GUIDELINES FOR CLINICAL AND PROGRAMMATIC MANAGEMENT OF TB, LEPROSY AND TB/HIV IN ETHIOPIA

FIFTH EDITION

APRIL, 2012
Addis Ababa
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FOREWORD

Tuberculosis is a major cause of morbidity and mortality in Ethiopia. Ethiopia is among the 22 High TB Burden Countries and among the 27 high MDR TB burden countries in the world. Compounded with HIV/AIDS, TB has become a formidable threat to the country.

Leprosy is a major cause of disability for people affected by it. Significant proportions of patients coming to health facilities have disability at diagnosis and many will be at risk of developing further disability after diagnosis.

Cognizant of the burden of TB, Leprosy and TB/HIV Co-infection in the country, the prevention and control of TBL and TB/HIV remains the priority health program in all phases of HSDP. Moreover, to guide the successful implementation of the interventions, a five years TBL and TB/HIV Strategic plan is developed(2010/11 – 2014/15) in line with HSDP IV and giving much focus on the scale up of community based TB care component of the Health Extension program packages.

Since the last edition of the manual in 2008, major developments and remarkable progresses have been made in the fight against TBL and TB/HIV both globally and nationally. Epidemiologic updates, treatment regimen shift and updates on the management of TBL and TB/HIV, and the development of an integrated training curriculum for general health workers are some of the major reasons for the revision.

This new guideline is accompanied by standardized Participants’ training manual with facilitators’ guide for general health workers to roll out the trainings on TBL and TB/HIV. The purpose of these guidelines is to provide guidance on the programmatic and clinical management of TBL and TB/HIV activities in the country. This guideline replaces the existing the fourth edition of TBL and TB/HIV Prevention and control program manual, the 2008 edition of Guidelines for implementation of TB/HIV collaborative activities in Ethiopia and the 2009 edition of Guidelines for prevention of transmission of TB in health care facilities, congregate and community settings in Ethiopia. However, Guidelines on Clinical and Programmatic management of MDRTB, community TB Care Implementation Guidelines and PPM DOTS Implementation Guidelines will continue serving to complement operational guidance on the respective initiatives.

The Guidelines is primarily intended for general health workers, policy makers, program managers at different levels of the health system and developmental partners in the health sector. Furthermore, it is also an important reference for academic and research institutions. It is with great pleasure that I recommend this new edition to be used as the primary guiding document on the program and clinical management of TB, Leprosy and TB/HIV in Ethiopia.

Dr Keseteberhan Admasu, MD, MPH
State Minister, Federal Ministry of Health
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<tr>
<th>NO</th>
<th>Name</th>
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<tbody>
<tr>
<td>1</td>
<td>Mr Biruck Kebede</td>
<td>FMOH</td>
</tr>
<tr>
<td>2</td>
<td>Dr Andargachew Kumsa</td>
<td>FMOH/ICAP</td>
</tr>
<tr>
<td>3</td>
<td>Dr Anteneh Kassa</td>
<td>FMOH/PHSP</td>
</tr>
<tr>
<td>4</td>
<td>Mr Kifle Sede</td>
<td>FMOH</td>
</tr>
<tr>
<td>5</td>
<td>Mr Dessalegn G/Yesus</td>
<td>FMOH</td>
</tr>
<tr>
<td>6</td>
<td>Mr Taddele Kebede</td>
<td>FMOH</td>
</tr>
<tr>
<td>7</td>
<td>Mr Sufyan Abdulber</td>
<td>FMOH/DELIVER</td>
</tr>
<tr>
<td>8</td>
<td>Dr Fitsum Girma</td>
<td>FMOH/JSI</td>
</tr>
<tr>
<td>9</td>
<td>Dr Eshetu Kebede</td>
<td>GLRA</td>
</tr>
<tr>
<td>10</td>
<td>Dr Dawit Assefa</td>
<td>ICAP</td>
</tr>
<tr>
<td>11</td>
<td>Dr Berhanemeskel Assefa</td>
<td>TB CARE I</td>
</tr>
<tr>
<td>12</td>
<td>Mr Addisu Liben</td>
<td>TB CARE I</td>
</tr>
<tr>
<td>13</td>
<td>Dr Abera Bekele</td>
<td>WHO</td>
</tr>
<tr>
<td>14</td>
<td>Dr Eshetu Gezahegn</td>
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<td>Dr Gani Alabi</td>
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<td>16</td>
<td>Dr Kassa Hailu</td>
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<td>17</td>
<td>Dr Kumlachew Abate</td>
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<td>18</td>
<td>Dr Getu Debele</td>
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<tr>
<td>20</td>
<td>Dr Yared Kebede</td>
<td>USAID</td>
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<tr>
<td>21</td>
<td>Dr Ahmed Bedru</td>
<td>TB CARE I</td>
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<tr>
<td>22</td>
<td>Dr Ezra Shimelis</td>
<td>TB CARE I</td>
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<tr>
<td>23</td>
<td>Dr Getachew Wondimagegn</td>
<td>TB CARE I</td>
</tr>
<tr>
<td>24</td>
<td>Dr Fekadesilassie Mikru</td>
<td>HEAL TB</td>
</tr>
<tr>
<td>25</td>
<td>Dr Tadesse Anteneh</td>
<td>HEAL TB</td>
</tr>
</tbody>
</table>

The finalization of this guideline is done by the following Experts:

Dr Andargachew Kumsa  Mr Habtamu Ayalneh, TB CARE I
Mr Biruck Kebede        Azmera Molla, FMOH/WHO
Mr Dessalegn G/Yesus    Ato Tesfaye Hunde, GLRA
Dr Anteneh Kassa        Addisalem Yilma, TB CARE I
Dr Ahera Bekele         

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<tr>
<th>ACRONYMS</th>
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<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
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<td>ART</td>
<td>Anti-Retroviral Treatment</td>
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<td>CSOs</td>
<td>Civil Society Organizations</td>
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<td>CDC</td>
<td>Centers for Disease Control and prevention</td>
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<td>CPT</td>
<td>Cotrimoxazole Preventive Treatment</td>
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<td>DOT</td>
<td>Directly Observed Treatment</td>
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<td>DOTS</td>
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<td>DST</td>
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<td>EQA</td>
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<td>FBOs</td>
<td>Faith Based Organizations</td>
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<td>FMOH</td>
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<td>HAART</td>
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<td>Human Immunodeficiency Virus</td>
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<td>HMIS</td>
<td>Health Management Information System</td>
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<td>HP</td>
<td>Health Post</td>
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<td>HPDP-D</td>
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<tr>
<td>IP</td>
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<td>IPT</td>
<td>Isoniazid Preventive Therapy</td>
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<td>IPLS</td>
<td>Integrated pharmaceutical Logistic system</td>
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<td>IRIS</td>
<td>Immune Reconstitution Inflammatory Syndrome</td>
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<tr>
<td>ISTC</td>
<td>International Standards for Tuberculosis Care</td>
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<td>LMIS</td>
<td>Logistic Management Information System</td>
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<tr>
<td>M&amp;E</td>
<td>Monitoring and Evaluation</td>
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<tr>
<td>MB</td>
<td>Multi-Bacillary</td>
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<tr>
<td>MDGs</td>
<td>Millennium Development Goals</td>
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<tr>
<td>MDR-TB</td>
<td>Multi-Drug Resistant TB</td>
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<tr>
<td>MDT</td>
<td>Multi-Drug Therapy</td>
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<tr>
<td>NGO</td>
<td>Non-Governmental Organization</td>
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<tr>
<td>NTLCP</td>
<td>National Tuberculosis &amp; Leprosy Control Programme</td>
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<tr>
<td>OI</td>
<td>Opportunistic Infection</td>
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<tr>
<td>PB</td>
<td>Pauci-Bacillary</td>
</tr>
<tr>
<td>PHCU</td>
<td>Primary Health Care Unit</td>
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<tr>
<td>PLHIV</td>
<td>People Living With HIV/AIDS</td>
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<tr>
<td>PPM</td>
<td>Public-Private Mix</td>
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PTB  Pulmonary Tuberculosis
PTB-ve  Smear Positive Pulmonary Tuberculosis
PTB +ve  Smear Negative Pulmonary Tuberculosis
QA  Quality Assurance
RHB  Regional Health Bureau
RRL  Regional Reference Laboratory
SCC  Short Course Chemotherapy
SOPs  Standard Operating Procedures
SSA  Sub Saharan Africa
TB  Tuberculosis
TBL  Tuberculosis & Leprosy
UNAIDS  The joint United Nations Program on HIV/AIDS
USAID  United States Agency for International Development
VCT  Voluntary Counseling and Testing
WHO  World Health Organization
XDR-TB  Extensively Drug Resistant Tuberculosis
INTRODUCTION

Tuberculosis and Leprosy have been recognized as major public health problems in Ethiopia. Efforts to control tuberculosis began in the early 1960s with the establishment of TB centers and sanatoriums in three major urban areas in the country. In 1976, in order to address effectively the TB challenge, the Central Office (CO) of the National Tuberculosis Control Programme (NTCP) was established. In view of the achievements made by combined tuberculosis and leprosy control programmes in other countries, including those in sub-Saharan Africa, it was decided in 1994 to combine the two programmes into the National Tuberculosis & Leprosy Control programme (NTLCP) under the co-ordination and technical leadership of the central office.

In June 2000, the previous Epidemiology/AIDS Department of the MOH was re-structured and named Disease Prevention and Control Department. The NTLCP was subsequently accommodated within this department as TB and Leprosy Prevention and Control Team. The leprosy component of the combined TB and Leprosy control program has been fully integrated into the general health services by the end of 2001. Since 2009, the national TB and leprosy prevention and control activities are coordinated under the Health Promotion and Disease Prevention Directorate.

Ethiopia has adopted the DOTS strategy since 1997 after success of the pilot program with the development of the first combined Tuberculosis and Leprosy Prevention and Control Program manual. TB/HIV collaborative activities was piloted in 2004 and subsequently scaled up nationally. PPM DOTS, Community TB Care and MDRTB programs have been also piloted and integrated into the TBL and TB/HIV control program.

This revised guideline contains both clinical and programmatic aspects of TB, Leprosy and TB/HIV. It was developed within the framework of the Stop TB Strategy for TB and the global enhanced strategy for leprosy. This guideline also addresses Multi-Drug Resistant-TB and Public Private Mix (PPM)-DOTS, community TB care and TB infection control.

This document considers the principles of International Standards for Tuberculosis Care (ISTC) which describe a widely accepted level of TB care that all practitioners should seek to achieve. Cross-referencing the applicable ISTC standards in this guideline should help providers in both public and private sectors to ensure their implementation.

The Guidelines is primarily intended for general health workers, program managers and developmental partners; moreover, policy makers, academic and research institutions may also benefit.

The major changes in the revised guideline are:

i. TB treatment regimen changed from EH to RH based treatment in the continuation phase

ii. TB case management is updated in line with the current WHO recommendations:
   - TB suspect and case definition among HIV co-infected and the issue of antibiotic trial in PLHIV is changed
   - New diagnostic methods such as LED microscope, GeneXpert, Culture and DST are incorporated
   - New updates in childhood TB and TB/HIV are included
• Updates on community TB care and PPM-DOTS initiatives included
• Basic principles of M(X)DR-TB management introduced

iii. Multiple program guidelines combined into one national programmatic and clinical management guideline with a comprehensive modular TBL and TB/HIV training curricula:

iv. The recording and reporting tools are customized with national HMIS and the principles of integrated supportive supervision.
2. BURDEN OF TUBERCULOSIS, HIV/AIDS AND LEPROSY

TB is a major public health problem throughout the world. About a third of the world’s population is estimated to be infected with tubercle bacilli and hence at risk of developing active disease. According to the WHO Global TB Report 2011, there were an estimated 9 million incident cases of TB globally, in 2010, of which 1.2 million were among people living with HIV. About 26% of the incident TB cases occurred in Africa in 2010. The proportion of TB cases co-infected with HIV is highest in countries in the African region; overall, the African region accounted for 82% of TB cases among people living with HIV.

In 2010, an estimated 1.1 million deaths occurred among HIV negative cases of TB including 0.32 million deaths among women. This is equivalent to 15 deaths per 100,000 population. In addition, there were an estimated 0.35 million deaths among incident TB cases that were HIV positive. Thus in total, approximately 1.4 million people died of TB in 2010 making the number of TB deaths per 100,000 population 20.

Of the 9 million annual TB cases, about 1 million (11%) occur in children (under 15 years of age). Of these childhood cases, 75% occur in the 22 high-burden countries. In countries worldwide, the reported percentage of all TB cases occurring in children varies from 3% to more than 25%.

The 22 High Burden Countries (HBCs) that have been given highest priority at the global level since 2000 accounted for 81% of all estimated cases worldwide. These countries have been the focus of intensified efforts in DOTS expansion. From the total 1.1 million deaths due to TB among HIV negative people, about 80% occurred in the 22 HBCs.

According to WHO 2011 report, globally 3.2% of incident cases of TB (290,000) are estimated to have MDR-TB. There are 27 identified high burden countries that carry 86% of the world MDRTB burden.

Globally, 244,796 new cases of leprosy were detected during 2009 and the registered prevalence at the beginning of 2010 was 211,903. Sixteen countries globally (7 in Africa including Ethiopia) accounted for 93% of all new cases detected during 2009. The proportion of cases with MB leprosy among new cases in the Africa region ranges from 32.7% to 94.27%. The proportion of children among new cases of leprosy in the African region ranges from 2.1% to 31.76%. Similarly the proportion of disability grade 2 ranged from 1.45% to 20.7%. In the region the proportion of females among newly detected cases of leprosy was in the range of 6.5% to 59.11% during 2009.

Ethiopia is one of the 22 HBCs. According to the WHO global TB report 2011, there were an estimated 220,000 (261 per 100,000) incident cases of TB in Ethiopia in 2010. According to the same report the prevalence of TB was estimated to be 330,000 (394 per 100,000). There were an estimated 29,000 deaths (35 per 100,000) due to TB, excluding HIV related deaths, in Ethiopia during the same period.

According to the 2002 EC (2009/10) health and health related indicators of the FMoH, tuberculosis is the second cause of death in Ethiopia. During the year 2010/11 (2003 EC), a total of 159,017 TB cases were notified in Ethiopia. Among these 151,866 (95.5%) were new cases of TB, all forms. The proportion of new smear-positive, smear negative and
EPTB among all new cases is 32.7%, 34.8%, and 32.5% respectively. Retreatment cases represent about 2.9% of all TB cases notified.

According to the 2002 EC (2009/10) report of FMoH, about 79% of HIV positive clients were screened for TB; of these 11% were found to have active TB. According to the same report only 45% of TB patients have undergone HIV test and 15% were tested HIV positive. About 69% and 39% of HIV positive TB patients were enrolled on CPT and ART, respectively.

According to the anti-TB drug resistance survey conducted nationwide in 2005 (EHNRI/FMOH), among 804 newly diagnosed TB cases 1.6% were found to be infected with MDR TB. The rate of MDR TB among specimens from 76 previously treated TB cases was 11.8%. WHO in 2011 reported, in Ethiopia, among new pulmonary TB and retreated pulmonary TB cases notified in 2010, there were an estimated 1600 and 580 MDR TB cases, respectively.

In Ethiopia, a total of 4430 (3922 MB and 378 PB) new cases and 5528 all forms of f Leprosy cases were registered in 2009/10. The proportion of children among new cases of leprosy was 7% during the same period. About 22% and 9% of new cases of leprosy had disability grade 1 and 2 respectively in 2010. The national registered prevalence in the same year was 5,303. The treatment outcome of cohort of 2008/09 was: 85% and 74% completion rate for MB and PB respectively.
3. NATIONAL TB, TB/HIV AND LEPROSY CONTROL PROGRAM

3.1 Goals and Objectives

Goal
The overall goal of the national TBL and TB/HIV Prevention and control program is to achieve the TB related MDG and STOP TB Partnership targets set for 2015 and the global targets for the control of leprosy.

General objectives

- Interrupt transmission of the infections;
- Reduce morbidity, mortality and disability;
- Prevent emergence and spread of drug resistance;
- Reduce burden of TB among people living with HIV;
- Reduce HIV burden among TB patients.

Specific objectives

- Expand and strengthen the access to high quality DOTS in order to meet the Stop TB Partnership and MDG targets for TB Control:-
  - To reduce the prevalence of TB to 156 per 100,000 population in 2015;
  - To reduce TB mortality to 20 per 100,000 population in 2015;
  - To increase treatment success rate to 90%;
- Expand and strengthen high quality leprosy prevention, control and care that is equitably distributed, affordable and easily accessible, in order to meet the targets for leprosy control:-
  - To decrease leprosy prevalence rate from 0.6/10,000 to 0.4/10,000;
  - To reduce disability grade II from 7% to 3%;
  - To achieve and maintain MDT completion rate of at least 90%;
- To address adequately TB/HIV, by strengthening the collaboration between TB and HIV Prevention and Control Programmes at all levels, in order to reduce burden of TB among People Living with HIV (PLHIV) and to reduce the burden of HIV and AIDS among TB patients:-
  - To increase proportion of TB cases screened for HIV to 90%
  - To increase proportion of PLHIV screened for TB to 100%
  - To reduce TB/HIV co-infection rate to 10%
- To increase the proportion of notified MDR-TB cases started on treatment to 100%.
- Enable and promote program-based operational researches

3.2 National Tuberculosis and Leprosy Control Strategy

National TB control Strategy
To build on the achievements of DOTS and address the remaining challenges, the STOP TB strategy was launched by WHO in 2006 to help achieve the millennium development goals for TB in 2015. Ethiopia also adopted this strategy to achieve the national TBL and TB/HIV targets.
This Strategy has six components where DOTS remains the most important component of the strategy. The components are:

1. **Pursue high quality DOTS expansion and enhancement**
   - Secure political commitment with adequate and sustained financing
   - Ensure early case detection and diagnosis through quality assured bacteriology
   - Provide standardized treatment with supervision and patient support
   - Ensure effective drug supply and management
   - Monitor and evaluate performance and impact

2. **Address TB/HIV, MDR-TB and the needs of poor and vulnerable population**
   - Scale up collaborative TB/HIV activities
   - Scale up prevention and management of MDR-TB
   - Address the needs of TB contacts and of poor and vulnerable population

3. **Contribute to health system strengthening based on primary health care**
   - Help improve health policies, human resource development, financing, supplies, service delivery and information
   - Strengthen infection control in health services, congregate settings and household
   - Upgrade laboratory networks and implement practical approach to lung health
   - Adapt successful approaches from other field and sectors, and foster actions on the social determinants of health

4. **Engage all care providers**
   - Involve all public, voluntary and corporate and private providers through public-private mix (PPM) approaches
   - Promote use the International Standard for TB care

5. **Empower people with TB, and communities through partnership**
   - Pursue advocacy, communication and social mobilization
   - Foster community participation in TB care, prevention and health promotion
   - Promote use of patients’ charter for Tuberculosis Care

6. **Enable and promote research**
   - Conduct program-based operational research
   - Advocate for and participate in research to develop new diagnostics, drugs and vaccines.

**National Leprosy Control Strategy**

The main principles of leprosy control, based on timely detection of new cases and their treatment with effective chemotherapy in the form of multi drug therapy, will not change over the coming years. The emphasis will remain on providing patient care that is equitably distributed, affordable and easily accessible.

The main elements of the strategy are:
- Sustain leprosy control activities in all endemic areas of the country
- Use case detection as the main indicator to monitor progress
- Ensure high-quality diagnosis, case management, recording and reporting
- Strengthen routine and referral services
- Discontinue the approach by campaign
- Develop tools and procedures that are home/community-based, integrated and locally appropriate for the prevention of disabilities/impairments and for the provision of rehabilitation services.
• Promote operational researches in order to improve implementation of a sustainable strategy.
• Encourage supportive working arrangements with partners at all levels.
4. TUBERCULOSIS

4.1 Basic of Tuberculosis

**Definition:** Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, a rod-shaped bacillus called “acid-fast” due to its staining characteristics in laboratory. Occasionally the disease can also be caused by *Mycobacterium bovis* and *Mycobacterium africanum*.

**Transmission:** Tuberculosis is most commonly transmitted by inhalation of infected *droplet nuclei* (the dried residua of larger respiratory droplets), which are discharged in the air when somebody with untreated sputum-positive pulmonary TB coughs or sneezes. Coughing produces droplets – as does talking, sneezing, spitting or singing – that may contain tubercle bacilli. As the droplets expelled into the air evaporate, some form droplet nuclei, which are infectious particles of respiratory secretions usually less than 5 mm in diameter containing one or a few tubercle bacilli. A single cough can produce 3,000 droplet nuclei and they can remain suspended in the air for several hours. Whereas larger particles either fall to the ground or, if inhaled, are trapped either in the nose or in the mucociliary system of the tracheo-bronchial tree, droplet nuclei are so small that they avoid the defences of the bronchi and penetrate into the terminal alveoli of the lungs where infection begins. Persons living in the same household, or who otherwise are in frequent and close contact with an infectious patient have the greatest risk of being exposed to the bacilli. In addition, consumption of raw milk containing *M.bovis* is a possible way of getting infected by TB, though it is much less frequent. Risk of infection depends on the extent of an individual’s exposure to droplet nuclei and on susceptibility to infection. Two factors determine an individual’s risk of exposure: the concentration of droplet nuclei in contaminated air and the length of time spent breathing that air. The extent of an individual’s exposure to droplet nuclei is determined by the proximity and duration of contact with an infectious source case, since the concentration of droplet nuclei to which the person is exposed depends on proximity, and the length of time spent breathing the contaminated air depends on duration of contact. The risk of infection of a susceptible individual is therefore high with close, prolonged, indoor exposure to a person with sputum smear-positive pulmonary TB.

TB affects individuals of all ages and both sexes. There are, however, groups, which are more vulnerable to develop the disease: Poverty, malnutrition and over-crowded living conditions have been known for decades to increase the risk of developing the disease. HIV infection has been identified as a major risk factor for developing tuberculosis. The age group mainly affected is between 15 and 54 years, and this leads to grave socio-economic consequences in a country with a very high prevalence of the disease.

**Pathogenesis:** primary infection occurs in persons without previous exposure to tubercle bacilli. Pulmonary infection occurs when TB bacilli, contained in a small infectious aerosol droplet, reaches a terminal airway and succeeds in establishing infection. A localized
granulomatous inflammatory process occurs within the lung and this is called the primary (Ghon) focus. From the Ghon focus, bacilli drain via lymphatics to the regional lymph nodes. The Ghon focus with associated tuberculous lymphangitis and involvement of the regional lymph nodes is called the primary (Ghon) complex. The development of the primary complex is asymptomatic. From the regional lymph nodes bacilli enter the systemic circulation directly or via the lymphatic duct. This occult haematogenous spread occurs during the incubation period, before adequate immune responses contain the disease. After dissemination, bacilli may survive in target organs for prolonged periods. The future course of the disease at each of these sites depends on the dynamic balance between host immunity and the pathogen.

**Natural history:** in the great majority (90-95%) of persons infected with M. Tuberculosis, the immunological defence either kills the inhaled or ingested bacilli or perhaps more often, keeps them suppressed (silent focus) causing latent Tuberculosis infection. Only about 5-10% of such infected persons (primary infection) develop active disease in their lifetime. **Active TB disease** arises from progression of the primary lesion as a continuous process within a year or so after infection, or from endogenous reactivation of latent foci, which remained dormant since the initial infection or exogenous re-infection. Post primary TB usually affects the lungs (more than 85%) but can involve any part of the body. The characteristic features of post-primary pulmonary TB are the following: extensive lung destruction with cavitation; positive sputum smear; upper lobe involvement; and usually no intra-thoracic lymphadenopathy.

If untreated, TB leads to deaths within 5 years in at least half of the patients. Without treatment, about 20 to 25% would have natural healing and 25 to 30% would remain chronically ill, thus continuing to spread the disease in the community.

### 4.2 TB Case Finding

Prompt identification of TB suspects within a health facility and community, and detection of infectious cases of tuberculosis is an essential and priority task of tuberculosis control program.

The main aim of TB case finding is to interrupt the chain of transmission by early initiation of treatment.

**TB Case finding strategies:**
- Awareness creation in the community on TB symptoms and the need to seek medical care
- Screening all clients entering a health facility for TB symptoms
- Identifying suspects and Perform three sputum smear examinations
- Tracing and examination of close contacts of TB patients
- Intensified TB screening in high-risk groups
- Increasing index of suspicion for TB by health care workers
- Integrate TB screening all service delivery points like VCT, ANC, EPI
- Engaging all relevant health care providers
IDENTIFICATION OF SUSPECTS

Identification of TB suspects involves screening of patients for signs & symptoms of TB, in particular cough of two weeks or more duration. Other symptoms that help to identify TB suspects include fever, night sweating, and weight loss. TB suspects’ identification should be made both at community and health facility levels. Health extension workers and community volunteers can perform the identification of suspects at community level. All identified TB suspects should be promptly referred to a nearby diagnostic HF for sputum smear examination and for further clinical evaluation.

**TB SUSPECT**: is any person with **cough of two weeks or more duration**.

4.3 Clinical Presentation of Tuberculosis

The symptoms of TB are grouped in to general, non-specific systemic symptoms and symptoms associated with organ specific TB.

The general symptoms of TB (pulmonary or extra-pulmonary) include: Weight loss, fatigue, malaise, fever, night sweats and loss of appetite.

**Symptoms of Pulmonary tuberculosis**: Since the predominant site of TB is the lungs, the commonest presenting symptoms are those of pulmonary TB – cough with or without sputum production, chest pain, haemoptysis, and breathlessness. Haemoptysis is often the result of cavitary lung disease causing erosion of pulmonary blood vessels – one large cavity or several smaller cavities may be associated with haemoptysis. Chest wall pain may be due to extensive lung inflammation, particularly if the pleural surface is involved. Breathlessness is an uncommon symptom in pulmonary TB, and usually indicates extensive lung disease or disease complications forms, such as pneumothorax, pleural effusion, or endo-bronchitis. Cough and haemoptysis are less common in HIV-positive pulmonary TB patients than in those who are HIV-negative. This is probably because there is less caviation, inflammation, and endo-bronchial irritation in HIV-positive patients.

Patients with respiratory symptoms attending a health facility must be asked about symptoms suggestive of tuberculosis, with particular attention to cough of 2 weeks or more duration.

A patient is most likely to be suffering from TB if, in addition to one or more of the above symptoms, the individual lives in close contact with a smear positive pulmonary TB (PTB+) patient. Moreover, any person who for any other medical reasons has got a chest x-ray examination and whose chest x-ray findings are suggestive of PTB must be dealt with as a TB-suspect.
Symptoms of extra-pulmonary TB: in addition to the general symptoms of TB, patients with extrapulmonary TB present with features related to the pathology of the affected organ. The most common forms of EPTB and the common presentations include:

**Tuberculous lymphadenitis:** Slowly developing painless Cervical Lymph node enlargement (regardless of HIV serostatus) is the commonest presentation. Lymphadenopathy can also be found in the axilla and intra-abdominally. Initially lymph nodes are firm and discrete, but later they become matted together and become fluctuant. The overlying skin may breakdown with the formation of abscesses and chronic discharging sinuses, which heal with scarring. In HIV infected patients, lymphadenopathies can be acute and resemble acute pyogenic lymphadenitis.

**Tuberculous pleurisy:** pain while breathing in, dull lower chest pain, intermittent cough, breathlessness on exertion.

**TB of bones and/or joints:** localized pain and/or swelling of insidious onset, discharge of pus, muscle weakness, paralysis, and stiffness of joints.

**Intestinal TB:** loss of appetite and weight, chronic abdominal pain, diarrhoea or constipation, mass in the abdomen, fluid in the abdominal cavity (ascites).

**Tuberculous meningitis:** Headache, fever, vomiting, neck stiffness and mental confusion of insidious onset.

4.4 Diagnostic Methods

TB can be diagnosed using different methods using bacteriological, molecular, histopathology and radiological diagnostic methods. Therefore, all TB suspects must be evaluated using the national standard TB diagnostic algorithm (see Anne 1).

A. Bacteriological methods

**Direct Light Smear Microscopy/conventional microscopy:** Sputum microscopy is the mainstay of diagnostic methods for TB in Ethiopia. It is most efficient and applicable method to identify infectious TB cases in peripheral laboratories. It is used for diagnosis, monitoring and defining cure.

Three sputum specimens must be collected and examined in two consecutive days (spot-early morning-spot). The sputum collection procedure is as follows.

- **Day 1:** the first "on-the-spot" sample is collected.
- **Day 2:** the early morning sample (**Sample 2**) is submitted, and then the second "on-the-spot" sample (**Sample 3**) is collected.

According to the national AFB microscopy laboratory manual, the result of the sputum smear should be reported as follows:
Examination finding | Result as recorded | Laboratory result | No. of fields examined
---|---|---|---
No AFB in 100 oil immersion fields | Negative | NEG | 100
1 to 9 AFB in 100 oil immersion fields | Positive | 1-9 (Scanty) | 100
10-99 AFB in 100 oil immersion fields | Positive | (+) | 100
1-10 AFB per oil immersion field | Positive | (+++) | 50
> 10 AFB per oil immersion field | Positive | (++++) | 20

The laboratory should keep all positive and negative slides (in separate boxes for positive and negative slides) to facilitate the Quality Assurance procedures according to the “AFB smear microscopy and external quality assurance Manual”.

The details of sputum specimen collection procedures, the guidelines for sputum smear examination and quality assurance are provided in the National TB and Leprosy Laboratory Manual.

**Light Emitting Diode (LED) Fluorescent Microscopy:** Light emitting diode (LED) microscopy is a newly introduced diagnostic tool to complement the conventional microscopy. It is recommended for centers with high case load as it saves time and improves sensitivity. However, the method requires additional training.

