety for doing TB microscopy
- Enquire about the working linkage of SCHW, treatment supporters, and health workers in the facility
- Check TB unit registers, TB laboratory registers, and district TB registers for numerical counting, patient classification, and overall completeness

Conducting supervisory visits

Using the list of insufficiencies prepared when planning the supervisory visit, discuss these issues with the health workers at the facility and the DTLS in order to find the cause of and solution for the insufficiencies. The following areas are important:

- Is someone responsible for carrying out a particular task?
- Is the person's knowledge and skill sufficient for the task?
- Has training been provided in this area?
- Are the staff motivated to perform their work?
- Are there barriers to performing work correctly?

At the end of the supervisory visits, present and discuss a summary of the main findings with the health workers at the appropriate level and agree on next steps. A copy of the written supervision report should be sent to the relevant officers.

Annex 5: Treatment Supporter

The treatment supporter is identified in the village meeting involving the VHT, LC1, and community members. The role of the treatment supporter is to help the TB patient adhere to taking anti-TB drugs. It is recommended that the treatment supporter should:

a) be a resident of the community, perhaps a neighbor, family member or other relative;
b) have a minimum level of literacy (able to read and write);
c) be identified by the community and accepted by the patient; and
d) understand and accept the role.

Note: A TB/HIV co-infected patient who is on both ART and anti-TB medication should have the same treatment supporter for both conditions.

The treatment supporter should live near enough to the patient to carry out the following tasks and responsibilities:

- ✓ Observe the patient taking the daily dose of anti-TB drugs correctly.
- ✓ Tally the drug intake day by day on the patient's treatment card.
- ✓ Ensure uninterrupted availability of drugs. In the rare event that the SCHW is delayed, the treatment supporter should collect the drugs from the health facility.
- ✓ Remind the patient to go for sputum follow-up examinations at two (3), five, and eight months of treatment.
- ✓ Encourage the patient to continue taking treatment.
- ✓ Keep the patient's drugs safe.
- ✓ Inform the SCHW of any problem related to the health of the patient or to any constraint in administering DOT.

The treatment supporter is therefore responsible to the SCHW and the community.

Basic facts about TB for the treatment supporter

- ✓ TB is caused by a germ that commonly affects the lungs.
- ✓ TB spreads to others when a TB patient coughs or sneezes.
- ✓ TB can be stopped from spreading by treating and curing the patient.
- ✓ The main symptom of TB is a cough lasting two or more weeks.
- ✓ TB can be cured if the patient takes anti-TB drugs daily for the recommended duration of treatment.
- ✓ If TB drugs are not taken for the recommended period, the disease may not be cured.
- ✓ Spread of TB can be prevented by *(i) patients covering their mouths or noses when coughing or sneezing, and (ii) opening windows and doors to allow fresh air to flow through the house*.

Annex 6: Tuberculin Skin Testing

Standard operating procedure for tuberculin skin testing

Administering the Mantoux Tuberculin Skin Test

Make sure that the area for administering the test has a firm, well-lit surface, and that equipment and supplies are ready. The Mantoux tuberculin skin test consists of an intradermal injection of exactly one tenth of a milliliter (mL), which contains 5 tuberculin units.

Look at the vial label to make sure the vial contains the tuberculin that you want to use, including the tuberculin unit strength. The label should indicate the expiration date. If it has been open more than 30 days or the expiration date has passed, the vial should be thrown away and a new vial used.

When you open a new vial, write the date and your initials on the label to indicate when the vial was opened and who opened it.

To avoid reducing the potency of the tuberculin, store it inside a refrigerator so that it remains between 2 and 8 degrees Centigrade. Also store and transport the tuberculin in the dark as much as possible and avoid exposure to light.

On a firm, well-lit surface, expose the patient's arm and slightly flex it at the elbow. The injection should be placed on the palm-side-up surface of the forearm, about 2–4 inches below the elbow. Your local institutional policy may specify the right or the left forearm for the skin test. The area selected should be free of any barriers to placing and reading the skin test such as muscle margins, heavy hair, veins, sores, or scars.

After choosing the injection site, clean the area with an alcohol swab by circling from the center of the site outward. Allow the site to dry completely before the injection. Because some of the tuberculin solution can adhere to the inside of the plastic syringe, the skin test should be given as soon as possible after the syringe is filled.

Pick up the syringe and be sure to fasten the needle tightly on the syringe by holding the cap and twisting it onto the tip of the syringe. Next, remove the needle cap.

The needle bevel should be perpendicular to the flange of the syringe. If necessary, turn and tighten the needle to line up the bevel correctly with the flange.

Place the vial on a flat surface, hold the vial between the thumb and fingers, and insert the needle through the neoprene stopper.

Invert the vial while keeping a firm hold on the syringe and plunger. The tip of the needle should be below the fluid level in the vial.

Pull back on the plunger and draw out slightly more than the one tenth of a milliliter needed for the test.

Remove the needle from the vial. Hold the syringe in an upright position, and then draw back slightly on the plunger. Tap the syringe lightly to break up air bubbles, and then push forward.

