

National Manual
for
Tuberculosis Control



**NATIONAL PROGRAMME FOR TUBERCULOSIS CONTROL AND
CHEST DISEASES**

2016

Acknowledgements

Editors in Chief

- ❖ Dr. Vineet Bhatia – WHO Independent Consultant
- ❖ Dr. Wijitha Senaratne – Consultant Respiratory Physician

Editorial Board

- ❖ Dr. Sudath Samaraweera – Deputy Director, NPTCCD
- ❖ Dr. Nirupa Pallewatte – Consultant Community Physician, NPTCCD
- ❖ Dr. Dhammika Vidanagama – Consultant Microbiologist, NTRL
- ❖ Dr. Pryadarshani Samarasinghe – Consultant Community Physician, NPTCCD
- ❖ Dr. Pramil Liyanage – Registrar in Health Informatics, NPTCCD
- ❖ Dr. Wasantha Perera – Medical Officer, NPTCCD

Contributors

Consultant Respiratory Physicians

Dr. Amitha Fernando
Dr. Anoma Siribaddana
Dr. Bandu Gunasena
Dr. Chandana Kulatunga
Dr. Chatura Wirasinghe
Dr. D. Madagedara
Dr. D.L.B. Dassanayake
Dr. Duminda Yasaratne
Dr. Eshanth Perera
Dr. Geethal Perera
Dr. Keerthi Gunasekara
Dr. M. Aflah Sadikeen
Dr. M.M.N. Masaima
Dr. Manil Pieris
Dr. N.L.A. Dissanayake
Dr. Nandika Harishchandra
Dr. R. De S. Karunatilaka
Dr. R.D. Wijetunga
Dr. R.R.G. Wimalarathne
Dr. Saman Kapilawansa
Dr. Saman Kularathne

Other Contributors

Dr. Sarath Amunugama : DDG (PHS I)
Dr. Sunil De Alwis : DDG (ET & R)
Dr. Kanthi Ariyaratne : Director, PHSD
Dr. Gamini Seneviratne : Former Director, NPTCCD
Dr. B.J.C. Perera : Consultant Paediatrician
Dr. Padma Gunarathna : Consultant Neurologist
Dr. T. Chang : Consultant Neurologist
Dr. Surantha Perera : Consultant Paediatrician
Dr. Mangala Gamage : Consultant Ophthalmologist
Dr. Ruwini Perera : DTCO, Colombo
Dr. A. Ramachandran : DTCO, Colombo
Dr. R.M.G. Rathnayake : DTCO, Gampaha
Dr. D. Waidhyarathne : DTCO, Anuradhapura
Dr. Ramya de Silva : MO, NPTCCD
Dr. Harshani Vitharana : MO, NPTCCD
Dr. Shyama Jayathilaka : MO, NPTCCD
Dr. Shyamalee Ratnayake : MO, NPTCCD
Dr. C.D. Hambange : MO, NPTCCD
Dr. Manilka Jayawardena : MO, NTRL
Ms. J.A.B.C. Croos : Chief Pharmacist, CDS
S.H.P.J.S.Thilakarathne : Acting MRO, NPTCCD

Compiled and Published by

Health Information Management Unit, NPTCCD

ISBN 978-955-0742-07-3

Foreword

Tuberculosis is a major health problem in the globe, causing ill health for millions of people each year. TB ranks alongside HIV as a leading cause of death due to communicable diseases.

Sri Lanka is a country with middle burden for TB. Nearly 10,000 patients of TB are detected each year. The incidence of TB in Sri Lanka remains static over the past five years though there is a gap of 3,000 - 4,000 patients remaining undetected, between the WHO estimated burden and the number detected.

The country has adopted WHO post 2015 strategies “zero deaths, disease and suffering due to tuberculosis” to control TB in Sri Lanka and taken initiatives to achieve its targets and objectives by year 2035.

The revision of National Manual for Tuberculosis Control is one of the key landmarks and a timely felt need for TB control in Sri Lanka. It has been updated according to revised WHO TB classifications of 2013 and contains chapters on new diagnostic methods, management of Childhood TB, as well as new indicators and recording and reporting formats.

This manual will serve as a guide for healthcare professionals in patient management, care and prevention and will enable implementation of NTP policies in TB Control.

I appreciate the efforts taken by National Programme for Tuberculosis Control and Chest diseases to update this manual and take this opportunity to wish the NPTCCD a success towards its journey in eliminating TB in Sri Lanka.



Dr. P.G. Mahipala,
Director General of Health Services,
Ministry of Health, Nutrition and Indigenous Medicine

Preface

There were several changes in the global TB Control Strategies during the past few years. New rapid diagnostics have been introduced in to practise. Classification of TB was revised accordingly. Post 2015 WHO TB Control Strategies were aimed to “End the TB epidemic by 2035” with targets to reduce TB deaths by 95% and to reduce incidence of TB by 90%.

Recognising the need of incorporating new developments into practise and the need of proper guidance in achieving the newly set targets, the NPTCCD has taken the initiative of updating the National Manual for TB control.

The new manual consist of two sections. Section one includes basic information on tuberculosis and technical guidelines. Section two is dedicated to operational guidelines. New chapters on new WHO classification, new diagnostics, childhood TB, drug resistant TB and management of TB in special situations are included.

This manual is a result of the joint venture of all stakeholders in TB care. Contribution made by College of Pulmonologists, College of Paediatricians and other professional colleges, previous Medical Administrators of NPTCCD, District Tuberculosis Control Officers, Consultant Community Physicians and Medical Officers of NPTCCD was a tremendous help to the writing panel in finalising the present National Manual. The inputs provided by Director of Private Health Sector Development, Director of Estate and Urban Health, Provincial and Regional Directors of Health, representatives from other health institutions, organisations and NGOO has given us an opportunity to address the operational issues in management of TB.

The deep engagement and the tremendous effort taken by Dr. Vineeth Bhathiya, WHO Consultant and Dr. Wijitha Senaratne, Senior Consultant Respiratory Physician in updating the manual contributed to the successful timely completion of this 3rd edition of manual of TB control in Sri Lanka.

This activity could not be fulfilled without the financial support provided by the WHO and GFATM to obtain technical assistance and for printing of the manual.

I hope this manual will be a useful guide to all health care professionals involved in TB patient care management and prevention. This would definitely be a milestone in pathway of elimination of TB in Sri Lanka.

I express my sincere gratitude to those who has contributed in numerous ways during this tremendous task of updating the National Manual.



Dr. Kanthi Ariyaratne,
Director, NPTCCD

Contents

| | |
|----------------------------------------------------------------------------------------------------------------------------------|-----|
| Acknowledgements..... | ii |
| Foreword..... | iii |
| Preface..... | iv |
| Contents..... | v |
| Abbreviations..... | ix |
| Introduction..... | xi |
| 1. Basic Information about Tuberculosis..... | 1 |
| 1.1 What is tuberculosis (TB)?..... | 1 |
| 1.2 How does tuberculosis spread?..... | 1 |
| 1.3 Risk of infection..... | 1 |
| 1.4 Tuberculosis infection and disease..... | 1 |
| 1.5 Risk of progression of infection to disease..... | 1 |
| 1.6 Pathogenesis..... | 2 |
| 1.7 Common symptoms of pulmonary tuberculosis..... | 2 |
| 1.8 Symptoms of extrapulmonary tuberculosis (EPTB)..... | 3 |
| 2. Case Definitions and Treatment Outcomes..... | 5 |
| 2.1 Presumptive TB (TB symptomatic)..... | 5 |
| 2.2 Who is considered a 'case' of tuberculosis?..... | 5 |
| 2.3 Classification based on anatomical site of the disease..... | 6 |
| 2.4 Classification based on history of previous TB treatment (patient registration group)..... | 7 |
| 2.5 Classification based on HIV status..... | 8 |
| 2.6 Classification based on drug resistance..... | 9 |
| 2.7 Treatment outcomes for TB patients (excluding patients treated for RR-TB or MDR-TB using the second line anti-TB drugs)..... | 10 |
| 3. Screening and Diagnosis..... | 13 |
| 3.1 Register of TB symptomatics..... | 13 |
| 3.2 Investigations..... | 13 |
| 3.3 Diagnosis of tuberculosis in children..... | 21 |
| 4. Treatment of TB..... | 23 |
| 4.1 Requirements for adequate chemotherapy..... | 23 |
| 4.2 Standard codes for TB treatment regimens..... | 23 |
| 4.3 Scientific basis of treatment of TB..... | 24 |
| 4.4 TB treatment regimens..... | 27 |

| | | |
|------|----------------------------------------------------------------------|-----|
| 4.5 | Categories and treatment regimens | 28 |
| 4.6 | Fixed-dose combination tablets (FDCs) | 31 |
| 4.7 | Treatment of TB in children | 35 |
| 5. | DOT and Patient Support | 39 |
| 5.1 | Directly observed treatment (DOT) | 39 |
| 5.2 | National policy for the implementation of DOT | 41 |
| 5.3 | Provision of drugs to DOT centres | 42 |
| 5.4 | Using a patient-centred approach to care and treatment delivery..... | 42 |
| 5.5 | DOT in children..... | 45 |
| 5.6 | Treatment interruption..... | 45 |
| 5.7 | Nutrition support | 46 |
| 6. | Monitoring Treatment and Assigning Outcome | 51 |
| 6.1 | Monitoring of treatment..... | 51 |
| 6.2 | Treatment outcome | 55 |
| 7. | Essential Anti-TB Drugs and Management of Adverse Reactions..... | 59 |
| 7.1 | Isoniazid | 59 |
| 7.2 | Rifampicin | 60 |
| 7.3 | Pyrazinamide..... | 62 |
| 7.4 | Ethambutol..... | 63 |
| 7.5 | Streptomycin..... | 64 |
| 7.6 | Management of side-effects of first-line anti-TB drugs..... | 65 |
| 8. | Preventing Tuberculosis..... | 71 |
| 8.1 | Infection control..... | 71 |
| 8.2 | BCG vaccination | 90 |
| 8.3 | Contact investigations..... | 93 |
| 8.4 | Preventive treatment (chemoprophylaxis)..... | 93 |
| 8.5 | Intensified case detection..... | 95 |
| 9. | TB in Special Situations | 99 |
| 9.1 | Pregnancy with TB..... | 99 |
| 9.2 | Treatment during breast-feeding | 99 |
| 9.3 | Management of a new-born child of a mother with active TB..... | 99 |
| 10. | Management of Co-Morbidities | 101 |
| 10.1 | HIV infection..... | 101 |
| 10.2 | Tuberculosis and diabetes | 105 |
| 10.3 | Tuberculosis and liver disease | 105 |
| 10.4 | Tuberculosis and renal insufficiency..... | 105 |

| | | |
|------|----------------------------------------------------------------------------------------------------|-----|
| 10.5 | Important drug interactions | 106 |
| 11. | Drug-Resistant Tuberculosis | 109 |
| 11.1 | Background information | 109 |
| 11.2 | Definitions and classifications..... | 111 |
| 11.3 | Strategies for case finding and diagnosis of DR-TB..... | 116 |
| 11.4 | Treatment of MDR-TB..... | 119 |
| 12. | Epidemiology of Tuberculosis in Sri Lanka..... | 129 |
| 13. | Administration and Planning | 131 |
| 13.1 | WHO End TB strategy for global TB control..... | 131 |
| 13.2 | National strategic plan 2015- 2020..... | 132 |
| 13.3 | National Programme for Tuberculosis Control and Chest Diseases (NPTCCD)..... | 134 |
| 13.4 | The central level..... | 136 |
| 13.5 | Provincial & regional level | 136 |
| 13.6 | District level | 137 |
| 13.7 | Health institutions..... | 145 |
| 13.8 | Duties of DOT provider | 146 |
| 14. | Organising Diagnostic Network | 147 |
| 14.1 | Network of laboratories..... | 147 |
| 14.2 | Laboratory quality assurance..... | 148 |
| 14.3 | Maintenance of adequate supply of quality laboratory consumables | 152 |
| 15. | Organising Treatment | 153 |
| 15.1 | Roles and responsibilities of the patient, TB programme staff, community and other providers | 153 |
| 15.2 | Organisation of DOT..... | 153 |
| 15.3 | Loss to follow-up retrieval action | 155 |
| 15.4 | Transfer of patients..... | 156 |
| 15.5 | Integration of TB services to general healthcare system for improved access to TB care..... | 157 |
| 16. | Logistics Management | 159 |
| 16.1 | Management of drugs and supplies | 159 |
| 16.2 | Selection of drugs and consumables | 159 |
| 16.3 | Process of indent and supply | 160 |
| 16.4 | Consumables supply at the district level | 160 |
| 16.5 | Estimation of anti-TB drug requirements at DCC level..... | 161 |
| 16.6 | Storage of drugs..... | 161 |

| | | |
|------|--------------------------------------------------------------------|-----|
| 17. | Recording and Reporting | 163 |
| 17.1 | Registration and notification process | 163 |
| 17.2 | Recording and reporting formats used in the NTP | 163 |
| 17.3 | Compilation and analysis | 168 |
| 18. | Supervision and Monitoring TB Control Programme..... | 169 |
| 18.1 | Supervisory visits..... | 169 |
| 18.2 | For the supervisory visit to be productive and effective | 169 |
| 18.3 | Monitoring and evaluation | 171 |
| 18.4 | Monitoring indicators | 172 |
| 19. | Capacity Building..... | 179 |
| 19.1 | Capacity building activities..... | 179 |
| 19.2 | Follow up after training..... | 180 |
| 20. | Inter-Sectoral Coordination | 183 |
| 20.1 | Engage providers outside the TB programme in providing DOT | 185 |
| 20.2 | NGOs and community involvement in TB care | 185 |
| 21. | Awareness Generation..... | 187 |
| 22. | Medical Certificates for Leave | 189 |
| 22.1 | Medical certificates for financial assistance | 190 |
| 22.2 | Conditions of eligibility for financial assistance | 190 |
| 22.3 | Administrative procedure for the TB Assistance scheme | 190 |
| 22.4 | Procedure for issue of medical certificates on form SS/TB/M1 | 191 |
| | Annexure..... | 195 |

Abbreviations

| | |
|---------|----------------------------------------------------------------|
| ACSM | Advocacy, Communication and Social Mobilization |
| AFB | Acid-Fast Bacilli |
| AIDS | Acquired Immune Deficiency Syndrome |
| ART | Anti-Retroviral Therapy |
| ARV | Anti-Retrovirals |
| CBO | Community-Based Organizations |
| CPT | Co-trimoxazole Preventive Therapy |
| DCC | District Chest Clinic |
| DCCL | District Chest Clinic Laboratory |
| DDG-PHS | Deputy Director General of Public Health Services |
| DGHS | Director General of Health Services |
| DOT | Directly Observed Therapy |
| DOTS | Directly Observed Treatment Short course |
| DR-TB | Drug-Resistant Tuberculosis |
| DST | Drug Susceptibility Testing |
| DTCO | District Tuberculosis Control Officer |
| EPTB | Extrapulmonary Tuberculosis |
| EQA | External Quality Assurance |
| FDC | Fixed-Dose Combination |
| FHW | Field Health Worker |
| FLD | First-Line (Anti-TB) Drugs |
| GDF | Global (TB) Drug Facility |
| GFATM | Global Fund to Fight AIDS, Tuberculosis and Malaria |
| HBC | High-Burden (TB) Country |
| HRD | Human Resource Development |
| HRH | Human Resources for Health |
| IC | Infection Control |
| IPT | Isoniazid Preventive Therapy |
| ISTC | International Standards for TB Care |
| LTBI | Latent TB Infection |
| MCH | Maternal and Child Health |
| MDG | Millennium Development Goals |
| MDR-TB | Multidrug-Resistant Tuberculosis |
| M&E | Monitoring and Evaluation |
| NGO | Non-Governmental Organization |
| NPTCCD | National Programme for Tuberculosis Control and Chest Diseases |
| NTRL | National Tuberculosis Reference Laboratory |
| NSP | National Strategic Plan |
| NTP | National TB Control Programme |
| PHC | Primary Health Care |
| PLHIV | Persons Living With HIV/AIDS |
| PMDT | Programmatic Management of Drug-Resistant Tuberculosis |
| PMCT | Prevention of Mother to Child Transmission |
| PPM | Public-Private Mix |
| PTB | Pulmonary TB |
| QA | Quality Assurance |

| | |
|--------|---------------------------------|
| RR | Rifampicin-Resistant |
| SCC | Short Course Chemotherapy |
| SDG | Sustainable Development Goals |
| SEA | South-East Asia |
| SEAR | South-East Asia Region (of WHO) |
| SLD | Second-Line (Anti-TB) Drugs |
| SOP | Standard Operating Procedures |
| TA | Technical Assistance |
| TB | Tuberculosis |
| TNF | Tumor necrosis factor |
| TWG-TB | Technical Working Group on TB |
| WHO | World Health Organization |
| XDR-TB | Extensively Drug-Resistant TB |