**Culture:** Sputum culture, to isolate Mycobacterium, is a highly sensitive diagnostic method which permits detection of a minimum of 10 to 100 viable bacilli in the volume of cultured materials (usually a tenth of an ml); hence; the method allows diagnosis of less infectious cases.

Culture remains the gold standard in mycobacterial detection because of its higher sensitivity and specificity. The technique is a relatively complex, requiring specialized laboratory set-up than smear microscopy. Culture with Drug Susceptibility Testing (DST) is used for the diagnosis and management of drug-resistant TB. The main disadvantage of culture is the lead time to diagnosis (- issuing result may take 12 weeks). Culture with DST is even longer.

**B. Molecular Tests for TB Diagnosis**

**Line Probe Assay (LPA):** Line Probe Assay is a new test that makes use of molecular technology and can identify the presence or absence of specific mutations on the genes of TB bacilli which are responsible for Isoniazid and Rifampicin resistance. It is a rapid and accurate test to identify cases with MDR-TB.

It is a DNA strip test that makes use of PCR + reverse hybridization that identify the
presence or absence of specific mutations on the genes of TB bacilli.

- **RIF**: rpoB gene (coding for the α-subunit of the RNA polymerase)
- **INH**: the katG gene (coding for the catalase peroxidise) and the inhA gene

LPA can be performed on either sputum specimen or on culture specimens depending on the smear result. If a patient with TB is smear positive the sputum contains enough bacilli to perform line probe assay directly on the sputum and MDR-TB can be proved within two days. However, if the sputum is smear negative it is recommended to perform TB culture first (preferably in liquid medium) and once growth of M. tuberculosis can be demonstrated, the isolate can be used to perform the line probe assay.

**Gene Xpert MTB/RIF**: Is a new rapid DNA test for TB which is fully automated, with minimal hand on time, diagnostic molecular test that uses a modern technology. Gene Xpert is indicated for the diagnosis of TB in high MDRTB and TB/HIV settings. It is also useful for the diagnosis of TB in children and Extrapulmonary TB.

### C. Histo-pathological examination

Pathology plays a complementary role in confirming the diagnosis of TB. 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 histo-pathological examination. Samples for pathologic examination can be collected using:

- **Fine needle aspiration** from accessible mass like peripheral enlarged lymph nodes
- **Aspiration of effusions** from serous membranes; however, serous fluid analysis is much less useful for diagnosis than histology and culture of a serous membrane biopsy specimen.
- **Tissue biopsy** from any body tissues such as serous membranes, skin, endometrium and bronchial, pleural, gastric or liver tissue

### D. Radiological examination

X-ray is a useful method to support the diagnosis of TB. It is sensitive but less specific. X-ray abnormalities suggestive of TB include Upper lobe infiltrates (bi-lateral or uni-lateral), Cavitation, Patchy, nodular shadows around the cavity. However, no shadow is typical for TB.

### 4.5 Case Definitions

The definitions below are based on the level of certainty of the diagnosis and on whether or not laboratory confirmation is available.

**Tuberculosis suspect:**

Any person who presents with symptoms and/or signs suggestive of tuberculosis, in particular cough of two weeks or more duration is a TB suspect. The most common symptom of pulmonary TB is a productive cough for more than 2 weeks, which may be accompanied by other respiratory symptoms (shortness of breath, chest pains, hemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue).
A Case of tuberculosis:
A definite case of TB (defined below) or one in which a health worker has diagnosed TB and has decided to treat the patient with a full course of TB treatment.

A Definite/proven case of tuberculosis:
A patient with two sputum smears (one sputum positive is enough for HIV positive patients) or culture positive for Mycobacterium tuberculosis. Definite case of tuberculosis is also defined as a patient with Mycobacterium tuberculosis complex identified from a clinical specimen, either by culture or by a newer method such as molecular line probe assay.

4.6 Classification of TB
Cases of TB are also classified according to the:
1. anatomical site of disease;
2. bacteriological results (including drug resistance);
3. history of previous treatment;
4. HIV status of the patient.

1. Anatomical site of TB disease:
In general, recommended treatment regimens are similar, irrespective of site. Defining the site is important for recording and reporting purposes and to identify the more infectious patients – those with pulmonary involvement who will be further subdivided by smear status below.

Pulmonary tuberculosis (PTB) refers to a case of TB involving the lung parenchyma. Miliary tuberculosis is classified as pulmonary TB because there are lesions in the lungs. Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of pulmonary TB.

Extrapulmonary tuberculosis (EPTB) refers to a case of TB involving organs other than the lungs such as pleura, larynx. Diagnosis should be based on at least one specimen with confirmed M. tuberculosis or histological or strong clinical evidence consistent with active EPTB, followed by a decision by a clinician (see Annex 2 for Lymph adenopathy) to treat with a full course of tuberculosis chemotherapy. The case definition of an EPTB case with several sites affected depends on the site representing the most severe form of disease. Unless a case of EPTB is confirmed by culture as caused by M. tuberculosis, it cannot meet the “definite case” definition given above.
2. **Bacteriologic classification**

Bacteriology refers to the smear status of pulmonary cases and the identification of *M. tuberculosis* for any case by culture or newer methods.

Smear-positive cases are the most infectious and most likely to transmit their disease in their surroundings; they are the focus for infection control measures and contact investigations. Bacteriological monitoring of treatment progress is most feasible and practicable in these patients.

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**Definitions of TB Cases Classifications**

**a. Smear-positive pulmonary TB (PTB+)**

A patient with at least two initial sputum smear examinations positive for AFB by direct microscopy,

Or

A patient with one initial smear examination positive for AFB by direct microscopy and culture positive,

Or

A patient with one initial smear examination positive for AFB by direct microscope and radiographic abnormalities consistent with active TB as determined by a clinician.

**b. Smear-negative pulmonary TB (PTB-)**

A patient having symptoms suggestive of TB with at least 3 initial smear examinations negative for AFB by direct microscopy,

And

1. No response to a course of broad-spectrum antibiotics,

And

2. Again three negative smear examinations by direct microscopy,

And

3. Radiological abnormalities consistent with pulmonary tuberculosis,

And

4. Decision by a clinician to treat with a full course of anti- tuberculosis

Or

A patient whose diagnosis is based on culture positive for *M. tuberculosis* but three initial smear examinations negative by direct microscopy

**c. Extra-pulmonary TB (EPTB)**

TB in organs other than the lungs, proven by one culture-positive specimen from an extra-pulmonary site or histo-pathological evidence from a biopsy,

Or

TB based on strong clinical evidence consistent with active EPTB and the decision by a physician to treat with a full course of anti-TB therapy.
3. **History of previous treatment: patient registration group**

At the time of registration, each patient meeting the case definition is also classified according to whether or not he or she has previously received TB treatment and, if so, the outcome (if known). It is important to identify previously treated patients because they are at increased risk of drug resistance, including MDR-TB. Treatment depends on whether the patient has relapsed or is returning after default or after prior treatment has failed.

**New patients** have never had treatment for TB, or have taken anti-TB drugs for less than 1 month. New patients may have positive or negative bacteriology and may have disease at any anatomical site.

**Previously treated patients** have received 1 month or more of anti-TB drugs in the past, may have positive or negative bacteriology and may have disease at any anatomical site. They are further classified by the outcome of their most recent course of treatment.

Patients whose sputum is smear-positive at the end of (or returning from) a second or subsequent course of treatment are no longer defined as “chronic”. Instead, they should be classified by the outcome of their most recent retreatment course: relapsed, defaulted or failed (e.g. failure after re-treatment, relapse after retreatment, return after defaulting retreatment regimen).

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### Registration Group by Outcome of most recent TB treatment

**New case (N):**
A patient who never had treatment for TB, or has been on anti-TB treatment for less than four weeks in the past.

**Relapse (R):**
A patient declared cured or treatment completed of any form of TB in the past, but who reports back to the health service and is now found to be AFB smear-positive or culture positive.

**Treatment after Failure (F):**
A patient who, while on treatment, is smear-positive at the end of the fifth month or later, after commencing. Treatment failure also includes a patient who was initially sputum smear-negative but who becomes smear-positive during treatment at two months or later.

**Return after default (D):**
A patient previously recorded as defaulted from treatment and returns to the health facility with smear-positive sputum.

**Transfer in (T):**
A patient who is transferred-in to continue treatment in a given treatment unit after starting treatment in another treatment unit for at least four weeks. The receiving treatment unit should register such patients as “transfer in” or “T” in the unit TB registers.

**Other (O):**
A patient who does not fit in any of the above mentioned categories. e.g. Smear negative PTB case who returns after default, EPTB case returning after default, previously treated TB patients with an unknown outcome of that previous treatment and who have returned to treatment with smear-negative PTB or bacteriologically negative EPTB.
4. HIV status

**Classifications of TB Cases in HIV positive individuals:**

**Smear-positive PTB:**
- One sputum smear examination positive for Acid-fast bacilli (AFB) and
- Laboratory confirmation of HIV infection

**Smear Negative PTB:**
- At least three sputum specimens negative for AFB, and
- Radiologic abnormalities consistent with active tuberculosis, and
- Laboratory confirmation of HIV infection, and
- Decision by a clinician to treat with full course of Anti-TB chemotherapy, or
- A patient with AFB smear-negative sputum which is culture-positive for MTB.

**Extra pulmonary TB:**
- One specimen from an extrapulmonary site culture or smear Positive for AFB, or
- Histological or strong clinical evidence consistent with active extrapulmonary TB.
- Laboratory confirmation of HIV infection, and
- Decision by a clinician to treat with full course of Anti-TB chemotherapy.

4.7 Treatment of TB

**The aims of TB Treatment:**

- To Cure the TB patient and restore quality of life and productivity
- To prevent death from active TB or its late effects
- To prevent relapse of TB
- To prevent the development and transmission of drug resistance
- To decrease TB transmission to others.

To achieve the aims of TB treatment, the patient should receive adequate chemotherapy and the Chemotherapy is considered to be adequate when it:
- Rapidly and substantially reduces the number of actively multiplying bacteria.
- Cures patients.
- Prevents relapse of the disease
- Prevents the development of resistance to the drugs.

The requirements for adequate chemotherapy are therefore:
- An appropriate combination of drugs.
- Prescribed in the correct dosage.
- Taken regularly by the patient.
- For a sufficient period of time.
**Drugs used for the chemotherapy of TB**

The drugs used for the TB treatment are safe and effective if properly used. First line drugs for the treatment of TB in Ethiopia include:

- Rifampicin (R);
- Ethambutol (E);
- Isoniazid (H);
- Pyrazinamide (Z) and
- Streptomycin (S).

The fixed dose combination (FDC) drugs available for adult and adolescent:
- RHZE 150/75/400/275 mg
- RHZ 150/75/400 mg
- RH 150/75 mg
- EH 400/150mg

TB drugs available as loose form:
- Ethambutol 400 mg;
- Isoniazid 300 mg;
- Streptomycin sulphate vials 1 gm.

**NB:** Streptomycin is administered by injection while the other anti TB drugs are to be taken orally.

All the drugs should be taken together as a single, daily dose, preferably on an empty stomach.

**Phases of chemotherapy**

The treatment of TB has two phases:

**Intensive (initial) phase**

This phase consists of treatment with combination of four drugs for the first 8 weeks for new cases, and with combination of five drugs for the first eight weeks followed by four drugs for the next four weeks for re-treatment cases. It renders the patient non-infectious by rapidly reducing the load of bacilli in the sputum, usually within 2-3 weeks except in case of drug resistance.

**Continuation phase**
This phase immediately follows the intensive phase and is important to ensure cure or completion of treatment. It is necessary in order to avoid relapse after completion of treatment. This phase requires treatment with a combination of two drugs, to be taken for 4 months for new cases and treatment with a combination of three drugs for re-treatment cases for 5 months.

**TB Patient Categories and How to select the correct Treatment Regimen**

Before you put patients on anti TB drugs:

- Determine the type of TB: PTB+, PTB- and EPTB
- Determine previous treatment history: New patient, Previously treated
- Select based on the three standard treatment regimens:
  - i. New patient regimen,
  - ii. Previously treated patient regimen,
  - iii. MDR-TB regimen

**Standard treatment regimens**

Standardized treatment means that all patients in a defined group receive the same treatment regimen. For assigning standard regimens, patients are grouped by the same patient registration groups used for recording and reporting, which differentiate new patients from those who have had prior treatment history. Registration groups for previously treated patients are based on the outcome of their prior treatment course: failure, relapse and default. The standardized TB treatment regimens for adults in Ethiopia are given in the following table1.
### Table 1: How to select the correct TB Treatment Regimens

<table>
<thead>
<tr>
<th>TB patient type</th>
<th>Recommended regimen</th>
<th>Additional Action(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td>Treatment as new:</td>
<td>Send sputum for culture &amp; DST if a contact of known MDR-TB case</td>
</tr>
<tr>
<td></td>
<td>2RHZE/4RH</td>
<td></td>
</tr>
<tr>
<td>Previously treated</td>
<td>Treatment after failure</td>
<td>Send sputum for culture &amp; DST while treating the patient</td>
</tr>
<tr>
<td></td>
<td>Treat as retreatment: 2RHZE/RHZE/5RHE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment after default or relapse after one course of treatment</td>
<td>Send sputum for culture &amp; DST while treating the patient</td>
</tr>
<tr>
<td></td>
<td>Treat as retreatment: 2RHZE/RHZE/5RHE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Relapse after second or subsequent courses of treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Failure of retreatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wait for DST result</td>
<td>Send culture &amp; DST and refer patient to MDR treatment initiating center</td>
</tr>
<tr>
<td>Transfer in</td>
<td>Continue same treatment regimen</td>
<td>Consider DST if eligible</td>
</tr>
<tr>
<td>Others</td>
<td>Previously successfully treated patients coming with PTB-ve or EPTB…</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment as new:</td>
<td>Send sputum/specimen for culture &amp; DST if a contact of a known MDR-TB case</td>
</tr>
<tr>
<td></td>
<td>2RHZE/4RH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Defaulted patients coming with smear negative TB, EPTB, or previously treated patients with unknown treatment outcome…</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treat as retreatment: 2RHZE/RHZE/5RHE</td>
<td>Send sputum/specimen for culture &amp; DST while treating the patient</td>
</tr>
</tbody>
</table>

**TREATMENT REGIMEN FOR NEW TB CASES**

News TB Patients will be treated with 2RHZE/4RH. Other Previously treated Smear Negative PTB and EPTB cases (Case definition ‘Other’) who were previously cured or treatment completed will be treated with New TB patient regimen.

This regimen consists of 8 weeks treatment with Rifampicin, Isoniazid, Pyrazinamide and Ethambutol during the intensive phase, followed by four months with Rifampicin and Isoniazid: 2RHZE/4RH.
Treatment Regimen for Previously treated TB Cases

Previously treated TB cases will be re-treated with 2S(RHZE) / 1(RHZE) / 5 (RH)E
Defaultered patients coming with smear negative TB, EPTB, or previously treated patients
with unknown treatment outcome (Case definition ‘Other’)

This regimen consists of eight weeks treatment with Streptomycin, Rifampicin, Isoniazid,
Pyrazinamide and Ethambutol followed by four weeks treatment with Rifampicin,
Isoniazid, Pyrazinamide and Ethambutol during the intensive phase, followed by five
months with Rifampicin, Isoniazid and Ethambutol: 2SRHZE/1RHZE/5(RH)E.

Anti-TB Drug dosages
The dose and type of anti-TB drugs are age & weight dependent. There is no sex specific
difference in TB treatment unless the patient is pregnant who should not be given
streptomycin.

Table 2: Recommended Doses of First-Line Anti-tuberculosis Drugs For Adults

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Recommended dose</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose and range</td>
<td>Maximum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(mg/kg Bwt)</td>
<td>(mg)</td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>5 (4–6)</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>10 (8–12)</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>25 (20–30)</td>
<td>2,000</td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
<td>15 (15–20)</td>
<td>1600</td>
<td></td>
</tr>
<tr>
<td>Streptomycin*</td>
<td>15 (12–18)</td>
<td>1000</td>
<td></td>
</tr>
</tbody>
</table>

*Patients aged over 60 years may not be able to tolerate more than 500–750 mg daily, so some guidelines recommend
reduction of the dose to 10 mg/kg per day in patients in this age group (2). Patients weighing less than 50 kg may not tolerate
doses above 500–750 mg daily.

Table 3: Anti TB Drugs Dosage of New TB cases

<table>
<thead>
<tr>
<th>Patient’s Weight in Kgs</th>
<th>Treatment Regimen and Dose</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intensive Phase 2RHZE</td>
<td>2RHZE</td>
</tr>
<tr>
<td></td>
<td>Continuation Phase 4RH</td>
<td>4RH</td>
</tr>
<tr>
<td>20-29*</td>
<td>1 ½</td>
<td>1 ½</td>
</tr>
<tr>
<td>30-39</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>40-54</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>≥55</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

*Remark: Because of difference in drug pharmacology between children and adults, the recommended dosage
in the weight range of 20–30kg is different*.
Table 4: Anti TB Drugs Dosage for Previously treated cases

<table>
<thead>
<tr>
<th>Patient’s Weight in Kgs</th>
<th>Treatment Regimen and Dose</th>
<th>Intensive Phase 2SRHZE/1RHZE</th>
<th>Continuation Phase 5 (RH)E</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>S*</td>
<td>RH</td>
</tr>
<tr>
<td>20-29</td>
<td></td>
<td>½ (0.5 g)</td>
<td>1 ½</td>
</tr>
<tr>
<td>30-39</td>
<td></td>
<td>½ (0.5 g)</td>
<td>2</td>
</tr>
<tr>
<td>40-54</td>
<td></td>
<td>¾ (0.75g)</td>
<td>3</td>
</tr>
<tr>
<td>≥ 55</td>
<td></td>
<td>1 g</td>
<td>4</td>
</tr>
</tbody>
</table>

*S*Streptomycin should not be included in the re-treatment for pregnant women.
*For patients over 60 years of age, the maximum dose of streptomycin is 0.75 gm.

4.8 Treatment of TB in Special Situations

Pregnancy
Ask female patients whether they are pregnant or not. Most anti-TB drugs are safe for use in pregnancy with the exception of streptomycin. Do not give streptomycin to a pregnant woman because it can cause permanent deafness in the baby. Pyridoxine supplementation is recommended for all pregnant women taking INH.

Oral contraception
Rifampicin interacts with oral contraceptive medications with a risk of decreased protection against pregnancy. A woman who takes the oral contraceptive pill may choose between the following two options while receiving treatment with rifampicin: following consultation with a clinician, she could take an oral contraceptive pill containing a higher dose of estrogen. Alternatively, she could use another form of contraception.

Breastfeeding
A breastfeeding woman who has TB can be treated with the regimen appropriate for her disease classification and previous treatment. The mother and baby should stay together and the baby should continue to breastfeed in the normal way. Give the infant a course of preventive therapy (INH). When preventive therapy is completed, give the infant BCG if not yet immunized. Pyridoxine supplementation is recommended for all breast feeding women taking INH.

HIV patients on Anti-retrovirals
TB patients with HIV infection or HIV/AIDS may experience a temporary worsening of symptoms and signs after beginning TB treatment. In TB patients infected with HIV, treatment with anti-retrovirals (ARV) may interact with treatment of TB, reducing the efficacy of anti-retrovirals and of anti-TB drugs and increasing the risk of drug toxicity. Detailed management of co-infected patients is provided under TB/HIV Collaborative activities section 6.
Treatment of patients with TB & Leprosy
Patients suffering from both diseases require appropriate anti-TB chemotherapy in addition to the standard MDT. Rifampicin will be common to both regimens and must be given in the doses required for TB. Once the anti-TB course is completed, the patient should continue his anti-leprosy treatment.

Treatment of patient with renal failure
Consult expert, if not possible to consult then avoid Streptomycin & Ethambutol; therefore the recommended regimen is 2RHZ/4RH.

Treatment of patients with liver disorder
Most anti-TB drugs can cause liver damage. Do not give Pyrazinamide because this is the most hepatotoxic anti-TB drug. Isoniazid & Rifampicin plus one or two non-hepatotoxic drugs such as Streptomycin and Ethambutol, can be used for total treatment duration of eight months. If the patient has severe liver damage, an alternative regimen is Streptomycin plus Isoniazid plus Ethambutol in the initial phase followed by Isoniazid & Ethambutol in the continuation phase with a total duration of 12 months. Hence, for TB patients with liver disease, recommended regimens are: 2SERH/6RH, 9RHE or 2SEH/10EH. Management of Ant-TB drug induced hepatitis is outlined in the Adverse Ant-TB drugs reaction section.

4.9 Treatment of Serious Forms of Extrapulmonary TB
In the extrapulmonary TB forms, lymphatic, pleural & bone or joint disease are the most common, while pericardial, meningeal and disseminated (miliary) forms are more likely to result in a fatal outcome. Pulmonary and EPTB should be treated with the same regimens. However, it’s recommended, given the serious risk of disability and mortality, for these patients to be managed with consultation of senior clinicians for a total duration of 9 to 12 months for TB meningitis and TB of bones or joints. Adjuvant corticosteroid treatment is recommended for TB meningitis and pericarditis. In TB meningitis Ethambutol should be replaced by Streptomycin.

Pericardial tuberculosis
For patients with pericardial tuberculosis, same regimen (as pulmonary) of anti-TB treatment is recommended (need expert opinion in diagnosis & treatment). Corticosteroids are recommended as adjunctive therapy for 11 weeks during the first period of anti-tuberculosis therapy.

Table 5: Dose of corticosteroid adjuvant therapy for Pericardial TB

<table>
<thead>
<tr>
<th>Weeks of treatment</th>
<th>Prednisolone dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>60mg/d</td>
</tr>
<tr>
<td>5-8</td>
<td>30mg/d</td>
</tr>
<tr>
<td>9-10</td>
<td>15mg/d</td>
</tr>
<tr>
<td>11th week</td>
<td>5mg/d (then discontinue at the end of the 11th week)</td>
</tr>
</tbody>
</table>
Pleural tuberculosis
Same regimen (as pulmonary) is also recommended for treating pleural tuberculosis. Tuberculous empyema, a chronic, active infection of the pleural space containing a large number of tubercle bacilli, usually occurs when a cavity ruptures into the pleural space. Treatment consists of drainage (often requiring a surgical procedure) and anti-TB drugs.

Tuberculous meningitis
Tuberculous meningitis remains a potentially devastating disease that is associated with a high mortality and sequelae, despite prompt initiation of adequate chemotherapy. HIV-infected patients appear to be at increased risk of developing Tuberculous meningitis but the clinical features and outcomes of the disease are similar to those in patients without HIV infection. Patients presenting with more severe brain impairment such as drowsiness, neurological signs, or coma have a greater risk of neurological sequelae and a higher mortality.

Chemotherapy should be initiated with RHZS in an initial phase for 2 months and RH should be continued for 7 to 10 months in the continuation phase.

Adjunctive corticosteroid therapy with dexamethasone is recommended for all patients. The recommended regimen is:

\[
\begin{array}{l}
\text{Dexamethasone- a total dose of 8 mg/day for children weighing less than 25 kg and 12 mg/day for adults and children weighing 25 kg or more. The initial dose is given for 3 weeks and then decreased gradually during the following 3 weeks.}
\\
\text{Prednisolone- a dose of 2-4mg/kg/day for children; 60mg/day for adults, for 3 weeks, then tapered of gradually over the following three weeks.}
\end{array}
\]

4.10 Management of Anti-TB Drugs’ Side-Effects
Generally anti TB drugs are safe and have fewer side effects. Most of the side-effects are minor and do not require stopping the anti-TB drugs. But the health workers or treatment supporter should monitor side effects by checking & asking the presence or absence of those anticipated side effects. Bear in mind that side effects are more common in HIV positive people.

Anti TB drugs adverse effects are grossly classified as:

a) **Minor side effects**: this may occur more frequently and managed symptomatically without interruption of anti-TB drugs. If the patient continues to be concerned about a minor side effect even after following the advice, refer/consult the patient to an experienced clinician

b) **Major side effects**: Not common and needs to stop the responsible offending drug or all drugs, and refer the patients to a higher level (hospital). The management of Anti-TB drugs side-effects is outline in the following table.
### Table 6: Symptom based approach to the management of Anti-TB drugs side-effects

<table>
<thead>
<tr>
<th>Side-effects</th>
<th>Responsible Drugs</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minor (Continue Anti-TB drug/s)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anorexia, nausea, abdominal pain</td>
<td>Rifampicin;</td>
<td>Give tablets with small meals or before bed time</td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide</td>
<td></td>
</tr>
<tr>
<td>Joint pains</td>
<td>Pyrazinamide</td>
<td>NSAIDs</td>
</tr>
<tr>
<td>Burning sensation in feet</td>
<td>Isoniazid</td>
<td>Pyridoxine 100mg daily</td>
</tr>
<tr>
<td>Orange/red urine</td>
<td>Rifampicin</td>
<td>Reassurance</td>
</tr>
<tr>
<td><strong>Major (Stop the responsible drug/s)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itching, skin reaction</td>
<td>Streptomycin;</td>
<td>Stop and replace with ethambutol; Stop, then reintroduce with desensitization¹</td>
</tr>
<tr>
<td></td>
<td>Rifampicin or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>isoniazid</td>
<td></td>
</tr>
<tr>
<td>Deafness</td>
<td>Streptomycin</td>
<td>Stop streptomycin and replace with Ethambutol</td>
</tr>
<tr>
<td>Dizziness (vertigo, imbalance and nystagmus)</td>
<td>Streptomycin</td>
<td>Stop streptomycin and replace with Ethambutol</td>
</tr>
<tr>
<td>Jaundice; hepatitis</td>
<td>Most anti-TB drugs</td>
<td>Stop all anti-TB drugs and refer</td>
</tr>
<tr>
<td>Vomiting and confusion</td>
<td>Most anti-TB drugs</td>
<td>Stop all anti-TB drugs and refer</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>Ethambutol</td>
<td>Stop Ethambutol and refer</td>
</tr>
<tr>
<td>Shock, purpura and acute renal failure</td>
<td>Rifampicin</td>
<td>Stop Rifampicin and refer</td>
</tr>
</tbody>
</table>

**Management of cutaneous reaction**

**Desensitization:** If a skin reaction develops, all anti-tuberculosis drugs must be stopped. Once the reaction has resolved, anti-TB drugs are reintroduced. The idea of desensitization is to start with a small dose of drugs: if a reaction occurs, it will be less severe than the reaction to a full dose. The dose is gradually increased over three days. There is no evidence that this process gives rise to drug resistance. It may be necessary to extend the treatment regimen. This prolongs the total time of TB treatment, but decreases the risk of relapse.

**Management of drug-induced hepatitis**

Most anti-TB drugs can damage the liver. Isoniazid, pyrazinamide and rifampicin are most commonly responsible ones where Ethambutol does so rarely. When a patient develops hepatitis during TB treatment, the cause may be the TB treatment or something else. It is important to rule out other possible causes before deciding that the hepatitis is drug induced.

If the diagnosis is drug-induced hepatitis, the anti-TB drugs should be stopped. The drugs must be withheld until liver function test have reverted to normal. Sometimes it is not possible to perform liver function test; in these situations, it is advisable to wait an extra 2
weeks after the jaundice has disappeared before recommencing TB treatment. Asymptomatic jaundice without evidence of hepatitis is probably due to rifampicin. Once drug-induced hepatitis has resolved, the same drugs are reintroduced. However, if the hepatitis produced clinical jaundice, it is advisable to avoid pyrazinamide. The suggested regimen in such patients is a 2-month initial phase of daily streptomycin, isoniazid and ethambutol, followed by a 10-month continuation phase of isoniazid and ethambutol (2 SHE/10EH). A severely ill TB patient with drug-induced hepatitis may die without antituberculosis drugs. In this case, the patient should be treated with two of the least hepatotoxic drugs, streptomycin and ethambutol. After the hepatitis has resolved, usual TB treatment should be restarted.

4.11 Monitoring of TB treatment

Directly Observed Treatment (DOT)
Health workers must take an active role to ensure that every patient takes the recommended drugs, in the right combinations, on the correct schedule, for the appropriate duration. The best way to ensure this is for a health worker or a community TB treatment supporter to watch each patient swallow every single dose of the drugs. This is called directly observed treatment - DOT. Directly observed treatment can take place at a hospital, a health center or health post, the patient’s workplace, or at the home of the patient. DOT ensures that all Anti-TB drugs are swallowed. DOT is supposed to build supportive relationship between patient and health worker or community TB treatment supporter. A good relationship enables the patient to discuss any question or fear about the disease and treatment.

The success of directly observed treatment requires the patient’s cooperation and motivation. Health workers and treatment supporters should have the appropriate communication skills when interacting with patients, provide all the necessary information about their treatment so that they understand the disease and adhere to the treatment. Essential information about TB disease includes:

- What is tuberculosis
- TB can be cured
- How TB spreads
- How to prevent TB from spreading
- Who else should be examined or tested for TB
- Importance and the necessity of DOT
- Details of treatment regimen
- What to expect, and what to do next.

As the health care worker or TB treatment supporter continue to see a patient daily to directly observe treatment, reinforcing messages about TB treatment needs to be continued. Support needs to be given for the patient to continue taking the drugs on schedule and to complete all the required doses. The patient should be informed about the dangers of
irregular or incomplete treatment. The following information needs to be reviewed with the patient periodically during the initial and continuation phase: Side-effects of drugs (if reported/observed); Type, color, amount, and frequency of drugs; Importance of continuing treatment; What happens if the patient takes only some of the drugs or interrupts treatment; Frequency and importance of required sputum examinations, etc.

**Monitoring during the Intensive phase**

During the initial phase of treatment, the patient must take the drugs in front of the health worker or trained HEW who is responsible for verifying that the patient swallows all of the prescribed drugs every day. The TB treatment can be followed either at health facility by the health worker or at a Health Post by trained HEWs.