Expel all air and excess fluid from the syringe and needle, leaving exactly one-tenth of a milliliter of tuberculin solution in the syringe.

The second step in administering the Mantoux tuberculin skin test is injection. You'll inject the tuberculin, discard the needle and syringe, check that the skin test was administered properly, and repeat the test if needed.

Stretch taut the selected area of skin between the thumb and forefinger. For an intradermal injection, the needle bevel is advanced through the epidermis, the superficial layer of skin, approximately 3 mm so that the entire bevel is covered and lies just under the skin. The injection will produce inadequate results if the needle angle is too deep or too shallow.

When the needle is inserted at the correct angle you can see the bevel of the needle just below the skin surface. Next, release the stretched skin and hold the syringe in place on the forearm. Grip the flange of the syringe between your first and middle fingers. Use your thumb to press on the plunger.

Now, slowly inject the tuberculin solution. You should feel fairly firm resistance as the tuberculin enters the skin. A tense, pale wheal that's 6–10 mm in diameter appears over the needle bevel. Remove the needle without pressing or massaging the area.

Next, discard the used syringe immediately in the designated puncture-resistant container

Reading the Mantoux Tuberculin Skin Test

To begin, collect the following supplies: a small, plastic, flexible ruler marked in millimeters to measure the test, a pen to mark the edges of the induration, and an alcohol pad to clean off the pen marks. You'll need the tuberculin testing forms for documenting the measurement results.

The skin test should be read between 48 and 72 hours after the skin test has been administered. The basis of reading the skin test is the presence or absence of induration, which is a hard, dense, raised formation. This is the area that is measured.

EQUIPMENT AND SUPPLIES

1) A single-dose disposable tuberculin syringe
2) Cotton balls and antiseptic
3) Purified protein derivative
4) A ruler with millimeter (mm) measurements

5) Forms to record placing of PPD and reading of skin test
6) Fridge for storing reagents
7) A puncture-resistant sharps disposal container
8) A pen

Annex 7: Field Guidelines for Taking Skin Smears for Leprosy

Selection of sites

- ✓ Only two sites are smeared: i) from the center of the most obvious, active skin lesion (usually nodule) in MB cases, and from the edge of the most active patch in PB cases;
  ii) from an ear lobe.
- ✓ If there is no suitable skin lesion, take the second smear from the other ear lobe or from sites where lesions were originally recorded.

Steps for taking the skin smears

- ✓ Explain the procedure to the patient (and attendant).
- ✓ Wash your hands and put on gloves.
- ✓ Take a clean slide and mark it using a slide marker with laboratory number and date.
- ✓ Clean the slide with methylated spirit.
- ✓ Make a skin fold and squeeze it between thumb and index finger to make it bloodless.
- ✓ Make a cut of 5 millimetres long and 3 mm deep with a sterile disposable scalpel blade, meanwhile maintaining the pressure on the skin fold with the fingers.
- ✓ If any blood or tissue fluid discharges, wipe it off with a sterile cotton wool swab.
- ✓ Firmly scrape the cut edge and bottom of the wound with the tip of the blade turned to 90 degrees.
- ✓ Gently and equally smear the tissue fluid and pulp on the slide in a circular shape with a diameter of 5–7 mm.
- ✓ Collect the smears of the two sites on one slide.
- ✓ Dress the small wound.
- ✓ Use a new disposable blade for the next patient.

Note: This is a skin piercing procedure with the potential risk of transmitting HIV. The procedure should be performed taking all necessary precautions.

- ✓ Details of the procedures for taking, fixing, staining, and reading skin smears are included in *How to do a skin smear examination for leprosy* (ILEP Learning Guide Four, 2006). Copies can be accessed at the NTLP Central Unit, the leprosy referral centres, and online at the ILEP website http://www.ilep.org.uk

Annex 8: TB Forms and Registers

8.1 Request for Sputum Examination
8.2 Patient Treatment Card
8.3 Referral and Transfer Form
8.4 Laboratory Register
8.5 Unit TB Register (part 1 and 2)
8.6 District TB Register
8.7 Sub-county Health Worker Register
8.8 Quarterly Case-finding Form (part 1 and 2)
8.9 Quarterly Treatment Outcome Form
8.10 Request for Culture and Sensitivity
8.11 Intensified TB Case-finding Form
8.12 TB/HIV Referral Form
8.13 TB Suspect Register
8.14 Stock Card
8.15 Dispensing Log
8.16 Facility Report and Request for Drugs
8.17 District Report and Request for Drugs

Annex 9: Leprosy Records and Registers

9.1 Leprosy Record Card (faces 1, 2, 3, and 4)
9.2 Unit Leprosy Register (right and left side)
9.3 District Leprosy Register (1 and 2)
9.4 Clinic Appointment Card
9.5 Quarterly Disability Reporting Form
9.6 Quarterly Report on Leprosy Control (1and 2)
9.7 Quarterly Report on Leprosy Treatment Outcomes

Annex 10: Map of Uganda showing the 100 hubs in the lab network