Introduction

Tuberculosis continues to be a major public health problem throughout the world, particularly in developing countries. Nearly one-third of the global population (i.e. two billion people) is estimated to be infected with *Mycobacterium tuberculosis* and is at risk of developing the disease. Globally, 10.4 million people are estimated to have fallen ill with TB in 2015 (new incident cases); 5.9 million men, 3.5 million women and 1.0 million children. Globally, 11% of the 10.4 million new incident TB cases in 2015 were HIV-positive¹. TB now ranks alongside HIV as a leading cause of death worldwide. In 2015, TB killed 1.8 million people (1.4 million HIV-negative and 0.4 million HIV-positive). The highest burden of the disease is in the most economically productive age group of our society (15-54 years). The World Health Organization (WHO) declared tuberculosis a global emergency in 1993 that provided much needed boost to global TB control efforts. Starting with the DOTS (Directly Observed Treatment Short course) strategy, the global efforts evolved into Stop-TB strategy and 2016 sees the global adaption of End-TB strategy. The Millennium Development Goals (MDG) target to halt and reverse TB incidence has been achieved on a worldwide basis, in each of the six WHO regions and in 16 of the 22 high-burden countries that collectively account for 80% of TB cases. Globally, TB incidence has fallen by an average of 1.5% per year since 2000 and is now 18% lower than the level of 2000.

Much concerted efforts are needed to control the tuberculosis epidemic. The first priority of tuberculosis control is the early detection, appropriate management using quality assured drugs in proper dosage and regimen, and cure of all tuberculosis patients, using a patient centred care approach that is accessible to all. Such approach not only cures patients but also prevents spread of the disease in community.

The fight against TB is best conducted within the setting of a National Tuberculosis Programme (NTP) integrated with the general health services of the country that coordinates with all relevant partners and stakeholders. The National Programme for Tuberculosis Control and Chest Diseases (NPTCCD), Sri Lanka, is primarily responsible for the control of tuberculosis in the country. The work of NPTCCD is under the supervision and guidance of the Director General of Health Services (DGHS) and the Deputy Director General of Public Health Services (DDG-PHS I). NPTCCD is assisted by a technical national advisory committee under chairmanship of the DGHS and has as its members, representatives from the directorates of health services, consultant respiratory physicians, consultant microbiologists, representatives from professional colleges, representatives from prison and Social Service Department, other senior administrators, public health specialists, university academia, private practitioners and NGOs.

¹Global tuberculosis report 2016, World Health Organization, Geneva 2016. ISBN 978 92 4 156539 4.

For effective control of tuberculosis and to prevent emergence of drug resistance, it is important to have a standard treatment policy for all patients in accordance with the internationally prescribed best-practices. Close co-operation of all healthcare providers at all levels is essential for successful implementation of the control programme. Similarly, the participation of community health workers, religious groups, political leaders and voluntary organizations is also essential for the successful tuberculosis control. It is important that the community is informed of the nature and extent of the problem, as well as its prevention and cure. It must be stressed that the disease is curable and preventable and there is no reason for discrimination or stigma. Another key element in controlling tuberculosis is to ensure that patients are supported to take their medicines regularly until they are cured. Non-adherence with treatment could be one of the major setbacks faced by all national tuberculosis programmes. Thus more than a medical problem, social dimensions of the disease also need to be addressed simultaneously for effective control.

After having successfully implemented the DOTS strategy in Sri Lanka, the country embarked on the other components of the WHO recommended Stop TB Strategy wherein the focus is on ensuring high quality DOTS, better outreach so that more number of patients have access to quality TB care, management of multi-drug resistant TB (MDR-TB) and TB-HIV co-infection, strengthening of health systems, involving all healthcare providers in the public sector, private sector and Non-Governmental Organizations (NGOs), strengthening the advocacy campaign, promoting Medical College involvement, and research. The country has now endorsed and adapted the WHO End-TB strategy². The three pillars of the strategy include – integrated, patient-centred care and prevention; bold policies and supportive systems; and intensified research and innovation. The strategy is based on principles of

- Government stewardship and accountability, with monitoring and evaluation;
- Strong coalition with civil society organizations and community; protection and promotion of human rights, ethics, and equity; and
- Adaptation of the strategy and targets at the country level, with global collaboration.

The manual is based on all policy updates as per the current international guidelines. The manual consists of two parts – technical guidelines which elaborate on the principles and policies of TB control, and operational guidelines which deal with implementation aspects.

Although the guidelines are up-to-date in their current form, it is possible that new international guidance on certain aspects of the disease control are issued in near future. Such changes would be informed to all potential users in form of circulars. At any point of time, the NTP manual should be used in conjunction with any recently issued circulars.

²<http://www.who.int/tb/strategy/en/> accessed 03 February 2016

**BASIC INFORMATION ON TUBERCULOSIS
AND
TECHNICAL GUIDELINES
FOR
TUBERCULOSIS CONTROL**

1. Basic Information about Tuberculosis

1.1 What is tuberculosis (TB)?

Tuberculosis is an infectious disease caused by the bacillus- *Mycobacterium tuberculosis* (MTB) and occasionally by *Mycobacterium bovis* and *Mycobacterium africanum*. Tuberculosis commonly affects the lungs, but can affect any other organ in the body except nails and hair.

1.2 How does tuberculosis spread?

Tuberculosis is an airborne infection. When a patient with infectious pulmonary tuberculosis coughs, sneezes or laughs, bacilli are expelled into the air in the form of tiny droplets. These droplets dry up rapidly to form droplet nuclei and may remain suspended in the air for several hours. When a healthy person inhales these droplet nuclei containing the tubercle bacilli, he/she may become infected. Adequate ventilation removes and dilutes these droplet nuclei, but they can survive in the dark ill-ventilated spaces for several days.

1.3 Risk of infection

An individual's risk of infection depends on the extent of exposure to an infectious source and susceptibility of the individual to infection. The risk of infection is therefore high in a person who has close, prolonged exposure to droplets from a person with untreated pulmonary TB. An untreated sputum positive patient has the potential to infect 10-15 persons per year. The risk of transmission of infection from extrapulmonary TB is lower.

1.4 Tuberculosis infection and disease

Tuberculosis develops in two stages. The first stage occurs when the tubercle bacilli enter the body of an individual but remain dormant without causing disease. This is called *tuberculous infection*. The second stage is *tuberculosis or tuberculous disease* where the infected individual actually develops the disease. Approximately 10% of people infected with bacillus but not suffering from any other concomitant immunosuppressive condition will develop the active disease during their lifetime.

1.5 Risk of progression of infection to disease

Once infected with *M. tuberculosis*, a person probably remains infected for rest of the life. Approximately 10% of people infected will develop the active disease during their lifetime. The majority (90%) will not develop the disease and the only evidence of infection in these people may be a positive tuberculin skin test. The organisms may remain dormant within the body and the disease can develop at any time. The chance of developing the disease is greatest within the first two years and lessens as time goes by, but the risk probably remains for the lifetime. Weakening of the immune system can cause rapid progress of the infection

to the disease status. Examples are HIV infection, diabetes, malnutrition, prolonged steroid therapy, chronic alcoholism, and malignancies.

1.6 Pathogenesis

1.6.1 Primary infection

Primary infection occurs on first exposure of a person to the tubercle bacilli. Once the tubercle bacilli enter the respiratory tract through inhalation, the organisms reach the alveoli of the lungs where they are engulfed by macrophages and presented to lymphocytes. This leads to an immune reaction against MTB which results in sub pleural Ghon focus with enlargement of the draining lymph nodes 4–6 weeks after primary infection. Ghon focus and the enlarged draining nodes comprise primary complex. In most cases the immune response is sufficient to stop the multiplication of bacilli and to prevent the development of the disease. The primary lesion may heal by fibrosis or by calcification. A positive tuberculin skin test may be the only evidence of infection.

In a few cases primary infection progresses and leads to complications of primary infection. Complications of primary infection can manifest as early complications such as pleural effusion, miliary TB, TB meningitis or late complications such as bone TB, renal TB etc.

1.6.2 Post-primary tuberculosis

Post primary tuberculosis occurs after a latent period of months or years after the primary infection. It may occur either by endogenous reactivation of the latent primary infection or by exogenous re-infection with TB bacilli. Site of post primary TB is usually the lungs and results in lung cavitation, fibrosis and patchy consolidation. They are the patients who may become sputum positive thus contributing to spread of the disease.

1.7 Common symptoms of pulmonary tuberculosis

1.7.1 Respiratory symptoms:

- Cough - usually more than two weeks. However in immunosuppressed and in the presence of any other risk factor, cough of any duration should lead to screening for TB.
- Shortness of breath
- Chest pain
- Haemoptysis (blood stained sputum)

1.7.2 Constitutional symptoms:

- Fever and night sweats
- Loss of appetite
- Loss of weight or failure to gain weight in case of children
- Tiredness (fatigue)

1.8 Symptoms of extrapulmonary tuberculosis (EPTB)

EPTB symptoms usually depend on the organ involved. Patients may present with constitutional features of the disease such as, fever, night sweats, loss of weight and loss of appetite or symptoms related to the affected system (e.g. neurological symptoms when nervous system is affected) or local symptoms like swelling (most commonly due to lymph nodes enlargement) related to the site of the disease.

2. Case Definitions and Treatment Outcomes

It is important to classify TB patients in order to determine the correct management including treatment regimen and the duration of treatment. It is also important for recording and reporting purposes which will facilitate cohort analysis of treatment outcome.

2.1 Presumptive TB (TB symptomatic)

A case of presumptive TB (TB symptomatic) is a person who presents with symptoms or signs suggestive of TB, particularly cough for two weeks or more.

2.2 Who is considered a 'case' of tuberculosis?

A case of tuberculosis is a patient in whom TB has been either bacteriologically confirmed in laboratory or clinically diagnosed based on a clinician's decision taking into account clinical picture, results of other investigations and risk factors.

2.2.1 A case of 'bacteriologically confirmed' TB

A patient whose sputum or another biological specimen is positive for AFB by smear microscopy or culture or WHO Approved Rapid Diagnostics (WRD) such as Xpert MTB/RIF.

Smear-positive pulmonary tuberculosis

- A patient with at least two sputum smears are positive for AFB by direct smear microscopy

OR

- A patient with at least one sputum smear positive for AFB by microscopy and as determined by a clinician based on Chest X-ray findings suggestive of TB

Culture positive TB

- A patient with or without sputum smear positive for AFB but sputum or any biological specimen culture testing positive by culture for *M. tuberculosis*

WRD positive TB

- A patient with or without sputum smear positive for AFB but sputum or any biological specimen testing positive on Xpert MTB/RIF for *M. tuberculosis*. (Xpert MTB/RIF may be used directly on biological specimen without subjecting the sample to microscopy examination as described later in this manual)

2.2.2 A case of 'clinically diagnosed' TB

A patient who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician and after consultation with a Consultant Respiratory Physician and decided to treat the patient with a full course of TB treatment

This definition includes cases diagnosed on the basis of clinical signs and symptoms, and/or radiological abnormalities and/or suggestive histology.

Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.

Bacteriologically confirmed or clinically diagnosed cases of TB are also classified according to:

- anatomical site of the disease;
- history of previous treatment;
- drug resistance;
- HIV status.

2.3 Classification based on anatomical site of the disease

2.3.1 Pulmonary tuberculosis (PTB)

Any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree with or without the involvement of any other organs in the body.

Miliary TB is classified as PTB because there are lesions in the lungs.

Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lung parenchyma, constitutes a case of EPTB. A patient with both pulmonary and EPTB should be classified as a case of PTB.

2.3.2 Extrapulmonary tuberculosis (EPTB)

Any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lung parenchyma or tracheobronchial tree, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, bones and joints, meninges.

A patient with both pulmonary and extrapulmonary tuberculosis should be classified as a case of pulmonary TB

2.4 Classification based on history of previous TB treatment (patient registration group)

In order to identify those patients at increased risk of acquired drug resistance and to prescribe appropriate treatment, a case should be defined according to whether or not the patient has previously received TB treatment. The registration group focuses only on history of previous treatment irrespective of bacteriological confirmation or site of disease.

Accordingly, all patients can be categorized as 'New' patients or 'Previously treated' patients.

They are defined as follows:

2.4.1 New patients

- A patient who has never taken treatment for TB

OR

- A patient who has taken anti-tuberculosis drugs for less than one month

New patients may have positive or negative bacteriology and may have disease at any anatomical site.

2.4.2 Previously treated patients

Those who have received 1 month or more of anti-TB drugs in the past are classified under this category. They 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 as 'relapse', 'treatment after failure' and 'treatment after loss to follow-up' (See Table 2.1).

- **Relapse**

Patients who have previously been treated for TB, were declared *cured* or *treatment completed* at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either reactivation of dormant bacilli or a new episode of TB caused by reinfection).

- **Treatment after failure**

Patients who have previously been treated for TB and whose *treatment failed* during or at the end of their most recent course of TB treatment.

- **Treatment after loss to follow-up**

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

- Other previously treated patients

Patients who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

2.4.3 Patients with unknown previous TB treatment history

Patients who do not fit into any of the categories listed above.

Table 2-1 Classification based on history of previous TB treatment

| Registration group (any site of disease) | Outcome of most recent prior treatment (defined in section 2.7) |
|-----------------------------------------------------|--------------------------------------------------------------------|
| New | - |
| Relapse | Cured |
| | Treatment completed |
| Previously treated | Treatment after failure |
| | Treatment after loss to follow-up |
| | Other previously treated patients |
| Patients with unknown previous TB treatment history | All cases that do not fit into above definitions |

New and relapse cases of TB are considered incident TB cases

2.5 Classification based on HIV status

HIV-positive TB patient refers to any bacteriologically confirmed or clinically diagnosed case of TB who has a positive result from HIV confirmatory test.

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

HIV status unknown TB patient refers to any bacteriologically confirmed or clinically diagnosed case of TB who has no result of HIV testing. If the patient’s HIV status is subsequently determined, he or she should be reclassified accordingly.

2.6 Classification based on drug resistance

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

- **Mono-resistance:** TB in a patient, whose infecting isolates of *M. tuberculosis* are resistant in-vitro to one of first-line anti-tuberculosis drugs except rifampicin. Rifampicin mono resistance is categorised separately.
- **Poly-resistance:** TB in a patient, whose infecting isolates of *M. tuberculosis* are resistant in vitro to more than one first-line anti-tuberculosis drug, other than to both isoniazid and rifampicin.
- **Multi Drug Resistant TB (MDR-TB):** Tuberculosis in a patient, whose infecting isolates are resistant in-vitro to both isoniazid and rifampicin with or without resistance to other first-line drugs.
- **Extensively Drug Resistant (XDR-TB):** TB in a patient, whose infecting isolates of *M. tuberculosis* are resistant in-vitro to both rifampicin and isoniazid along with resistance to any quinolone and one of the second-line injectable anti-TB drugs.
- **Rifampicin resistance (RR):** Resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti TB drugs except isoniazid.