- If the patient chooses a health facility with TB DOTS clinic, he/she can attend his/her daily treatment follows up in the same health facility.
- If the patient chooses to follow treatment at Health post level, HEWs should take the responsibility of observing patient while taking their daily Anti-TB drugs. More information on this issue can be found in the Community DOTS section of this Guideline.
- If directly observed treatment cannot be provided on an out-patient basis, the patient should be hospitalized during the course of the intensive phase of treatment.

**Monitoring during the continuation phase**

The continuation phase of the treatment of TB should also be administered under the direct observation of health care worker, HEWs or a designated trained TB treatment supporter either at health facility (Health Center, TB DOTS Clinic or Hospital), Health Post or patients’ home. For TB patients choosing health facilities to follow their treatment during continuation phase, the Health facility’s TB focal person takes the responsibility to ensure direct observation of treatment. Besides directly supervising the TB treatment during this phase, there is a recommended fixed scheduled visit for the TB patient at the health facility serving as the patient’s treatment unit.

For those patients choosing health posts to follow their continuation phase of treatment at health post, the HEWs will be responsible for ensuring the direct observation of treatment. Whereas, if the patient cannot follow his/her continuation phase treatment either at health facilities or at health post level and chooses to follow his/her treatment at his/her home, the designated trained treatment supporter will be responsible for ensuring the patient takes each and every dose of ant-TB drugs during this phase under direct observation.

The recommended scheduled follow up visits at the treatment unit during the continuation phase of treatment for TB patients following their continuation phase treatment at health posts or at their home is:

- HEWs collect Anti-TB drugs from HC on monthly basis.
- The patient, accompanied by the TB treatment supporter, collect anti TB drugs weekly from the health post.
The follow up dates should be arranged jointly by the health worker and the patient, depending on the ease of access to the health facility and the adherence requirements. Whatever facility is providing drugs during the continuation phase, all TB patients must be clearly advised to go the TB clinic where they are registered, for clinical check and bacteriological tests, at defined dates and at the end of their treatment. During these follow up visits, efficiency and outcome of treatment is monitored, drug tolerance is assessed and sputum is taken for microscopic examination for PTB+ patients. Follow up laboratory tests is necessary in order for cure to be confirmed and the patient's final status to be correctly recorded.

For tuberculosis patients who are in a precarious situation (homeless) and those who are drug addicts, alcoholics or who have mental problems, the organization of follow-up must aim at reducing the lack of compliance common in these population groups.

**Monitoring TB patient’s Progress:**
During the follow up in the intensive and continuation phase of treatment, monitoring of patient’s progress involves:

- Signs and symptoms /clinical assessment
- Weight measurement: weight should be measured at the beginning of TB treatment to determine treatment dose. Subsequent weight measurements are taken at the end of 2nd months of treatment and drug dose should be adjusted accordingly.
- Follow up AFB sputum examination (for new and re-treatment PTB+ cases): at 2nd, 5th and 6th for new, and at 3rd, 5th, and 8th for retreatment patients.

*NB. The sputum sample for the AFB monitoring test should be requested during the last week of the indicated month.*

**a) Follow up of New Smear Positive PTB cases**
In general, the response to anti-TB treatment in smear positive Pulmonary TB patients is monitored by follow up sputum smear examinations (see Annex 5). For new smear-positive pulmonary TB patients treated with first-line drugs, sputum smear microscopy should be performed at completion of the intensive phase of treatment.

As a routine, all new sputum-positive patients on TB treatment must have one sputum specimen examined at the end of the 2nd, 5th and 6th ‘month’ of therapy. Dates and results of direct sputum examinations should be entered in the Unit TB Register.

- If the sputum smear at the end of 2nd month is negative for AFB, the continuation phase will be started.
- If the sputum smear at the end of the 2nd month of intensive phase is positive for AFB, start continuation phase treatment and repeat sputum smear microscopy at the end of the 3rd month of therapy (extension of the intensive phase by one month is not recommended)
- If the sputum smear at the end of 3rd month of therapy is negative, continue with the continuation phase and sputum smear should be obtained for microscopy at the end of 5th month of therapy. However, if the sputum smear at the end of 3rd month of
therapy is positive for AFB, two sputum samples should be taken and sent for culture and DST. The main purpose of obtaining cultures at this stage is to detect drug resistance without waiting the fifth month to change to appropriate therapy (Note that treatment is declared a failure if a patient is found to harbor MDR-TB at any point in time during treatment).

- In the continuation phase of treatment, if the sputum smear result at the end of 5th month of treatment is negative for AFB, the patient should continue with the same treatment. If the first smear result is positive for AFB at the end of 5th month, sputum smear examination should be repeated. If the second sputum smear result is positive, the patient is declared as treatment failure. But if the second sputum is negative go for third tie breaker sputum test and decide accordingly. The patient should be registered as treatment failure and re-started with regimen for previously treated cases.

- The sputum is examined again at the end of 6th month. If the result is negative the patient is declared cured. If the result is positive in two smears at 5th or 6th months, the patient is a treatment failure and should re-start the treatment regimen for previously treated cases.

- If for whatever reason after 6 months of treatment, the final sputum examination cannot be done and the sputum result at 5th month was negative or not done, the patient should be declared treatment completed.

b) Follow up of previously treated Smear Positive PTB Cases
Sputum smear examination is performed at the end of the intensive phase of treatment (the 3rd month), at the end of the 5th and 8th months of treatment.

- In previously treated patients, if the specimen obtained at the end of the intensive phase (month 3) is smear negative, the continuation phase of re-treatment regimen is started and sputum is examined at the end of 5th month of therapy. However, if the sputum smear result at the end of 3rd month of therapy is smear-positive, sputum culture and drug susceptibility testing (DST) should be performed. But patient should continue treatment till the result comes. Decision on treatment will made based on the DST result.

- If the smear result at the end of 5th month of re-treatment regimen is negative for AFB, the continuation phase is continued and sputum is examined at the end of 8th month of therapy. However, if the patient is found smear-positive at the end of 5th month of treatment in 2 different specimens, the patient is declared as treatment failure. Further decision on treatment must be guided by DST.

- If the sputum smear result at the end of 8th month is found to be negative, the patient is declared cured (if in at least one previous occasion either 3rd or 5th month of therapy is negative). However, if the smear result at the end of the 8th month of therapy is positive in two different specimens, the patient is declared treatment failure. Further decision on treatment must be guided by DST.

- If for whatever reason after 8 months of treatment, the final sputum examination cannot be done and the sputum result at 5th month was negative or not done, the patient should be declared treatment completed.
c) Follow up of New Smear Negative PTB and EPTB Cases

Follow-up for smear negative PTB and EPTB patients is by monitoring weight and the clinical condition. For pulmonary TB patient whose sputum microscopy was negative (or not done) before treatment, should have a repeat sputum test at the end of intensive phase in case the disease progressed or symptoms persistent. If the sputum smear microscopy is found to be negative, continue same treatment.

If sputum result turns positive, (it could be due to non-adherence, or drug resistance or an error at the time of initial diagnosis i.e. a true smear-positive patient was misdiagnosed as smear-negative), wait for the third month and repeat sputum smear microscopy. If remains positive, send for DST.

4.12 Management of TB Treatment Interrupters

a) Retrieval of absentees or Interrupters

If, during the intensive phase, a patient has not attended on the appointed clinic day for Directly Observed Therapy and fails to report for 2 days thereafter (- and has interrupted treatment), he/she has to be considered as an Absentee and should be retrieved.

In case of absenteeism, the following measures are suggested:

i. Confirm that the patient did not attend the daily DOT

ii. Communicate with the TB treatment supporter

iii. Communicate with health extension worker or community volunteer

iv. Assist to identify and solve the problem, if any

v. Close follow up and encourage the patient to adhere to treatment

vi. Arrange for home visit whenever possible

When the patient is found, further care and treatment is based on the duration of treatment already received and the patient's bacteriological status.

Treatment interrupters are patients who took treatment for at least one month and discontinue treatment for less than eight consecutive weeks.

Defaulters are patients who took treatment for at least one month and discontinue treatment for more than consecutive eight weeks; and

Both should be managed as follows:

- EPTB and smear negative PTB, with the consultation of trained clinician, the missed doses should be supplemented at the end of each phases of treatment.

- Management of smear positive PTB Treatment interrupters depends on:
  - prior treatment duration before interruption
  - period of treatment interruption, and
  - Current smear result.
b) Management of New PTB+ Treatment Interrupters

Table 7: Management of New PTB+ Treatment Interrupters

<table>
<thead>
<tr>
<th>Duration of treatment before interruption</th>
<th>Duration of interruption</th>
<th>Smear result at return</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4 Weeks</td>
<td>&lt; 2 consecutive weeks</td>
<td>Smear not needed</td>
<td>Continue the same treatment(^1)</td>
</tr>
<tr>
<td></td>
<td>2-8 consecutive weeks</td>
<td>Smear not needed</td>
<td>Re-start the same treatment</td>
</tr>
<tr>
<td>4-8 Weeks</td>
<td>&lt; 8 consecutive weeks</td>
<td>Negative</td>
<td>Continue the same treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Positive</td>
<td>Start regimen for Previously treated</td>
</tr>
<tr>
<td>&gt;8 Weeks</td>
<td>&lt;8 consecutive weeks</td>
<td>Negative</td>
<td>Continue the same treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Positive</td>
<td>Start regimen for Previously treated, send sputum for culture &amp; DST(^2)</td>
</tr>
</tbody>
</table>

\(^1\) taking into account the administered doses and continue same treatment.
\(^2\) DST is indicated for New smear positive patients if the third month result remains positive.

A patient who returns after default and who is PTB+ should be registered in a new cohort as “return after default” and should be treated with regimen for previously treated cases.

c) Management of Smear Negative PTB and EPTB treatment defaulters/interrupters

The treatment of Smear negative PTB is followed up by monitoring the clinical progress and the regularity of drug collection.

Any smear negative PTB patient who returned after interruption of treatment, whose condition has not improved or gets worse by the end of the intensive phase, should be assessed by an experienced medical officer and two specimens of sputum should be examined. If one smear is positive, two other specimens should be examined. If out of these, one more is positive, the patient has PTB+ve and has to start regimen for previously treated cases. This group of patients are registered under the category = ‘failure’.

If the condition of the patient deteriorates while the sputum remains negative, X-ray is advisable to aid the diagnosis. If findings on X-ray are consistent with active TB, the initial anti-TB treatment may be repeated. This group of patients are registered under the category = ‘others’.
Any PTB-ve patient, who interrupted the treatment for more than 8 consecutive weeks (defaulting) and returns for continuation of treatment should be assessed by an experienced medical officer and two specimens of sputum should be examined. Out of these smears, if one or more is positive, the patient has PTB+ve and should start regimen for previously treated cases (case definition = return after default). If the smears remain negative, the patient should be treated with the original regimen (case definition = ‘other’).

A patient who returns after default and who is PTB-ve (as proven by deterioration of the X-ray not due to other diseases) should be registered in a new cohort as “other” and be treated with a full course of the original regimen.

Any EPTB patient, who interrupted the treatment for more than 8 consecutive weeks (defaulting) and who returns for continuation of treatment, should be assessed by an experienced medical officer. If the condition remains the same or gets worse the patient should be treated with the full course original regimen.

Medical Referrals and Indications for Hospitalization

Referral of TB patients
A TB and/or leprosy patient is said to be referred when they are sent to another health facility temporarily for better diagnosis, consultation & management and/or other programmatic reasons.

Reasons for Patient referral:
- For diagnosis (X-ray, histo-pathology…)
- For better management (serious side effect management, comorbid conditions, in-patient care, MDR-TB…)
- Programmatic (to initiate treatment after diagnosis, patient preference…)

N.B.: a patient who is diagnosed to have TB in one health facility and referred to another health facility before starting anti-TB treatment or before four weeks of treatment will be recorded in the unit TB register, and begins TB treatment in the later one. In the receiving HF, the patient should be classified and reported as ‘New" not as “Transfer in”.

Therefore, if the HF is planning to refer this kind of patient, the patient should not be registered in the TB unit register.

Indications for Admission of TB patients
In the majority of cases, admission is not necessary for TB patients. However, admission may be indicated when there is:
- Severe clinical deterioration of the patient's condition
- Tuberculosis related complications like massive hemoptysis, pneumothorax, empyema…
- Serious side-effects such as jaundice or severe allergic skin reaction…
- Severe comorbid conditions diseases such as uncontrolled or complicated diabetes, kidney failure, chronic liver diseases…

The period of hospitalization depend on their clinical condition; it often lasts less than two weeks, and the patient can be discharged as soon as the reasons for hospitalization resolved.
4.13 TB Treatment Outcomes

**Cured:**
A patient whose sputum smear or culture was positive at the beginning of the treatment but who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.

**Treatment completed:**
A patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion.

**Treatment failure:**
A patient whose sputum smear or culture is positive at 5 months or later during treatment. or Patients found to harbour a multidrug-resistant (MDR) strain at any point of time during the treatment, whether they are smear-negative or -positive.

**Died:**
A patient who dies for any reason during the course of TB treatment.

**Defaulter:**
A patient who has been on treatment for at least four weeks and whose treatment was interrupted for eight or more consecutive weeks.

**Transfer out:**
A patient who has been transferred to another recording and reporting unit and whose treatment outcome is unknown.

**Treatment success:**
A sum of cured and completed treatments.
5. CHILDHOOD TUBERCULOSIS

5.1 Basics of Childhood Tuberculosis

The source of infection in most children is an infectious adult in their close environment (usually the household). This exposure leads to the development of a primary parenchymal lesion (-Ghon focus) in the lung with spread to the regional lymph node(s). The immune response (delayed hypersensitivity and cellular immunity) develops about 4–6 weeks after the primary infection. In most cases, the immune response stops the multiplication of M. tuberculosis bacilli at this stage. However, a few dormant bacilli may persist. A positive tuberculin skin test (TST) would be the only evidence of infection.

In some cases, the immune response is not strong enough to contain the infection and disease occurs within a few months. Risk of progression to disease is increased when primary infection occurs before adolescence (less than 10 years of age) – particularly in the very young (0–4 years) – and in children with immunocompromised/ postmeasles/malnourished, etc.

Progression of disease occurs by: (i) extension of the primary focus with or without cavitation, (ii) the effects of pathological processes caused by the enlarging lymph nodes, or (iii) lymphatic and/or haematogenous spread. Children who develop primary TB e usually do so within 2 years following exposure and infection. A small proportion of children with TB (generally older children) develop post-primary TB either due to reactivation or reinfection.

5.2 Clinical manifestations

In most children, TB presents with symptoms of a chronic disease after they have been in contact with an infectious source case. The key risk factors for TB are:

- Household contact with Pulmonary TB case
- Age less than 5 years
- HIV infection
- Severe malnutrition.

In children TB disease presents in various clinical forms:

Pulmonary Tuberculosis: The most common clinical presentation is persistent respiratory symptoms and poor weight gain. A child may have nonproductive cough and/or mild wheezes. Pulmonary TB in infants and HIV infected children may present as acute pneumonia.

Extra-pulmonary tuberculosis: Children of less than 2 years of age are at risk of disseminated disease causing miliary TB or TB meningitis. The common EPTB in children are:
• **Tuberculous lymphadenitis**: is the commonest form. Regardless of HIV status, the lymph nodes most commonly involved are the cervical nodes. Generalized lymphadenopathy can occur in children with HIV infection, reduced immunity and in symptomatic HIV children who are given BCG vaccination.

• **Tuberculosis of the spine or joints** is the second commonest form of childhood EPTB, and may occur within the first few years following primary infection. It usually affects weight bearing bones or joints and the most common sites are spine, hip, knee and ankle. Early diagnosis of TB of the spine is essential to prevent the disastrous consequence leading to paralysis.

• **Miliary Tuberculosis**: Patients present with constitutional features rather than respiratory symptoms. Early symptoms are vague and lack specificity. Lassitude, anorexia, failure to thrive and prolonged unexplained fever are common. Therefore, a high index of suspicion is necessary. TB meningitis is the commonest cause of death if miliary TB is untreated.

• **CNS TB**: is the result of haematogenous spread of the bacilli to the CNS. The patient may present with constitutional features and chronic meningitis and there is gradual onset and progression of headache and decreased consciousness. If it forms tuberculoma (a large, solid lesion, rather like a malignant tumor) it may present with focal neurological deficits, seizures and obstructive hydrocephalus. Young children, especially those under 2 years of age have the highest incidence and the worst prognosis.

• **Tuberculosis of the serous membranes**: Inflammatory Tuberculous effusions may occur in any of the serous cavities of the body, i.e. pleural, pericardial or peritoneal cavities.

### 5.3 Diagnosis of TB in children

It is easy to over diagnose TB in children and it is also easy to miss TB in children. Even though bacteriological confirmation of TB is not always feasible, it should be sought whenever possible. A trial of treatment with anti-TB medications **is not recommended** as a method to diagnose TB in children. The decision to treat a child should be carefully considered and once such a decision is made, the child should be treated with a full course of therapy.
**Key features suggestive of TB**
- Chronic symptoms suggestive of TB
- Physical signs highly of suggestive of TB
- X-ray suggestive of TB
- A positive tuberculin skin test

**Recommended approach to diagnose TB in children**

The diagnosis of TB in children relies on careful and thorough assessment of all the evidence derived from a careful history, clinical examination and relevant investigations because bacteriological confirmation of TB is often difficult. Carefully assess all the evidence before making the diagnosis.

**Clinical Assessment**

**A. Typical symptoms**
- Cough especially if persistent and not improving
- Weight loss or failure to gain weight
- Fever and/or night sweats
- Fatigue, reduced playfulness, less active

*Especially, if symptoms persist (>2-3 weeks) without improvement following other appropriate therapies (e.g. broad-spectrum antibiotics for cough; antimalarial treatment for fever; or nutritional rehabilitation for malnutrition)*

**B. History of contact**
- Close contact: such as with a source case of Pulmonary TB living in the same household or a chronic cougher
- Contact may be with a source case of Pulmonary TB from outside the household with whom the child has had frequent contact even from school in cases of older children.
- A source case with sputum smear-positive PTB is more likely to infect contacts than cases with sputum smear-negative PTB; however, cases with EPTB are not infectious.
- Children usually develop TB within 2 years after exposure and most (90%) within the first year.

**C. Clinical examination**
- Conduct through physical examination with special emphasis on weight measurement (look for weight loss or poor weight gain), fever, signs of respiratory distress and chest finding.
Children can also present with acute severe pneumonia (especially in infants and HIV-infected children) and asymmetrical and persistent wheeze.

D. Tuberculin skin test
TST is useful to support a diagnosis of TB in children with suggestive clinical features who are sputum smear negative or who cannot produce sputum.
A positive TST indicates infection:
- positive in any child if $\geq 10$ mm irrespective of BCG immunization
- also positive if $\geq 5$ mm in HIV-infected or severely malnourished child

A positive TST is particularly useful to indicate TB infection when there is no known TB exposure on clinical assessment i.e. no positive contact history.

**Caution:** *a positive TST does not distinguish between TB infection and active Disease. A negative TST does not exclude TB disease.*

E. Bacteriological confirmation
Children usually have paucibacillary pulmonary disease (low organism numbers), as cavitating disease is relatively rare. All attempts must be made to confirm diagnosis of TB in a child using whatever specimens and laboratory facilities are available. Appropriate specimens from the suspected sites of involvement should be obtained for microscopy (and, if available, for culture and histopathological examination, too). Appropriate clinical samples include sputum, gastric aspirates and lymph node fine-needle aspiration or other tissue biopsy.

F. Chest X-Ray
CXR remains an important tool for diagnosis of PTB in children who are sputum smear negative or who cannot produce sputum. The following abnormalities on CXR are suggestive of TB:
- Enlarged hilar lymph nodes and opacification in the lung tissue
- Miliary mottling in lung tissue
- Cavitation (tends to occur in older children)
- Pleural or pericardial effusion

The finding of marked abnormality on CXR in a child with no signs of respiratory distress (no fast breathing or chest in-drawing) is supportive of TB.

G. Investigations for Common forms of extrapulmonary TB in children
The investigations usually used to diagnose the common forms of extrapulmonary TB are shown below:
Table 8: Common forms of extrapulmonary TB in children

<table>
<thead>
<tr>
<th>Site</th>
<th>Practical approach to diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral lymph nodes (especially cervical)</td>
<td>Lymph node fine needle aspiration or biopsy</td>
</tr>
<tr>
<td>Miliary TB (e.g. disseminated)</td>
<td>Chest X-ray and lumbar puncture (to test for meningitis)</td>
</tr>
<tr>
<td>TB meningitis</td>
<td>Lumbar puncture (if not contraindicated)</td>
</tr>
<tr>
<td>Pleural effusion (older children and adolescents)</td>
<td>Chest X-ray, pleural tap for biochemical analysis (protein and glucose concentrations), cell count and culture</td>
</tr>
<tr>
<td>Abdominal TB (e.g. peritoneal)</td>
<td>Abdominal ultrasound and ascitic fluid analysis</td>
</tr>
<tr>
<td>Osteoarticular</td>
<td>X-ray, joint tap or synovial biopsy</td>
</tr>
<tr>
<td>Pericardial TB</td>
<td>Ultrasound and pericardial tap</td>
</tr>
</tbody>
</table>

H. HIV testing

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

Approach to TB diagnosis in HIV-uninfected child

TB suspected on basis of typical and persistent symptoms

Sputum:  
- Negative or not done  
- Smear-positive

Clinical Diagnosis
- Positive contact history
- Physical signs suggestive of PTB*
- CXR suggestive of PTB

If only one or none of the features are present

- If child sick, admit to hospital for further investigation
- Make a diagnosis of TB if two or more of these features are present

If child well, review after 2-4 weeks

*Treat for TB

*The clinical and CXR signs suggestive of TB are listed above  
(Source: pediatric desk guideline for diagnosis TB in children, 2010, IUATLD)
Presence of any one of the followings suggests the diagnosis of TB in a child:
- Radiological picture of miliary pattern
- Pathologic findings compatible with TB
- Culture positive
- Isolation of organism by AFB.

5.4 Standard Case Definitions and Treatment Classification of TB in Children

The standard case definitions of TB in children are similar to that of adults. Treatment classification of childhood TB is the same as adults: New,Previously treated and MDRTB cases.

5.5 TB Treatment in Children

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

Recommended treatment regimens

Anti-TB treatment is divided into two phases: an intensive phase and a continuation phase. During the intensive phase, TB in children should be treated with four drugs regimen (HRZE) for two months followed by two drug regiment (HR) for four months at the following dosages:

Table 9: Recommended doses of first-line anti-TB drugs for adults and children

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose (mg/kg body weight)</th>
<th>Recommended dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>10 (10-15)</td>
<td>300</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>15 (10-20)</td>
<td>600</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>35 (30-40)</td>
<td>–</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>20 (15–25)</td>
<td>–</td>
</tr>
</tbody>
</table>


All Anti-drugs should be administered daily and intermittent therapy is not recommended.

Streptomycin should not be used as part of first line treatment regimen for children with pulmonary tuberculosis or TB peripheral lymphadenitis because of lack of strong
evidence on the efficacy and taking into account of the risk of toxicity associated with the use of the drug. Also considering the problems associated with injection-based treatment and presence of more effective oral alternatives.

Pyridoxine is recommended for children who have severe malnutrition, HIV positive on ART.

In general, extra-pulmonary tuberculosis in children can be treated with the same regimens as pulmonary disease. Exceptions are: TB meningitis and osteo-articular TB.

Children with suspected or confirmed Tuberculous meningitis and osteo-articular TB should be treated with a four-drug regimen (HRZE) for 2 months, followed by a two-drug regimen (HR) for 10 months; the total duration of treatment being 12 months. The recommended treatment dosages are the same as those described for pulmonary tuberculosis.

**Treatment failure**
Most children with TB will start to show signs of improvement after 2 to 4 weeks of anti-TB treatment.

If assessment at 1-2 months of anti-TB treatment shows the following, consider treatment failure:

- No symptom resolution or symptoms getting worse
- Continued weight loss
- Smear-positive at 2 month follow-up sputum

Poor adherence is a common cause of “treatment failure”. If a child stops anti-TB treatment for less than 2 weeks in the intensive phase and less than 2 months in the continuation phase and becomes symptomatic, then restart treatment for new cases and refer to higher level.

Treatment failure is more common in HIV-infected children. It also suggests the possibility of MDR TB and needs careful assessment.

**Nationally Available Pediatric formulations**

**Pediatric FDC:**
- Rifampicin + Isoniazid(RH): 60mg + 30mg tab/dispersible
- Rifampicin + Isoniazid(RH): 60mg + 60mg tab/dispersible
- Rifampicin + Isoniazid(RH) + Pyrazinamide: 60mg + 30mg + 150mg tab/dispersible

**Pediatric drugs as loose form:**
- Ethambutol: 100mg tab

*Notes:*
1. Children receiving treatment must be weighed at least every month
2. Treatment doses should be adjusted as soon as a child changes weight bands
3. Check table strengths carefully, especially tables containing RH 60/30 and RH 60/60, to avoid toxicity.
4. Children weighing more than 30 kg should be treated according to the current adult treatment guidelines.
5. Children with TB should not be treated with intermittent regimens.
6. Streptomycin shouldn’t be used as part of the first line treatment regimen for children with susceptible TB.
7. Ethambutol is safe in children at a dose of 20 mg/kg (range 15–25 mg/kg) daily.
8. Because of difference in drug pharmacology between children and adults, the recommended dosage in the weight range of 20-30kg is different*.

**Table 10: Pediatric FDC Dosing Regimens for New and Retreatment**

**A. FDC dosing regimens for NEW CASES**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Intensive phase (2 months)</th>
<th>Continuation phase (4 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RHZ (60,30,150)</td>
<td>RHZE (150,75,400,275)</td>
</tr>
<tr>
<td>5 to 7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8 to 14</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>15 to 20</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>21 to 30*</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

**B. FDC dosing regimens for Retreatment Cases**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Intensive phase (3Months)</th>
<th>Continuation phase (5Months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RHZ (60,30,150)</td>
<td>RHZE (150,75,400,275)</td>
</tr>
<tr>
<td>5 to 7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8 to 14</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>15 to 20</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>21 to 30*</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>
*Remark:* Because of differences in drug pharmacology between children and adults, the recommended dosage in the weight range of 20-30kg is different.

**Corticosteroids**

Corticosteroids may be used for the management of some complicated forms of TB, e.g. TB meningitis, airway obstruction by TB lymph glands, and pericardial TB. The drug used is prednisone, in a dosage of 2 mg/kg daily, increased up to 4 mg/kg daily in the case of the most seriously ill children, with a maximum dosage of 60 mg/day for 4 weeks. The dose should then be gradually tapered over 1–2 weeks before stopping.

**Monitoring TB treatment in children**

Children, parents/caregivers, and other close family members should be educated about TB. The support of the child's parents and immediate family is vital to ensure a satisfactory outcome of treatment. DOT should be used for all children with tuberculosis. Even when drugs are given under DOT, tolerance of the medications must be monitored closely.

Each child should be assessed: two weeks after treatment initiation, at the end of the intensive phase and every two months until treatment completion. The assessment should include symptom assessment, assessment of treatment adherence, enquiry about any adverse events and weight measurement. Adherence should be assessed by reviewing the treatment card. A follow-up sputum sample for smear microscopy at 2 months after treatment initiation should be obtained for any child who was smear-positive at diagnosis. Follow-up CXRs are not routinely required in children, particularly as many children will have a slow radiological response to treatment. A child who is not responding to anti-TB treatment should be referred for further assessment and management.

**Adverse Reactions to TB Drugs in Children**

Adverse events are less common in children than in adults. The most common adverse reaction is the development of hepatotoxicity, which can be caused by Isoniazid, Rifampicin or Pyrazinamide. Serum liver enzyme levels should not be monitored routinely, as an increment of liver enzymes (<5 times normal values) is not an indication to stop treatment. However, the occurrence of liver tenderness, hepatomegaly, or jaundice should lead to investigation of serum liver enzyme levels and immediate interruption of all potentially hepatotoxic drugs.

Isoniazid may cause symptomatic pyridoxine deficiency, particularly in severely malnourished children. Supplemental pyridoxine (5-10 mg/day) is recommended in malnourished children.
5.6 Contact Screening and Management

Background and rationale: Young children living in close contact with a source case of smear-positive pulmonary TB are at particular risk of TB infection and disease. The risk of infection is greatest if the contact is close and prolonged. The risk of developing disease after infection is much greater for infants and young children under 5 years. If disease develops, it usually does so within 2 years of infection, but in infants the time can be as short as a few weeks. Isoniazid preventive therapy (IPT) for young children with infection who have not yet developed disease will greatly reduce the likelihood of developing TB during childhood.

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

IPT is recommended for all young children (<5 years) that are household contacts of a case with sputum smear-positive TB with no evidence of TB disease. Recommended treatment is isoniazid 10 mg/kg daily for 6 months. Follow-up should be carried out at least every one month until treatment is complete. Contacts with TB disease should be registered and treated. After a course of IPT, give one dose of BCG vaccine to children aged less than 2 years who have not already had BCG immunization.
Figure 2: Approach contact management in children

Child contacts of infectious MDR-TB cases
The chemoprophylaxis regimens that have been studied are Isoniazid and to a lesser extent Rifampicin. Since MDR-TB is resistant to both of these drugs, it is unlikely that use of these drugs to treat latent infection caused by resistant *M. tuberculosis* strain will prevent the development of active TB disease. Therefore, Close contacts of MDR-TB patients should receive careful clinical follow-up for a period of at least 2 years. If active disease develops, *prompt initiation* of treatment with a regimen designed to treat MDR-TB of the index case is recommended. At present, second-line drugs are not recommended for chemoprophylaxis for contacts of known MDR-TB patients.

Prevention of TB for a newborn
Once a pregnant woman has been on anti TB treatment for at least 2–3 weeks, she is generally no longer infectious. If a pregnant woman with TB has been on treatment for TB for several weeks before delivery, it is less likely that the baby will become infected. The risk is highest if a mother is diagnosed at the time of delivery or shortly thereafter. If a pregnant woman is found to have pulmonary TB shortly before delivery, then the baby, and if possible, the placenta, should be investigated for evidence of congenital TB infection and, if found, the baby should be treated.
If the newborn is asymptomatic he/she should receive 6 months of IPT, followed by BCG immunization. Breastfeeding can be safely continued during this period. An alternative policy is to give 3 months of IPT followed by TST. If the test is negative, IPT should be stopped and BCG vaccination given. If the test is positive, IPT should be continued for another 3 months followed by BCG vaccination.

5.7 Management of TB/HIV Co-Infection in Children

Incidence of tuberculosis in HIV-infected children is much higher compared to HIV negative children. The prevalence of HIV in TB-infected children ranges from 10% to 60%. Establishing the diagnosis of tuberculosis in HIV-infected children may be difficult because the manifestations of tuberculosis are similar to many HIV related infections and conditions like PCP pneumonia, lymphoid interstitial pneumonitis, viral and bacterial pneumonias. TB can coexist with lymphoid interstitial pneumonitis, broncheicctasis or any other lung conditions. As a result of this, there is risk of either under or over diagnosing tuberculosis.

In HIV infected children tuberculosis is often severe, progressive and likely to involve extra-pulmonary sites. The mortality rate for TB/HIV co-infected children is high particularly if there is evidence of advanced immune suppression. HIV counseling and testing should be offered to all children with diagnosis of tuberculosis, and all HIV-exposed and infected children should be screened for TB using a combination of targeted history, Tuberculin Skin Test (TST) if available and laboratory tests.

TB Screening in infants and children

**Symptom screen:** Children living with HIV who have any one of the following symptoms – poor weight gain\(^1\), fever, current cough or contact history with a TB case – may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, they should be offered IPT regardless of their age. Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB (see Annex 8).

Based on the recent available data WHO concluded IGRA are not recommended to screen children living with HIV for eligibility to receive IPT. Hence, do not use IGRA in Ethiopia for this purpose.

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\(^1\) Poor weight gain is defined as reported 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.
**Approach to TB diagnosis in HIV-infected child**

TB suspected on basis of typical and persistent symptoms

- **Sputum:**
  - Negative or not done ➔ **smear positive**
  - Consider contact history

- **Contact:**
  - smear negative or not known ➔ **smear positive**

- **Clinical Diagnosis:**
  - physical signs or CXR suggest
    - Not PTB#
    - **PTB**

---

# It can be difficult to clearly define what is “suggestive of PTB” on clinical or radiological findings in HIV-infected children because of clinical overlap between PTB and other forms of HIV-related lung disease.

# CXR abnormalities of PTB in HIV-infected child are similar to those in HIV-uninfected child.

(Source: pediatric desk guideline for diagnosis TB in children, 2010, IUATLD)

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**Figure 3: Approach to TB diagnosis in HIV-infected child**

**Treatment of TB/HIV Co-infection in children**

Four areas of intervention need emphasis in the management of TB/HIV Co-infection:

- **i. Anti-TB Medication**
  The principle of treatment for children with TB/HIV co-infection is similar to HIV uninfected children. Most HIV infected children respond well to the standardized anti-TB regimen.

- **ii. Cotrimoxazole Preventive Therapy**
  All children with tuberculosis have to be provided with prophylactic cotrimoxazole. It prolongs survival and decreases the incidence of respiratory tract illnesses, diarrheal illnesses and hospital admissions.

- **iii. Antiretroviral Therapy**
In HIV-infected infants and children co-infected with tuberculosis, initiation of anti-TB regimen is the priority. Start ART as soon as tolerated in the first 8 weeks of TB therapy. Children on ART and anti-TB medication need to be closely monitored as there are clinically significant drug-drug interactions between Rifampicin and some ARV drugs (mainly NNRTIs and PIs). These drugs have similar routes of metabolism and co-administration results in sub-therapeutic levels of antiretroviral drugs. Rifampicin can decrease serum level of protease inhibitors by as much as 80% or more, and NNRTI by between 20% and 60%. In addition to this there is significant overlap of adverse reaction of anti-TB medications and ARVs. Close monitoring for possible toxicity has to be carried out on regular basis.

Table 11: Shared toxicities of Antiretroviral drugs and Anti-TB medications

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Antituberculous therapy</th>
<th>Antiretroviral therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral neuropathy</td>
<td>Isoniazid</td>
<td>Stavudine, Didanosine</td>
</tr>
<tr>
<td>Rash</td>
<td>Rifampcin, Isoniazid</td>
<td>NNRTI</td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>Pyrazinamide</td>
<td>Stavudine, Zidovudine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Protease inhibitors</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>Rifampcin, Isoniazid</td>
<td>NNRTI</td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide</td>
<td>Protease inhibitors</td>
</tr>
</tbody>
</table>

Table 12: ART regimen choices in a child who has started TB therapy

<table>
<thead>
<tr>
<th>Regimen of 3NRTI:</th>
<th>AZT+3TC+ABC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D4t+3TC+ABC</td>
</tr>
<tr>
<td>Alternative firstline ART regimen:</td>
<td></td>
</tr>
<tr>
<td>Children over 3 years of age or &gt;10 Kg</td>
<td>AZT+3TC+EFV</td>
</tr>
<tr>
<td>Regimen of 2NRTI plus EFV</td>
<td>d4T+3TC+EFV</td>
</tr>
<tr>
<td>Children under 3 Years of age or &lt;10 Kg</td>
<td>AZT+3TC+ NVP</td>
</tr>
<tr>
<td>Regimen of 2NRTI plus NVP</td>
<td>d4T+3TC+ NVP</td>
</tr>
</tbody>
</table>


Notes:
- NVP should be started at full dosage in children receiving rifampicin. A lower lead-in dose of NVP should be avoided because this results in sub-therapeutic NVP levels.
- NVP be used at the maximum of 200mg/m2/dose
- The effects of rifampicin on ART metabolism lasts for 2 weeks after rifampicin is stopped.
**HIV-infected infants and children who develop TB while on ART**

For all HIV-infected children, anti-TB therapy should be started immediately upon the diagnosis of TB; ART should continue.

Make adjustments to ART regimens as needed to decrease the potential for toxicities and drug interactions:

- If on a regimen of 2 NRTIs + NVP, substitute EFV for NVP if child is 3 years of age and above.
- If on a regimen of 2 NRTIs + NVP and substitution with EFV is not possible, ensure NVP is dosed at the maximum dose of 200 mg/m² per dose twice daily.
- If on a regimen of LPV/r, consider adding RTV to a 1:1 ratio of LPV: RTV to achieve the full therapeutic dose of LPV.

**INH prophylaxis in infants and children (IPT)**

TB risk assessment and INH prophylaxis (IPT) should be part of management of TB/HIV co-infection. Risk assessment should focus on regular evaluation of patients based on targeted history, including contact history with a known TB patient. IPT should be administered after excluding active TB.

- All HIV-infected infants and children exposed to TB through household contacts, but with no evidence of active disease, should begin IPT.
- Children living with HIV (older than 12 months of age and including those previously treated for TB), who are unlikely to have active TB, and are not known to be exposed to TB, should receive 6 months of IPT as part of a comprehensive package of HIV care.
- In children who are living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive a six months of IPT if the evaluation shows no TB disease. If they are unlikely to have active TB and have had no known contact history with a TB case, IPT should not be given.
- All children living with HIV who have successfully completed treatment for TB disease should receive INH for an additional six months.

**BCG Vaccination for HIV-exposed infants**

BCG vaccination is contraindicated in HIV infected infants. Recent evidence shows that HIV infected infants who were routinely vaccinated with BCG at birth, when asymptomatic, and who later developed AIDS, are at high risk of developing disseminated BCG disease.

The implementation of selective BCG vaccination strategies may not be feasible in most of the TB high endemic settings including Ethiopia. However, BCG vaccination strategies in
infants born to HIV-infected women need strategies to reduce the risk of vertical HIV transmission and disseminated BCG disease in infants. Current national recommendation for BCG immunization of infants continues until all programs for implementing selective deferral of HIV exposed infants are in place.

**Who should receive IPT** due to limited resources and high national TB prevalence, IPT is only given to the most vulnerable children, those at highest risk to develop TB following *M. tuberculosis* exposure/infection. The two groups of children who qualify to benefit most from initiation of IPT are

- The very young (infants and children <5yrs of age)
- The HIV-infected children (irrespective of their age)

It is mandatory to rule out active disease (TB) prior to consideration of IPT. Once started with IPT the child must be evaluated every month. If Tuberculosis is suspected at subsequent follow up visits rescreening for active TB disease should be carried out. INH should not be given to children who have contraindications to INH or suspected to have active TB.

INH dosage and follow up schedule for infants and children with HIV **is the same as HIV negative under five children.** It is desirable that Vitamin B6 be supplied with INH at a dose of 25 mg daily.

### 5.8 Multi Drug Resistant (MDR) TB in children

- Incidence of MDR-TB and primary drug resistance TB has been shown to be the same for children as for adults
- Since MDR-TB is life threatening, no anti tuberculosis drugs are absolutely contraindicated in children including fluoroquinolones.
- Children who have received treatment for DR-TB generally tolerate the second-line drugs well.
- The MDR-TB treatment regimen and duration of therapy in children is similar with adults.
- A child with household contact of MDR-TB should be evaluated actively and followed closely.

Drug-resistant TB should be suspected if any of the features below are present:

- **Known to have household contact with a person known or suspected to have MDR-TB.**
- **Experiencing failure to first line treatment**
- **Re-treatment TB patients [e.g., return after default, relapse]**

**Remark:** Every effort should be made to bacteriologically confirm MDR-TB in these children. (For additional information see national MDR-TB guideline)
6 TB/HIV COLLABORATIVE ACTIVITIES

The HIV/AIDS pandemic presents a major challenge to the control of TB in Ethiopia. The dual epidemic has a number of impacts on the health sector. It increases TB and HIV burden, demand for care and worsen the situation of the already overstretched health care delivery system in the country. The expanded scope of the strategy for tuberculosis control in Ethiopia comprises interventions against tuberculosis and HIV. Therefore, the National Tuberculosis and HIV Prevention and Control programs must strengthen the health system’s ability to respond to the health care needs of TB/HIV patients’ in the country.

Impact of HIV on TB Prevention and Control
HIV increases susceptibility to infection with M. tuberculosis, the risk of progression to TB disease, and the incidence and prevalence of TB. The life time risk of HIV positive individuals to develop TB is 20-37 times greater than HIV negative individuals. It also increases the likelihood of re-infections and relapses of TB. In a population where TB/HIV is common, health services struggle to cope with the large and rising number of TB. HIV/AIDS has a number of impacts on TB patients and the control program; primarily, requiring more resources for diagnosis and treatments; overstretching the human resources. Moreover, it has the following consequences:

- The high stigma attached to TB/HIV hinders health seeking in TB patients.
- The relatively high proportion of smear-negative PTB and EPTB in HIV infected individuals creates a challenge in the diagnosis of TB, requiring improved diagnostic capacity.
- Poor treatment outcome (failure, recurrence, default) and high morbidity and mortality in TB patient co-infected with HIV.
- Increased transmission of TB including drug-resistant strains among HIV-infected patients and health care workers in health facilities and other congregate settings.
- High rates of drug-drug interactions and side effects.

Impact of Tuberculosis on HIV
In an individual infected with HIV, the presence of TB affects in many ways.

- TB increases HIV replication, which leads to increased viral load. This results in more rapid progression of HIV disease including development.
- TB increases occurrence of other OIs.
- The management of TB and HIV co-infected individual is challenging because of high pill burden, increased adverse effects, drug-drug interactions and immune reconstitution inflammatory Syndrome (IRIS).

6.1 Rationale and Objectives of TB/HIV Collaboration

Rationale
Tuberculosis and HIV Prevention and Control programs share mutual challenge of high impact of TB on HIV and high impact of HIV on TB. Therefore, two programs must
collaborate to provide better service for the co-infected patients. Thus, TB and HIV collaboration is justified because of the shared benefit from the implementation of TB/HIV collaborative activities and efficient utilization of resources allocated by both programs.

Objectives
General objective:
- To reduce the burden of TB/HIV among populations affected by both diseases.
Specific objectives are to:
- Strengthen the mechanisms for collaboration
- Reduce the burden of TB among HIV-positives
- Reduce the burden of HIV among TB patients

6.2 Nationally Recommended TB/HIV Collaborative Activities
A. Strengthen the Mechanisms for integrated TB and HIV services delivery
   - Strengthen the coordination mechanism for integrated TB/HIV services at all levels
   - Conduct Surveillance to determine HIV burden among TB patients and TB burden among HIV patients
   - Carry out joint TB/HIV planning for integrated TB and HIV services delivery
   - Conduct monitoring and evaluation of collaborative TB/HIV activities
B. The three Is for HIV/TB and earlier initiation of ART to reduce the burden of TB among HIV positive individuals
   - Intensify TB case finding and ensure quality TB treatment
   - Initiate TB prevention with earlier initiation ART and Isoniazid preventive therapy (IPT)
   - Ensure Tuberculosis infection control in health care and congregate settings
C. Decrease the burden of HIV among TB patients
   - Provide HIV testing and counselling to presumptive and confirmed TB patients
   - Introduce HIV prevention interventions for presumptive and confirmed TB patients
   - Provide cotrimoxazole preventive therapy for HIV positive TB patients
   - Ensure HIV/AIDS prevention, treatment and care for HIV positive TB patients
   - Provide antiretroviral therapy for HIV positives TB patients

6.3 TB/HIV Collaboration at Program Management Level

A. Strengthen the Mechanisms for integrated TB and HIV services delivery

I. Strengthen the coordination mechanism for integrated TB/HIV services at all levels

To strengthen the TB/HIV collaborative activities, coordinating mechanism at all program management levels (Federal, Regional, Zonal/Sub-City, Woreda and Health Facility) should be strengthened. The role and responsibility at each level will follow their respective
structural arrangement or level. Developing and implementing national policies and strategies and implementation guidelines, ensuring sufficient resources are mobilized for TB/HIV collaborative activities, conducting supportive supervision and capacity building of health workers, conducting surveillance and operational research activities will be among the key responsibilities of the federal, regional and district levels.

Similarly health facilities are responsible to ensure the implementation of integrated TB/HIV collaborative services as per the national guidelines, strengthen referral linkages between the TB and HIV services and compile and use TB/HIV data for improvement of the service.

II. Determine the prevalence of HIV among TB patients and TB prevalence among PLHIV

Surveillance of HIV should be conducted among TB patients and surveillance of active TB disease among PLHIV in order to inform program planning and implementation.

HIV surveillance among TB patients improves TB/HIV Programmatic decisions. Since Ethiopia has a generalized HIV epidemic, routine HIV testing and counseling for all TB patients should form the basis of surveillance. However, data from routine HIV testing and counseling of TB patients should be complemented by periodic survey. HIV testing should be considered as an integral part of TB prevalence and anti TB drug resistance surveys.

III. Carry out joint TB/HIV planning for integrated TB and HIV services delivery

A joint TB/HIV plan should clearly define the roles and responsibility of TB and HIV programs in implementing, monitoring and evaluating collaborative TB/HIV activities at all levels of the health system.

IV. Conduct monitoring and evaluation of collaborative TB/HIV activities

TB/HIV collaborative activities should be recorded and reported using the standardized tools.

B. Reduce the burden of TB among HIV positive individuals (The three I’s for HIV/TB and earlier initiation of ART)

I. Intensify TB case finding and ensure quality TB treatment

Tuberculosis case finding should be intensified in all HIV testing and counseling services for HIV positive clients by using a set of simple questions for early identification of TB suspects. HIV positive clients coming through HCT services should be informed the advantages of being screened for TB. Once informed the risk of developing active TB, they should undergo screening for TB (see Annex 7).
Table 13: TB screening questions for HIV Positive adults and adolescents

<table>
<thead>
<tr>
<th>Questions to be asked at each visit</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you have cough currently?</td>
<td>Yes</td>
</tr>
<tr>
<td>(current cough = within the last 24 hours)</td>
<td>No</td>
</tr>
<tr>
<td>2. Do you have fever?</td>
<td>No</td>
</tr>
<tr>
<td>3. Do you have weight loss?</td>
<td>No</td>
</tr>
<tr>
<td>4. Do you have night sweats?</td>
<td>No</td>
</tr>
</tbody>
</table>

**Interpretation of result:**
- If YES to any one of the symptoms, then patient is a TB suspect (screened positive) and should be evaluated for TB.
- If NO to all four symptoms, patient is screened negative and should be provided with IPT if patient has no any contraindication for INH.

All HIV positive clients with active TB should be treated with standard anti TB treatment regimen.

II. Initiate TB prevention with Isoniazid Preventive Therapy and early initiation of ART

_Isoniazid Preventive Therapy (IPT)_ is the use of Isoniazid to sterilize latent TB infection. Thus, isoniazid is given to individuals with latent infection with *Mycobacterium tuberculosis* in order to prevent progression to active disease. Screening for exclusion of active TB in HIV infected persons, is the single most important step that should precede the decision to initiate IPT.

So far, evidences strongly favor the benefit of IPT in eligible individuals. Studies have shown that providing IPT to people living with HIV does not increase the risk of developing INH-resistant TB. Therefore, concerns regarding the development of INH resistance should not be a barrier to providing IPT.

The dose of INH is 300mg/day for adults and 10mg/kg for children. The duration of IPT is for six months, and it is desirable to provide vitamin B6 (25mg/day) to prevent INH-induced peripheral neuropathy.
Table 14: Dosage of INH for Children according to weight band

<table>
<thead>
<tr>
<th>Weight Ranges (kg)</th>
<th>Number of 100 mg tablets of INH per dose</th>
<th>Dose given (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5</td>
<td>½ tablet</td>
<td>50</td>
</tr>
<tr>
<td>5.1-9.9</td>
<td>1 tablet</td>
<td>100</td>
</tr>
<tr>
<td>10-13.9</td>
<td>1 ½ tablet or ½ adult tablet</td>
<td>150</td>
</tr>
<tr>
<td>14 -19.9</td>
<td>2 tablets</td>
<td>200</td>
</tr>
<tr>
<td>20 -24.9</td>
<td>2 ½ tablets</td>
<td>250</td>
</tr>
<tr>
<td>&gt;25</td>
<td>3 tablets or one adult tablet</td>
<td>300</td>
</tr>
</tbody>
</table>

Contraindications of IPT

Individuals with any one or more of the following conditions should not receive IPT.

- Symptoms compatible with tuberculosis, even if the diagnosis of TB cannot be confirmed.
- Active hepatitis (chronic or acute)
- Regular and heavy alcohol consumptions
- Prior allergy or intolerance to isoniazid
- Symptoms of peripheral neuropathy

Past history of TB and current pregnancy should not be contraindications for starting of IPT.

Isoniazid drug interactions

Isoniazid may interact with other drugs. The patient who is on IPT and anyone of the following drugs should be referred to higher level health facility for monitoring.

- Phenytoin, warfarin, and carbamazepine (their serum levels may increase).
- Ketoconazole and diazepam (their serum levels may decrease).
- Procainamide and chlorpromazine (the half-life of isoniazid can be increased)

Placement of IPT clients

The most frequent entry point to care and treatment for HIV-infected persons is HIV Counseling and Testing (HCT) services. After active TB is ruled out IPT should be part of a comprehensive care for HIV positive individuals. It should be initiated and continued at the HIV care/ART clinic. The particulars of the patient should be documented in the ART and Pre-ART register for HIV positive clients without active TB who receive IPT.

Follow up of patients on IPT

Patients should be given one-month supply of Isoniazid and assessed at each follow-up visit to:

- Evaluate adherence to treatment and to educate client
- Evaluate for drug toxicity
• Evaluate for signs and symptoms of active tuberculosis or other OIs and eligibility for ART
• Stop IPT if active TB is diagnosed and to immediately start anti-TB.

III. Ensure Tuberculosis infection control in health care facilities and congregate settings
• Program managers at each level should provide managerial direction for the implementation of TB IC in health care facilities and congregate settings.
• Each Health care and congregate settings should have a TB IC plan included in general infection control plan of the facility to reduce transmission of TB in health care and congregate settings.
• Health care workers, community health workers and care providers living with HIV should be provided with ART and IPT if eligible. Furthermore, opportunity to reduce the risk of TB transmission to this high-risk group must be offered.

C. Reduce the burden of HIV in patients with presumptive and confirmed TB

I. Provide HIV testing and counselling to presumptive and confirmed TB patients

HIV testing is an entry point for HIV care and treatment services including ART and this apply equally to TB patients. Significant proportions of TB patients are co-infected with HIV. Among TB patients who are also HIV-infected, other Opportunistic Infections (OIs) are significant causes of morbidity and mortality even with a successful treatment of TB. Hence, HIV testing and counseling should be routinely offered to all TB patients.

II. Introduce HIV prevention interventions for presumptive and confirmed TB patients

All clients attending TB clinics should be screened for sexually transmitted infections using a set of simple questions. Those with symptoms of sexually transmitted infections should be treated or referred to the treatment providers. (Refer to the National Guideline for the Treatment of STI Using the Syndromic Approach). Condoms should be made available in TB clinics.

III. Provide cotrimoxazole preventive therapy for HIV positive TB patients

Cotrimoxazole is a safe and broad-spectrum antibiotic acting on broad range of bacterial, fungal and protozoal infections that cause major morbidity and mortality in adults and children living with HIV. CPT has an impact in reducing morbidity and mortality in TB/HIV co-infected people. Therefore CPT is recommended to all TB/HIV co-infected patients regardless of the CD4 Count.
Cotrimoxazole could be dispensed at the HIV clinic and TB clinic (for the duration of TB treatment). All clients receiving CPT should be registered on Unit TB register, Pre ART/ART Register and should be monitored monthly (Refer to the National Co-trimoxazole Prophylaxis Guideline for details on Co-trimoxazole Prophylaxis).

IV. Ensure HIV/AIDS prevention, treatment and care for HIV positive TB patients

Referral linkages between TB and HIV services must be strengthened to provide comprehensive HIV prevention services for TB patients and their families. Tuberculosis control should implement procedures for prevention of occupational and nosocomial exposure to HIV infection in their services. Health units should be equipped with protective materials and routinely follow standard precautions to prevent HIV transmission in the health care settings. Linkage should be ensured for pregnant and non-pregnant HIV positive clients to access services for prevention of mother to child transmission.

TB clinics should establish linkage with HIV services to provide the continuum of care and support for HIV positives during and after completion of anti-TB treatment.

V. Provide antiretroviral therapy for HIV positive TB patients

ART should be offered to HIV positive TB patients eligible for ART according to the national guidelines for ART (See table 6.3).

6.4 Diagnosis of TB in PLHIV

Diagnosis of TB is challenging in HIV positive individuals especially when the stage of disease is advanced. Standard TB diagnostic approaches and clinical algorithms should be followed to guide the diagnosis of TB in PLHIV (See Annex 3 & 4).

Clinical Assessment: Thorough clinical evaluation of the patient including exclusion of other OIs should be done. For patients with respiratory symptoms in whom tuberculosis is less likely and who are treated empirically for bacterial pneumonia or Pneumocystis pneumonia (PCP), clinical response should not automatically exclude the diagnosis of tuberculosis. Acute bacterial pneumonia or PCP may occur in patients with underlying tuberculosis and patients should, therefore, be re-evaluated for tuberculosis, particularly if respiratory symptoms persist after treatment.

AFB microscopy: three sputum specimens should be taken and examined for AFB. One of the specimens should be early-morning sputum produced after an overnight sleep. One positive AFB smear will be sufficient to classify a patient as a smear-positive case if the patient is HIV-infected or if there is strong clinical suspicion of HIV infection.

Chest radiography: Chest X-ray plays a significant role in shortening delays in diagnosis of TB in PLHIV. It can also be an important entry point to diagnose non-tubercular chest
diseases, which are common among HIV positives. Suggestive radiological findings need sound clinical judgment to put a seriously ill patient with negative sputum smear results on anti-TB treatment.

**Sputum culture:** Sputum culture is the gold standard for the diagnosis of tuberculosis. In patients with negative sputum smears, sputum culture should be encouraged as part of the diagnostic procedure for people living with HIV.

**Molecular Tests:** New tools such as LPA and geneXpert are useful rapid tests to diagnose TB in PLHIV. These tests also offer the opportunity to provide DST information to identify potential/suspected MDR-TB/HIV confected patients.

**Diagnosis of extra-pulmonary tuberculosis in HIV positive**
Extra-pulmonary tuberculosis is more HIV-related than pulmonary tuberculosis. The accurate diagnosis of extrapulmonary tuberculosis is complex and difficult, particularly in peripheral health facilities with limited diagnostic capacity. Therefore, it is important for health care workers to have high-index of suspicion and critically evaluate using clinical algorithms (see Annex 2 for enlarged Lymph nodes). For other sites, do organ specific investigations.

**Antibiotic trial:** Antibiotic trial has a role to treat concomitant bacterial infection PLHIV with cough or serious illness. However, antibiotic trial is not helpful in the diagnosis of TB in HIV positives. Broad-spectrum antibiotics to cover for typical and atypical causes of pneumonia, should be used to reduce the time delay for tuberculosis diagnosis. In such circumstances, fluoroquinolones should be avoided, as they may cause delay in the diagnosis of tuberculosis.

**6.5 Management of TB/HIV Co-infections**
The first priority for HIV-positive TB patients is to initiate TB treatment, followed by cotrimoxazole and ART.

**If an HIV positive patient not on ART develops TB disease**
The following group of HIV/TB co-infected patients can safely be started on TB treatment at any health facility:
- HIV infected smear positive pulmonary TB patients who are not yet on ART;
- Patients diagnosed of smear negative pulmonary TB or extra-pulmonary TB at the hospital and referred to lower level health facilities for TB treatment and
- Any patient who has previously defaulted from TB treatment, anti-TB can be started after investigating and solving the adherence problem promptly.

The following points should be considered sequentially to start anti-TB treatment:
- Determination of TB disease site and type of patient/Case definition (based on previous TB treatment) (See TB disease classification)
- Starting anti-TB treatment based on previous treatment history
  - New patient regimen: same as HIV negative individuals (refer TB treatment section)
- Retreatment regimen: same as HIV negative individuals (refer TB treatment section)

**If an HIV positive patient on ART develops TB disease**
If the patient is diagnosed to have TB while already on ART, urgent consultation or referral to an experienced clinician (preferably the one who started the ART) is needed to decide on TB-ART co-treatment plan. The ART should not be stopped. Anti-TB drugs can interact with ARV drugs, therefore the clinician need to decide whether it is necessary to adjust the treatment.

Adjustment of the ART should be made based on the ART regimen the patient is on as follows:
- A change to Efavirenz based regimen is recommended for patients on Nevirapine whenever possible
- If Efavirenz based regimen is not possible (e.g. first trimester pregnancy), Nevirapine can be continued with close clinical & laboratory monitoring.

**Care for TB patient who is found to be HIV positive**

*Patient evaluation and linkage for HIV Care services:* As soon as HIV is identified in a TB patient, the patient should be enrolled to HIV chronic care. The HIV care can be delivered at the TB clinic for the duration of TB treatment or the patient may be referred to the HIV Chronic Care/ART clinic. In the HIV clinic appropriate clinical, psychosocial & laboratory evaluations should be done as per the national guidelines for ART as soon as possible so that the patient can get other services besides the TB treatment. These evaluations include clinical evaluations to look for additional OIs, & laboratory investigations including complete blood count, chemistry tests & CD4 count tests. Patients should be initiated on Cotrimoxazole preventive therapy as soon as possible.

*Decide when to start ART in relation to TB treatment:* The decision to initiate ART to TB patients must be made by a trained clinician. However, the health workers at the first-level health facility need to decide whether and when to consult with or refer the patient to an experienced clinician. The guidelines for when and what ART regimen to start for TB patients found to be HIV positive is described below.
<table>
<thead>
<tr>
<th>CD4 count</th>
<th>Recommendation</th>
<th>Preferred ARV regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200/mm³</td>
<td>• Start TB treatment.</td>
<td>• Start EFV containing regimen(^2) However, if drugs are unavailable or there are problems with EFV (adverse effects with intolerance and risk of pregnancy) use triple nucleoside regimen with caution.</td>
</tr>
<tr>
<td></td>
<td>• Start ART as soon as TB treatment is tolerated (usually between 2-8 weeks of TB treatment)(^1)</td>
<td>• If patient develops ABC hypersensitivity continue NVP but monitor liver function every month(^3).</td>
</tr>
<tr>
<td>200-350/mm³</td>
<td>• Start TB treatment.</td>
<td>• Start EFV containing regimen</td>
</tr>
<tr>
<td></td>
<td>• Start ART as soon as TB treatment is tolerated (within 8 weeks of TB treatment)(^4)</td>
<td>• If a non-pregnant woman has CD4 of &gt;250 use EFV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• In pregnant women with CD4 &gt;250 use triple NRTI containing ABC/3TC/ZDV</td>
</tr>
<tr>
<td>&gt;350/mm³</td>
<td>• Start TB treatment.</td>
<td>• Start EFV containing regimen</td>
</tr>
<tr>
<td></td>
<td>• Defer ART</td>
<td>• Re-assess eligibility for ART at 24 weeks clinically and immunologically, in the course of TB-treatment, at completion of TB treatment, or as indicated.</td>
</tr>
<tr>
<td>CD4 not available</td>
<td>• Start TB treatment.</td>
<td>• Start EFV containing regimen (unless the continuation phase is EH)</td>
</tr>
<tr>
<td></td>
<td>• Start ART after 2-8 weeks TB treatment if patient has severe disease and/or other clinical indicators of advanced immune deficiency</td>
<td>• If a non-pregnant woman has CD4 of &gt;250 use EFV</td>
</tr>
<tr>
<td></td>
<td>• Start ART after completion of intensive phase when patient is not seriously ill or other signs of advanced immune deficiency are absent</td>
<td>• In pregnant women with CD4 &gt;250 use triple NRTI containing ABC/3TC/ZDV</td>
</tr>
</tbody>
</table>

\(^1\) HIV positive TB patients with profound immunosuppression (CD4 counts less than 50 cells/mm\(^3\)) should receive ART immediately within the first 2 weeks of initiating TB treatment. Otherwise, timing of ART initiation should be up to clinical judgment based on other signs of immunodeficiency indicating progression of HIV disease. For TB patients in WHO clinical Stage IV, ART should be started as soon as TB treatment is tolerated irrespective of CD4 count.