Rifampicin resistance tuberculosis is not mutually exclusive with MDR or XDR TB since all MDR and XDR TB cases are also classified as Rifampicin Resistance Tuberculosis

Treatment outcomes

The treatment outcome definitions make a clear distinction between two types of patients:

- Patients treated for drug-susceptible TB;
- Patients treated for drug-resistant TB using second-line treatment (defined as combination chemotherapy for drug-resistant tuberculosis which includes drugs other than those in Group 1 and streptomycin in Group 2).

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

2.7 Treatment outcomes for TB patients (excluding patients treated for RR-TB or MDR-TB using the second line anti-TB drugs)

All bacteriologically confirmed and clinically diagnosed TB cases should be assigned an outcome from this list **except** those with RR-TB or MDR-TB³, who are placed on a second-line drug regimen.

2.7.1 Cured

A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who is smear negative or culture negative in the last month of treatment and on at least one previous occasion.

2.7.2 Treatment completed

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

2.7.3 Treatment failed

A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.

2.7.4 Died

A TB patient who dies for any reason before starting or during the course of treatment.

2.7.5 Lost to follow-up

A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.

2.7.6 Not evaluated

A TB patient for whom no treatment outcome is assigned. This includes cases for whom the treatment outcome is unknown to the reporting clinic.

2.7.7 Treatment success

The sum of cured and treatment completed.

Patients found to have an RR-TB or MDR-TB strain at any point in time should be started on an adequate second-line drug regimen. These cases are excluded from the main TB cohort when calculating treatment outcomes and included only in the second-line TB treatment cohort analysis. If treatment with a second-line drug regimen is not possible, the

³For further details on registration and management of RR/MDR-TB cases, please refer to the National PMDT guidelines.

patient is kept in the main TB cohort and assigned an outcome from among those listed above.

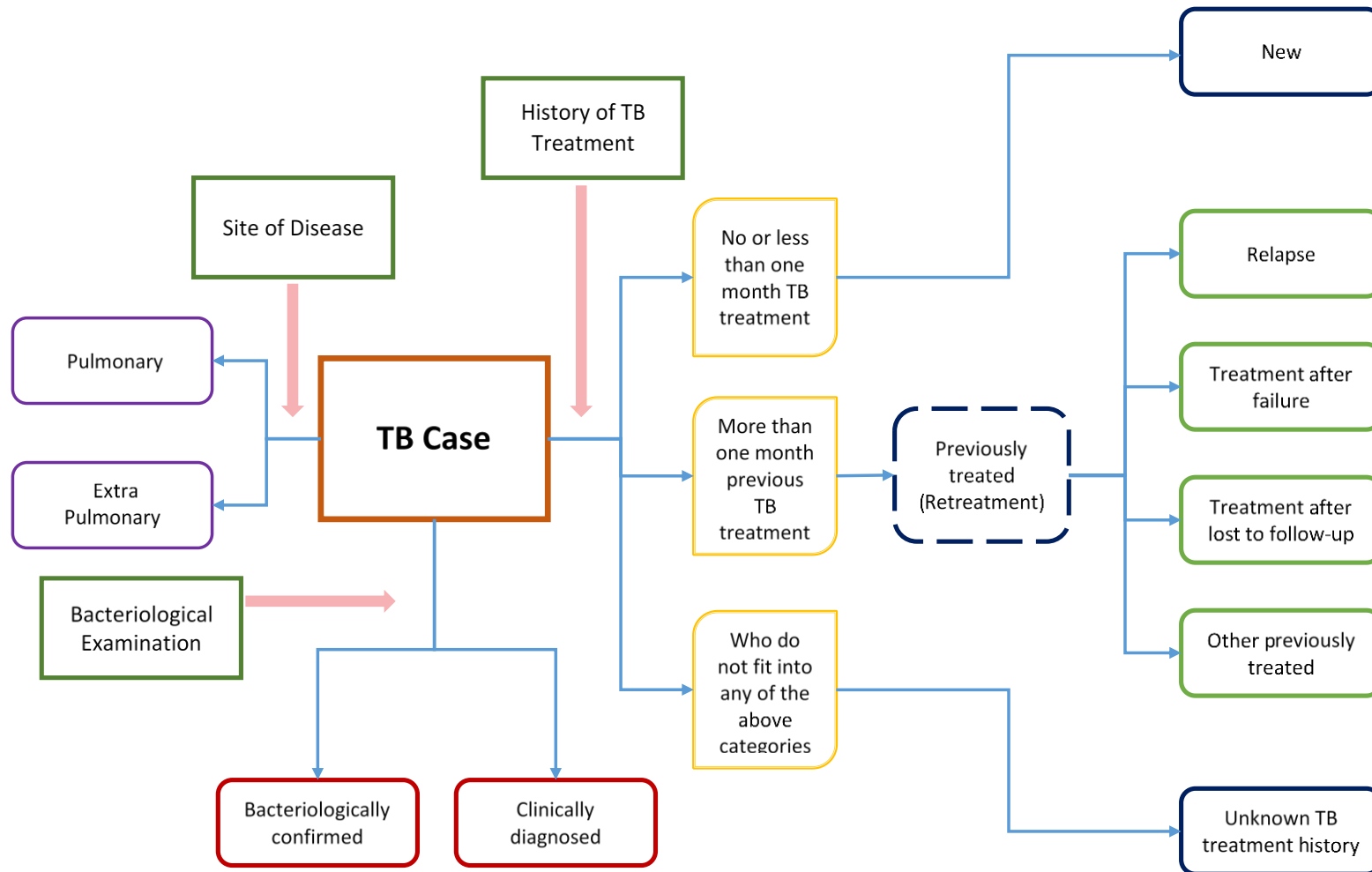


Figure 2-1 Classification of TB cases

3. Screening and Diagnosis

The highest priority for tuberculosis control is early identification and cure of all tuberculosis cases. Therefore any person with symptoms suggestive of tuberculosis, particularly cough for more than two weeks and close contacts of known TB cases should be investigated. Screening is also sometimes carried out in individuals with risk factors like HIV infection, prisons, for immigration purposes based on country specific requirements, priority groups as determined by local epidemiology as well as certain pockets of unreached populations. However mass screening of general population is not recommended. Active screening for intensified case detection is further explained in section 8.5.2

3.1 Register of TB symptomatics

A register of TB symptomatics should be maintained at all health institutions. This is a record of all the patients identified with symptoms suggestive of TB at the health centre and referred for examination of sputum/ biological samples.

The register is useful:

- To review the case finding activity of the health institution.
- To monitor whether TB symptomatics have been referred to the laboratory and the results of laboratory examinations have been received for all samples sent.

Whenever a TB symptomatic is identified, it should be recorded in the register. The referring medical officer or a nursing officer assigned the duty should be responsible for maintaining this register. The Medical Officer-in-charge or the Senior Medical Officer of the OPD should oversee this activity. The head of the institution may entrust these responsibilities to any other officer depending on the situation in the particular institution. Person who is responsible for the register should ensure that full name, complete address and contact telephone numbers, if available, are entered in the register legibly, so that all TB symptomatics with positive results could be located if he/she does not return for the results.

3.2 Investigations

3.2.1 Sputum smear microscopy

Sputum smear microscopy is among the least expensive methods of diagnosing infectious cases of pulmonary tuberculosis. Whenever tuberculosis is suspected in a patient who has had a cough for two weeks or more with or without any history of previous TB treatment, three sputum samples should be collected and examined microscopically for Acid Fast Bacilli (AFB).

Collection of sputum samples⁴

A patient with symptoms suggestive of pulmonary TB (PTB) needs to submit three sputum samples for microscopy. Patient should be advised to collect sputum and not saliva by vigorous coughing following a deep inspiration.

Three early morning samples are preferred. However, outpatients may provide sputum specimens as follows:

- | | |
|-------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| First spot specimen | - Supervised spot specimen at the first visit |
| Early morning specimen | - Patient is given a sputum container to collect early morning specimen on the following day. |
| Second spot specimen | - Second supervised spot specimen is collected when the patient returns with the early morning specimen on the second day. |

In clinics or wards, sputum samples should be produced in a designated place with good ventilation and sunlight, and away from other people

Correct procedure to collect a sputum sample

In order to obtain valid results, it is very important to instruct patients how to collect a sputum sample correctly. It is not uncommon for patients to produce a sample of saliva rather than sputum if they were not instructed.

How to produce a good sputum sample?

- Rinse mouth with water
- Inhale deeply 2-3 times with mouth open
- Cough out deeply from the chest
- Open the container and bring it closer to the mouth
- Spit out the sputum into it and close the container

This should be done in a well-ventilated space, as far away as possible from other people.

Inhaling steam facilitates sputum production.

3.2.2 Chest X-ray

While Chest X-ray is a good screening tool, diagnosis of tuberculosis by means of X-ray alone is unreliable. Abnormalities seen on a chest X-ray may be mimicked by a variety of other conditions. Therefore, the chest X-ray has a limited role in confirming the diagnosis of pulmonary tuberculosis. The decision to start on anti-TB treatment on patients should not be based solely on abnormal chest X-ray findings and all efforts should be made to perform sputum microscopy and other microbiological tests on sputum. If microbiological

⁴For methods of collection of other biological specimen, please refer to the laboratory manual

tests are negative, then Chest X-ray findings may be substantiated with a thorough history, clinical examination and other available tests.

Chest X-rays may also be used at the end of the treatment to assess extent of lung damage and to detect any residual complications like bronchiectasis, fibrosis, pleural thickening and lung collapse. However, as in case of diagnosis, Chest X-ray have no role in declaring cure from TB as some of the radiological changes may persist even after the disease has been cured.

3.2.3 Culture for AFB

Culture examination of sputum for AFB is more sensitive and specific than direct smear microscopy and are useful in detecting cases where the number of organisms are fewer than that can be detected by direct smear microscopy. But this is more expensive and takes at least 6-8 weeks to get the results by conventional methods of culture. Culture methods based on liquid media are more sensitive and can show positive results relatively early when compared with solid media.

Under ideal circumstances pre-treatment sputum cultures for *Mycobacteria* should be performed on all PTB patients. However, due to limited facilities available, at present sputum cultures are recommended in the following situations: -

- All previously treated TB cases before initiating treatment
- Pre-treatment cultures in new patients who have a high risk of drug resistance. (example: health care workers, prisoners, drug addicts, patients returning from abroad, contacts of known drug resistant TB patients and unknown drugs or regimen administered for TB outside the programme) or those with high risk of mortality in case of drug resistance e.g. HIV positive patients and those with other immunocompromised conditions
- All paediatric patients
- All new smear negative and EPTB cases where appropriate and adequate samples are available
- New PTB patients who fail to convert at the end of two months or later
- Previously treated patients (initially direct smear positive or negative) started on first line anti-TB drugs who fail to convert at the end of three months or later

3.2.4 Rapid diagnostic tests

There are new rapid diagnostic methods available for detection of TB such as Xpert MTB/RIF, and line probe assay.

Xpert MTB/RIF

Xpert MTB/RIF is an automated nucleic acid amplification test recommended by World Health Organization (WHO) for early detection of TB and resistance to rifampicin, which is one of the most important drugs used in the first line regimen for treating TB. Resistance to rifampicin is also used as a proxy indicator of multidrug resistance. The test takes around two hours, and requires minimal man power to perform. Xpert MTB/RIF can detect TB bacilli at much lower concentrations as compared to smear microscopy and hence is considered much more sensitive. At present, this test is only offered for following groups of patients

- All cases with a history of TB treatment in past and now presenting with symptoms suggestive of TB (retreatment cases)
- Other new cases/ symptomatics with a risk of drug resistance
 - Contacts of known DR-TB cases
 - Healthcare workers
 - Patients who return from abroad with active TB
 - Prisoners
 - Drug addicts
 - Patients treated outside the programme
- People living with HIV are at higher risk of morbidity and mortality due to TB. Given the urgency in detecting resistance to drugs, the samples from such patients are subject to Xpert MTB/RIF testing
- New PTB patients remaining positive at 2 months of treatment.
- Retreatment patients started on first line anti-TB drugs remaining positive at 3 months or later
- Patients with possible central nervous system TB
- Paediatric TB cases

With the wider availability of this test in future (**expected by mid-2017**) it will be used as an initial test in the confirmation of diagnosis on all groups of patients with sputum smear negative PTB as well as EPTB cases.

Line probe assay

Line probe assay (LPA) is a molecular method for diagnosing TB and the most common genetic mutations causing resistance to rifampicin and isoniazid. This technology can diagnose MDR-TB directly from smear positive sputum specimens and from culture isolates providing results in five hours. Turnaround time could be longer when the test is

performed in batches of selected cultures. This test does not work well on smear negative specimens. Since this test is technically more demanding it is used only at National Tuberculosis Reference Laboratory (NTRL) to confirm the diagnosis of MDR-TB alongside conventional DST.

As of now the LPA is performed on solid or liquid culture isolates and for confirmation on specimen where the Xpert MTB/RIF (GeneXpert) tests show rifampicin resistance.

3.2.5 Tuberculin skin test

Tuberculin is a purified protein derived from tubercle bacilli. Infection with *M. tuberculosis*, causes the development of hypersensitivity to tuberculin. This is useful in identification of tuberculous infection. However, the Tuberculin skin test is of limited value in clinical work, especially in countries with a high prevalence of TB. A positive test only indicates the infection but not the presence or the extent of tuberculous disease. A negative test does not necessarily exclude active TB. It also does not have a value in the diagnosis of re-activation of tuberculosis. Repeat test has no value in the diagnosis of tuberculosis. There are several methods of performing the Tuberculin skin test. They are, Mantoux, Heaf and Tine methods. In Sri-Lanka, Mantoux is used as the tuberculin skin testing method.

Mantoux test is indicated only as an ancillary investigation to diagnose active tuberculosis only after performing examination of other biological specimen like sputum. Mantoux should not be used as a screening test on contacts or others. However, in instances, where, Mantoux testing is a requirement for medical examination to go overseas for education or employment, this test can be carried out at District Chest Clinics on a fee levied basis.

Technique of Mantoux test

Several preparations of Tuberculin are available. The tuberculin that is used in NTP in Sri Lanka at present is 5 TU PPD-S which is bioequivalent to formerly used solution 2 TU PPD RT-23. Currently available Mantoux solution (tuberculin) comes in multi dose vials of 1ml and contains 5 TU (tuberculin units) per 0.1ml. The Mantoux test is done by intradermal injection of 0.1 ml of tuberculin to the anterior aspect of the left forearm. The transverse diameter of the induration is measured after 48-72 hours.

Interpretation of Mantoux depends on two factors:

- Diameter of the induration
- Person's risk of being infected with TB and of progression to disease if infected

Induration of diameter ≥ 5 mm is considered positive in:

- HIV-positive individuals including children
- Severely malnourished children

Induration of diameter ≥ 10 mm is considered positive in:

- All other children (whether or not they have received BCG vaccination) and adults

Mantoux skin test (PPD skin test)



CORRECT
Only the induration
is being measured

INCORRECT
The erythema is
being measured

(CDC 1995)

Figure 3-1 Reading Mantoux test

The following precautions should be taken to ensure the quality and potency of the Mantoux solution:

- Optimal temperature for storage is 2-8°C.
- Should not be frozen but be kept refrigerated.
- Skin test should be performed as soon as possible after the syringe is filled.

The multi-dose vials, once opened may be used up to a maximum period of 4 weeks, if all the following conditions are met (Opened multi dose vials policy WHO/V&B/00.09)

- The expiry date has not passed
- The Tuberculin PPD is stored under appropriate cold chain conditions
- The product vial septum has not been submerged in water
- Aseptic technique has been used to withdraw all doses

Interpretation of Tuberculin test

3.2.6 A positive Tuberculin test

Tuberculin test per se is not a diagnostic test for TB. It should be interpreted in the context of clinical picture and other investigations. A positive tuberculin test is only one piece of evidence in favour of a diagnosis of tuberculosis more so in children. Wherever possible a bacteriological examination should be done to confirm the diagnosis of tuberculosis.

Tuberculin test can be positive in the absence of active TB in the following conditions:

- Incorrect interpretation of test
- Past TB disease
- BCG vaccination
- Primary TB infection
- Infection with non-tuberculous mycobacteria

3.2.7 A negative Tuberculin test

The following conditions may result in a negative Tuberculin skin test even in the presence of active tuberculous infection:

- Incorrect administration or interpretation of test
- HIV infection
- Improper storage of tuberculin
- Viral infections (e.g. measles, varicella)
- Vaccinated with live viral vaccines (within 6 weeks)
- Malnutrition
- Bacterial infections (e.g. typhoid, leprosy, pertussis)
- Immunosuppressive medications (e.g. corticosteroids)
- Neonatal patient
- Primary immune-deficiencies
- Diseases of lymphoid tissue (e.g. Hodgkin's disease, lymphoma, leukaemia, sarcoidosis)
- Low protein states
- Severe TB
- Diabetes and other immunocompromised conditions

A Tuberculin test has no value in diagnosis of re-activation. Repeat Mantoux testing is not recommended for the diagnosis of TB since repeat test is known to have a booster effect and may provide a false positive result.

3.2.8 Diagnosis of extrapulmonary TB/non respiratory specimens

Tissue biopsy

Tissue biopsy is useful in the diagnosis of extrapulmonary TB (EPTB). Biopsy will also exclude another pathological process like malignancy. Therefore biopsy should be attempted in suspected EPTB if lesion is amenable to biopsy specifically when a confirmed diagnosis cannot be made using Xpert MTB/RIF on tissue aspirate or there is no clinical progress even after administering effective TB treatment for 2 months or more. In pulmonary TB (PTB) too lung biopsy may be indicated in the diagnosis of miliary TB or in case of lung lesions atypical of TB when the sputum is negative for AFB. Histology will reveal granulomatous inflammation with central caseation and cell infiltration with

lymphocytes, epithelioid cells and Langhan's giant cells. Biopsy specimens collected in normal saline can be cultured for AFB. Direct smear for AFB and Xpert MTB/RIF can also be done on biopsy samples when an adequate volume of sample can be obtained. Xpert MTB/RIF is recommended in addition to AFB culture for diagnosis of TB in EPTB cases (except pleural effusion, blood, urine and stools) which is expected to be introduced for the purpose in Sri Lanka from mid-2017 when sufficient capacity for conducting tests is available.

Tissue aspirate

Cytology and direct smear for AFB can be done on aspirates from extrapulmonary sites such as lymph nodes, collections of pus. If an adequate amount (at least 0.8 ml) of aspirate is obtained, Xpert MTB/RIF can be performed which, if positive, confirms the diagnosis microbiologically. For AFB culture and Xpert MTB/RIF at least 1 ml of aspirate would be required.

Pleural fluid

Pleural fluid aspiration should be done on all pleural effusions. Exudative effusions with lymphocyte predominance suggest TB pleural effusion but does not confirm the diagnosis. The yield of direct smear for AFB is low and AFB culture should be performed on pleural fluid. In non-smoking young patients, elevated pleural fluid adenosine deaminase (ADA) strongly suggest tuberculous aetiology especially when Mantoux test is also positive. This obviates the necessity to do pleural biopsy. Some patients may need thoracoscopy. However such decision will be taken by Consultant Respiratory Physician based on clinical situation and other available test reports.

Cerebrospinal fluid (CSF)

Diagnosis of neurological TB is difficult. High protein content in CSF with high lymphocyte count suggest TB aetiology but not confirmatory. Xpert MTB/RIF is a sensitive rapid molecular diagnostic test on CSF which should be done as a first line investigation when neuro TB with meningeal involvement is suspected. At least 0.8ml of CSF should be sent for the test. Direct microscopy for AFB on CSF has poor sensitivity. Mycobacterial culture can also be done and needs at least 1 ml of the specimen.

Urine

In the diagnosis of genitor-urinary TB, direct smear of urine for AFB is unreliable as urine can be contaminated with atypical mycobacteria. However urine culture for AFB should be done. For this, three early morning samples of urine (each sample at least 20ml) should be sent in culture bottles separately. (If 50ml sterile, screw capped, conical tubes are provided from the culture laboratory 40ml urine can be collected). Xpert MTB/RIF on urine is not recommended in the diagnosis of genito-urinary TB.

3.3 Diagnosis of tuberculosis in children

Diagnosis of TB in children is often difficult since only a small proportion of children have sputum smear positive tuberculosis, and many children cannot produce sputum for examination. Detailed clinical history of symptoms and contact with a known or likely case of tuberculosis followed by thorough clinical examination should precede diagnostic tests.

Diagnosis of TB in children should be considered in the following situations.

- Respiratory symptoms more than two weeks not responding to broad-spectrum antibiotics.
- Undiagnosed illness continuing for more than 2- 4 weeks.
- Unexplained fever (even if low-grade)
- Meningitis not responding to antibiotic treatment or sub-acute in onset and/or raised intracranial pressure
- History of contact with an infectious pulmonary TB case, particularly in the same household.
- An abnormal chest X –ray.
- A positive Tuberculin skin test.
- Unexplained weight loss or failure to gain weight in spite of adequate nutrition.
- Fatigue, reduced playfulness, decreased activity.
- Failure to thrive in an infant.
- Enlarged lymph nodes (especially non painful), abdominal mass, ascites, CNS signs, signs of pleural or pericardial effusion, enlarged joints.
- Gibbus deformity of spine.

The diagnosis should be based on:

- Careful history (including history of TB contact and symptoms consistent with TB)
- Clinical examination (including growth assessment)
- Tuberculin skin testing
- Chest X-ray
- Bacteriological confirmation whenever possible – In case of suspected PTB, early morning sputum (where a good sample can be obtained), gastric aspirate or sputum obtained after nebulisation with normal/ hypertonic saline can be sent for direct smear and culture for *M. tuberculosis* and Xpert MTB/RIF
- Other investigations relevant for suspected pulmonary TB and suspected extrapulmonary TB
- HIV testing

Bacteriological examination for tuberculosis in children

As per the recent WHO guidelines on Xpert MTB/RIF as well as the childhood TB guidelines⁵ the following recommendations are included for diagnosing TB in children

- Xpert MTB/RIF should be used rather than conventional microscopy and culture as the initial diagnostic test in children suspected of having MDR TB or HIV-associated TB
- Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial test in all children suspected of having TB
- Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture, and/or histopathology) for testing of specific non-respiratory specimens (lymph nodes and other tissues) from children suspected of having extrapulmonary TB
- Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test in testing cerebrospinal fluid specimens from children suspected of having TB meningitis
- Interferon-gamma release assays (IGRAs) should not replace the tuberculin skin test (TST) for the diagnosis of latent TB infection in children or for the diagnostic work-up of children (irrespective of HIV status) suspected of TB disease in these settings
- Routine HIV testing should be offered to all patients, including children, diagnosed with TB

Smear microscopy for AFB can be used as an initial test only for the older children who can expectorate an adequate volume of sputum and when the Xpert MTB/RIF test is not immediately available. Even when sputum smear is AFB negative or microscopy facility is not readily available an early morning sputum sample should be transported to the nearest laboratory with facilities for Xpert MTB/RIF test and culture for *M. tuberculosis*.

Since most young children swallow sputum, gastric aspirate or induced sputum may be obtained early morning and sent for Xpert MTB/RIF test and culture for *M. tuberculosis*.

⁵Guidance for national tuberculosis programmes on the management of tuberculosis in children – 2nded, 2014. WHO. ISBN 978 92 4 154874 8

4. Treatment of TB

Treatment of tuberculosis is the cornerstone of any NTP. The modern treatment strategy is based on standardized short course chemotherapy regimens and proper case management to ensure completion of treatment and cure.

Aims of treatment of TB are:

- To cure the patient of TB
- To prevent death from active TB or its late effects
- To prevent relapse of TB
- To decrease transmission of TB in the community
- To prevent the emergence of drug resistant TB

Short Course Chemotherapy (SCC) is the recommended treatment for tuberculosis. When properly applied, it fulfils the above aims of anti-TB drug treatment.

4.1 Requirements for adequate chemotherapy

- An appropriate combination of quality assured anti-tuberculosis drugs
- Prescribed in correct dosage according to the weight band
- Taken regularly by the patient
- For the prescribed period of time

It is essential for the patients to receive and to adhere to the recommended course of treatment (usually 6-8 months) in order to be cured. If patients fail to take their combination of drugs regularly, the bacilli may become resistant to the drugs. The best way to support patient adherence to treatment is patient-centred Direct Observation of Treatment (DOT). This means that the patient swallows the tablets under the direct observation of a health worker or a trained person.

4.2 Standard codes for TB treatment regimens

There are five essential first line anti-TB drugs namely isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin. There is a standard code for TB treatment regimens and each anti-tuberculosis drug has an abbreviation.

| | | |
|---|---|--------------|
| H | - | Isoniazid |
| R | - | Rifampicin |
| Z | - | Pyrazinamide |
| E | - | Ethambutol |
| S | - | Streptomycin |

A TB treatment regimen consists of two phases, the intensive phase and the continuation phase. The number before a phase is the duration of that phase in months.

E.g.: 4 HR means 4 months of isoniazid and rifampicin daily.

4.3 Scientific basis of treatment of TB

The strategies adopted in the treatment of TB are based on both scientific and operational research. The following three components are discussed in brief.

- Domiciliary/ ambulatory treatment
- Short course chemotherapy
- Direct observation of treatment

4.3.1 Domiciliary treatment

Domiciliary chemotherapy has been proved to be as effective as institutional treatment. Soon after the initiation of appropriate and effective treatment on domiciliary basis, patients do not pose an additional risk as a source of infection among contacts at home.

4.3.2 Short course chemotherapy

Short course chemotherapy is recommended for the treatment of pulmonary TB, as well as all forms of extra-pulmonary TB in all new cases. The introduction of rifampicin and pyrazinamide has made it possible to shorten the duration of treatment regimens for a period as short as six to eight months. The shorter duration has also contributed to the improvement of treatment adherence.

4.3.3 Basis of chemotherapy

- **Bacteriological basis of treatment**

i. Existence of naturally occurring drug resistant mutants

In an untreated tuberculosis patient, naturally occurring drug resistant mutants exist to different drugs at varying frequencies. The larger the bacterial population higher is the probability that resistant mutant strains to be present. The number of viable bacilli commonly found inside the cavities sized about 2 cm in diameter on an average, is likely to be in excess of 100 million (10^8). As a rule of thumb the frequency of spontaneous occurrence of drug resistant mutants would be roughly ~ 1 in 10^6 to isoniazid (H), ~ 1 in 10^6 to streptomycin (S) and ~ 1 in 10^8 to rifampicin (R). Based on these frequencies, the chances of naturally occurring organisms that is resistant to both H and R would be roughly ~ 1 in 10^{14} , which is virtually negligible.

There would be appreciable numbers of mutants resistant to any single drug before initiating treatment that are capable of multiplying and will not be affected by a single drug, e.g. isoniazid. This accounts for frequent failures observed with monotherapy of patients harbouring large number of bacilli. As a rule, mutants resistant to one drug are susceptible to other drugs and vice versa. Therefore, during the initial intensive phase (when the bacterial load is high), if four effective drugs are given concurrently, the chances of survival and selection of drug resistant organism to any single drug would be very small. This is the basis for the use of multi-drug therapy in the treatment of tuberculosis.

Role of intensive phase

The objective of combining four drugs in the intensive phase (IP) is to achieve rapid killing of actively multiplying bacillary population. This phase will eliminate naturally occurring drug resistant mutants and prevent the further emergence of drug resistant mutants. An optimal minimum duration of two months in new cases is essential for achieving smear conversion of 90% and above, thereby significantly reducing the infectiousness of the patient.

Role of continuation phase

Continuation phase (CP) with fewer drugs for a comparatively longer period will ensure elimination of persisters and those bacilli that were initially dormant but activate after some time, which are responsible for relapses. The optimum duration of continuation phase is four months for new patients and five months for re-treatment patients.

ii. Existence of sub-bacillary population

In a given lesion of TB, there are 4 bacterial sub-populations that are having different metabolic rates depending on their surrounding environment. They are acted upon with different intensity by different anti-TB drugs. The bacillary population and different drugs acting on them are shown in the figure below.

The bacillary sub populations B and C are referred as semi-dormant or persisters which are difficult to eliminate and are the source for relapses.

❖ Actions of anti-TB drugs

Anti-TB drugs have the following three actions:

- Early bactericidal activity
- Sterilizing activity
- Ability to prevent emergence of drug resistance

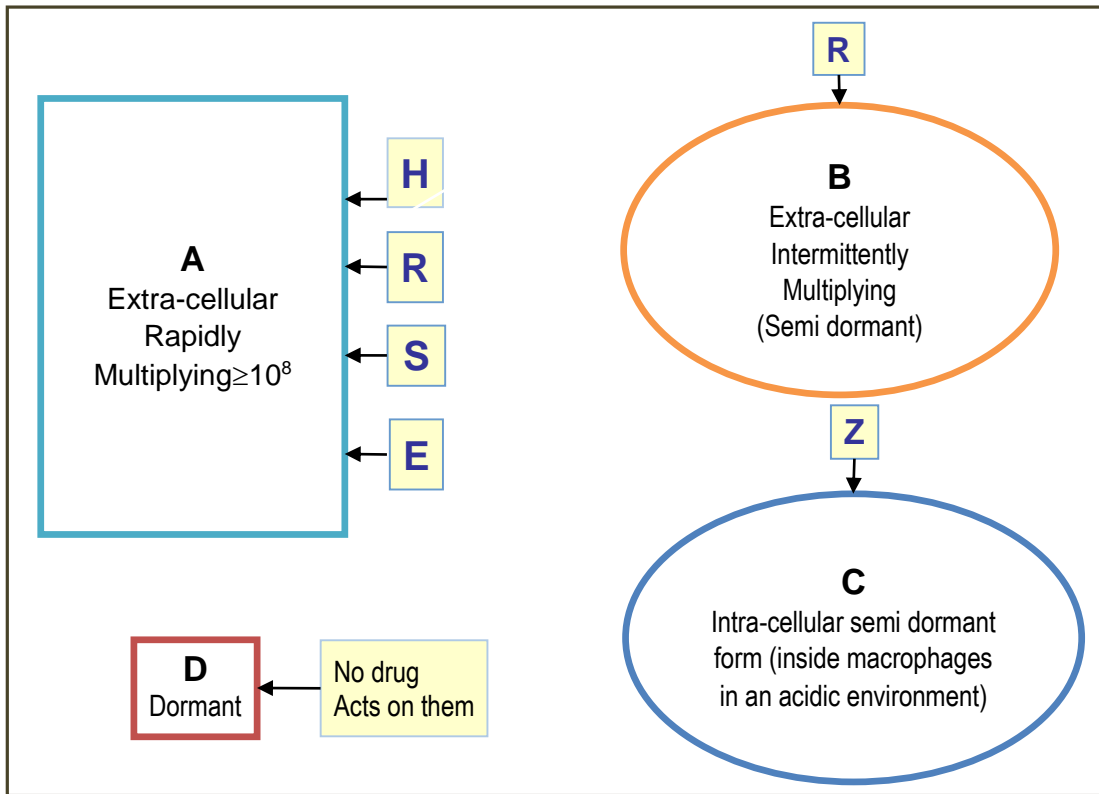


Figure 4-1 Bacillary sub-populations

Isoniazid (H) is a potent drug exerting early bactericidal activity, prevents emergence of drug resistant mutants to any companion drug and has low rates of adverse drug reactions.