\(^2\) EFV containing regimens include d4T/3TC/EFV or ZDV/3TC/EFV.

\(^3\) NVP (200 mg daily for 2 weeks followed by 200 mg twice daily) may be used in place of EFV in absence of other options. NVP containing regimens include: d4T/3TC/NVP or ZDV/3TC/NVP.

\(^4\) Since the current TB treatment regimen contains Rifampicin throughout the treatment duration, there is no need to wait until the completion of intensive phase to start ART.

\(^5\) Start ART if non-TB Stage IV conditions are present.
**Immune Reconstitution Inflammatory Syndrome (IRIS):**

Immune reconstitution inflammatory syndrome (IRIS) is a condition seen in some cases of AIDS or immunosuppression, in which the immune system begins to recover, but responds to a previously acquired opportunistic infection with an overwhelming inflammatory response that paradoxically makes the symptoms of infection worse.

If the CD4 count rapidly increases (due to effective treatment of HIV, or removal of other causes of immunosuppression), a sudden increase in the inflammatory response produces nonspecific symptoms such as fever, and in some cases a worsening of damage to the infected tissue. There are two common IRIS scenarios. The first is the “unmasking” of an occult opportunistic infection. The second is the “paradoxical” symptomatic relapse of a prior infection despite microbiologic treatment success. Often in paradoxical IRIS, microbiologic cultures are sterile. In either scenario, there is hypothesized reconstitution of antigen-specific T cell-mediated immunity with activation of the immune system following HIV therapy against persisting antigen, whether present as intact organisms, dead organisms, or debris.

Though these symptoms can be dangerous, they also indicate that the body may now have a better chance to defeat the infection. The best treatment for this condition is unknown. In paradoxical IRIS reactions, the events will usually spontaneously get better with time without any additional therapy. In unmasking IRIS, the most common treatment is to administer an antibiotic, antiviral or anti-fungal drugs against the infectious organism. In some severe cases anti-inflammatory medications, such as corticosteroids are needed to suppress inflammation until the infection has been eliminated. Infections most commonly associated with IRIS include cytomegalovirus, herpes zoster, Mycobacterium avium complex (MAC), Pneumocystis pneumonia, and tuberculosis. AIDS patients are more at risk for IRIS if they are starting HAART for the first time, or if they have recently been treated for an opportunistic infection.
7. DRUG-RESISTANT TUBERCULOSIS

7.1 Basics of Drug Resistant Tuberculosis

Drug-resistant TB is a man-made problem, largely being the consequence of human error as a result of individual or combination of factors related to management of drug supply, patient management, prescription of chemotherapy, and patient adherence. Poor infection control practice also has been identified as a major contributing factor for the spread of DR-TB. DR-TB, like drug susceptible TB, is transmitted through inhalation of infected droplet nuclei, and clinical manifestations are also similar. More recently the emergence of Extensively Drug-Resistant TB (XDR-TB) has added to the complexity of TB care and treatment.

The diagnosis of DR TB is made only by laboratories performing DST. Treatment of MDR-TB is more complicated and longer than treatment of drug susceptible TB. It is important to treat MDR-TB patients both to prevent morbidity, mortality and to limit the spread of drug-resistant TB in the community.

This chapter is intended to serve as a brief overview of the MDRTB diagnosis and treatment in Ethiopia. For detailed information and guidance refer to recent the national programmatic Management of drug resistant Tuberculosis.

7.2 Case Finding Strategies

Risk factors for MDR-TB

Routine testing of mycobacterial strain for DR-TB by culture and DST from every patient is not recommended and cost-effective. Culture and DST should therefore be used selectively for patients at risk of DR-TB based on a careful history. Specific elements of the history that suggest an increased risk for drug resistance are described below:

- Previous exposure to Anti-TB treatment
- Exposure to a known MDR-TB case
- History of using poor or unknown quality TB drugs
- Treatment in poorly-performing control program
- Co-morbid conditions associated with mal-absorption
- HIV/AIDS

Case Definition & Classification of DR-TB

i) Case definitions for DR-TB are used for the following reasons:
   - To allow proper patient registration and epidemiological notification;
   - To facilitate case allocation to appropriate treatment categories;
   - To facilitate case evaluation according to site, bacteriology and treatment history;
   - To evaluate program performance through cohort analyses.

ii) Case definitions:
• **Mono-resistance**: Resistance to only one first line anti-TB drugs.

• **Poly-resistance**: Resistance to more than one first line anti-TB drugs, but not to both isoniazid and rifampicin.

• **Multidrug-resistance (MDR)**: Resistance to at least isoniazid and rifampicin.

• **Extensive drug-resistance (XDR)**: Resistance to isoniazid and rifampicin (i.e. MDR) as well as any fluoroquinolone, and any of the second line injectable Anti TB drugs (capreomycin, kanamycin, and amikacin).

**Classification based on treatment history**

*Classification based on History of previous TB treatment*: allows categorization of M(X) DR-TB patients into three categories. These categories are essential for epidemiological monitoring of the M(X) DR-TB epidemic and help to identify patients that may be at risk. M(X) DR-TB patient categories are as follows:

**New**: A patient who has received no or less than one month of antituberculosis treatment.

**Previously treated with first-line drugs only**: a patient who has been treated for one month or more for TB with only first-line TB drugs.

**Previously treated with second-line drugs**: a patient who has been treated for one month or more for TB with one or more second-line drugs, with or without first-line TB drugs.

*Classification based on site of disease*: is where the used to classify cases according site of disease as pulmonary or extra-pulmonary form:

**Pulmonary M(X) DR-TB** refers to disease involving the lung parenchyma.

**Extra-pulmonary M(X) DR-TB** refers to organs other than the lungs.

*N.B.*: A patient with both pulmonary and extra-pulmonary M(X) DR-TB constitutes a case of pulmonary M(X) DR-TB.

**Procedures for suspect identification, evaluation and referral**

In Ethiopian context, DST is targeted for selected high risk groups who are at increased risk of developing/acquiring drug resistant TB.

<table>
<thead>
<tr>
<th><strong>MDR-TB suspects:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Treatment Failure of previously treated cases</td>
</tr>
<tr>
<td>• Symptomatic close contacts of confirmed MDR-TB cases</td>
</tr>
<tr>
<td>• Symptomatic individuals from known high risk groups (Ex: HCWs)</td>
</tr>
<tr>
<td>• Previously treated cases (treatment failure of new cases, return after relapse, return after default)</td>
</tr>
<tr>
<td>• Previously treated cases who remain smear positive at the end of intensive phase</td>
</tr>
<tr>
<td>• New cases( smear +ve &amp; -ve) who remain smear positive at the end of third month</td>
</tr>
<tr>
<td>• Other retreatment cases: defaulted patients coming with smear negative TB, EPTB, or previously treated patients with unknown treatment outcome, SS+ve interrupters who took treatment for more than 8 weeks…</td>
</tr>
</tbody>
</table>
Remark: Previously treated TB patients may have had DST results in the past that may no longer reflect the current resistant pattern they have; therefore, DST should be repeated for patients whose last DST dated older than one month at the time of MDR-TB enrolment.

Suspect identification and referral Procedure:

- Identify TB patients meeting the above criteria for suspect
- Educate the patient on basics of DR-TB, its transmission and need for contact investigation
- Inform about importance of sputum culture and DST for confirmation of the diagnosis
- Arrange sputum sample transport mechanism to the designated laboratory like with courier system
- Treat patient as per the national TBL guideline till result is ready and teach on Infection control measures at household level
- Collect the result of culture & DST and Decide on the subsequent management
- Facilitate early referral of cases with confirmed DR-TB to the designated MDRTB treatment initiating center.

Contact Tracing and Management

Opportunities to halt the spread of drug resistant mycobacterium in communities and to treat DR-TB are often missed. Therefore, all cases from the risk group and confirmed cases of DR-Tuberculosis should be traced for their close contact.

Active contact tracing

In the case of M(X)DR-TB in Ethiopia, all close contacts of confirmed M(X) DR TB cases must be actively traced with emphasis given to:

- Children under five years
- HIV positive patients
- All symptomatic close contacts
- Individuals with comorbid conditions

Chemoprophylaxis of contacts of M(X)DR-TB index cases

So far, the only chemoprophylaxis regimens studied extensively are isoniazid and, to a lesser extent, rifampicin. M(X)DR-TB by definition is resistant to both of these drugs; hence, the use of these drugs to treat latent infection caused by an M(X)DR-TB strain will not prevent the development of active TB disease. On the other hand, On the basis of the currently available evidence, it is not recommend to use second-line drugs for chemoprophylaxis in M(X)DR-TB contacts.
Close contacts of M(X)DR-TB patients should have careful clinical follow-up for a period of one to two years. If active disease is suspected, prompt culture and DST is indicated. Based on the DST result, initiation of treatment with a regimen designed to treat M(X)DR-TB is recommended.

7.3 Laboratory Diagnosis of DR TB

**Microscopy:** Although direct smear microscopy is the cornerstone for diagnosis of drug-susceptible pulmonary TB, it cannot distinguish between drug-susceptible and resistant *M. tuberculosis*, or between different species of mycobacteria.

The main uses of microscopy for drug-resistant TB are therefore limited to assessing the infectiousness of patients, confirming that microbes growing on (or in) artificial media are mycobacteria or not, and guide the procedure of tests like LPA.

**Line Probe Assay:** is a new test that makes use of molecular technology and can identify the presence or absence of specific mutations on the genes of TB bacilli responsible for resistant to isoniazid (H) and rifampicin (R). The benefits of this test are the high degree of sensitivity (98%) and specificity (99%), the speed of the test (within 48 hours) and the potential to perform high volumes of test per day.

**Culture:** Mycobacterial culture provides definitive diagnosis of tuberculosis. *Mycobacterium tuberculosis* multiplies extremely slowly with generation time 18-24 hours; therefore, results of TB culture may take several weeks. Mycobacteria also require special culture media (e.g. Lowenstein Jensen, Middle Brook and different liquid Medias).

**Drug Susceptibility Testing:** is required to make a definitive diagnosis of M(X) DR-TB and guide clinical management. DST can be done by either phenotypic or genotypic methods.

7.4 Treatment of Drug Resistant Tuberculosis

**A. Programmatic treatment approach**
The Programmatic approach to MDRTB treatment in Ethiopia is either standardized individualized or empiric treatment approaches.

- **Standardized treatment:** Drug Resistance Survey (DRS) data from representative patient populations are used to base regimen design in the absence of individual DST. All patients in a defined group or category receive the same regimen.

- **Individualized Treatment:** Each regimen is adopted according to guidelines based on the patient’s past history of TB treatment, individual FL- and SL-DST results and possible side-effects.

- **Empiric Treatment:** Each regimen is individually designed based on the patient’s past history of TB treatment and with consideration of DRS data from the representative patient population. An empirical regimen is adjusted when DST on individual patient becomes available.

**B. Grouping of anti-tuberculosis agents**
**Group 1**: First-line oral agents: Isoniazid (H); Rifampicin (R); Ethambutol (E); Pyrazinamide (Z); Rifabutin (Rfb)

**Group 2**: Injectable agents: Kanamycin (Km); Amikacin (Am); Capreomycin (Cm); Streptomycin (S)

**Group 3**: Fluoroquinolones: Moxifloxacin (Mfx); Levofloxacin (Lfx)

**Group 4**: Oral bacteriostatic second-line agents: Ethionamide (Eto); Cycloserine (Cs); para-aminosalicylic acid (PAS)

**Group 5**: Agents with unclear role in DR-TB treatment: Clofazimine (Cfz); Linezolid (Lzd); Amoxicillin/clavulanate (Amx/Clv); Thioacetazone (Thz); Imipenem/cilastatin (Ipm/Cln); High-dose isoniazid (High-dose H).

C. **Principles of Designing MDRTB Treatment**

- Start with first line drugs if sensitivity confirmed
- Each MDR TB regimen will consist of at least four new drugs
- As standard all patients will receive Pyrazinamide, Kanamycin/Amikacin, Levofloxacin, Ethionamide, and Cycloserine
- Ethambutol is continued if DST suggests susceptibility to the drug. However, as most patients have already used Ethambutol for prolonged periods and DST for Ethambutol is not fully reliable, this drug will not count as one of the 4 effective drugs 'with certain effectiveness', even if the DST shows susceptibility
- Pyrazinamide will be used throughout in all patients as resistance uncommon and no reliable DST available, but it will also not be counted as an effective drug.
- Kanamycin DST is used as a surrogate marker also for Amikacin. In case of resistance to Kanamycin/Amikacin, Capreomycin can be used as injectable and can be counted as effective drug.
- Ofloxacin DST is used as a surrogate marker for quinolone resistance. However, in case of resistance to Ofloxacin, Levofloxacin, a higher generation of quinolone, will be kept in the regime, unless Moxifloxacin is available which should then be used. In case of quinolone resistance neither Levofloxacin nor Moxifloxacin will count as one of the drugs 'with certain effectiveness'. Thus PAS is added when resistance to quinolones is confirmed.
- The drugs dosages are determined by body weight.

D. **MDR-TB Treatment Regimens in Ethiopia**

The standardized treatment regimen addresses 5 patient categories:

1. Patients with MDR-TB confirmation, but no full DST results available yet: Regimen:
   
   E-Z-Km(Am)-Lfx-Eto-Cs
2. MDR-TB Patients susceptible to both Kanamycin and Quinolone: **Regimen is the same as above**

3. MDR-TB Patients susceptible to Kanamycin, but resistant to Quinolone: Regimen:
   
   **E-Z-Km(Am)-Mfx-Eto-Cs-PAS**

4. MDR-TB Patients susceptible to Quinolone, but resistant to Kanamycin: Regimen:

   **E-Z-Cm-Lfx-Eto-Cs**

5. XDR-TB Cases (i.e.: MDR-TB and resistance to Quinolone and Kanamycin)

   Regimen: **E-Z-Cm-Mfx-Eto-Cs-PAS**

Clinical team at M(X)DR-TB treatment referral hospital may modify the regimen after receiving the result of DST.

**Duration and Phases of Treatment**

*Intensive phase:* The injectable agent is used for minimum of 6 months and at least 4 months after culture conversion.

The use of an individualized approach which reviews the cultures, smears, x-rays, and the patient’s clinical status may also aid in deciding whether or not to continue an injectable agent longer than the above recommendation, particularly in the case of patients for whom the susceptibility pattern is unknown, effectiveness is questionable for an agent(s), or extensive or bilateral pulmonary disease is present.

*Continuation phase:* The treatment period following the intensive phase. The total treatment is for minimum duration of 18 months beyond culture conversion (eg. pediatric patients receiving second line treatment with baseline culture negative result). Thus if the culture is negative at completion of first month of MDR-treatment, intensive phase will be 6 months and continuation phase 13 months. However, if culture conversion (two consecutive negative cultures, from samples collected at least 30 days apart) is at completion of second months, intensive phase will be 6 months and continuation phase 14 months. If culture conversion is at completion of fourth months, intensive phase will be 8 months and continuation phase will be 14 months. Extension of therapy to 24 months may be indicated in chronic cases with extensive pulmonary damage.

**E. Management of Extra-pulmonary M(X)DR-TB**

Extra-pulmonary DR-TB is treated with the same strategy and length of time as pulmonary M(X)DR-TB. If the patient has symptoms suggestive of central nervous system involvement and is infected with DR-TB, the regimen should use drugs which have adequate penetration into the central nervous system. Pyrazinamide, ethionamide and cycloserine have good penetration; kanamycin, amikacin, and capreomycin do so only in the presence of meningeal inflammation; whereas PAS and Ethambutol have poor or no penetration. The fluoroquinolones have variable CSF penetration, with better penetration seen in the higher generations.
8. TB INFECTION CONTROL

8.1 Basic of TB infection control

TB infection control (TB IC) is a combination of measures aimed at minimizing the risk of TB transmission within populations. The foundation of such infection control is early and rapid diagnosis, and proper management of TB patients. TB IC requires and complements the implementation of core interventions in TB control, HIV control and strengthening of health systems.

Rationale

TB infection control is growing in importance because of the association of TB with HIV and the emergence of DR-TB. The situation is worsened by the increasing number of patients without corresponding infrastructure expansion and health care worker enrolment, leading to overcrowding of patients, delayed diagnosis and treatment resulting in increased TB transmission.

Health care workers are at increased risk of TB infection compared to the general population. Non-medical staff in health care settings are also at risk, where undiagnosed pulmonary TB patients with cough are presenting the risk of TB infection to close contacts and health care workers. Waiting rooms and corridors where patients wait to receive medical care are often areas of particular risk.

Incidence of TB among people living or working in congregate settings (e.g. correctional facilities or nursing homes) and among household contacts of TB patients also exceeds the incidence found in the general population. Therefore, this document also provides guidance on preventing TB transmission in health facilities, congregate settings and households.

8.2 Set of TB IC activities

The set of national and regional level managerial activities is given & described in detail below. At this level, activities 1–6 are all managerial, they provide policy makers at national and subnational level with a comprehensive framework that can support and facilitate the implementation, operation and maintenance of TB infection control in health-care facilities, congregate settings and households. This managerial framework should be based within existing national and regional infection control management structures.

Set of activities for national and Regional TB infection control:

1. Identify and strengthen a coordinating body for TB infection control, and develop a comprehensive budgeted plan that includes human resource requirements for implementation of TB infection control at all levels.
2. Ensure that health facility design, construction, renovation and use are appropriate.
3. Conduct surveillance of TB disease among health workers, and conduct assessment at all levels of the health system and in congregate settings.
4. Address TB infection control advocacy, communication and social mobilization (ACSM), including engagement of civil society.
5. Monitor and evaluate the set of TB infection control measures.
6. Enable and conduct operational research.
8.3 Reducing transmission of TB in health-care facilities

This section describes the various elements that can be combined to achieve TB infection control at facility level.

Set of control measures – facility level

The set of TB infection control measures that apply at facility level are listed below. Implementation of the national and regional managerial activities described above facilitate the implementation of measures described in this section and should therefore be implemented as a set.

Managerial Activities:
Facility-level managerial activities constitute the framework for setting up and implementing the other controls at facility level. The managerial activities should ensure political commitment and leadership at facility level as well as at national level. Other types of control measures at this level also include administrative and environmental controls, and personal protective equipment, each of which is discussed below. These types of control should be implemented together because they complement one another.

Administrative controls:
Administrative controls should be implemented as a first priority because they have been shown to reduce transmission of TB in health-care facilities. Such controls are a vital part of sound infection control practices, which require people with TB symptoms to be promptly identified, separated and treated. The physical separation of TB patients or people suspected of having TB requires rational design, construction or renovation, and use of buildings.

Environmental controls:
Environmental controls include methods to reduce the concentration of infectious respiratory aerosols (i.e. droplet nuclei) in the air, and methods to control the direction of infectious air. The choice of environmental controls is intimately related to building design, construction, renovation and use, which in turn must be tailored to local climatic and socioeconomic conditions.

Personal protective equipment:
Personal protective equipment (particulate respirators) should be used together with administrative and environmental controls in situations where there is an increased risk of transmission.
**Set of measures for facility-level TB infection control:**

**Managerial activities:**

- a) Identify and strengthen local coordinating bodies for TB infection control, and develop a facility plan (including human resources, and policies and procedures to ensure proper implementation of the controls listed below) for implementation.
- b) Rethink the use of available spaces and consider renovation of existing facilities or construction of new ones to optimize implementation of controls.
- c) Conduct on-site surveillance of TB disease among health workers and assess the facility.
- d) Address advocacy, communication and social mobilization (ACSM) for health workers, patients and visitors.
- e) Monitor and evaluate the set of TB infection control measures.
- f) Participate in research efforts.

**Administrative controls**

- g) Promptly identify people with TB symptoms (triage), separate infectious patients, control the spread of pathogens (cough etiquette and respiratory hygiene) and minimize time spent in health-care facilities.
- h) Provide a package of prevention and care interventions for health workers, including HIV prevention, antiretroviral therapy and isoniazid preventive therapy (IPT) for HIV-positive health workers.

**Environmental controls**

- i) Use ventilation systems.
- j) Use ultraviolet germicidal irradiation (UVGI) fixtures, at least when adequate ventilation cannot be achieved.

**Personal protective equipment**

- k) Use particulate respirators.

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### 8.4 Infection control for congregate settings

The recommendations for congregate settings are less specific than those for health-care facilities, because congregate settings are so diverse. They include a mix of settings that range from correctional facilities and military barracks, to homeless shelters, refugee camps, dormitories and nursing homes. Each facility differs in the type of population it contains and the duration of stay of dwellers; in turn, this affects the dynamics of TB transmission.

The incidence of TB infection and TB disease among individuals in congregate settings exceeds the incidence among the general population. The association of HIV and the emergence of MDR-TB and XDR-TB increase the need to give urgent and appropriate attention to implementation of TB infection control in congregate settings, and to prioritize some elements.
Managerial activities:

As a first step, policy makers responsible for congregate settings should be made part of the coordinating system for planning and implementing interventions to control TB infection. In particular, the medical service of the ministry of justice and correctional facilities should be fully engaged and encouraged to implement TB infection control. In any congregate setting, overcrowding should be avoided because it can lead to non-infected individuals being exposed to TB.

Congregate settings should be part of the country surveillance activities, and should be included in facility assessment for TB infection control. Such assessment will be useful in determining the level of risk of the facility or building.

Any advocacy and information, education and communication material should include a specific focus on congregate settings, as should monitoring and evaluation of TB infection control measures. Facility-level managerial activities should also apply with some adaptation to congregate settings. These activities will facilitate the implementation of the different types of controls described below.

Administrative controls:

To decrease TB transmission in congregate settings, cough etiquette and respiratory hygiene, and early identification, followed by separation and proper treatment of infectious cases should be implemented. In particular, all inmates of long-term stay facilities and inhabitants of other congregate settings should be screened for TB before entry into the facility. All staff should be given appropriate information and encouraged to undergo TB diagnostic investigation if they have signs and symptoms suggestive of TB. People suspected of having TB should be diagnosed as quickly as possible. People suspected of having TB and infectious patients should always be separated and/or isolated in an adequately ventilated area, until sputum smear conversion. Directly observed therapy (DOT) while a patient is on treatment is also recommended. In short-term stay congregate settings, such as jails and shelters, a referral system for proper case management of cases should be established.

In congregate settings, patients living with HIV and other forms of immunosuppression should be separated from those with suspected or confirmed infectious TB. All staff and persons residing in the setting should be given information and encouraged to undergo HIV testing and counselling. If diagnosed with HIV, they should be offered a package of prevention and care that includes regular screening for active TB.

In congregate settings with patients having, or suspected of having, drug-resistant TB, such patients should be separated from other patients (including other TB patients), and referral for proper treatment should be established.

Environmental controls:
Buildings in congregate settings should comply with national norms and regulations for ventilation in public buildings and specific norms and regulations for prisons.

**Personal protective equipment:**
When a person residing in a long-term stay congregate setting is suspected or diagnosed as having TB and is physically separated, the same recommendations on infection control apply as for health-care facilities. In short-term stay congregate settings, appropriate referral should be organized.

**8.5 Reducing transmission of TB in households**

Various actions are needed to reduce transmission of TB in households because household members of persons with infectious TB are at high risk of becoming infected with TB and consequently developing the disease.

Studies show that the major risks for infection are through close contact (exposure) to the infectious case before diagnosis. Whether the patient subsequently remains at home or moves to a sanatorium appears to have little impact on household transmission, provided the patient is treated effectively.

Patients with MDR-TB usually sputum convert later than those with drug-susceptible TB. This is probably due to the limited efficacy of second line drug armamentarium. For this reason, patients with drug-resistant TB remain infectious for much longer, even if treatment is initiated. This may prolong the risk of transmission in the household.

Early case detection remains one of the most important interventions for reducing the risk of TB transmission in the household. TB contact investigation should be undertaken. In addition, basic infection control behaviour-change campaigns should be part of any community information, education and communication messages. The infection control messages need to promote the importance of early identification of cases, adherence to treatment and implementation of proper TB infection control measures in the household, before and after diagnosis of TB.

Behaviour-change campaigns for family members of smear-positive TB patients and health service providers should aim to minimize stigma and the exposure of non-infected patients to those who are infected.

To reduce exposure in households:
- 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 respiratory hygiene, and should follow such practices at all times
- while smear positive, TB patients should:
  - spend as much time as possible outdoors
  - sleep alone in a separate, adequately ventilated room
- minimize contact with children (<5yrs) and immunosuppressed individuals
- spend as little time as possible in congregate settings or in public transport

Additional IC measures for confirmed MDRTB patients:

- While culture positive, MDR-TB patients who cough should always practice cough etiquette (including use of masks) and respiratory hygiene when in contact with people. Health service providers should wear particulate respirators when attending patients in enclosed spaces.

- Family members living with HIV, or family members with strong clinical evidence of HIV infection, should not provide care for patients with culture-positive MDR-TB. If there is no alternative, HIV-positive family members should wear respirators, if available.

- 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 and, if positive, drug-susceptibility testing and treatment.

- While culture positive, XDR-TB patients should be isolated at all times, and any person in contact with a culture-positive XDR-TB patient should wear a particulate respirator. If at all 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, potential renovation of the patient’s home should be considered, to improve ventilation.
9. LEPROSY

9.1 Basics of Leprosy

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, an acid-fast, rod-shaped bacillus. The disease mainly affects the skin, the peripheral nerves, mucosa of the upper respiratory tract and also the eyes, apart from some other structures. It affects persons in all age groups and both sexes. The age group mainly affected is between 15 and 45 years. Factors related to poverty increase the risk of developing the disease.

Mode of transmission

Leprosy is believed to be transmitted through air-borne spread of droplets, from the nose and mouth, containing the bacilli expelled by untreated leprosy patients and inhaled by healthy persons. 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.

Infectiousness of Leprosy

Leprosy is not highly infectious as evidenced by the following facts:

- Over 95% of the population has a natural immunity against leprosy.
- Over 85% of the leprosy cases are non-infectious.
- With MDT (Multi Drug Treatment) an infectious case is rendered non-infectious within a few days.

Natural evolution

Under normal circumstances, only a very small proportion (less than 5%) of all individuals who are infected by the leprosy bacilli will develop the disease during their lifetime. In the majority of people, the immunological defence kills all the bacilli. The disease has a long incubation period, ranging from 3 to 5 years, but it may vary from 6 months to more than 20 years. If not treated, leprosy can cause severe disability, mainly as a result of peripheral nerve damage.

Association of Leprosy with HIV

Researches conducted in various countries showed that there is no strong association between these two diseases. However, some data suggest that immune-mediated reactions that complicate leprosy occur at a higher frequency in co-infected patients. Leprosy has now been reported presenting as immune reconstitution disease among patients commencing highly active antiretroviral treatment.

9.2 Leprosy Case Finding

Leprosy case-finding is the detection of active cases of leprosy by examination of suspects attending health facilities. The major objectives of case finding are to:

- Identify the sources of infection in the community, that is, individuals who are discharging large number of leprosy bacilli.
- Treat those infectious patients rapidly and make them non infectious thereby interrupting the chain of transmission
- Diagnose and cure leprosy cases before irreversible nerve damage has occurred
- Minimize the delay in initiating treatment, thereby increasing the possibility of cure before irreversible nerve damage ensues

**Strategies for leprosy case finding**

**Self reporting/voluntary case finding:** All health care personnel should ask for symptoms of leprosy (e.g. skin changes) among persons who voluntarily visit health services at OPD to identify suspects.

**Contact tracing:** Examination of all household contacts, especially children, of confirmed cases of leprosy patients is important to identify leprosy cases early. A close contact is defined as a person living in the same household or being in frequent contact with a person who is diagnosed to have leprosy. When a new case is detected, the health worker should examine all household contacts of the patient for evidence of leprosy. Thereafter, the contacts should be educated on the early signs of the disease and requested to return if any suspect skin lesions or motor or sensory changes occur. The health worker should do contact tracing and examination either by:
- telling the patient to bring all household contacts to the health facility, or
- Visiting the home of the patient to examine the households

**Encourage suspects to visit health facility:** people suspected with leprosy shall be encouraged to report voluntarily to the nearby health facility. HEWs, community volunteers and the community at large shall advice leprosy suspects to visit the nearby HF.

**Active case finding** includes the use of small scale campaigns in restricted special situations and suspected or known leprosy pocket areas. It should be a onetime activity with the principal aim of establishing sustainable services.

Efforts to increase case detection are focused on facilitating self referral by people who suspect themselves of leprosy. Promote and educate the public about early signs and symptoms of leprosy to increase their awareness and to facility self-reporting of suspected cases to the health facility. In addition, public education will promote the breakdown of barriers such as stigma, discrimination and fear associated with leprosy.