Rifampicin (R) is a potent bactericidal and sterilizing drug acting on extracellular semi-dormant bacilli which multiply intermittently and cause relapses.

Pyrazinamide (Z) is a bactericidal and sterilizing drug effective in eliminating intracellular semi dormant bacilli multiplying slowly in an acidic environment, thus reducing the relapse rate.

Ethambutol (E) is an effective bacteriostatic drug helpful in preventing emergence of resistance to other companion drugs.

Streptomycin (S) is a bactericidal drug.

The ranking of the drugs with respect to their type of activity is indicated in the following table.

Table 4-1 Activity of Anti-TB drugs

| Drugs | Early bactericidal | Sterilizing activity | Prevention of emergence of drug resistance |
|--------------|--------------------|----------------------|--------------------------------------------|
| Isoniazid | ++++ | ++ | ++++ |
| Rifampicin | +++ | ++++ | +++ |
| Streptomycin | +++ | -- | ++ |
| Pyrazinamide | ++ | +++ | + |
| Ethambutol | + | -- | ++ |

- **Pharmacological basis of treatment**

In the treatment of TB, it is important to achieve peak serum levels of all the drugs simultaneously, so that maximum bactericidal effect is obtained. This is achieved by administration of all the drugs at the same time. This also renders operational convenience of advising the patients to consume all the drugs at the same time.

4.4 TB treatment regimens

Treatment regimens consist of two phases:

1. Initial intensive phase (IP)
2. Continuation phase (CP)

4.4.1 Intensive phase

During the initial intensive phase, there is the rapid killing of TB bacilli as explained above. Infectious patients quickly become non-infectious (within about two weeks) and symptoms improve when given proper dosage of quality assured drugs in right combination. Most patients with sputum smear-positive pulmonary TB become smear negative within two months of effective treatment. Patient support in taking medicines using Directly Observed Therapy (DOT) is essential in the initial phase for every single dose. This prevents the development of drug resistance as the risk is higher during the early stages of anti-TB treatment, when there are abundant bacilli.

4.4.2 Continuation phase

During the continuation phase, fewer drugs are necessary, but for a longer period. The sterilizing effect of the drugs eliminates the remaining bacilli, thus preventing subsequent relapses. During the continuation phase, at least once a week observation of drug intake is desirable

Patients who have taken anti-tuberculosis drugs previously are much more likely to develop drug resistance, which may have been acquired through inadequate prior chemotherapy.

Therefore before starting treatment, it is essential to inquire all patients closely and carefully to determine whether or not they have previously treated for tuberculosis, so that they can be screened for drug resistance and put on the proper treatment regimen.

4.5 Categories and treatment regimens

The recommended treatment regimen depends on the treatment category of each patient. There are two treatment categories, new and retreatment, and two standardized treatment regimens in Sri Lanka (Table 4.2).

Table 4-2 Case definitions, treatment categories and recommended regimens

| Case Definition | Treatment Category | Treatment Regimen | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|--------------------------------------------------------------------------------|--------------------|
| | | Intensive Phase | Continuation Phase |
| New cases <ul style="list-style-type: none"> • Pulmonary • Extrapulmonary TB | New | 2 HRZE | 4 HR |
| Previously treated cases without drug resistance <ul style="list-style-type: none"> • Relapses • Treatment after failure • Treatment after loss to follow-up • Other previously treated cases | Retreatment* | 3HRZE Add S for 2 months if there is perceived risk of mono/poly resistance | 5 HRE |

* Sputum specimen from all retreatment cases would be subject to Xpert MTB/RIF test and simultaneously be sent for Culture and DST (C&DST). In case the results of Xpert MTB/RIF are reported MTB positive/ rifampicin resistance (RR) not detected, and the clinician decides to initiate the patient on TB treatment, standard first line anti-TB drugs RHZE on IP and RHE in CP should be administered. However where the Consultant Respiratory Physician considers the risk of having drug resistance as high (e.g. repeated treatment interruption, treatment failure), Streptomycin may be added to the first line regimen for initial two months of treatment while awaiting results of complete DST. The regimen may be modified again as per the drug sensitivity pattern after the results of C&DST are obtained. In case the results of Xpert MTB/RIF are reported MTB positive/ RR detected or there is any drug resistance found on C&DST, then the algorithm as per the PMDT guidelines needs to be followed under the guidance of Consultant Respiratory Physician.

4.5.1 Treatment regimen for new cases

This regimen is applicable to all **new** patients which include new bacteriologically confirmed or clinically diagnosed cases of TB (including extrapulmonary TB patients).

Recommended Treatment Regimen

2 HRZE – intensive phase

4 HR – continuation phase

In case of neurological involvement (e.g. TB meningitis) continuation phase should be extended to 10 months. Ethambutol may be replaced with streptomycin in case of neuro TB with meningeal inflammation or as decided by the Consultant Respiratory Physician in consultation with the neurologist. In osteoarticular TB too, continuation phase should be extended to 7 – 10 months.

4.5.2 Treatment regimen for previously treated cases (Re-treatment Regimen)

This regimen is applicable to all previously treated cases. They are:

- Relapses
- Treatment after failure
- Treatment after loss to follow-up
- Other previously treated patients

Two samples of sputum should be collected for AFB culture and DST and Xpert MTB/RIF testing on all patients who are going to be commenced on retreatment, prior to commencement of treatment. If Xpert MTB/RIF shows RR, refer to PMDT guidelines. If RR not detected by Xpert MTB/RIF, such patients should be commenced on retreatment regimen. Re treatment ATT regimen consists of three months of RHZE (intensive phase) followed by five months of RHE (continuation phase)

3HRZE / 5HRE

Streptomycin may be added for initial two months of retreatment regimen in consultation with a Consultant Respiratory Physician when RR is not detected on Xpert MTB/RIF but the patient is considered to be at high risk of drug resistance. Such cases include:

1. Treatment failure
2. History of recurrent treatment interruption
3. Unknown regimen or unknown quality of anti-TB drugs outside the national programme

Further reference to PMDT guidelines is advised in cases where mono or poly-resistance is confirmed at a later stage.

Pulmonary and extrapulmonary disease should be treated with the same regimens.

Unless drug resistance is suspected, adjuvant corticosteroid treatment is recommended for TB meningitis and pericarditis.

4.5.3 Role of steroids

Rationale of adding oral steroids to anti TB treatment is that steroids will reduce the organization and subsequent fibrosis of exudates and reduce inflammation. There is no consensus of opinion on the use of steroids in the treatment of TB. However, in general routine addition of oral steroids to anti TB treatment is recommended in;

- a) TB meningitis and other forms of neuro-TB
- b) TB pericardial effusion
- c) Genitourinary TB with ureteric obstruction
- d) Laryngeal TB with life-threatening airway obstruction (ENT opinion should be sought)
- e) Spinal TB with cord compression (Neuro Surgeon's opinion should be sought)

Addition of steroids should be decided on an individual basis in the following situations:

- a) TB pleural effusion
- b) Abdominal TB including TB peritonitis
- c) TB salpingitis
- d) TB lymphadenitis: progressive enlargement of existing nodes and appearance of new nodes

Steroids are also recommended in the management of immune reconstitution inflammatory syndrome (IRIS) which occurs as a complication of treating HIV-TB co-infection. Rifampicin increases metabolism of steroids through liver enzyme induction. Therefore, the recommended dose of prednisolone is 0.75 – 1 mg per kg per day (children 1 – 2 mg/kg daily) or an equivalent. Rifampicin also can precipitate hypoadrenalism due to increased metabolism of adrenocortical hormones which necessitates addition of intravenous hydrocortisone. Tuberculosis can affect adrenal glands leading to TB adrenalitis resulting in hypoadrenalism. In which case, hydrocortisone replacement therapy should be initiated.

4.5.4 Role of surgery

Surgery, although sometimes required for diagnosis, plays little role in the treatment of extrapulmonary TB. It is reserved for management of late complications of disease such as hydrocephalus, obstructive uropathy, constrictive pericarditis, and spinal cord compression from Pott disease (spinal TB). TB lymphadenopathy with abscess formation

can be drained if considered amenable for intervention. Tuberculous pyrothorax not drained adequately with chest tube may need decortication

4.6 Fixed-dose combination tablets (FDCs)

In the management of TB patients with first line drugs, fixed-dose combination anti-TB drugs are recommended over individual drugs. Sri Lanka has introduced FDCs for TB treatment regimens in 2005. There are several advantages as well as disadvantages of using fixed drug combination tablets over individual drugs.

Advantages

- Prescription errors are likely to be less frequent because dosage recommendations are more straightforward and adjustment of dosage according to patient weight is easier
- The number of tablets to ingest is less and may thus encourage patient adherence to treatment
- If treatment is not observed, patient cannot be selective in the choice of drugs to ingest
- Resistance is less likely to emerge because monotherapy is avoided

Disadvantages

- Over dosage or under dosage (sub therapeutic blood levels) if number of tablets is more or less than the prescribed number
- Health care workers may be tempted to evade Directly Observed Therapy, erroneously believing that adherence is automatically guaranteed
- Poor rifampicin bioavailability is a problem with low quality FDCs. Quality assurance is therefore essential
- Using FDCs does not obviate the need for individual drugs for a minority of patients who develop drug toxicity

Table 4-3 WHO recommended formulations of FDC (adult) used in Sri Lanka

| FDC formulation | | |
|-----------------|------|---------------------------------------------------------------------------|
| FDC 2 | RH | rifampicin 150mg + isoniazid 75mg |
| FDC 3 | RHE | rifampicin 150mg + isoniazid 75mg + ethambutol 275mg |
| FDC 4 | RHZE | rifampicin 150mg + isoniazid 75mg + pyrazinamide 400mg + ethambutol 275mg |

Table 4-4 Number of FDC tablets used in TB treatment in adults according to body weight

| Treatment regimen | No. of tablets/grams according to body weight (kg)* | | | Duration of treatment |
|-------------------------------------------------------|-----------------------------------------------------|----------|----------|-----------------------|
| | <35 kg | 35-54 kg | ≥55 kg** | |
| New patients | | | | |
| Intensive phase-daily RHZE tablet (FDC 4) | 2 | 3 | 4 | 2 months |
| Continuation phase-daily RH tablet (FDC 2) | 2 | 3 | 4 | 4 months |
| Previously treated patients*** (retreatment) | | | | |
| Intensive phase – daily RHZE tablet (FDC 4) | 2 | 3 | 4 | 3 months |
| Streptomycin**** (IM) | 0.5g | 0.75g | 1g | 2 months |
| Continuation phase-daily RHE tablet (FDC 3) | 2 | 3 | 4 | 5 months |

*Change the number of tablets/grams if the weight band change overtime.

** for patients over 70 kg bodyweight, additional 400 mg Pyrazinamide may be added by the clinician in the intensive phase

***For retreatment cases, the use of additional drugs like Streptomycin would be decided by Consultant Respiratory Physician depending on history, risk assessment and available DST reports

****Patients over 60years, the dose of streptomycin is 0.5 g, irrespective of the weight

Table 4-5 Management of new cases who interrupted treatment

| Length of treatment | Length of interruption | Do a smear? | Result of smear | Register again as | Treatment |
|-------------------------|------------------------|-------------|---------------------|------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| < 1 month | < 2 weeks | No | - | - | Continue new patient regimen* |
| | 2-8 weeks | No | - | - | Start again on new patient regimen** |
| | > 8 weeks | Yes | Positive | Treatment after loss to follow-up | Start on retreatment patient regimen** after Xpert MTB/RIF test and Culture & DST |
| | | | Negative | - | Continue new patient regimen* |
| 1-2 months | < 2 weeks | No | - | - | Continue new patient regimen* |
| | 2-8 weeks | Yes | Positive | - | 1 extra month of intensive phase of new patient regimen after Xpert MTB/RIF testing if RR not found |
| | | | Negative | - | Continue new patient regimen* |
| | > 8 weeks | Yes | Positive | Retreatment case – treatment after loss to follow-up | Start on retreatment regimen after a Xpert MTB/RIF test and Culture & DST |
| Negative | | | - | Continue new patient regimen* | |
| 2 months or more | <2 weeks | No | - | - | Continue new patient regimen* |
| | 2-8 weeks | Yes | Positive With no RR | Retreatment case – treatment after loss to follow-up | Start on retreatment regimen after a Xpert MTB/RIF test and Culture & DST |
| | | | Negative | - | Continue new patient regimen* |
| | > 8 weeks | Yes | Positive with no RR | Retreatment case – treatment after loss to follow-up | Start on retreatment regimen after a Xpert MTB/RIF test and Culture & DST |
| Negative | | | - | Continue new patient regimen* | |

*A patient must complete all 60 doses of the initial intensive phase. Treatment taken before interruption is also counted.

**A patient who must “start again” should re-start treatment from the beginning

This is only a guide. Consultant opinion should always be sought especially in cases who have history of treatment interruption after taking drugs for 2 months or more or those who have repeated treatment interruptions.

Table 4-6 Management of retreatment cases who have interrupted treatment

| Length of treatment | Length of interruption | Do a smear? | Result of smear | Register again as | Treatment |
|---------------------|------------------------|-------------|--------------------------------------|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| < 1 month | < 2 weeks | No | - | - | Continue retreatment regimen* |
| | 2-8 weeks | No | - | - | Start again on retreatment regimen** |
| | > 8 weeks | Yes | Positive | Treatment after loss to follow-up | Start again on retreatment regimen**Check previous pre-treatment culture & DST reports. Request another culture if previous reports were negative. Repeat Xpert MTB/RIF |
| | | | Negative | - | Continue retreatment regimen* |
| 1-2 months | < 2 weeks | No | - | - | Continue retreatment regimen* |
| | 2-8 weeks | Yes | Positive | - | 1 extra month of intensive phase of retreatment regimen after a repeat Xpert MTB/RIF test and RR not found. Repeat culture if previous pre-treatment culture is negative |
| | | | Negative | - | Continue retreatment regimen* |
| | > 8 weeks | Yes | Positive | Treatment after loss to follow-up | Start again on retreatment regimen** after a repeat Xpert MTB/RIF test and RR not found. Repeat culture if previous pre-treatment culture is negative |
| | | | Negative | - | Continue retreatment regimen* |
| | 2 months | <2 weeks | No | - | - |
| 2-8 weeks | | Yes | Positive with no RR on Xpert MTB/RIF | Treatment after loss to follow-up | Start again on retreatment regimen** after a repeat Xpert MTB/RIF test and RR not found. Repeat culture if previous pre-treatment culture is negative |
| | | | Negative | - | Continue retreatment regimen* |
| > 8 weeks | | Yes | Positive with no RR on Xpert MTB/RIF | Treatment after loss to follow-up | Start again on retreatment regimen** after a repeat Xpert MTB/RIF test and RR not found. Repeat culture if previous pre-treatment culture is negative |
| | Negative | | - | Continue retreatment regimen* | |

*A patient must complete all 90 doses of the initial intensive phase. Treatment taken before interruption is also counted.

**A patient who must “start again” should re-start treatment from the beginning

This is only a guide. Should always seek CRP opinion before deciding treatment course. DST is essential in all retreatment cases and may need to be repeated if treatment is

interrupted. Xpert MTB/RIF will yield immediate results on Rifampicin sensitivity. First line drugs may be continued for all patients found not to have RR till such time complete DST results are available.