**How to identify leprosy suspect**

Suspect leprosy in any individual who presents with:
- Pale or reddish patches (skin patch with discoloration) on the skin
- Painless swelling or lumps in the face and earlobes
- Loss of, or decreased sensation on the skin
- Numbness or tingling of the hands and/or the feet
- Weakness of eyelids, hands or feet
- Painful and/or tender nerves
- Burning sensation in the skin
- Painless wounds or burns on the hands or feet
Confirming Leprosy case:

Over 95% of leprosy cases can be diagnosed on clinical grounds. Laboratory investigation is indicated for confirmation in doubtful cases and sometimes for patient classification.

A. **Take History**

Obtain the following information from the suspect and record findings:

- General information: name, sex, age, complete address, distance from home to the clinic and occupation.
- History of onset, duration of symptoms, including history of contact with a leprosy patient; painless wounds/burns; burning sensation; weakness in picking or holding objects or closing eyelids; unusual sensation in hands and feet (numbness, tingling), presence of itching and history of previous leprosy treatment

B. **Carry out physical examination** thus:

1. **Examination of the skin**:

   Examination must always be carried out with adequate light (preferably natural light) and sufficient privacy for the patient to feel at ease.

   - Inform client/patient about the examination and why
   - Ask the client/patient to remove all garments.
   - Examine systematically from head to neck to shoulders, then arms, trunk, buttocks, hands and finally legs and feet in that order to ensure that no important signs are missed. Do the front side of the body and then the backside.

   Examination of the skin:

   - Check for presence of skin lesions (patches or nodules).
   - Check for loss of sensation in the skin lesions (patches) using a wisp of cotton wool
   - Count the number of skin lesions

   **Sensation testing**

   Check the sensation of the skin lesions using a wisp of cotton wool as follows:

   - **Explain** to the patient the purpose of the test and what is expected from him

| The most common & early symptom of Leprosy is pale or reddish discoloration of the skin. |
• **Roll** the end of a wisp of cotton wool into a fine point. Touch the skin with the fine point of the cotton wool until it bends

• **Touch** the skin with the fine point of the cotton wool until it bends with the patient’s eyes opened and instructing the patient to point to the location where s/he feels the wisp of the cotton, then continue until the patient has demonstrated understanding of the test

• **Repeat** the step with the patient eyes closed, first on the normal skin and then on the skin patch, touching the normal now and then

• **Watch** that the patient’s eyes are closed when the test is being done.

Confirm definite loss of sensation in the skin patch when the patient can not feel the points of contacts within the skin patch but does point to other places where the skin is normal

Note that a **definite loss of sensation on a skin lesion** is indicative of leprosy.

A patient points accurately to areas of normal skin, but sometimes points away from where the skin in a 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 a diagnosis of leprosy is made.

2. Examination of the nerves:

**Nerve palpation**

Nerves most commonly affected by leprosy are greater auricular, ulnar, median, radial cutaneous, peroneal and posterior tibial (See below). However, the two most commonly affected are the ulnar and peroneal nerves. Hence, these two nerves are commonly enlarged and can be felt quite easily.

![Figure 3: Peripheral Sites where nerves can be felt](image-url)
Nerves are palpated to check for enlargement and/or tenderness.

- Palpate the nerves starting from the head and going down to the feet. Compare the right and left sides.
- When palpating a nerve, always use the pulp of two or three fingers; the nerves should be rolled over.

A definite ENLARGEMENT of one or more nerves is indicative of LEPROSY.

3. Examination of skin smears

Bacteriological examination of a skin smear is done for doubtful cases to confirm the diagnosis and/or classification of leprosy. Only one slide, with smears taken from 2 sites must be collected and examined. One positive smear result is enough for diagnostic and justifies starting MB treatment. However, skin smear should not be carried out routinely for all suspects. Its use should be limited for doubtful cases only. The finding of a negative smear examination result doesn’t rule out leprosy.

A case of leprosy is a person with one of the cardinal signs of leprosy, and who requires chemotherapy. A leprosy patient who has completed a full course of chemotherapy should no longer be regarded as a case of leprosy, even when sequelae of leprosy such as skin lesions, disability and/or disfiguration remain or are present.

The **cardinal signs** of leprosy are:
1. Definite loss of sensation in a pale (hypo-pigmented) or reddish skin lesion.
2. Thickened or enlarged peripheral nerve with or without tenderness
3. The presence of acid-fast bacilli in a slit skin smear.

**Presence of one or more of the three cardinal signs of Leprosy is a confirmation of a leprosy case**

**Differential diagnoses of leprosy**

Without careful examination, leprosy can easily be 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 other common skin diseases. The differential diagnoses of leprosy are listed below.
Table 16: Differential diagnosis of leprosy

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinea versicolor</td>
<td>The lesions are hypo-pigmented, but without loss of sensation. They often itch. When an anti-fungal ointment is applied they usually clear up within 6 weeks.</td>
</tr>
<tr>
<td>Ringworm (Tinea corporis)</td>
<td>The lesions are well-defined areas of hypo-pigmentation with white scales and without loss of sensation. They usually clear up within 6 weeks when an anti-fungal ointment is applied.</td>
</tr>
<tr>
<td>Vitiligo</td>
<td>There are usually completely white areas of skin. The skin texture is normal and there is no loss of sensation</td>
</tr>
<tr>
<td>Birthmarks</td>
<td>Lightly or deeply pigmented areas of different sizes, which are present since birth or shortly after birth and do not change.</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>Raised areas with white fatty scales, which itch and bleed easily on scratching (pin point bleeding). There is no loss of sensation</td>
</tr>
<tr>
<td>Molluscum contagiosum</td>
<td>Nodular lesions with a depression in the centre. Firm squeezing results in the appearance of a creamy substance</td>
</tr>
<tr>
<td>Onchocerciasis</td>
<td>Hypopigmented macules are often one of the manifestations. There is itching and no loss of sensation. In a later stage there are mottled lesions, in particular on the loins and shins.</td>
</tr>
<tr>
<td>Cutaneous leishmaniasis</td>
<td>Small erythematous papules appearing after bite of sand fly and later changing to dry crusted lesions</td>
</tr>
<tr>
<td>Post kala-azar cutaneous</td>
<td>Nodular, papular lesions and diffuse infiltrates, usually located on the face. These may occur one or more years after treatment of visceral leishmaniasis. Skin smears are negative for AFB</td>
</tr>
<tr>
<td>leishmaniasis</td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td>Secondary syphilis presents with a considerable variety of lesions, e.g. papular and nodular lesions. Skin smears are negative for AFB. Positive serology for treponematosis.</td>
</tr>
<tr>
<td>Pityriasis alba</td>
<td>The lesions are often restricted to the face making differentiation from leprosy difficult since loss of sensation in the face is not easy to demonstrate. The lesions subside spontaneously, leaving hypopigmented macules. Besides, new lesions may appear at other sites.</td>
</tr>
<tr>
<td>Nutritional deficiencies</td>
<td>Usually over the cheek, single or multiple, ill-defined, hypopigmented patches with other features of vitamin deficiencies such as glossitis, stomatitis. The patches will clear after the administration of vitamins.</td>
</tr>
</tbody>
</table>

In doubtful cases, Do any one of the following:

- Consider the possibility of another skin disease and treat appropriately.
• Discuss the cases with colleagues who have experience on managing leprosy and manage the patient accordingly.
• Refer the suspect to a health facility where there are experienced health worker or a dermatologist.
• If referral is not possible, give 3 months appointment for reevaluation.

### 9.3 Classification of Leprosy

For the choice of the treatment regimen, patients should be classified according to the WHO classification based on the number of leprosy skin lesions and nerve involvement into either the paucibacillary (PB) or Multibacillary (MB) group. Doubtful cases should be classified as MB and treated accordingly.

1. **Paucibacillary (PB) leprosy**
   - One to five leprosy skin lesions.
   - Only one nerve trunk enlarged

2. **Multibacillary (MB) leprosy**
   - Six or more skin lesions.
   - Less than six skin lesions, which have a positive slit skin smear result.
   - If there is involvement (enlargement) of more than one nerve

#### Pure neural leprosy

These are patients who do not have any skin lesion, but who have clearly thickened nerves with or without signs of nerve damage. Patients with pure neural leprosy should be reported and treated as a MB case (See Annex 9).

### 9.4 Nerve Function Testing

After diagnosis of leprosy is made, CARRY OUT the following nerve functions tests:

- Voluntary Muscle Testing (VMT)
- Sensory Testing (ST)
- Autonomic nerve function test for dryness of palms and soles

#### Voluntary Muscle Testing (VMT)

VMT is done to check Muscle strength of eye, hands and feet. The strength should be graded as

- Strong (S)
- Weak (W)
- Paralyzed (P)

Test the muscle strength of eyes, hands and feet as follows:

**Voluntary muscle testing (VMT) of the eyes: eye closure**

- Ask the patient to close his eyes lightly as in sleep.
- Observe whether or not the closure on both eyes is complete or not. Inability to fully close the eye is called lagophthalmos (paralysis “labeled as P” of the eyelid muscles).
- If there is lagophthalmos, measure the lid gap in mm as shown in the diagram below.

**Lid gap measuring procedures**

1. Explain the procedure to the patient
2. Ask the patient to close his/her eyes lightly, as in sleep.
3. Measure and record any gap in mm as illustrated on the right side.
4. If closure is normal, record: “0 mm.”

If the patient is able to fully close his/her eyes, then ask the patient to close his eyes firmly, gently try to open the eye lids using the pulp of your thumbs to check for strength.

Grade the eye muscle strength as weak (W) if the eye lids open easily; or strong (S) if it is difficult to open the lids.

*Voluntary Muscle testing (VMT): hands and feet:*

**Check for range of movement** on the fifth finger as follows:

- ASK patient to abduct 5th finger (move finger away from the rest). If patient cannot move the finger, record as paralysis (P), an indication of ULNAR nerve damage.
- If movement is normal, test for resistance by PRESSSING gently over the proximal phalanx of the 5th finger using your (examiner’s) index finger as shown in the diagram below, holding the other 3 fingers steady and ask the patient to maintain the position and RESIST the pressure of the examiner's index finger as strongly as possible.
- Press gradually more firmly and judge whether resistance is strong (S) or weak (W).

COMPARE the right hand with the left hand always.
Check for range of movement of both thumbs

- **ASK** the patient to first flex the thumb over the palm (touch the root of 5th finger) and later point the thumb to his/her nose while you hold the remaining 4 fingers. If patient can not move the thumb, record as paralysis (P), an indication of MEDIAN nerve damage
- If movement is normal, **test for resistance by PRESSSING** gently over the proximal phalanx of the thumb using your (examiner’s) index finger as shown in the diagram below, holding the other 4 fingers steady and the ask the patient to maintain the position and RESIST the pressure of the examiner’s index finger as strongly as possible
- **Press** gradually more firmly and judge whether resistance is strong (S) or weak. (W)

COMPARE the right hand with the left hand always

Check for the range of movement of the wrist

- **ASK** the patient to extend the wrist. If patient can not extend the wrist, record as paralysis (P), an indication of RADIAL nerve damage called WRIST DROP
- If movement is normal, **test for resistance by PRESSING** gently over the dorsum of the hand as shown in the diagram below, whilst you (examiner) hold the wrist with your other hand. And ask the patient to maintain the position and resisting the pressure as strongly as possible
- Press gradually more firmly and judge whether resistance is strong (S) or weak. (W)

COMPARE the right hand with the left hand always

Check the movement of the feet

- **ASK** patient to dorsi-flex his foot (move up his foot at the ankle). If patient can not dorsi-flex the foot, record as paralysis (P), an indication of PERONEAL nerve damage called FOOT DROP.
- If movement is normal, **test for resistance by PRESSING** gently over the dorsum of the foot as shown in the diagram below, whilst you (examiner) hold the leg with your other hand. And ask the patient to maintain the position and resisting the pressure as strongly as possible
- Press gradually more firmly and judge whether resistance is strong (S) or weak. (W)
**COMPARE** the right foot with the left foot always

<table>
<thead>
<tr>
<th>a. Is movement full?</th>
<th>b. Is resistance full?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Little finger in</strong>...a test of ulnar</td>
<td>Nerve function</td>
</tr>
<tr>
<td>Hold these 3 fingers straight</td>
<td>Patient tries to hold a card between ring- and little fingers. Assessor pulls card gently.</td>
</tr>
<tr>
<td><strong>Straight Thumb up</strong>...a test of</td>
<td>Median nerve function</td>
</tr>
<tr>
<td>Straight Thumb up...a test of</td>
<td>Median nerve function</td>
</tr>
<tr>
<td>Patient moves thumb base fully out and across</td>
<td>Assessor resists at side of thumb (not at front or back)</td>
</tr>
<tr>
<td><strong>Wrist up</strong>.......a test of radial</td>
<td>Nerve function</td>
</tr>
<tr>
<td><strong>Foot up</strong> ....a test of peroneal</td>
<td>Nerve function</td>
</tr>
</tbody>
</table>

**Sensory testing (ST)**

Sensory testing is done to check the presence of sensation in the eyes, hands and feet.

Test the sensation of eyes, hands and feet as follows:

*Sensation of the eyes (cornea):*

ASK patient to blink his/her eyes.
Observe the patient's spontaneous blinking while talking to him/her. If the there is a blink, corneal sensation is normal. If there is no blink, the eye is at risk.

*Sensation of palms and soles:*
ST on palms and soles should be done with a ball-point pen. The tests are done on ten standard points.

**Hand and foot mapping, including sensation test (ST)**

<table>
<thead>
<tr>
<th>1. Explain the test to the patient. Rehearse it with the patient. Then test. The eyes of the patient should be covered.</th>
<th>2. Compare sensation of the little finger with that of the thumb and sensation of one hand with the other, to see if there is difference. Compare findings with those shown on any earlier records.</th>
</tr>
</thead>
</table>
| 3. Support the patient’s hand or foot so that fingers/toes are well supported to prevent joint movement during the test. | 4. Record:  
If the patient feels, ✓  
If not, x |
| 5. Mark any wounds ( ), open crack ( ) clawing of digits (c) and bone loss or absorption ( ) on the Patient Record Card or VMT/ST Form. |
| 6. Dent the patient’s skin by 1-2 mm at dot sites using a ball-point pen - asking the patient to point to the exact site whenever he/she feels. The stimuli should be irregular in timing and placing. |
| 7. Look for any CHANGE. Make sure that the change is real and not due to inaccuracies in testing. |
9.5 Examination of Eyes, Hands and Feet for Disabilities

i. Examination of the eye

- **Visual Acuity:**

Vision of both eyes of the patient should be tested according to the demonstration below and should be recorded on the Patient Record Card.

- Test vision with good light falling on the assessor.
- Ask the patient to cover one eye, then count the number of fingers that the assessor holds up.
- Test at 6 meters. If the patient cannot see at 6 meters, re-test at 3 meters.
- Record the findings

- **Other eye problems/complications:**

Look for: Injury of cornea and loss of vision due to incomplete blink and/or eye closure.

ii. Examination of hands and feet

Patients should also be examined for the following complications, which result from nerve damage:

- Skin cracks on palms and soles with sensation loss.
- Wounds on palms and soles with sensation loss.
- Clawed fingers and toes.
- Foot drop.
- Wrist drop.
- Shortening and scarring in fingers and toes with sensation loss.

9.6 Disability Grading

For all confirmed cases of leprosy, nerve function testing must be done to grade the disability status at the time of diagnosis. The disability grades are Grade-0, Grade-1 or Grade-2. Each eye, hand and foot should be graded separately. Disabilities should be graded as follows:

**Eyes**

**Grade 0:** No disability found. This means there is no eye problem due to leprosy and no loss of vision.

**Grade 1:** The eyes are not given a grade of 1.
Grade 2: Visible damage or disability is noted. This includes the inability to close the eye fully (lagophthalmos) or obvious redness of the eye (typically caused by a corneal ulcer or uveitis). Visual impairment or blindness (vision less than 6/60 or inability to count fingers at 6 meters) due to leprosy should be graded as grade 2.

Hands and feet

Grade 0: No disability found. This means there is no loss of sensation or visible deformity or damage.
Grade 1: There is loss of sensation in the palm of the hand or sole of the foot, but no visible deformity or damage.
Grade 2: There is visible damage or disability due to leprosy. This includes weakness or paralysis of muscles on the hands and feet, wounds and ulcers as well as visible deformities such as a foot drop or a claw hand or absorption of fingers.

The highest grade in one of the six sites (eyes, hands or feet) is the overall disability grade for that patient.

9.7 Case Definition and Treatment of Leprosy

Case definitions

Leprosy patients who need treatment are grouped into either as “New cases” or “Other cases”;
New cases: leprosy patients who have never received treatment before
Other cases include: Relapse, Return after default, Transfer in, People with a change in classification from PB to MB, patients who relapse after treatment with Dapsone mono-therapy in the past.

Table 17: Case definitions & management of Leprosy case

<table>
<thead>
<tr>
<th>Case definition</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>New case</td>
<td>Treat according to the clinical assessment (and/or laboratory diagnosis)</td>
</tr>
<tr>
<td>Relapse after MDT</td>
<td>Treat according to the new clinical assessment (and/or laboratory diagnosis) independent of the previous category of treatment</td>
</tr>
<tr>
<td>Return after default</td>
<td>Treat MB according to the new clinical assessment (and/or laboratory diagnosis) independently from the previous treatment category</td>
</tr>
<tr>
<td>Transfer in</td>
<td>Treat according to the previous classification assessed in the original health facility</td>
</tr>
<tr>
<td>Other</td>
<td>Treat according to the clinical assessment (and/or laboratory diagnosis)</td>
</tr>
</tbody>
</table>
Treatment of Leprosy

The objective of the treatment is to:
- Cure leprosy by rapidly eliminating the bacilli
- Prevent the emergence of drug resistance
- Prevent relapse
- Prevent disability

Patients are no longer infectious after taking the first dose of treatment. There are virtually no relapses or recurrences of the disease after completion of treatment with MDT.

Multi-drug therapy (MDT) is a combination of drugs that is very safe and effective in treating leprosy to prevent the emergence of drug resistance; under no circumstance should leprosy be treated by a single drug as it may result in drug resistance. MDT is available free of charge to all who need it. The drugs are all taken by mouth. The drugs are supplied in special and convenient blister packs for both MB and PB cases. Each blister pack contains treatment for 4 weeks (28 days). Pauci-bacillary (PB) MDT blister pack contains Rifampcin and Dapsone. Multi-bacillary (MB) blister pack contains Rifampcin, Clofazemine and Dapsone. The best way to prevent the spread of leprosy is to treat all patients with MDT.

Drugs used in MDT

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin (R)</td>
<td>150mg, 300mg</td>
</tr>
<tr>
<td>Clofazimine (C)</td>
<td>50mg, 100mg</td>
</tr>
<tr>
<td>Dapsone (DDS)</td>
<td>50mg, 100mg</td>
</tr>
</tbody>
</table>

Rifampicin is given once a month. No toxic effects have been reported. Rifampicin may cause slight discoloration (reddish) of the urine and this should be explained to the patient before starting MDT.

Clofazimine is most active when administered daily. The drug is well tolerated and virtually nontoxic in the dosage used for MDT. The drug may cause brownish discoloration and dryness of the skin. However, this disappears within few months after stopping treatment. This should be explained to patients being started on treatment.

Dapsone is very safe in the dosage used in MDT and side effects are rare. The main side effect is allergic reaction, causing itchy skin rashes and exfoliative dermatitis. Patients known to be allergic to any of the sulpha drugs should not be given dapsone.

MDT drugs are provided in blister calendar packs each containing a four weeks (one month) supply, except for children below 10 years.

The appropriate dose for children under 10 years of age can be decided on the basis of body weight. [Rifampicin: 10 mg per kilogram body weight (mg/kg); clofazimine: 1 mg/kg daily and 6 mg/kg monthly; dapsone: 2 mg/kg daily. The standard child blister pack may be broken up so that the appropriate dose is given to children under ten years of age. Clofazimine administration can be spaced out as required.
MDT regimen

There are two types of MDT regimens. The Paucibacillary (PB)-MDT and Multibacillary (MB)-MDT:

**PB-MDT regimen**

This regimen consists of Rifampicin and Dapsone for a total duration of 6 months. It is to be prescribed to all cases classified as Paucibacillary (PB) leprosy.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>0-5 yrs old</th>
<th>6-14 yrs old</th>
<th>≥ 15 yrs old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin (4-weekly supervised)</td>
<td>300 mg</td>
<td>450 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>Dapsone (daily, unsupervised)</td>
<td>25 mg</td>
<td>50 mg</td>
<td>100 mg</td>
</tr>
</tbody>
</table>

**MB-MDT regimen**

This regimen consists of Rifampicin, Dapsone and Clofazimine to be taken for 12 months. It is to be prescribed to all cases classified as Multibacillary (MB) leprosy.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>0-5 yrs old</th>
<th>6-14 yrs old</th>
<th>≥ 15 yrs old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin (4-weekly supervised)</td>
<td>300 mg</td>
<td>450 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>Clofazimine (4-weekly supervised)</td>
<td>100 mg</td>
<td>150 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>Clofazimine (unsupervised)</td>
<td>50 mg twice a week</td>
<td>50 mg every other day</td>
<td>50 mg daily</td>
</tr>
<tr>
<td>Dapsone (daily, unsupervised)</td>
<td>25 mg</td>
<td>50 mg</td>
<td>100 mg</td>
</tr>
</tbody>
</table>
MDT blister packs for adults

**PB adult blister pack**

**PB adult treatment:**

*Once a month:* Day 1
- 2 capsules of rifampicin (300 mg X 2)
- 1 tablet of dapsone (100 mg)

*Once a day:* Days 2–28
- 1 tablet of dapsone (100 mg)

**Full course:** 6 blister packs

---

**MB adult blister pack**

**MB adult treatment:**

*Once a month:* Day 1
- 2 capsules of rifampicin (300 mg X 2)
- 3 capsules of clofazimine (100mg X 3)
- 1 tablet of dapsone (100 mg)

*Once a day:* Days 2–28
- 1 capsule of clofazimine (50 mg)
- 1 tablet of dapsone (100 mg)

**Full course:** 12 blister packs

---

MDT blister packs for children
9.8 Administration of MDT and Phases of Chemotherapy

Phases of Treatment of Leprosy

The drug administration for treatment of leprosy with MDT has two phases;
- Daily-self administered treatment and taken every day at home.
- Monthly, Directly- Observed treatment taken at a health facility with the presence of a health worker to observe the patient taking the drugs.

The health worker should instruct the patient how to take the daily self-administered dose at home every day. The patient should also be instructed to come to the health facility every 28th day to take the monthly directly observed dose. The health worker shall supervise/observe while the patient takes the monthly dose. The health worker should make sure that patients understand which drugs they have to take once a month and which drugs they have to take every day. MDT regimens consist of two phases:
1. **Supervised:** drugs are administered under the direct observation by the health worker on fixed clinic days at four weekly intervals.

2. **Unsupervised:** drugs are self administered by the patient.

The drugs are to be taken orally and should be taken in a single dose on an empty stomach or two hours after a meal.

**Duration of MDT**

**PB:** the duration of treatment for PB patient is for 6 months. The monthly supervised dose is Rifampcin & Dapsone (R & DDS) and is taken at the start of treatment (day 1) and then every 28th day of the month for 6 consecutive months. The daily, Self Administered dose is Dapsone and is taken every day for 6 months. The full course of treatment must be completed within 9 months after initiation of treatment.

**MB:** the duration of treatment for MB patient is for 12 months. The monthly, supervised dose is with Rifampcin, Clofazemine & Dapsone (R, C & DDS) and is taken at the start of treatment (day 1) and then every 28th day of the month for 12 consecutive months. The daily, self-administered dose is with Clofazemine and Dapsone and is taken every day for 12 months. The full course of treatment must be completed within 15 months.

**9.9 Treatment in Special Conditions**

**Pregnancy and breast-feeding**

The standard MDT regimens are safe, both for the mother, the unborn child and the child and therefore can be administered during pregnancy and breast-feeding.

**Patients co-infected with HIV**

Patients infected with HIV usually respond equally well to leprosy treatment as those without HIV infection.

**Patients co-infected with TB**

Patients suffering from both TB and leprosy require standard TB treatment in addition to the standard MDT. Hence, skip the monthly dose of the rifampicin in the leprosy MDT regimen. Once the TB treatment is completed, the patient should continue his/her MDT, or the other way round.
9.10 Management of Adverse Effects of Leprosy Drugs

MDT is remarkably safe and serious adverse effects are very rare. Nevertheless, patients have to be educated on the side-effects of the drugs and on the need to report whenever such side-effects occur.

Table 18: Adverse effects of MDT Drugs

<table>
<thead>
<tr>
<th>Side-effects</th>
<th>Responsible Drug (s)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itching and skin rash</td>
<td>Rifampicin</td>
<td>Reassurance</td>
</tr>
<tr>
<td>Loss of appetite, nausea and abdominal pain</td>
<td>Rifampicin</td>
<td>Give drugs with food</td>
</tr>
<tr>
<td>Orange/red urine, faeces, saliva and sputum</td>
<td>Rifampicin</td>
<td>Reassurance (harmless and will disappear after cessation of MDT)</td>
</tr>
<tr>
<td>Brown discoloration of skin lesions and</td>
<td>Clofazimine</td>
<td>Reassurance (harmless and will disappear after cessation of MDT)</td>
</tr>
<tr>
<td>pigmentation of the conjunctiva</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dryness of the skin and ichthiosis (thick,</td>
<td>Clofazimine</td>
<td>Apply Vaseline ointment</td>
</tr>
<tr>
<td>rough and scaly skin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia (sleeping difficulties and</td>
<td>Dapsone</td>
<td>Give the drug in the morning</td>
</tr>
<tr>
<td>disturbances)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaemia</td>
<td>Dapsone</td>
<td>Give iron and folic acid</td>
</tr>
<tr>
<td>Major</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jaundice (Yellowish discoloration of the</td>
<td>Rifampicin</td>
<td>Stop treatment and refer</td>
</tr>
<tr>
<td>sclera, skin and mucous membranes)</td>
<td>Dapsone</td>
<td></td>
</tr>
<tr>
<td>Skin rashes, severe itching and urticaria</td>
<td>Dapsone &amp; Rifampicin</td>
<td>Stop treatment and refer</td>
</tr>
<tr>
<td>(pale red, raised itchy bumps)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

9.11 Treatment Monitoring and Follow-up

MDT should be given on fixed clinic days. Patients who cannot attend on the fixed clinic day should be allowed to collect drugs on the following days. If the patient is unable to collect the drugs for reasons related to illnesses or age, drugs could be given to family members.

During every clinic visit for MDT administration or monitoring follow-up, do the following:

Educate the patient about the importance of regularly taking of the medications, the major side effects of the drugs and signs and symptoms of reactions/neuritis and on the need to report immediately to the nearby treatment center whenever any problem occurs.

Carry out nerve function tests (VMT and ST of the eyes, hands and feet) to detect nerve function impairment early and to prevent the occurrence of disability.

REMEMBER to Examine the eyes, hands and feet (including VMT-ST) at any time if the patient complains loss of sensation and/or change in muscle strength or problem with vision, routinely every month as long as the patient is on MDT and just before Release From Treatment (RFT)
Nerve function assessment at the end of treatment should be compared with that at the beginning of treatment. This includes comparing disability grades and VMT-ST status at the beginning and completion of treatment. The assessment should be scored as improved (I), same (S) or deteriorated (D) and recorded in the patient record card and unit leprosy register.

9.12 Treatment Outcome

**Multibacillary (MB) cases** should complete 12 four weekly doses of MDT (12 months) within a maximum period of 15 months.

- After completion of the 12 doses of MDT, the patient should be released from treatment (RFT) and recorded as *treatment completed*.
- If a patient misses some treatment, the number of doses missed should be added on at the end, so that the complete course of treatment is given. A patient who has missed more than 3 four-weekly doses of MDT (3 months) in total should be recorded as *default*.
- If an MB patient recorded as a default reports at a clinic, a second course of MDT should be started, after the importance of regular treatment is discussed with the patient.
- Patients who restart treatment must be entered into a new treatment cohort, which is currently open for intake. They should be re-registered as return after default with a new registration number. The previous number should be recorded in the column ‘remarks’. This implies that such patients have been included in two different cohorts, the first one being the cohort in which they did not successfully complete their treatment, the second one being the cohort whose intake period includes the point at which they started their second MDT course.
- After completion of the second course of MDT, the patient should be declared *treatment completed*.
- Patients who fail to complete the second course of MDT should not be given a third chance. These patients should be recorded as *default* immediately after they have missed the 4th four weekly doses of MDT. They should be told to report immediately as soon as signs of active disease return.

**Paucibacillary (PB) cases**

Paucibacillary (PB) patients should complete 6 four-weekly doses of MDT (6 months) within a maximum period of 9 months.

- After completion of the 6 doses of MDT the patient should be released from treatment (RFT) and recorded as *treatment completed*.
- Patients who have missed more than 3 four-weekly doses of MDT in total should be recorded as *default*.
- If they return to the clinic again, they should not be given a second course of MDT unless they are found to have signs of active disease.
Table: Definitions of treatment outcome

<table>
<thead>
<tr>
<th><strong>Treatment completed:</strong></th>
<th>A patient who has completed a full course of MDT within the prescribed period (6 doses for PB in nine months and 12 doses for MB in 15 months).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Died:</strong></td>
<td>A patient who dies of any cause during the course of MDT.</td>
</tr>
<tr>
<td><strong>Default:</strong></td>
<td>A patient who has failed to collect more than three (consecutive or cumulative) four-weekly (monthly) doses of MDT.</td>
</tr>
<tr>
<td><strong>Transfer out:</strong></td>
<td>A patient who has started treatment and has been transferred to another health institution and for whom the treatment outcome is not known at the time of evaluation of the results of treatment.</td>
</tr>
</tbody>
</table>

**Retrieval of absentees**

If a patient has neither attended the fixed clinic day nor during the two weeks thereafter, he/she has to be considered as an absentee and should be retrieved. The following measures are suggested:

- Inquire from fellow patients as to why the patient has failed to collect his/her drugs and ask them to contact and advise the absentee.
- Notify the contact person, recorded in the register, through available means and request his/her assistance to encourage the patient to return for treatment.
- Send out messages through health workers who may travel to the patient’s village for outreach health programmes like EPI.
- Communicate with the health extension worker or community volunteers to assist in retrieving the patient.
- Visit the home of the patient if possible.

The above measures can be taken either in combination or separately and all efforts must be exerted to ensure the continuation of treatment.

**Treatment for patients living in inaccessible areas**

Some patients who live in geographically inaccessible areas or whose lifestyle does not permit regular visits to the health facility (e.g. pastoralists) or who cannot attend clinics at certain times (e.g. rainy season) should be given a sufficient supply of MDT blisters to cover their period of absence. In exceptional cases it is acceptable to give a full course supply of MDT blisters to these patients. However, the involvement of a formal or informal community leader or community health worker in the monitoring of drug intake should always be sought. Such patients should strongly be advised to report to the nearest health facility if they develop any problem or complication.

**Referral of leprosy patients for special care**

The patient requires referral to an experienced physician or hospital if s/he has:
- Severe reaction not responding to steroid treatment for 2 or 4 weeks (respectively for PB patients and MB patients)
- Recurrent/chronic reaction
- Red and/or painful eye
- Diabetes
- Not improved with current treatment
- Developed a reaction for the second time
- Deep ulcer(s)
- Permanent paralysis that is suitable for reconstructive surgery

When a patient is referred, make copies of the sensation maps and strength records which show recent changes and send it with the referral form. If a patient does not return to referring health facility to continue his/her treatment, contact the hospital to determine the patient’s treatment outcome.

9.13 Follow Up and Care After Release from Treatment (RFT)
Most patients will have no further problems after release from treatment. However, after being congratulated for completing treatment, they need to be made aware of possible complications:
- The skin patches caused by the leprosy will not disappear immediately.
- Loss of sensation, muscle weakness and other nerve damage may also persist.
- Leprosy reaction can still develop after MDT and these reactions can be effectively treated. If any unusual symptoms occur, the person should come back immediately for examination and treatment.
- Recurrence of the disease (relapse) is rare, but if they suspect the disease has returned, they should come for further examination.
- Return to the health facility in 12 months’ time for a routine follow-up review. Patients should be reviewed annually for 2 years after release from treatment, to identify any late occurring reaction or nerve function impairment.
- Visit or report to the nearby health facility whenever they have complaints.

Care to leprosy patients include:
- Management of neuritis
- Provision of protective foot wears
- Provision of vaseline ointment
- Basic medications such as analgesics, antibiotics, eye ointments have to be provided.

These are provided to the patients free of charge if and only if they are made available by the control programme. When this is not the case, patients should be encouraged to buy by themselves. All these care activities should be recorded in the RFT register and some of them (like neuritis treatment and provision of protective foot wears) should be reported quarterly.

9.14 Leprosy Reactions, Complications and Their Management

Complications in leprosy
Complications of leprosy may occur or may have already occurred at the time of treatment. These include adverse drug reaction, leprosy reaction, Complications of advanced disease and psychosocial problems. Advanced disease of leprosy may be eye problems leading to blindness because of damage to the cornea, or due to damage to the internal structures of the eye. The health worker must refer to an eye specialist any patient who reports decreased vision or has a red or painful eye. Patients may already have sunken nose, loss of eyebrows and the so-called ‘leonine’ face which used to be characteristics of untreated MB leprosy are cosmetic problems
and visible disfigurements that lead to severe stigma and discrimination. Plastic surgery is needed to correct these lesions.

Psychosocial problems are related to widely-held beliefs and deep rooted prejudices concerning leprosy and its underlying causes, and not merely to the problem of disability. People with leprosy often suffer from low self-esteem and depression, as a result of rejection and hostility they endure at the hands of the family and community. Such negative attitudes are also observed among staff of the health services, including doctors. These need to be addressed with urgency. People suffering from psychosocial problems may need to be referred for counselling or other help.

**Patients With suspected complication SHOULD be referred to the nearest hospital for appropriate management**

**Leprosy reactions**
Leprosy reaction is an immunological response to the bacilli, presenting as acute inflammatory episodes. It is the sudden appearance of symptoms and signs of inflammation on the skin, eyes and peripheral nerves. Clinically, there is redness, swelling and sometimes tenderness of skin lesions. There may be swelling, pain and tenderness of nerves, often accompanied by loss of function. New skin lesions may also appear. The long-term problems related to leprosy (deformity and disability) are due to nerve damage from leprosy reactions. Therefore, early detection and adequate management of reactions is very important.

**There are two types of leprosy reactions:**

1. **Reversal Reaction (or Type 1 reaction)**
2. **Erythema Nodosum Leprosum (ENL) or Type 2 reaction**

Both types of leprosy reactions can occur before the start of treatment, during treatment and after release from treatment. Both can be divided into mild or severe reactions. A mild reaction is one that occurs in the skin only (as long as it does not occur over a major nerve or in the face); there may be mild fever and slight swelling (oedema) of the limbs. Severe reactions affect the nerves or eyes. **Only when the reaction is severe, treatment with corticosteroids is necessary.**

**Type I (reversal) reaction**

Both PB & MB patients can develop this type of reaction. Suspect Type 1 reaction in patients with the following Signs and symptoms:

- Pain over the lesion
- The lesion becomes more red, warm, swollen and tender
- Oedema of the face, hands and feet
- Deterioration in the nerve function
Mild reversal reaction and treatment

Suspect/Confirm Mild reversal reaction if only oedema and erythema of skin lesions (excluding the face and overlying nerve trunk) are present. If there are any signs of neuritis such as nerve pain or tenderness or loss of nerve function, the reaction is no longer mild, and should be managed as a severe reaction.

TREAT mild Type I reaction with analgesics acetylsalicylic acid (Aspirin 600 mg up to 6 times per day [adult dosage], or Paracetamol if Aspirin is not available).

Examine the patient after one week. If there are still signs of reaction, the treatment should be continued for another week, after and examine again for new nerve damage at every clinic attendance. If nerve damage occurs, the patient is suffering from a severe reaction, then manage as for severe reaction accordingly.

Severe reversal reaction and treatment

Suspect/Confirm a severe reversal reaction when a patient has one or more of the following signs:

- Pain or tenderness on palpation in one or more nerves, with or without loss of nerve function.
- Change in VMT (including eye closure) of less than six months duration. The change can be from strong to weak, from weak to paralysis, or from strong to paralysis.
- Change in ST of less than six months duration. A change is considered to be significant when any hand or foot has increased loss of sensation at two or more points.
- A raised, red swollen patch overlying a nerve trunk or around an eye.
- Red, raised and ulcerating skin lesions.
- Oedema of hands or feet.
- A mild reaction lasting more than 6 weeks.

Give prednisolone treatment to patients who present with one or more of the signs given above and who do not present with any condition which requires referral to hospital.

ADVISE patients with nerve involvement to rest the affected limb.

Prednisolone is a potent corticosteroid drug. The drug is supplied in blister packs. Each blister contains 2 weeks treatment at different strengths, so that only one tablet is taken daily, in the morning after a meal. Patients should be carefully educated on the requirements for successful treatment and the risks involved in steroid treatment.

Conditions to be treated before starting prednisolone treatment

Appropriate treatment should be given for the following concurrent diseases:

- Diarrhoea, with blood and/or mucus
- Fungal infections
- Scabies
- Worm infestations
- Epigastric pain (gastritis/peptic ulcer disease)
- Conjunctivitis and trachoma

Treatment for the above conditions should be started immediately, but need not be finalised before the start of treatment with prednisolone.
Type II Reaction (Erythema Nodosum Leprosum: ENL)

ENL occurs in MB patients only. It usually appears quickly and may disappear within 1-2 weeks. Erythematous (red) and tender (painful) sub-cutaneous nodules are usually present and are more commonly seen on the face and/or the external surface of the limb.

Severe ENL: signs and treatment

Suspect/Confirm Type II reaction if a patient has one or more of the following signs:

- Appearance of Erythematous Sub-cutaneous Nodular Lesions with ulceration (ulcerating ENL).
- Tenderness on palpation or spontaneous pain in (a) nerve trunk(s).
- Loss of muscle strength and/or loss of sensation in eyes, hands or feet, for less than 6 months.
- Painful eyes, with redness around the limbus cornea, increased lacrimation, fixed narrowing (constriction) of the pupil and diminishing vision (irido-cyclitis).
- Painful testicular swelling (orchitis).
- Painful swollen fingers (dactylitis).
- General condition: fever and malaise.

Patients may experience several episodes of ENL, one after the other (recurrent ENL). MB patients may develop a reversal reaction and an ENL reaction simultaneously. All patients with ENL should be referred (to a hospital where experienced health workers are available) immediately with their clinical records to hospital for treatment. Patients with ENL reaction should always be admitted as this may be a life threatening condition.

N.B All ENL (Type II) reactions are severe

Criteria for referral to a hospital during reaction

- ENL reaction
- Deep ulcer(s)
- Red and/or painful eye
- Pregnancy
- Younger than 12 years of age
- Severe peptic ulcer disease
- Diabetes
- General illness with fever
- Patient who improved during previous courses, but who develops a reaction for the 3<sup>rd</sup> time
- Severe depression or psychosis
- Suspected relapse
Table 19: Ambulatory treatment of severe reversal reaction with Prednisolone

<table>
<thead>
<tr>
<th>Duration of treatment</th>
<th>MB</th>
<th>PB</th>
<th>Daily dose (do not exceed 1 mg per kg body weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 weeks</td>
<td>2 weeks</td>
<td></td>
<td>40 mg</td>
</tr>
<tr>
<td>4 weeks</td>
<td>2 weeks</td>
<td></td>
<td>30 mg</td>
</tr>
<tr>
<td>4 weeks</td>
<td>2 weeks</td>
<td></td>
<td>20 mg</td>
</tr>
<tr>
<td>4 weeks</td>
<td>2 weeks</td>
<td></td>
<td>15 mg</td>
</tr>
<tr>
<td>4 weeks</td>
<td>2 weeks</td>
<td></td>
<td>10 mg</td>
</tr>
<tr>
<td>4 weeks</td>
<td>2 weeks</td>
<td></td>
<td>5 mg</td>
</tr>
<tr>
<td>Total 24 weeks</td>
<td>Total 12 weeks</td>
<td>STOP</td>
<td></td>
</tr>
</tbody>
</table>

Follow up patients on prednisolone treatment (for reaction) every 2 weeks.

- Assess the patient condition and do VMT and ST at each visit.
- REFER any patient in whom nerve function deteriorates during the standard course or who does not show improvement after 4 weeks on prednisolone treatment to hospital where higher dosages of prednisolone can be given.
- REFER a patient who has responded positively to a previous full course of prednisolone, but the reaction re-occurs or the nerve function deteriorates.

Management of severe reactions in hospitals

For hospitalized patients the initial dose of prednisolone will be as high as 80mg in a daily single morning dose. The dose can be tapered by 10mg every 2-4 weeks depending on the severity and response to treatment until a level of 40mg is reached. Then normal tapering off should recommence as indicated in the table above. If at any dosage, the clinical signs of reaction fail to improve after 5-7 days or if nerve damage increases, the prednisolone dosage should be doubled for about 2 weeks. Then reduce step wise at intervals of 2-4 weeks or so till it returns to the previous level and then normal tapering off should then recommence.
### Table 20: Side effects of steroids (Prednisolone) treatment & their management

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs of diabetes (thirst or excessive urination)</td>
<td></td>
</tr>
<tr>
<td>Development of sepsis</td>
<td>Refer the patient</td>
</tr>
<tr>
<td>Osteoporosis and pathological fractures</td>
<td></td>
</tr>
<tr>
<td>Myopathy (muscle pain)</td>
<td></td>
</tr>
<tr>
<td>Worsening of tuberculosis</td>
<td>AFBs or refer the patient</td>
</tr>
<tr>
<td>Diarrhea or dysentery</td>
<td>Re-hydration, stool examination</td>
</tr>
<tr>
<td></td>
<td>and specific treatment</td>
</tr>
<tr>
<td>Swelling of the face, increased hair growth and acne</td>
<td>Reassure</td>
</tr>
<tr>
<td></td>
<td>No specific treatment is required</td>
</tr>
<tr>
<td>Abdominal (Epigastric) pain (This might be due to peptic ulceration)</td>
<td>Give antacids</td>
</tr>
</tbody>
</table>

_N.B. If prednisolone is not properly tapered, adrenal insufficiency may occur resulting in shock and death._

### Relapse in Leprosy

Relapse 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 is diagnosed by the appearance of definite new skin lesions and/or an increase in the bacterial index (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. MDT is a very effective treatment for leprosy. If a full course of treatment has been administered properly, relapse is generally rare. Most relapses occur long after the treatment was given, sometimes more than 10 years later.

Refer all suspected cases of relapse for further investigation at a leprosy referral center. Use the table below to guide you on how to suspect leprosy relapse and differentiate it from leprosy reaction.
Table 21: Table showing differentiation between relapse and Reactions

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Relapse</th>
<th>Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development of signs</td>
<td>Slow</td>
<td>Sudden</td>
</tr>
<tr>
<td>Site</td>
<td>New patches</td>
<td>Over old patches</td>
</tr>
<tr>
<td>Tenderness/ pain</td>
<td>No (unless also in reaction)</td>
<td>Nerves usually, skin sometimes</td>
</tr>
<tr>
<td>Damage</td>
<td>No (unless also in reaction)</td>
<td>Sudden and rapid</td>
</tr>
<tr>
<td>General condition</td>
<td>Not affected (unless also in reaction)</td>
<td>Often fever, joint pain etc.</td>
</tr>
<tr>
<td>Duration after treatment completion</td>
<td>&gt; 2 years</td>
<td>&lt; 2 years</td>
</tr>
</tbody>
</table>

*N.B. Relapses after the complete course of MDT are very rare.*

9.15 Prevention of Disability (POD) in Leprosy

Disability is preventable and is not inevitable for people affected by leprosy. However, all leprosy patients are at risk of developing disability at any time (before, during and after treatment). Most disability and deformity result directly or indirectly from loss of function of peripheral nerves supplying the eyes, hands and/or feet.

Disability and deformity can be prevented by timely detection and prompt treatment of neuritis, Poor treatment of leprosy can cause permanent disability and deformity, which fosters hopelessness, and stigma and fear against those affected. It is therefore the task of all health staff working with leprosy patients to *preserve nerve function*, and to prevent further deformity and disability in patients who already have irreversible disability at the time of diagnosis. The best To prevent disabilities do the following:

- Early diagnosis of leprosy and prompt treatment.
- Recognise nerve function impairment at the time of diagnosis and start treatment with steroids if it began recently (less than 6 months).
- Recognise and promptly treat new signs and symptoms of leprosy reactions with nerve involvement during treatment.
- Educate patients to recognise early signs of nerve function impairment and to report this immediately.
- Train (with demonstration and practice by patient in the presence of care giver) patients about self care.directed at the disabilities they are at risk of developing. Training should be individualized as much as possible

Interventions for preventing (further) disability

Patients as well as individual health workers should learn how to manage specific Leprosy-related problems and disabilities. There are three categories under which useful interventions can
be practiced to prevent (further) disability in leprosy. These are:

1. Home-based self-care
2. Simple interventions organized at the local clinic
3. Referral services for more complex interventions that require inputs from specialists

**Home-based Self care to prevent (further) disability**

Health workers have the responsibility to diagnose, treat and educate the patients in order to prevent disability. Prevention of Disability (POD) is the patients’ responsibility for the rest of the time! Therefore health workers must educate patients on how to avoid the complications of the disease and prevent further disability by practicing self-care.

**How can health workers promote effective self care in patients with leprosy related disabilities?**

Health workers should educate leprosy patients about self care while they are on treatment and after released from treatment to help them prevent disability. The most effective self-care training is:

- **Specific** to the patient (targets disabilities they have / are at risk of)
- **Practical** (the patients actually do the self-care with the health worker)
- **Achievable** by the patient (promotes simple, affordable methods)
- **Repeated** (what was taught is reviewed each time the patient visits, to make sure they understood and are practicing it).
- **Empowering** – the patient believes “I can do it” in terms of self-care and prevention of further impairments

**Self care groups**

Self care can be encouraged by establishing ‘self-care groups’ of patients with similar disabilities who live close to one another. Self-care groups who meet together regularly promote:

- Independence and interdependence among group members living close together.
- The use of locally available self-care materials for skin and wound care, and encourage group members to support each other to maintain interest in lifelong self-care.
- Self-care succeeds when people fully take charge of their own care

**What are the activities to prevent disability which can be performed by the person at home?**
Self care for the eyes

If there is:

- **Motor weakness**: can’t close eyes fully (lagophthalmos)
  - Exercise (close the eyes strongly) if the muscles are weak, or
  - Do ‘passive blink’ often if eyelid muscles are completely paralyzed

- **Sensory impairment** (corneal anaesthesia)
  - Do “Think-blink” exercises (consciously blink eyes frequently)

The patient must be advised to:

- Cover the eyes with a clean cloth when sleeping.
- Protect eyes during the day. E.g. use spectacles, hat, scarf.
- Inspect the eyes daily using mirror. Check for foreign bodies or redness.
- Clean eyes daily with clean water.
- Apply lubricating eye drops or one drop of caster oil in the morning and evening.

Self care for the hands

When the patient has problems on the hands, advice the patient to do the following at home:

- Inspect the hands daily for signs of injury
- Soak the insensitive hand in water for about 30 minutes every day to maintain skin elasticity and prevent dryness of the skin
- Use a rough stone to smoothen the callus, and then apply oil or petroleum jelly when the skin is still wet to prevent the skin from drying out.
- Use a clean cloth to prevent any open wound.
- Avoid handling hot materials with bare hand
- If there is weakness of the muscle in the hand, passive stretching and active exercises to prevent contractures and to get some strengthening

Self care for the feet

When the patient has problems on the feet, advice the patient to do the following at home:

- Inspect the feet daily for signs of injury.
- Soak and then apply oil the feet. As for the hands use a rough stone to rub away the callus.
- Walk as little as possible and walk slowly. Rest frequently.
- If ulcers are present, rest is essential.
- Use a clean cloth to cover open wounds.
- If there is a foot-drop, do passive stretching to prevent a contracture of the Achilles tendon.

Simple interventions organized at the local/peripheral clinic.

When General health workers have a patient with certain disability, they can arrange to see person so that specific interventions relevant to that person can be discussed. Individual health
workers should learn how to manage the specific problems seen in their own patients. Provide any help that may be needed by the person to carry out the home-based self-care tasks mentioned above.

**Intervention on the eyes**

When the patient has eye problems, do the following at the clinic:

- **Provide** to the patient saline drops for use at home if the eyes are very dry.
- **Treat** conjunctivitis with antibiotics and an eye pad.
- **Refer more serious eye problems to an eye clinic/ophthalmologist**

**Intervention on the hands**

When the patient has problems on the hand, do the following at the clinic:

- **Provide** cooking gloves if the patient has insensitive hands (if available)
- **Refer** More serious hand problems to the referral centers for physical Rehabilitation

**Intervention on the feet: Provision of protective footwear**

Patients with sensory loss in the feet must wear protective footwear. Any kind of footwear will protect the feet as long as it has:

1. Hard sole (so thorns, glass etc. on the road can’t penetrate)
2. Soft insole (to spread force and prevent blisters)
3. Back-strap or heel cup (so footwear can’t fall off), and
4. Flexible, adjustable, good fit (e.g. made of leather or cloth, with laces, buckles, or Velcro)

If no deformity is present, provide proper protective footwear (canvas shoes, embedded with MCR) or market shoes

Patients can collect canvas shoes, embedded with micro cellular rubber (MCR), and other orthopaedic appliances from MDT providing health facilities and nearby orthopaedic workshops respectively. Otherwise advise them to buy their own appropriate protective footwear from the local market.

If significant foot deformity is present, use special orthopedic appliances made in orthopedic workshops.

**Refer more serious problems to the referral centers for physical Rehabilitation**

Closed plastic shoes are not suitable as they exacerbate sweating, blisters, and infection of the skin and underlying tissues.
Referral services for more complex interventions.
These are interventions which can usually only be done at a referral centre and require inputs from specialists.

Intervention on the eyes
When the patient has eye problems, the following interventions can be performed by an eye specialist at the clinic:

- Any acute eye problem should be managed at an eye clinic.
- Corrective surgery may be helpful in severe cases of lagophthalmos.
- Remember that cataract is the commonest cause of blindness in elderly people, whether or not they have leprosy. Leprosy does not prevent routine cataract surgery.

Intervention on the hands
When the patient has problems on the hands, the following interventions can be performed at the referral clinic:

- Help the person adapt tools to avoid injury to insensitive hands
- Remove thick callus and trim ulcers with a scalpel blade
- If there is weakness or a contracture, make a splint to wear at night
- An invasive infection (the hand is hot, red and swollen) is an emergency and must be referred for intensive antibiotic treatment and surgery
- Surgery may be useful in some cases of weakness or claw-hand

Intervention on the feet
When the patient has problems on the feet, the following interventions can be performed at the referral clinic:

- Remove thick callus and trim ulcers with a scalpel blade.
- Chronic ulcers may be helped by orthotics, or by surgery.
- For a foot-drop, make a spring-loaded device to keep the foot in the correct position while walking.
- An invasive infection (the foot is hot, red and swollen) is an emergency and must be referred for intensive antibiotic treatment and surgery.
- Foot-drop surgery can be performed

Septic and re-constructive surgery
There are surgical procedures and techniques to correct or limit the deterioration of deformities and disabilities. Refer patients in need of sophisticated surgical procedures and techniques like tendon transfer operations, plastic surgery and others to specialized hospitals like ALERT.

9.16 Prevention of Leprosy

Chemo prophylaxis
Unlike TB, there is no indication for chemoprophylaxis for leprosy.

BCG
BCG vaccination has a documented and substantial effect in preventing leprosy and is therefore considered as an important tool for prevention of leprosy.
10. COMMUNITY PARTICIPATION IN TB AND TB/HIV CONTROL

10.1 Community TB Care (CTBC)
Community Based TB care is a working partnership between the health sector and the community in the prevention and care activities of TB. Communities’ involvement is one of the key components of the National TB Prevention and Control Strategy with the aim of empowering community to contribute to TB suspect identification, referral, and treatment support and follow up. However, community’s contribution to TB care is explicitly a contribution to, and not a substitute for, basic health services of TB control activities.

10.2 Objectives of CTBC
- To increase community awareness on TB transmission, prevention and treatment
- To identify and promptly refer TB suspects for early diagnosis and initiation of treatment
- To improve access to DOT service
- To ensure retrieval of absentees/interrupters

Components of CTBC
- Community awareness creation and social mobilization on TBL and TB/HIV prevention and control activities.
- Promotion of TB Infection control at community and household level
- Identification and referral of TB suspects
- TB contacts tracing and referral
- Community based DOT and treatment follow up
- TB treatment absentees/ interrupters and defaulters retrieval

10.3 Implementation of Community TB Care
CTBC implementation is a collective responsibility of all stakeholders including political administrators, health administrators, health workers, partners and the community at large. National TB Control Program has developed CTBC implementation guideline to guide the operational implementation processes. For details, refer the updated version of this guideline.

Area of engagement for health centers
They are required to be engaged in capacity building of HEWs and TB treatment supporters, strengthening of referral linkages with health posts and monitoring the implementation of CTBC activities. Additionally, they must ensure supply of IEC materials, recording and reporting materials and anti-TB drugs.
Area of engagement of health posts

1. Implementation of the CBTC components as per the details the implementation Guidelines.
2. Coordination of the implementation of the CBTC components by local partners such as civil society organizations and community structures.

TB treatment supporters

TB Treatment Supporter (TTS) is a volunteer who provides close support to TB patient in making sure that daily doses of anti-TB drugs are taken as directed until the end of treatment. TTS can be a health extension worker, a family member, a community leader, a religious leader or facility health worker. The following are roles of TB treatment supporters in CTBC:

- Daily supervise treatment and tick on the patient’s Treatment card
- Educate and support TB patients and family
- Accompany the patient on weekly bases to refill drug from the DOTS clinic
- Collect drugs if the TB patient is clinically unstable to collect Anti-TB drugs
- Report any difficulties encountered during the treatment to health post/health center
- Trace patients interrupting treatment and help them return to treatment

Criteria for selection of treatment supporters:

- Accepted by the patient
- Resident in the nearby
- Agree to support the daily treatment throughout the course of treatment
- Sympathetic and considerate individual
- Must maintain Confidentiality of the client

Patients not eligible for TTS at Community level

- Patients on injectable
- Clinically unstable patients
- History of non-adherence to treatment
- TB/HIV co-infected Patients on ARVs and Ant-TB treatment, and
- MDR-TB patients on the intensive phase of treatment and suspected/confirmed XDR-TB cases
11 PUBLIC-PRIVATE MIX IN TB CARE

11.1 Introduction

Engaging all relevant health care providers in TB care and control through public-private mix approaches is an essential component of the National TB control Strategy.

Public-Private Mix (PPM) for TB Care and Control represents a comprehensive approach for systematic involvement of all relevant health care providers in TB control to achieve national TB control targets set in the HSDP IV. PPM encompasses diverse collaborative strategies such as public-private (between public and the private-for-profit and private for-non-profit sector), public-public (between public and other public sector care providers such as general hospitals, prison or military health services and social security organizations), and private-private (between an NGO or a private hospital and the neighbourhood private providers) collaboration. PPM also implies engaging relevant care providers in prevention and management of Drug Resistant-TB and in the implementation of TB/HIV collaborative activities. PPM can play significant role in TB suspect identification and referral service as well as in TB treatment supervision. This demonstrates that virtually all types of potential health care providers including traditional healers fit within the umbrella of PPM. At present, Ethiopia's PPM model focused on private for-profit private, private not for profit (NGO) and workplace health providers. In PPM, all certified facilities are expected to meet the national standards and Guidelines for TB care; in addition, The International Standard for TB Care (ISTC) have to be maintained by all care providers, public and private, in managing patients who have, or are suspected of having TB.

RATIONALE

- Strong Political commitment to encourage the contribution of private sector in health care delivery system of the country (HSDP IV, GTP, health policy...)
- Growing contribution of the private sectors in health sector
- Enhanced quality of TB diagnosis, care and treatment
- The growing need to improved equity and access to services
- The need to standardize case management practices to reduce treatment errors and rational use of anti-TB drugs through formal engagement of the providers.
- Increasing workload of public Health facilities health care workers.

11.2 Service Areas for Engaging Private Sectors in PPM DOTS

Private sectors and all other relevant providers outside of the realms of the NTP are allowed/encouraged to be engaged in the delivery of following services:

- Advocacy, communication and social mobilization
- Identification and referral of TB suspects to nationally accredited diagnostic centers
- Participation in diagnostics and Quality assurance services
- Treatment delivery services
- Community TB care services
- Mentoring, Supportive supervisions and monitoring of performance
- Delivering TB/HIV interventions
- Sputum sample collection and transportation services to the designated diagnostic centers
- Delivering MDR-TB diagnostic and/or treatment services
- Participate in operational researches

Potential Private Care providers for engaging in PPM DOTS program in Ethiopia include:
- Private-for-profit:
  - Private hospitals, Clinics, centers, diagnostic labs, drug outlets
- Private-for-non-profit
  - FBO clinics, NGO clinics, workplace clinics
- Other governmental organizations
  - Uniformed service clinics, prison, factory
- Civic Society Associations and community structures
  - Idir, anti-TB clubs, formal association, local NGOs

The delivery of one or combination of services can apply to one private facility after fulfilling the requirements, completion of preparatory procedures and signing memorandum of understanding (MOU) with the responsible governmental body. The details of the implementation guidance can be obtained on the updated edition of the National PPM DOTS implementation guidelines.
12 ADVOCACY, COMMUNICATION AND SOCIAL MOBILIZATION FOR TBL AND TB/HIV

12.1 Principles of Advocacy, Communication and Social Mobilization

Advocacy, communication and social mobilization (ACSM) embrace: advocacy to influence policy changes and sustain political and financial commitment; two-way communication between the care providers and people with TB as well as communities to improve knowledge of TB control policies, programmes and services; and social mobilization to engage society, especially the poor, and all allies and partners in the campaign to Stop TB. Each of these activities can help build greater commitment to fighting TB. ACSM efforts in TB control should be linked with overarching efforts to promote public health and social development.

Advocacy is intended to secure the support of key constituencies in relevant local, national and international policy discussions and is expected to prompt greater accountability from governmental and international actors. It is a process to create change in policies, laws and practices. It is a broad set of interventions designed to place TB high on the political and development agenda and foster political will to increase and sustain financial and other recourses. It has the following three components:

- **Policy advocacy**: Informs politicians and administrators on how TB related issues will affect the country and outlines actions to take to improve laws and policies,
- **Programme advocacy**: Targets opinion leaders at nation and community levels on the need for sustained resources and local action and
- **Media advocacy**: Puts issues on the public agenda, encourage the media to cover TB related topics regularly and in a responsible manner to raise awareness of possible solutions.

Communication is concerned with informing, and enhancing knowledge among, the general public and people with TB and empowering them to express their needs and take action. Equally, encouraging providers to be more receptive to the expressed wants and views of people with TB and community members will make TB services more responsive to community needs. Behavior Change or Programme Communication aims at increasing knowledge, attitude changing and practice among various groups of people by creating awareness about TB, improving interpersonal communication between patients and providers and empowering people to take actions.