In case of drug resistance to Rifampicin (RR) or any drug at any stage found on Xpert MTB/RIF or Culture & DST, PMDT guidelines need to be followed with referral to the Consultant Respiratory Physician.

4.7 Treatment of TB in children

The basic principles of treatment and the regimens (drug combinations and duration) are as same as that for adults. However if inclusion of ethambutol is a concern in very small children, intensive phase with RHZ followed by continuation phase with RH may be given as incidence of isoniazid resistance and the burden of HIV are low in Sri Lanka. Such decision should be taken by a clinician experienced in managing paediatric TB.

The following dosages of anti-TB medicines should be used daily for the treatment of TB in children:

- isoniazid (H) 10 mg/kg (range 7–15 mg/kg); maximum dose 300 mg/day
- rifampicin (R) 15 mg/kg (range 10–20 mg/kg); maximum dose 600 mg/day
- pyrazinamide (Z) 35 mg/kg (range 30–40 mg/kg)
- ethambutol (E) 20 mg/kg (range 15–25 mg/kg)

Treatment may require dose adjustment to reconcile the effects of age and possible toxicity in young infants. The decision to adjust doses should be taken by a clinician experienced in managing Paediatric TB.

Streptomycin should not be used as part of first-line treatment regimens for children with pulmonary TB or tuberculous peripheral lymphadenitis.

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

New paediatric FDC formulations

- RHZ rifampicin 75mg + isoniazid 50mg + pyrazinamide 150mg
- RH rifampicin 75mg + isoniazid 50mg

The child-friendly fixed dose combinations offer the following advantages:

- Correct, WHO-recommended dose – no need for breaking, crushing or chopping of tablets
- Quickly dispersible in liquid - easy for children of all ages to take
- Palatable flavours
- Expected to improve treatment adherence and outcomes

Table 4-7 Paediatric formulation fixed dose combination drugs dosages according to the body weight (New formulations*)

| Phase and Drug | Weight (Kg)** | | | | |
|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|-------|-------|-----------------------|
| | 4- 7 | 8-11 | 12-15 | 16-24 | >25 |
| Intensive phase – daily | | | | | |
| RHZ (75 mg +50mg + 150 mg) | 1 | 2 | 3 | 4 | |
| E 100*mg | Ethambutol should be added in the intensive phase for children with extensive disease or living in settings where the prevalence of HIV or of isoniazid resistance is high | | | | Use adult formulation |
| Continuation phase – daily | | | | | |
| RH (75 mg + 50 mg) | 1 | 2 | 3 | 4 | |

* Likely to be available by 2017

** rounded off to nearest Kg

Table 4-8 Old paediatric formulations – till such time these are phased out*

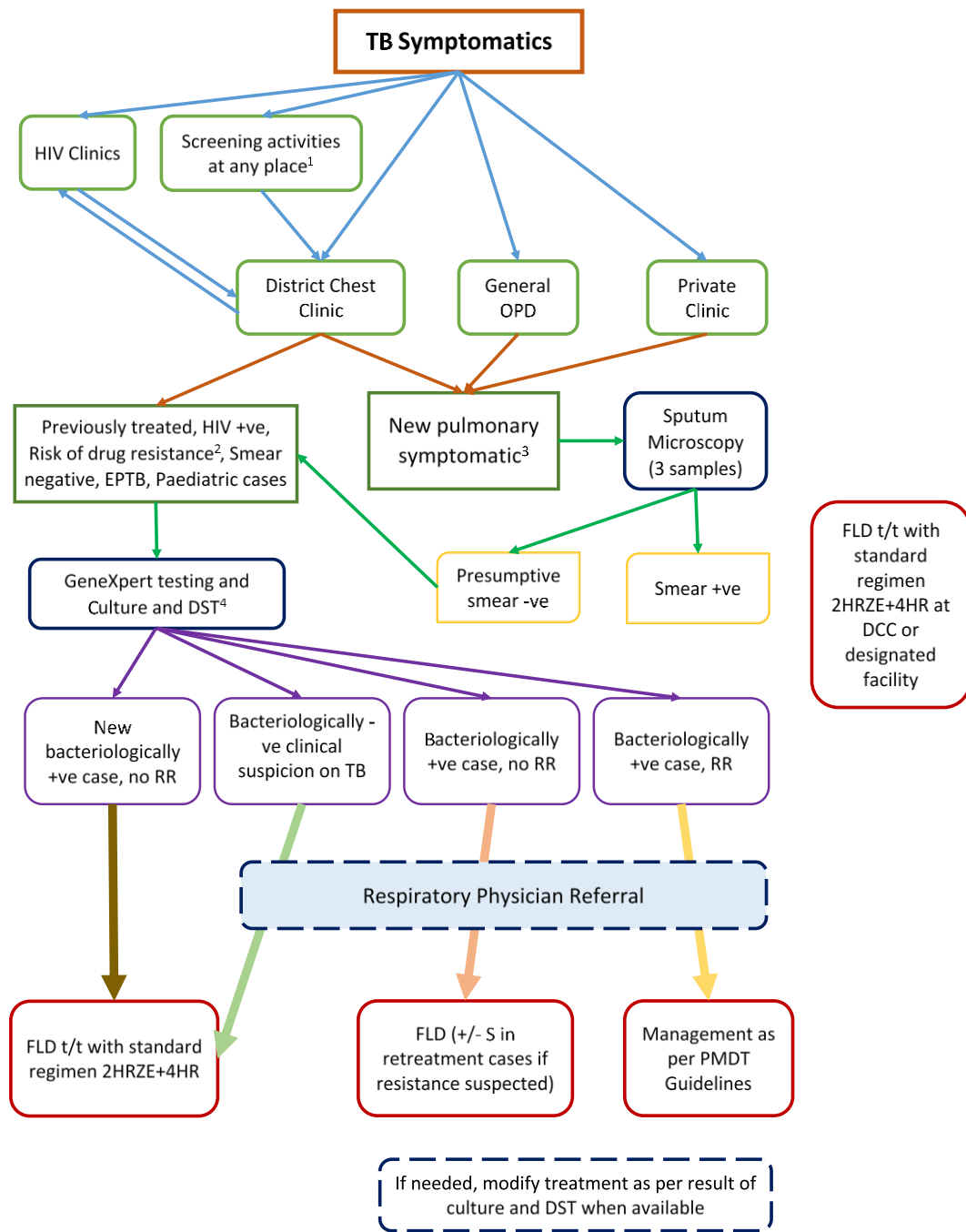
| Phase and Drug | Weight (Kg)** | | | | |
|-----------------------------------|---------------|------|-------|-------|------------------|
| | 5-7 | 8-14 | 15-20 | 21-29 | >30 |
| Intensive phase – daily | | | | | |
| HRZ (30mg + 60mg + 150mg) | 1 | 2 | 3 | 4 | |
| HR (60mg + 60mg) | 1 | 1 | 2 | 2 | |
| E 100mg | 1 | 2 | 3 | 3 | Use adult dosage |
| Continuation phase – daily | | | | | |
| HR (30mg + 60 mg) | 1 | 2 | 3 | 4 | |
| HR (60mg + 60 mg) | 1 | 1 | 2 | 2 | |

* These formulations will be phased out soon and replaced with new formulations as above

** rounded off to nearest Kg

Adherence to treatment may also be an issue as the children would depend upon the parents to bring them to the treatment centre and the timings may also interfere with their school hours. In such situations directly observed treatment by parents or by a community volunteer will be more appropriate.

The management of adverse drug reactions is similar to that in adults. However there will be a need to consult a Consultant Paediatrician and/or a Respiratory Physician in such cases. Supplemental pyridoxine (5-10) mg per day is recommended in children who are malnourished, HIV infected and in breast-fed infants.



1. Active screening, screening among immigrants etc. where findings are suggestive of TB
2. Likely cases – treatment failure, repeated treatment interruption, unknown TB treatment in private sector and other such cases where RIF is found sensitive on treatment testing
3. Case with no history of previous treatment, without any associated risk factors for resistance like contact with a known DR-TB case
4. Initial decision will be based on Xpert MTB/RIF test and whether the sample is found RIF resistant (RR) or sensitive

Figure 4-2 Patient pathway

The clinical follow up of the children during treatment is preferably every two weeks during the intensive phase and monthly during the continuation phase. It includes assessment of symptoms, treatment adherence, adverse effects and weight measurement.

The other investigations during follow up such as sputum examination and chest x-ray are done at the same frequency as in adults.

A non-responding child should be referred for further assessment and management to Consultant Paediatrician or Respiratory Physician.

5. DOT and Patient Support

This chapter describes

- the role and responsibility of the patient, TB programme, other providers, and the community in the cure of TB
- directly observed therapy
- patient-centred care
- measures to prevent treatment interruption

Adherence to TB treatment is crucial in achieving cure while avoiding the emergence of drug resistance. Regular and complete medication intake provides individual TB patient the best chance of cure, and also protects the community from the spread of TB. The emergence and spread of MDR and XDR-TB further reinforces the absolute necessity of helping a TB patient not to miss any drug doses. Supervision and patient support remains the cornerstone of appropriate TB treatment, and help programmes to achieve the desired treatment success.

5.1 Directly observed treatment (DOT)

DOT is a supportive mechanism that ensures the best possible results in treatment of TB. Here a DOT Provider helps the patient to take the treatment regularly by direct observation of intake of each dose daily along with proactive monitoring of adverse effects and psychological support, thereby ensuring adherence. DOT provider should be a responsible person accountable to NTP who is easily accessible and acceptable to the patient.

5.1.1 Why is directly observed treatment (DOT) necessary?

Patient adherence to treatment is a key factor in treatment success. Many patients who receive self-administered treatment are at risk of taking drugs irregularly and stopping treatment before completion due to various reasons. Studies in various countries have consistently shown that at least one third of patients do not consume medicines regularly. Many patients who do not receive directly observed treatment stop taking drugs once they feel better. It is neither possible to predict who these patients will be nor to prevent non-adherence through health education. Studies also have shown that there will be poor treatment outcome and high death rates in the absence of DOT, even when regular supply of drugs is ensured. Therefore, patient support through directly observed treatment is required to ensure treatment adherence and it also helps to motivate the patient to continue treatment. A patient who misses one attendance for DOT can be traced immediately, counselled and returned to treatment. DOT contact should also be seen as an opportunity to address issues that prevent patient from adhering to treatment.

Hence, by providing DOT, the NTP ensures that patients receive the correct drugs, in the correct doses, at the correct intervals and for the correct duration of time.

DOT should be seen as a part of a support package to address patient's needs. Such a support package should ensure that DOT is undertaken in a way that is sensitive and supportive to the patient's needs. A treatment supporter observing intake of every dose ensures that the patient takes the right anti-tuberculosis drugs, in the right doses, regularly over the recommended period. Regular supervision and support helps patients to be in frequent communication with a health worker or treatment observer, which provides more opportunities for education, identification and resolution of barriers to treatment, as well as early identification of non-adherence and initiating interventions to bring back the patient on prescribed treatment. Regular supervision also allows the prompt detection and management of adverse drug reactions and clinical deterioration.

DOT is associated with high cure and treatment completion rates. The highest rates of success were achieved in programs that used DOT in the context of a full support package, with components such as incentives and enablers.

DOT of each drug dosage is most critical in the intensive phase. It is particularly important in the treatment of patients who have poor family support, loners, alcoholics, substance abusers, mentally handicapped patients, prison inmates, patients with poor social and educational backgrounds and patients receiving second line anti TB drugs. Supervised treatment should be carried out in a context-specific and patient-friendly manner. There must be flexibility in how DOT is applied, with adaptation in different settings at the patient's convenience. The whole purpose of treatment observation could be lost if it is limiting access to care, turn patients away from treatment, or add to their hardships.

Depending on the local conditions, treatment observation may be undertaken at a health facility, in the workplace, in the community or at home (least preferred). A treatment supporter (DOT provider) must be identified for each TB patient. The treatment supporter should be a person acceptable to and chosen in consultation with the patient. For patients who live close to a health facility, the best treatment supporter would be one of the staff in the health facility, and this should be the choice of option if it is convenient to the patient. Collaboration with other programmes allows identifying staff from these programmes who may be observers to TB treatment.

Some TB patients may be living far away from a health facility. For them, preferred treatment observer would be a community health worker or a trained and supervised local community member. Cured TB patients could be successful DOT providers, as can traditional healers, friends, co-workers, a family member, neighbour, religious leader, etc. In fact, any person willing and acceptable to the patient, and also easily approachable and answerable to the health system can be a treatment supporter.

The NTP is responsible for training and monitoring the non-medical treatment observers. There must be a clearly defined line of accountability from NTP staff to general health

services staff and the treatment supporters. It is important to ensure the confidentiality and that the supervised treatment is acceptable to the patient. Patient's drugs should remain with the treatment supporter and only be given to the patient at the time of ingestion.

5.1.2 DOT in Sri Lanka

As described above DOT is one of the important elements of the internationally recommended strategy for TB control and Sri Lanka also follows the same. This ensures that all TB patients take the right anti-tuberculosis drugs, in the right doses daily without interruption over the recommended period and ensures that the patient completes the full course of treatment.

5.2 National policy for the implementation of DOT

5.2.1 All TB patients will be given DOT

- **New Pulmonary TB and extrapulmonary TB cases (all bacteriologically confirmed as well as clinically diagnosed)**

Intensive phase:

All patients should be given DOT **daily** during the **intensive phase**. This should be community based or a health centre close to the patient's residence as far as possible, and hospital based wherever necessary as in the case of very ill patients or those patients who are unable to attend daily for supervised treatment. However the final decision on the location of the facility should be based on mutual agreement between the patient and the clinician or a responsible health staff taking into consideration roles and responsibilities at each end.

Continuation phase:

Since the continuation phase also contains rifampicin, every effort should be made to provide each dose under observation. Wherever this is not possible patients should be advised to attend the chest clinic or the DOT centre **at least once a week** where the first dose can be given under direct observation and the remaining doses for the week are issued for administration at home. DTCO and PHI should make arrangements for supervisory visits to check drug intake (including pill counts). The patient is required to bring empty drug foils every time he/she visits the DOT provider or the clinic for drug collection.

- **All previously treated cases**

Directly Observed treatment should be given preferably **throughout the entire period** of treatment daily, both in the intensive and continuation phase of treatment of previously treated patients.

Since streptomycin may need to be injected during the first two months of intensive phase, this could be arranged at a local hospital or at a general practice on an out-patient basis. In

case there are no options for administering injectables on ambulatory basis, hospital admission may become necessary.

5.2.2 DOT providers

The following categories are identified as potential providers of Direct Observation of Treatment.

- Healthcare workers in state healthcare facilities
- Field healthcare workers
- General practitioners
- Healthcare workers in private health facilities
- Trained community volunteers
- Community leaders or any person in community who can be trained and is ready to take the necessary responsibility.

Trained community volunteers or community leaders need regular support, motivation and supervision by the NTP staff to ensure that quality is maintained.

5.3 Provision of drugs to DOT centres

Drugs for each patient are delivered to the DOT centres from the District Chest Clinic (DCC) by the PHI or any other staff assigned by the DTCCO. One month stock of drugs for each patient on treatment should always be ensured at each DOT centre

5.4 Using a patient-centred approach to care and treatment delivery

DOT has to be tailored to the needs of the patients. Locally appropriate measures should be consciously undertaken to identify and address physical, financial, social and cultural as well as health system barriers to access TB treatment services. Particular attention should be paid to the poorest and most vulnerable groups. Efforts should be made to explicitly address gender issues, to improve staff attitudes, and to enhance inter personal communication. It is essential that these approaches are based on ethical principles where the needs, rights, capabilities and responsibilities of patients, their families and their communities are appropriately addressed.

Whatever the chosen method of supervision and administration of treatment, there should be high sputum smear conversion and cure rates under routine conditions, irrespective of whether the setting is rural or urban. If, evaluation of the method of supervision and administration of the regimen shows suboptimal results, it should be altered and tested in demonstration and training districts.

In addition to DOT, other measures to support patient adherence with regular and complete treatment include:

- (a) A regular supply of quality assured drugs
 - provided free of charge;
 - in fixed-dose combinations to help reduce medication errors in addition to facilitating adherence;
 - maintaining buffer stock at all levels as per the number of patients and the usual drugs delivery cycle;
- (b) Accessible, high quality, continuous ambulatory TB care
 - expanding treatment outlets in the difficult rural and urban settings and involving providers who practice close to where patients live. This will reduce travel costs and loss of time and wages;
 - ensuring convenient clinic hours with minimized waiting times;
 - training sufficient number of motivated health workers with managerial support;
 - with flexibility to make appropriate arrangements for transfer to another facility;
 - by make arrangements upon release from hospital or prison to continue care on an ambulatory basis in the patient's community;
- (c) Positive action to remove barriers to treatment and care
 - ensuring that all services provided are affordable (if not free), and eliminating cost of care as a barrier to access services;
 - training health staff and DOT providers to ensure that treatment is administered in a non-discriminatory and non-stigmatising manner;
 - educating patient, including information regarding the regimen, duration, adverse drug reactions and possible treatment outcomes, provided repeatedly by well-trained and considerate staff;
 - prompt detection and management of adverse drug reactions;
 - ensuring that other forms of treatment support (such as community, workplace, or other) are available when facility-based treatment poses an obstacle for the patient;
 - provision or financing of transportation, and other treatment enablers that can compensate for the patient's indirect costs of care through collaboration with NGOs;

- provision of incentives such as food or hygienic packages for patients and their families, if appropriate for the context and individual patient in collaboration with NGOs;
- arranging patient and peer support groups, which may also help to reduce stigma;
- referring for psychological, social and legal support and other services including substance abuse treatment. Joint (integrated) support for TB patients with addictive behaviours;
- ensuring that concomitant HIV treatment is also easily obtainable.

(d) Health education

The patient and the family should be educated on the following aspects:

- Curability of the disease if drugs are taken as prescribed
- The disease and mode of its spread
- Treatment, duration, dosages, number of tablets, colour of tablets etc.
- Importance of directly observed treatment and regular, uninterrupted treatment for the entire duration.
- The need for sputum examination at regular intervals for monitoring
- Possible common side-effects and reporting them on visit
- Examination of close contacts

(e) Availability of hospitalization

Hospitalization may be needed for severely ill patients, those with complications or associated co-morbidities requiring closer clinical monitoring. It might also be an alternative, especially during the initial phase of treatment, for a small number of patients for whom other options of ensuring treatment adherence and support are not available. However, hospitalization per se does not ensure regular drug intake or completion of the treatment. Patient-centred support and supervision is just as important to success in an inpatient setting as it is in the community. Under the following conditions patients may be admitted for indoor treatment:

- Too ill for outdoor treatment.
- Having co-morbidities that need inward treatment.
- Unable to attend daily DOT treatment.
- Having severe adverse drug reactions.
- Having complications of the disease.

- Substance or alcohol abuse which increase the risk of defaulting treatment under ambulatory DOT.
- Poor family support

Duration of hospitalization of patients depend upon their clinical condition or social needs. Irrespective of patient being in hospital, provision of DOT should be done under the observation of the nursing staff. Patients should be provided with health education regarding the disease and the treatment. When the patient is taking in ward treatment, the Bed Head Ticket should be maintained with required details such as the clinical condition, investigations, diagnosis and management. However, TB Treatment Card which is used during DOT provision is not required to maintain at the hospital.

Diagnostic algorithm and regimens used should be in accordance with the National Guidelines. Follow up sputum examination should also be done according to the National Guidelines before discharging the patient from the ward.

On discharge, the TB Referral Form (TB 07) should be filled in triplicate and the patient is referred to the appropriate DCC with the original. The second copy of the Referral Form should be posted to the referring chest clinic and remaining copy is retained at the hospital.

5.5 DOT in children

Adherence to treatment may also be an issue as children would depend on the parents or other care-givers to bring them to the treatment centre and the timings may also interfere with their school timings. In such situations directly observed treatment by parents or by a community volunteer will be more appropriate.

5.6 Treatment interruption

5.6.1 Prevention of treatment interruption

Treatment interruption can be prevented, and if it occurs, can be limited so that there is no altogether total interruption of therapy. Promoting adherence through a patient-centred approach is probably more effective than spending resources for tracing patients whose treatment is interrupted.

Major factors influencing treatment interruption are substance abuse or mental illness, difficult access to treatment (distance, cost of transport), time and wages lost, sub-optimal quality and speed of drug delivery, low knowledge levels about TB and the need to complete treatment, and lack of flexibility for transfer to another facility.

All visits of the patient to the health facility should reinforce the need for regular and complete intake of treatment and elicit any problems that may cause interruption. At the time of registration, sufficient time should be set aside to discuss with the patient (and preferably also with the patient's family members or a designated treatment supporter). This initial meeting provides an important opportunity to inform the patient and the family

about the duration of treatment, and the need to consult ahead of time in case of a change of address. During the meeting, it is important to record the patient's address and other relevant contact details (e.g. partner or spouse, parents, work place, place of study, family physician) in order to maximize the probability of locating patients in the event of a treatment interruption. Recording cellular phone numbers of the patient and family has been very helpful in many settings.

It is helpful for a health staff member to accompany the patient to his or her residence. This allows verification of the patient's exact address, and provides an opportunity to arrange screening of household contacts.

When the patient is met at the end of the initial phase of treatment, the health worker should reassess patient's needs, and should inquire about future plans (work, family, moving to another location) during the continuation phase of treatment. Any changes should be discussed and concerns are addressed.

5.6.2 Management of patients who interrupt treatment

It is important to promptly act upon patients not able to come for DOT for any reason. They should be contacted within a day after missing daily dose during the intensive phase and within one week during the continuation phase. Reason/s for the patient's absence should be explored in detail in order to take appropriate remedial actions and to ensure that treatment is continued.

5.7 Nutrition support

Nutritional status is often poor in patients suffering from Tuberculosis. The wasting commonly found in patients with active TB is most likely the result of a combination of factors, including decreased appetite and subsequent food intake, and increased losses and altered metabolism associated with the inflammatory and immune response.

Effect of TB on the nutritional status are severe weight loss (loss of lean and fat mass), altered protein metabolism, micronutrient Deficiencies (such as Vitamins A, D, E, C; minerals zinc, selenium) and anaemia. Good nutritional status has an impact on "quality of life" and the ability to return back to normal life.

This guideline provides protocol for effective treatment of acute undernutrition which can easily be followed by health staff in provision of outpatient and inpatient care to the patients. This guideline will help to improve the case management and outcome among patients.

Nutritional support within TB programs may include the following components:

- (a) Nutritional assessment to determine nutritional status and necessary referrals or intervention

- (b) Nutrition education and counselling on symptom-management and improved dietary intake during and after TB treatment and microbial cure
- (c) Targeted micronutrient supplementation (e.g., vitamin B6)
- (d) Food support for treatment of malnutrition in TB patients
- (e) Food support as a safety net program to increase treatment adherence

(a) Nutritional assessment to determine nutritional status and necessary referrals or intervention.

Nutrition screening of TB patients

- i. Take the weight and height of all patients except in pregnant women on the first visit
- ii. Calculate the Body Mass Index (BMI)

$$\text{BMI} = \text{Weight in kgs} / (\text{height in meters})^2$$
- iii. Determine the nutritional status of the adult male, non pregnant women as follows:

Table 5-1 Nutritional status according to BMI

| Classification | BMI (kg/m ²) Principal cut-off points |
|-------------------------|---------------------------------------------------|
| Severe undernutrition | < 16.0 |
| Moderate undernutrition | 16.0-16.99 |
| Mild undernutrition | 17.0-18.49 |
| Normal | 18.5-24.9 |
| Overweight or obese | >=25.0 |

- iv. In children between 5-18 years use the BMI for age and sex charts to determine the nutritional status and for children below 5 years the weight for height growth chart provided by the Ministry of Health (CHDR).
- v. If weight and height can not be measured (ex- elderly with kyphosis) and in pregnant women, measure Mid Upper Arm Circumference (MUAC) to determine the current nutritional status
 - a. MUAC < 19 cm - Severe Undernutrition
 - b. MUAC 19-21.9 cm - Moderate Undernutrition

Treatment plan

It depends on the current nutritional status. Table 5.1 below provides the management plan and the criterias for discharge from the particular programme. It is recommended to eat 5-6 meals per day. The 5-6 meals should also include the suggested **special diet**.

Table 5-2 Suggestive diet for nutritional management

| Nutritional status | Management plan | Discharge criteria |
|--------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Severe undernutrition | <ul style="list-style-type: none"> • TB patients with severe undernutrition need an extra 1200kcal of energy per day. • Suggested special diet in addition to normal diet per day <p>Chicken egg fresh cooked - 1 Supplementary food - 100g Rice parboiled cooked - 2 cups Nuts (peanut / cashew etc.) - 60g</p> <p>It provides 1200 kcal and 60g protein</p> | <p>Once patients achieve a;</p> <ul style="list-style-type: none"> • BMI of 16, or • MUAC 19cm (if BMI can not be taken, or with pregnant women), or • W/H \geq - 3SD (if adolescents) <p>They should be transferred to the schedule of treatment of moderate undernutrition</p> |
| Moderate undernutrition | <ul style="list-style-type: none"> • TB patients with moderate undernutrition need extra 700kcal of energy • Suggested special diet in addition to normal diet per day <p>Chicken egg fresh cooked - 1 Supplementary food - 50g Rice parboiled cooked - 1 cup Nuts (peanut / cashew etc.) - 45g</p> <p>It provides 718 kcal and 32g protein.</p> | <p>Once patients achieve a;</p> <ul style="list-style-type: none"> • BMI of 17, or • MUAC 22cm (if BMI can not be taken, or with pregnant women), or • W/H \geq -2SD (if adolescents) <p>they should be transferred the Normal BMI schedule</p> |
| Normal BMI | <p>TB patients with normal BMI need extra energy of 200kcal and a total protein intake of approximately 75 - 100 g per day.</p> <ul style="list-style-type: none"> • Suggested special diet in addition to normal diet per day <p>Chicken egg fresh cooked - 1 Peanut / cashew etc.) - 25g</p> <p>It provides 215 kcal and 13g protein.</p> | <p>Follow up continuously till they take treatment</p> |

Outpatient follow up

- Patients should usually be followed up monthly. In the case of severe undernutrition fortnightly followup is recommended.
- It is also important to plot their weight gain as it gives a clear picture of progress made.

- Outpatient follow up should be coordinated with other clinic visits.
- If patients fail to gain weight within the first 2-4 weeks, reassess them.
- All patients who are not responding after three months should be reviewed by a respiratory physician along with a nutrition specialist.

(b) Nutrition education and counselling on symptom-management and improved dietary intake during and after TB treatment and microbial cure

- Nutrition education and counselling should be provided using the Food based dietary guidelines published by the Ministry of Health.

(c) Targeted micronutrient supplementation (e.g., vitamin B6)

- A good multivitamin and mineral supplement providing 50% -150% of the recommended daily allowance, is needed since it will be most unlikely that a person with TB will be able to meet the increased requirements for vitamins and minerals with diet alone due to a poor appetite.
- TB patients treated with isoniazid should be given Vitamin B6

(d) Food support for treatment of undernutrition in TB patients

- Following food items can be used as supplementary food for severe and moderate undernutrition of TB patients.
 - Thripasha or any other available supplementary food

**For food items to be avoided due to drug interactions, please refer
Chapter 7**

6. Monitoring Treatment and Assigning Outcome

6.1 Monitoring of treatment

Monitoring of tuberculosis patients on treatment include:

- Bacteriological monitoring for pulmonary TB cases by examination of sputum smears at regular intervals during treatment. Cases where resistance is suspected, additional tests like Culture & DST, and Xpert MTB/RIF are also used
- Clinical monitoring by symptomatic improvement and weight gain especially in the case of extrapulmonary and clinically diagnosed pulmonary TB.
- Monitoring the drug intake during intensive phase and drug collection during the continuation phase by reviewing the treatment cards.

Patient weight should be monitored each month and dosage should be adjusted if weight changes. A written record of all medications given, bacteriological response and adverse reactions should be maintained for every patient on the patients' records including the TB Treatment Card.

Response to treatment in both new and retreatment bacteriologically confirmed cases should be monitored by sputum smear examination at the end of the intensive phase of treatment, end of fifth month and end of treatment. Generally two sputum samples should be collected for smear examination at each follow up sputum examination.

The best way to monitor the patients is by sputum examination. Conversion of bacteriologically confirmed PTB cases to negative is the best indicator that the intensive phase of chemotherapy has been regular and is effective. After two months of chemotherapy, more than 80% of new PTB cases should be smear negative and after 3 months, the rate should be more than 90%.

In a new PTB case if the sputum smear is positive at the end of 5th month or later, these cases are considered as treatment failures and investigated for drug resistance. They are reregistered as 'treatment after failure' and are put on the regimen for previously treated cases.

Bacteriologically confirmed EPTB cases are monitored clinically and radiologically. If the patient develops cough during the course of treatment, smears should be examined for AFB though this could also be due to another concomitant pathology. Non responding EPTB cases should have a repeat Xpert MTB/RIF test for possible resistance and review by Consultant Respiratory Physicians as well as other specialists depending on the site of the disease.

It is reiterated here that Xpert MTB/RIF has no role as a follow-up test to monitor course of treatment. However this could be used to test Rifampicin resistance in case of non-responding disease.

6.1.1 Monitoring new PTB cases

Intensive phase

During the intensive phase, isoniazid, rifampicin, pyrazinamide and ethambutol (as 4 FDC) are given daily for two months under direct observation.

At the end of the two-month intensive phase, sputum smear examination of two samples should be carried out on all PTB patients.

Smear positive PTB

If sputum smear positive patients become sputum smear negative at the end of two months, continuation phase of treatment with two drugs – isoniazid and rifampicin (as 2 FDC) should be started.

If the smear is positive at the end of two months, two samples of sputa for AFB culture should be collected preferably after omitting ATT for three days, and Xpert MTB/RIF test performed on one sample. If Xpert MTB/RIF detects rifampicin resistance (RR), refer to Consultant Respiratory Physician for management as per programmatic management of drug resistant TB (PMDT) guidelines. If not, the intensive phase of four drugs should be extended for further one month. At the end of the 3rd month, sputum smear examination should be repeated which if negative, continuation phase commenced.

If sputum smear is positive at the end of 3rd months, repeat Xpert MTB/RIF should be performed on sputum. If this detects rifampicin resistance, refer to Consultant Respiratory Physician for management as per PMDT guidelines. If RR not detected, start on the continuation phase of treatment, regardless of the sputum result. These patients have a high risk of drug resistant TB. Therefore, request LPA on culture isolates. Results of culture, LPA (if done) and DST done at the end of two months should be followed up and treatment is modified if drug resistant TB detected. If end of two months culture is negative while sputum is positive at the end three months, two samples of sputum should be collected for repeat AFB culture. In all cases of documented or suspected drug resistance, referral to Consultant Respiratory Physician is essential.

Clinically diagnosed (sputum negative) PTB

In clinically diagnosed PTB patients, sputum culture for AFB should be performed prior to commencement of ATT. It is expected that the country will have adequate Xpert MTB/RIF facilities by mid-2017. An Xpert MTB/RIF test will then be performed on all smear negative PTB cases as well. If positive this test will change clinical diagnosis to microbiological diagnosis and indicate whether there is RR. In case pre ATT Xpert MTB/RIF detects RR, then the case should be managed as per the PMDT guidelines under guidance of Consultant Respiratory Physician.