Social mobilization is the process of bringing together all feasible and practical inter-sectoral allies to raise people’s knowledge of and demand for good-quality TB care and health care in general, assist in the delivery of resources and services and strengthen community participation for sustainability. Social mobilization is important to create community will and commitment to be involved and to participate in TB control and prevention within the context of the community. Major target audiences of social mobilization are communities, religious leaders and social networks.
12.2 Objectives and National Strategies of TBL ACSM

Objectives
- To ensure the commitment of policy and decision makers to mobilize resources for TBL prevention and control
- To build the ACSM skills of managers/officers, service providers and promoters at all levels
- To improve communities’ health care seeking behavior on TBL
- To fight stigma and discrimination against TBL

Strategies:
The key TB controls challenges (commitment and resources, case finding & treatment adherence, stigma and discrimination and sustainability and self-reliance) are addressed through the following ACSM strategies. ACSM activities can be used to achieve all six major goals of stop TB strategy.

- Empower and involve people affected by the diseases in the prevention and control activities
- Strengthening evidence-based advocacy to ensure political commitment and resource mobilization
- Promote the use of guidelines, strategies, culture sensitive messages and materials,
- Educate different segments of the population to take action through mass media and health education programs in HFs.
- Improve ACSM skills of program managers, service providers and promoters by continuous capacity building on TBL ACSM
- Encourage operational researches to provide reliable data for messages/materials development, monitoring and evaluation.

12.3 Key TBL Messages for Patients and Service Providers

Communication with patients about TB disease is a continuous process. This process goes on as long as the patient requires chemotherapy or, as in leprosy ‘released from treatment’ (RFT), is at risk to develop further disability. The health staff must be trained and motivated to ensure effective communication with their patients.

Communication with patients should be performed in groups as well as with individual patients. The education should never be a one-way approach. A two-way communication flow should always be maintained. Patients should be stimulated to give their comments, communicate their feelings, ask questions and give suggestions. Demonstrations should accompany the explanations and the patients should be requested to practice any procedures with their actions observed and encouraged accordingly. Group education is important before starting chemotherapy in order to explain the new treatment and the importance of regular attendance. Education in self-care to leprosy patients with similar disability problems can also be done in groups. Direct communication with the patients is the best way to obtain feedback, to understand the problems patients face and also to find solutions.
### General TB Messages
- TB is communicable disease caused by bacteria
- Any person with cough of two weeks or more duration is a TB suspect and must be evaluated for TB
- With appropriate treatment TB and Leprosy are curable
- Tablets need to be taken daily, as prescribed, and at the same time each day
- TB patients will become less-infectious after two weeks of starting the treatment
- Both HIV-positive and HIV-negative TB patients respond well to TB treatment
- TB, HIV & Leprosy drugs should never be shared to anyone else
- Coughing patients should practice cough hygiene
- Household contacts of TB patients need to be screened for TB
- TB Treatment is free of charge
- TB treatment standard is the same in public and private HFs in the country
- TB treatment is given under direct observation of an health care workers and designated Treatment supporter

### Messages for TB/HIV Co-infection
- All PLHIV should be screened for TB at each visit to HFs
- All TB patients must be tested for HIV
- All TB/HIV co-infected patients must be provided with integrated TB/HIV services

### Messages on MDR-TB
- MDR TB is the result of failure to strictly adhere to TB treatment
- Transmission, symptoms and signs of MDR TB is similar with that of drug-susceptible TB
- MDR TB suspects should be investigated to confirm the diagnosis
- With an appropriate and timely treatment with second line anti-TB drugs, MDR-TB is curable
- Treatment of MDR TB requires strict adherence to treatment

### Leprosy specific messages
- Leprosy is caused by bacteria and not by curse or heredity
- MDT drugs are free of charge to Leprosy patients
- Disability caused by leprosy can be prevented and reduced through early diagnosis and treatment
In order to achieve sustainable program implementation, it is very important to ensure that every health unit involved in the prevention, diagnosis and treatment of Tuberculosis & Leprosy has an adequate and uninterrupted supply of drugs, laboratory reagents, medical supplies and equipment.

To ensure the uninterrupted availability of sufficient amount of pharmaceuticals, there must be:

- Appropriate selection, quantification, procurement, warehousing, distribution and inventory management systems where applicable
- Accurate inventory records with clear SOPs to fill and update the records.
- Timely requisition of pharmaceuticals by health facilities.
- Effective and efficient pharmaceutical delivery system to health facilities
- Sufficient pharmaceutical stores which fulfils standard storage principles at PFSA and health facilities.
- Well-defined responsibilities for the various activities and steps.
- Regular communication between the pharmacy and TBL and TB/HIV program sections at all levels.

In addition to this, ensuring the rational use of these pharmaceuticals is crucial in achieving proper program implementation.

PFSA is mandated for all the responsibilities of Pharmaceuticals Supply Management (PSM). Accordingly, all the responsibilities which were handled by FMOH/NTP such as quantification, procurement and distribution of all TBL commodities will be handled by PFSA in an integrated manner with other pharmaceuticals; and all the necessary pharmaceuticals will be directly delivered to health facilities by PFSA. The integrated delivery of TBL commodities to health facilities has been started by PFSA and will be scaled up throughout the country in a phased manner.

13.1 TBL Drugs Supply Management

According to the Integrated Pharmaceutical Logistics System (IPLS), all pharmaceuticals are handled and managed in an integrated manner and the distribution pipeline has only three levels, namely; Central PFSA, PFSA Hubs/branches and Health Facilities (health centers and hospitals).
All TBL pharmaceuticals quantification, procurement and storage are done at the central PFSA level in collaboration with NTP/FMOH.

**Forecasting**
Forecasting of anti-TBL pharmaceuticals will be conducted by PFSA, in collaboration with all stakeholders such as the NTP, RHBs and partners. As much as possible, forecasting should be conducted on annual basis; but it can also be conducted every 2 to 3 years with annual revision of the forecast. All possible data, including consumption and morbidity data, can be used for the forecasting.

**Procurement**
TBL pharmaceuticals procurement should be done in a timely and effective manner by PFSA. Sometimes, depending on different factors, the NTP/FMOH might conduct direct procurement for some pharmaceuticals. It will also be the responsibility of the NTP/FMOH to arrange and facilitate emergency procurements and donations in collaboration with PFSA and partners.

Concerning laboratory reagents, after the bulk reagents are procured by PFSA, the Central and Regional/sub regional laboratories are responsible to prepare the reagents with standard procedure for periphery laboratories.

**Storage, Distribution and Inventory Management**

TBL pharmaceuticals will be stored only at central PFSA warehouses, PFSA branch warehouses, and health facility stores. PFSA is responsible to distribute pharmaceuticals to its branches, and the branches are responsible to deliver pharmaceuticals to the public health facilities, on bi-monthly basis, and to distribute to accredited private health facilities based on their consumption.

Health facility stores are responsible to develop distribution schedule for the different dispensing units, including the TB clinics; and facility TB clinics are required to submit filled *Internal Facility Report and Resupply (IFRR)* Form and collect the anti-TBL drugs from their respective stores according to their schedule.

All stores are also required, depending on their capacity, to have electronic and/or paper-based inventory management system in place. They are also expected to:

- Keep sufficient stock of supplies;
- Order new supplies in time from PFSA branches and safe-guard timely distribution to dispensing units;
- Check the shelf lives of the pharmaceuticals and take necessary action;
- Keep up-to-date records on stock on hand, consumption, loss/adjustments, etc;
Where applicable, health centres collect reports from their catchment HPs, as per the structure of the PHCU, and supply them with the necessary pharmaceuticals on a monthly basis. The HPs, using standard form, reports on stock on hand, consumption and loss/adjustments and submit the report to their respective HCs. The HCs will calculate the HPs’ requirements and resupply them accordingly.

At each level of the health system the issuance should be governed by first-expire-first-out (FEFO) and first-in, first-out (FIFO) storage principles.

**13.2 Operational rules for shelf life of TB pharmaceuticals**
In order to avoid or minimize wastage due to expiry, pharmaceuticals procured should have at least 5/6 (80%) of their shelf life when they arrive at the central store; and FMHACA is the responsible body to ensure this.

**13.3 Ordering of Pharmaceuticals**
In every health facilities, the TBL clinics should report data for drug consumption using the “completed by unit” section of the IFRR to the health facility stores regularly as per schedule. The facility stores will complete the “completed by store” section of the form and supply the TBL clinic with the necessary pharmaceuticals.

Every two months, the health facility stores are required to fill the Report and Requisition Form (RRF) and submit it to their respective PFSA branches. They should also send a copy of the RRF to the respective WorHO/ZHD/RHB for administration reasons. Based on their report and request, PFSA branches will refill facilities with the required pharmaceuticals. PFSA will also aggregate the RRFs and the information collated will be used for decision making, such as forecasting and procurement planning.
13.4 Rational Use of Drugs

Patients must receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time free of charge.

Rational use of drugs implies promotion of rational prescribing, ensuring good dispensing practice and encouraging appropriate drug use by the patient and the community at large. This should be part and parcel of programmatic activities at each and every level and the implementation is the responsibility of all stakeholders including PFSA, the NTP and partners.

13.5 Records and Forms

The following records and forms are used for all pharmaceuticals:

1. Report and Requisition Form (RRF) – to be used by the facility to report on and request pharmaceuticals and submitted to PFSA branches
2. Internal Facility Report and Resupply Form (IFRR) - to be used by TBL clinics to report on and request pharmaceuticals from health facility stores
3. All government Vouchers (models) Stock Record Cards and Bin Cards. According to the IPLS, all TBL clinics are required to fill and regularly update bin cards.

The necessary formats and registers will be distributed to health facilities by PFSA and FMOH.

13.6 Quality Check and Quality Control
It is the responsibility of PFSA to procure quality pharmaceuticals with all recommended steps from WHO prequalified manufacturers/suppliers; but the Food, Medicine and Healthcare Administration and Control Authority (FMHACA) will ensure the registrations, onsite inspection at port arrival and sample analysis of all pharmaceuticals and take necessary measures. FMHACA is also responsible to supervise and control illegal drug trafficking in the country. In addition, supervising and controlling of private health facilities, including clinics and retail drug outlets such as pharmacies, drug shops and rural drug vendors, directly or through delegation of RHBs, in relation to handling pharmaceuticals, is the responsibility of the Authority.

RHBs, ZHDs, WorHOs and Health Facilities are required to report immediately if they face quality complains from patients, health care staffs and store workers using the standard Adverse Drug Reporting forms developed by FMHACA. Central and Regional/sub regional laboratories are responsible to implement EQA regularly.

13.7 Responsibilities

It is the responsibility of the TBL team members and pharmacy units at all levels to:

- Keep sufficient stock of pharmaceuticals;
- Order new supplies and distribute them timely;
- Check the shelf-life of the drugs routinely and take necessary actions;
- Keep up-to-date record and report on pharmaceuticals received, distributed, consumed and losses/adjustments;
- Promote and ensure rational prescribing, dispensing and use of drugs.

According to the IPLS, distribution of all anti-TBL pharmaceuticals, directly to HCs and hospitals, will be handled by PFSA. HPs will be supplied with the necessary pharmaceuticals by their respective HCs. Accordingly, HFs are responsible to report on and request pharmaceuticals timely and PFSA branches are expected to deliver the necessary pharmaceuticals in efficient manner.

FMOH, RHBs, ZHDs, WorHOs will be responsible for resource mobilization, supportive supervision, follow up, technical assistance, etc on the pharmaceutical supply management system.
14. MONITORING AND EVALUATION OF TBL AND TB/HIV CONTROL ACTIVITIES

Monitoring and Evaluation (M&E) is an action-oriented and pre-planned management tool that operates on adequate, relevant, reliable and timely collected, compiled and analyzed information on program objectives, targets and activities. The objectives of M&E are to improve the management and optimum use of resources of program to make timely decisions and resolve constraints and problems of implementation.

Monitoring
Monitoring is a continuous and periodic tracking of program implementation using input, process and outcome data that are collected, collated and analyzed on a regular basis. Monitoring is also used to assess whether or not planned activities are carried out according to the plan.

Evaluation
Evaluation is an episodic in depth assessment of program implementation and achievement of objectives. Evaluation explains the relationship between the program and its effects. It helps to answer the why and how questions of program implementation. Evaluation is very helpful to improve programmatic implementation and experience sharing among stakeholders. After an evaluation process a judgment should be made about the worth of the program.

M & E is very essential for program management and is specifically used to:
- Monitor and evaluate the program performance
- Identify problem and measure its magnitude
- Evidence based planning (e.g. resource allocation for drug and laboratory supplies, designing interventions, etc).
- Systematically evaluate patient progress and treatment outcome

The M & E process involves data collection, reporting and analysis.

14.1 TBL, TB/HIV M & E Tools

Recording and reporting of TBL & TB/HIV prevention and control activities
Effective TBL and TB/HIV prevention and control requires proper and standardized recording and reporting system. Recording and reporting is used to systematically monitor and evaluate progress of patient/s and treatment outcome as well as the overall program performance. Monitoring and evaluation is done at different levels of the health system where epidemiological and operational indicators for monitoring of the TBL and TB/HIV prevention and control program are compiled, calculated and analyzed.
The reporting of TB, Leprosy and TB/HIV collaborative activities is integrated into the Health Management Information System (HMIS) and all forms and registers are standardized and in line with HMIS throughout the country. Health facilities are the primary sources of data (the community TB care activities are compiled at Health Post level and reported to health centers). Every information concerning TB patients should be completely and correctly recorded. Registers and reporting forms should be kept neatly and maintained properly.

**Table 22: List of standardized registers and formats in TBL and TB/HIV**

<table>
<thead>
<tr>
<th>Forms and registers</th>
<th>Data content</th>
<th>Data recording point</th>
<th>Responsible person</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unit TB register</td>
<td>Category of TB patient, treatment &amp; lab. follow up, HIV screening status, treatment outcome</td>
<td>HF (TB clinic)</td>
<td>Facility TBL focal persons</td>
<td>Routine</td>
</tr>
<tr>
<td>Unit Leprosy register</td>
<td>Leprosy Patient category, Disability grade, treatment follow up, treatment outcome</td>
<td>HF (TB clinic)</td>
<td>Facility TBL focal persons</td>
<td>Routine</td>
</tr>
<tr>
<td>AFB Lab register</td>
<td>AFB lab result of new &amp; follow up cases</td>
<td>HF (Laboratory unit)</td>
<td>Lab staff</td>
<td>Routine</td>
</tr>
<tr>
<td>TB Treatment follow up card</td>
<td>Lab &amp; Evaluation result, Treatment &amp; Lab follow up, Treatment outcome</td>
<td>HP/Community</td>
<td>HEWs and Treatment supporter</td>
<td>Routine</td>
</tr>
<tr>
<td>HMIS Health Center/Clinic/Hospital Quarterly Service Delivery report form</td>
<td>Information on TBL case finding and treatment outcome and TB/HIV collaborative activities</td>
<td>HF</td>
<td>Health facility HMIS/TB focal persons</td>
<td>Quarterly</td>
</tr>
<tr>
<td>WoHO /ZHD / RHB Quarterly Service Delivery report form</td>
<td>Information on TBL case finding and treatment outcome and TB/HIV collaborative activities by type of health facility</td>
<td>WoHO /ZHD / RHB health offices</td>
<td>HMIS/TB focal persons at respective health office</td>
<td>Quarterly</td>
</tr>
<tr>
<td>Lab request form</td>
<td>Lab exam. request and result</td>
<td>HF</td>
<td>Health worker and lab technicians</td>
<td>Routine</td>
</tr>
<tr>
<td>Leprosy patient card &amp; VMT and ST (follow up) form</td>
<td>VMT/ST status</td>
<td>HF</td>
<td>Health worker at TBL clinic</td>
<td>At diagnosis and then on a quarterly basis</td>
</tr>
<tr>
<td>TB &amp; Leprosy ID cards</td>
<td>Patient information, disease classification and category of patient and follow up dates</td>
<td>HF</td>
<td>Health worker at TBL clinic</td>
<td>Routine</td>
</tr>
<tr>
<td>TB &amp; Leprosy transfer/referral forms</td>
<td>Details on TB &amp; Leprosy patient treatment status and reason for referral</td>
<td>HF</td>
<td>Health Worker</td>
<td>Routine</td>
</tr>
<tr>
<td>TB Suspect referral form</td>
<td>Information on TB suspect</td>
<td>HP</td>
<td>HEWs</td>
<td>Routine</td>
</tr>
<tr>
<td>HMIS HP Monthly Service Delivery report form</td>
<td>CTBC activity report (suspect identified and referred)</td>
<td>HP</td>
<td>HEWs</td>
<td>Monthly</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>------------------------------------------------------</td>
<td>----</td>
<td>------</td>
<td>---------</td>
</tr>
<tr>
<td>Report and Requisition Form</td>
<td>Drug/supplies consumption report and requisition</td>
<td>HF (drug store)</td>
<td>Health workers</td>
<td>Quarterly</td>
</tr>
</tbody>
</table>

NB: ART & Pre-ART registers from ART clinic are used for reporting of TB/HIV collaborative activities in addition to the Unit TB register.

### 14.2 Key Indicators in TBL and TB/HIV Prevention and Control

An indicator is a variable used to measure progress towards the stated goals, objectives and targets of the program, allowing managers to assess progress towards benchmarks. It is a specific measure of program performance that is tracked over time by the monitoring system. The value of an indicator in itself is usually of limited use but rather unexpected values or changes in the indicator suggest the need for further investigation. Therefore the following below mentioned TBL and TB/HIV indicators are used in tracking the achievements of the program. For further description and understanding of nationally used indicators, see the National HMIS/M&E Information Use Guidelines and Display Tools Technical Area 1, HMIS Indicators Definition.

1. **Tuberculosis case detection rate (All forms of TB):** is the percentage of new all forms of TB cases notified among the total number of TB cases estimated to occur in the area.

2. **Tuberculosis re-treatment rate:** is the proportion of TB re-treatment TB cases (relapse, failures & return after default and other re-treatments) among all forms of TB cases notified in the reporting period.

3. **Pulmonary Tuberculosis treatment success rate:** is the percentage of a cohort of new smear positive TB cases registered in a specified period that successfully completed treatment, whether with bacteriologic evidence of success (“cured”) or without (“treatment completed”).

4. **Pulmonary Tuberculosis cure rate:** is the percentage of a cohort of new smear-positive TB cases that were cured as demonstrated by bacteriologic evidence.

5. **Tuberculosis death rate (All forms of TB):** is the percentage of a cohort of all forms of TB cases registered in a specified period that died during treatment, irrespective of the cause.

6. **Tuberculosis re-treatment failure rate:** is the percentage of retreatment (treatment-after-failure, treatment-after-relapse, and treatment-after-default) sputum smear-positive pulmonary cases registered during a specified period that are smear positive at the end of five months or later after initiation of the retreatment regimen.
7. **Percentage of health posts providing community DOTS service:** is the percentage of health posts that provide community DOTs service.

8. **Leprosy case detection rate:** is the number of new leprosy cases detected per 100,000 population in a specified area.

9. **Leprosy Grade II disability rate among new cases of Leprosy:** is the proportion of new leprosy cases with disability grade II among the newly detected leprosy cases.

10. **Leprosy in Children (<15yrs) detection rate among new cases of Leprosy:** is the proportion of new children leprosy cases among the newly detected leprosy cases.

11. **Leprosy treatment completion rate:** is the percentage of a cohort of leprosy cases registered in a specified period that successfully completed treatment.

12. **HIV testing for TB Patients:** The proportion of TB patients who are tested for HIV.

13. **TB/HIV co-infection rate:** The proportion of TB patients tested HIV positive.


15. **Percentage of HIV-positive patients who were screened for TB in HIV care:** is the proportion of adults and children enrolled in HIV care who are screened for TB symptoms during their last visit.

16. **Anti-retroviral therapy (ART):** Proportion of HIV-positive registered TB patients who are started on ART or continue previously initiated ART, during or at the end of TB treatment.

17. **Percentage of new HIV-positive patients started on IPT:** Proportion of adults and children who started IPT among newly enrolled PLWH in HIV care during the reporting period.

18. **Number of laboratory confirmed MDR TB patients by culture & DST:** The number of MDR TB cases confirmed by Culture and DST notified to NTP during the specified period of assessment (number).

19. **Confirmed MDR-TB cases enrolled on SLDs:** 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.

20. **MDR TB Treatment Interim results – culture conversion at six months:** Number and percentage of MDR-TB cases initiated on a second-line anti-TB treatment regimen who have a negative culture at the end of six months of treatment during the specified period of assessment (number and percentage).

21. **Treatment success rate of cases with laboratory confirmed MDR-TB:** Laboratory-confirmed MDR-TB cases successfully treated (cured plus completed treatment) among
those enrolled on second-line anti-TB treatment during the year of assessment (number and percentage)

14.3 Data Reporting, Data flow and Quality Assurance

Routine HMIS data are assembled and reported on a quarterly and annual basis. Facilities aggregate and review their data monthly and report to their respective facility and administrative office quarterly. The administrative office aggregates the data it receives, adds its own administrative data, and monitors its own performance based on these reports and self-generated data, and forwards the HMIS report to the next level. Annual reports include additional data that are not collected quarterly. These reports follow the same line and principles of desegregation as the quarterly reports. Data aggregation methodology is maintained throughout the reporting chain so that even at the federal level it is possible to disaggregate data by facility type and ownership. HMIS Data flow from the facilities to the federal level is depicted below.

Figure 5: HMIS Data flow in TBL and TB/HIV control program

**TBL and TB/HIV Data Quality Assurance**

Data Quality Check is one of the components of the HMIS system. Once TBL and TB/HIV data are collected, the data are checked for any inaccuracies and obvious errors at every level. The data quality assurance is done at two levels: facility level and administrative level/district health
offices. At facility level, such a mechanism is the Lot Quality Assurance Sampling (LQAS) methodology which is done on monthly basis. In this procedure randomly selected data elements from the monthly reports are checked against the register or the source of the report. The findings are then compared to a standard Data Accuracy Table. And again at district health offices, the same procedure is done on quarterly basis before the data are sent to the next higher reporting unit. Hence, in HMIS all reports are quality checked at every level; from the healthcare institution to the federal level.

14.3 Supportive Supervision and Review Meetings

Supportive Supervision
Supervision aims at ensuring and improving quality, effectiveness and efficiency of services provided; it should also enhance competence and satisfaction of the staffs at all levels. Supervision consists of observation, discussion, support and guidance. Therefore, it is an essential tool in the management of staff and facilities and should be done on a regular basis. The overall aim of supervision is the promotion of continuous improvement in the performance of the staff.

Supervisions at all levels is conducted in an integrated manner using standardized checklist as clearly identified in the Integrated Supportive Supervision guideline. It is carried out on a regular basis and is done from every administrative level to the respective office and health facility. The ISS guideline shows the actual process of implementation, the team composition and checklist.

Besides ISSs, in depth TB Program-Specific supervisions using standardized TBL and TB/HIV supportive supervision tool can also be conducted whenever critical gaps that require intensive technical approach are identified/flagged during the ISS.

Review Meetings
Review meetings organized at various levels create a very good opportunity to review the status of programme implementation, achievements and challenges and come up with workable solutions for the problems and challenges encountered. They are key elements for program management. Furthermore, review meetings are forums for exchange of ideas and experiences among the health professionals and programme coordinators. In these meetings, programme coordinators from the next lower levels will present activity reports of their respective area, including major achievements and challenges/constraints encountered during the period under review.

Integrated review meeting is conducted on regular bases at every level. In this manner, activities taking place at all levels will then be brought forward to the respective review meeting sessions where TBL and TB/HIV program performance is reviewed as part of the overall review meeting.
REFERENCES
FMOH. 2011. Community TB care implementation guidelines
WHO. 2006. PPM DOTS Policy documents.
WHO. 2010. Public- Private Mix for TB care and control: Toolkit
WHO. 2012. WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders
Patient with symptoms suggestive of TB

2 or 3 positive
Sputum microscopy for AFB (three samples)

3 negative smears

Only 1 positive

Examine 2 additional sputum samples

Both negative

Treat with non-specific broad-spectrum antibiotics (excluding anti-TB drugs and fluroquinolones) for 7-10 days

No improvement

Review after 2-4 weeks

Repeat sputum microscopy (three samples)

1-3 positive*

Chest X-ray and physician’s judgment

Smear-positive Pulmonary TB**

Smear-negative Pulmonary TB

No Tuberculosis: Treatment based on clinical

No Tuberculosis
Annex 2: Management of Enlarged Lymph Nodes

ENLARGED LYMPH

LYMPH NODES ARE FIRM / HARD and

REFER PATIENT FOR BIOPSY

LYMPH NODES ARE MOBILE, SOFT AND

EXTRA-INGUINAL

INGUINAL SITE

SIGNS AND/OR SYMPTOMS OF

BROAD-SPECTRUM ANTI-BIOTICS FOR 3 WEEKS

NO

REVIEW AFTER 4-8 WEEKS

YES

SPUTUM AFB x3 + CLINICAL

IMPROVED

CONDITION SAME OR WORSE

DISCHARGE

INVESTIGATE FOR OTHER SITES OF ACTIVE TB

PRESENT

INITIATE ANTI-TB TREATMENT

ABSENT

REFER PATIENT FOR BIOPSY
Annex 3: Algorithms for the Diagnosis of TB in Ambulatory HIV-Positive TB

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

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

b. The investigations with in the box should be done at the same time wherever possible in order to decrease the number of visits and speed up the diagnoses.

c. For countries with the adult HIV prevalence rate >1% or prevalence rate of HIV among TB patients >5%

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

e. PCP: Pneumocystis carinii pneumonia

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

g. AFB positive is defined as at least one positive and AFB Negative as two or more negative smears.

h. Reassessment for TB includes AFB examination and clinical assessment
Annex 4: Algorithms for the Diagnosis of TB in seriously ill HIV-positive Patients

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

1. The danger signs include anyone of: respiratory rate >30/min, fever>39°C, pulse rate >120/mm and unable to walk unaided
2. The investigations with in the box should be done at the same time wherever possible in order to decrease the number of visits and speed up the diagnoses.
3. For countries with the adult HIV prevalence rate >1% or prevalence rate of HIV among TB patients >5%
4. Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered
5. PCP: Pneumocystis carinii pneumonia
6. In the absence of HIV testing, classify HIV status unknown into HIV positive depends on clinical assessment or national and/or local policy
7. AFB positive is defined as at least one positive and AFB Negative as two or more negative smears.
8. Reassessment for TB includes AFB examination and clinical assessment
Annex 5: Flow Chart of Sputum Follow up Examinations for New PTB Positive Patients

**New smear positive PTB patient**

1. **Intensive phase for 2 months**
   - **Smear at the end of 2nd month**
     - **Neg (1x)**
     - **Pos (1x)**
       - **Start continuation phase**
       - **Continue Rx & Send for DST**

2. **Smear at the end of 5th month**
   - **Neg**
   - **Pos**
     - **Cured**
   - **Neg**

3. **Smear at end of 6th month**
   - **Pos**
     - **Treatment Failure**
   - **Pos**
     - **Retreatment regimen, Send DST**

1. *No prolongation of the Intensive phase is required (as RH is the continuation phase) if the smear is positive at the end of 2nd month.*
2. *If one smear is positive at the end of the 3rd month; take second sputum smear for confirmation.*
3. *Treatment decision should be guided by DST result.*
Annex 6: Flow Chart for Sputum Follow Up Examinations for Re-treatment PTB Positives

*Previously treated smear positive PTB patient*

- **Intensive phase for 3 months**
  - Smear at the end of 3rd month:
    - Neg (1x) → Start continuation phase
    - Pos (1x) → Send two sputum samples for culture and DST and start continuation phase

- Smear at end of 5th month:
  - Neg → Cured
  - Pos → Treatment Failure
    - Send two sputum samples for culture and DST and manage according to the results of DST

1: Prolongation of the Intensive phase by 1 additional month is not recommended. If the DST result of the sputum samples taken at the end of 3rd month of therapy confirms MDR TB diagnosis, link the patient to MDRTB treatment Initiating center.
Annex 7: TB Screening Tool for HIV Positive Adults and adolescents
Annex 8: TB Screening Tool for Children

Child over 12 months of age and living with HIV*

Screen for TB with any one of the following:
- Poor weight gain**
- Fever
- Current cough
- Contact history with TB patient

No

Assess for contraindications to IPT***

No

Give IPT

Yes

Defer IPT

Yes

Refer/Work up for TB****

Active TB diagnosed?

Yes

Treat for Tuberculosis

Child improved?

Yes

Give IPT

No

Treat for common Childhood diseases

Consult for further Workup

No

No

Defer IPT

* All children and infants less than one year of age should be provided with IPT if they have a history of household contact with a TB case.

** Poor weight gain is defined as reported 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.

*** Contraindications include: active hepatitis (acute or chronic) and symptoms of peripheral neuropathy. Past history of TB should not be a contraindication for starting IPT. Although not a requirement for initiating IPT, TST may be done as a part of eligibility screening in some settings.

**** Investigations for TB must be done in accordance with existing national guidelines.
Annex 9: Flowchart for Diagnosis and Classification of Leprosy

1. Skin patch
   - Test the skin patches for sensation (use cotton wool)
   - No sensory loss
   - Doubtful sensory loss
   - Definite sensory loss
2. Major nerve trunks
   - Palpate the nerves
   - Thickened/Tender nerve(s) With or without sensory/motor deficit
   - Review after 6 months
   - Not Leprosy

LEPROSY

Classifying Leprosy (Clinically)

Types of Leprosy

Classifying Leprosy (bacteriologically)

Skin Smear negative

Skin Smear positive

1 to 5 skin patches or 1 thickened/tender nerve trunk

Pauci-Bacillary Leprosy (PB)

6 or more skin patches or more than 1 thickened/tender nerve trunk

Multi-Bacillary Leprosy (MB)