In case pre ATT Xpert MTB/RIF is negative, and the patient is clinically diagnosed as having tuberculosis, such patients should be assessed again after one month of ATT (chest x ray, weight gain and symptomatic improvement). If there is clinical and radiological improvement, ATT should be continued. Otherwise, the diagnosis should be reviewed. Sputum negative patients should have their sputum direct smear done at the end of two months of ATT and their pre-treatment culture should be traced and documented

If the sputum is negative at the end of two months with clinical improvement ATT should be continued as usual.

In the unlikely event of clinically diagnosed PTB patients on ATT becomes positive at the end of two months, there are three possibilities:

- (a) An error at the time of initial diagnosis- i.e., a true smear positive patient incorrectly diagnosed as smear negative at the beginning of the treatment.
- (b) Progression of the disease due to non- adherence to treatment
- (c) Development of drug resistance

In this case, repeat Xpert MTB/RIF on sputum (even if done earlier). If it is positive and RR detected, refer to Consultant Respiratory Physician for management as per PMDT guidelines. If not, send two samples of sputum for AFB culture and DST, check on pre ATT sputum culture result which will be ready by now. If pre-treatment is positive, request LPA in addition to routine DST. If RR is not detected and LPA also does not report any drug resistance, continue 4FDC for one more month and repeat sputum direct smear. If sputum direct smear at the end of 3rd month too is positive, follow the instructions given above for sputum positive patients who remain sputum positive after three months.

If Xpert MTB/RIF or LPA shows any drug resistance, refer to Consultant Respiratory Physician for treatment as per PMDT guidelines.

Continuation Phase

During the continuation phase, isoniazid and rifampicin (as 2 FDC) are given daily for four months extended up to 10 months in case of neuro TB and osteoarticular TB.

- Do follow up sputum smear examination at the end of 5th month and end of treatment.
 - (a) If sputum smear is negative at the end of 5th month and at the end of 6th month of treatment, the patient is declared cured and anti-TB drugs are stopped.
 - (b) If the sputum smear is positive at the end of 5th month or 6th months with clinical and radiological evidence of active disease that patient is diagnosed as treatment failure. Such patients are at a high risk of having drug resistant TB. In such cases, two samples of sputum should be collected for AFB culture and Xpert MTB/RIF performed on one sample. If RR not detected, patient

should be commenced on re treatment regimen after registering the outcome as “treatment failure”. If RR detected on Xpert MTB/RIF refer to PMDT guidelines on further management.

- (c) If sputum examination cannot be done at the end of the treatment due to any reason and there is no evidence of failure, the treatment can still be stopped after completion of complete duration. The outcome in such cases is given as Treatment Completed.

Table 6-1 Schedule for follow-up sputum examination

| Patient category | When to do sputum smear (PTB Positive Patients) |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bacteriologically confirmed new Cases Includes <ul style="list-style-type: none"> smear-positive PTB smear negative PTB cases and EPTB cases confirmed bacteriologically using Xpert MTB/RIF or on culture | <ul style="list-style-type: none"> End of 2nd month <i>End of 3rd month if smear- positive at the end of 2nd month</i> End of 5th month End of treatment |
| Clinically diagnosed new cases Includes <ul style="list-style-type: none"> Smear negative PTB and EPTB cases who were not bacteriologically confirmed using Xpert MTB/RIF or culture | <ul style="list-style-type: none"> End of 2nd month <i>End of 3rd month if smear becomes positive at the end of 2nd month</i> End of 5th month End of treatment |
| Previously Treated patients <ul style="list-style-type: none"> Relapse Treatment after failure Treatment after loss to follow-up Other previously treated Unknown previous treatment history | <ul style="list-style-type: none"> End of 3rd month <i>End of 4th month if smear positive at the end of 3rd month</i> End of 5th month End of treatment |

6.1.2 EPTB patients

EPTB patients should be monitored clinically after one month of treatment. If there is symptomatic improvement with weight gain, anti-TB treatment should be continued. If not, the diagnosis should be reviewed as patient may be suffering from pathology other than TB.

6.1.3 Retreatment cases

Patients on retreatment regimen should have their sputum examined for AFB at the end of three months of treatment. Their pre-treatment sputum cultures (and possibly DST) will be ready by this time and these reports should be traced. If sputum direct smear is positive at the end of three months of retreatment, possibilities and appropriate actions are listed below. Relapse cases should have approximately the same rates of sputum conversion as new pulmonary cases. Other re-treatment cases such as treatment failures may have sputum conversion rates of more than 75% after three months of receiving the re-treatment regimen

Table 6-2 Course of action to be followed when sputum direct smear on patients on treatment regimen is positive at the end of three months of treatment

| Condition | Course of action |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| Sputum direct smear positive, but there is clinical and chest x ray improvement with pre-treatment culture positive and isolates sensitive to RHSE. Repeat Xpert MTB/Rif test does not show RR | Continue RHZE for another month* |
| Sputum direct smear positive, pre-treatment culture positive and isolates show drug resistance | Refer to Consultant Respiratory Physician for management as per PMDT guidelines |
| Sputum direct smear positive, pre-treatment culture positive but DST not available Repeat Xpert MTB/RIF test | If RR detected, refer to Consultant Respiratory Physician for management as per PMDT guidelines. If not continue RHZE until DST report is ready |
| Sputum direct smear positive, pre-treatment culture negative/not available Collect two samples of sputum for repeat AFB culture and do Xpert MTB/RIF on one sample | If RR detected, refer to PMDT guidelines. If not RHZE for another month* |

**If intensive phase of retreatment is extended by one month with RHZE sputum direct smear for AFB should be done again at the end of fourth month. If it is negative, start continuation phase with RHE and sputum direct smears should be done monthly. If end of fourth month or subsequent direct smears become positive, DR TB is highly likely even if initial culture DST does not show drug resistance and RR not detected on Xpert MTB/RIF. Such patients should be discussed in PMDT site and central committees and further management done according to a joint decision.*

6.2 Treatment outcome

For each patient, at the end of the treatment course of each patient, treatment outcome should be recorded in the District Tuberculosis Register. There are six possible treatment outcomes, i.e., cured, treatment completed, treatment failure, died, lost to follow-up or not evaluated.

(These outcome definitions are to be used only when the patient has been treated on first line drugs. For patients treated on second line drugs for drug-resistance, please refer the PMDT guidelines)

6.2.1 Cured

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

6.2.2 Treatment completed

A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least

one previous occasion were negative, either because tests were not done or because results are unavailable.

6.2.3 Treatment failure

A TB patient whose sputum smear or culture is positive at the end of fifth month or later during treatment.

6.2.4 Died

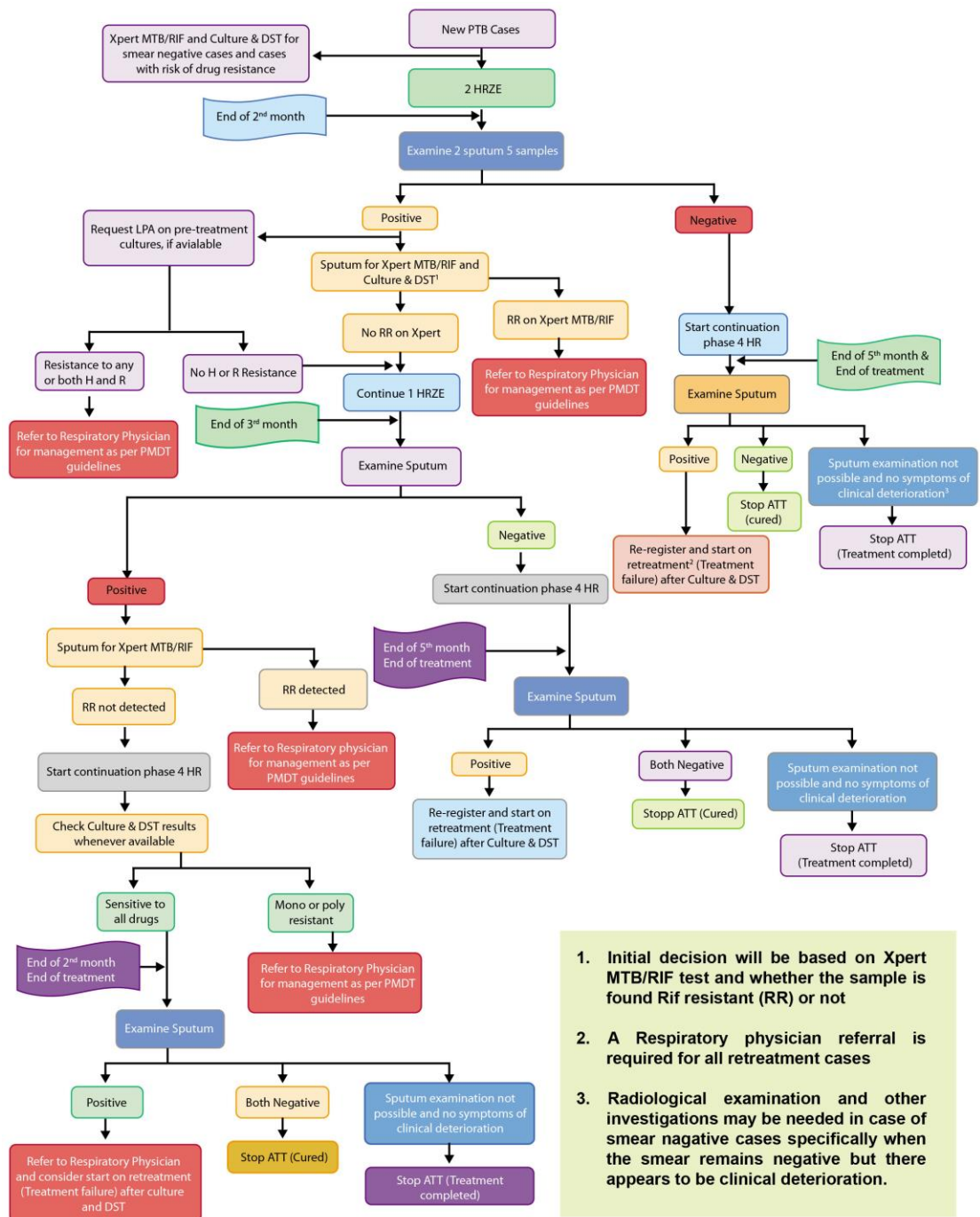
A TB patient who dies for any reason before starting or during the course of treatment.

6.2.5 Lost to follow-up

A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.

6.2.6 Not evaluated

A TB patient for whom no treatment outcome is assigned. This includes cases for whom the treatment outcome is unknown to the reporting unit.



1. Initial decision will be based on Xpert MTB/RIF test and whether the sample is found Rif resistant (RR) or not
2. A Respiratory physician referral is required for all retreatment cases
3. Radiological examination and other investigations may be needed in case of smear negative cases specifically when the smear remains negative but there appears to be clinical deterioration.

Figure 6-1 Treatment and follow-up of new patients

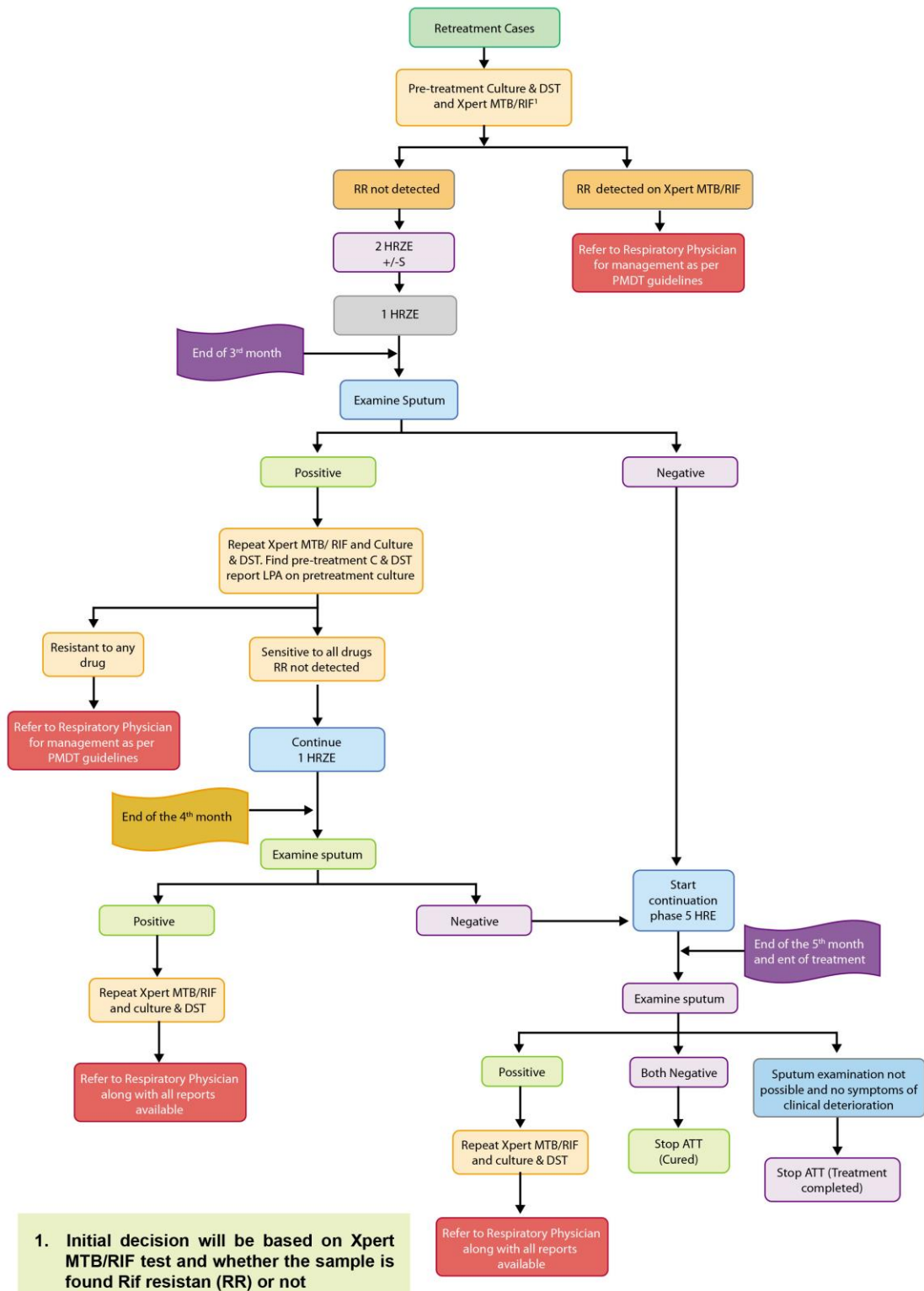


Figure 6-2 Treatment and follow-up of retreatment patients

7. Essential Anti-TB Drugs and Management of Adverse Reactions

Essential anti-TB drugs

Isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin are considered as first line anti-TB drugs.

7.1 Isoniazid

Isoniazid (INH/H) is highly bactericidal against replicating tubercle bacilli. It is rapidly absorbed and diffuses readily into all fluids and tissues. It is metabolized in the liver. The plasma half-life, which is genetically determined, varies from less than one hour in fast acetylators to more than three hours in slow acetylators. It is largely excreted in the urine within 24 hours, mostly as inactive metabolites.

7.1.1 Uses

- Isoniazid is a component of all first line anti-TB chemotherapeutic regimens currently recommended by the WHO as well as second line anti-TB chemotherapeutic regimens when resistance to INH is not documented.
- Isoniazid alone is used in chemoprophylaxis.

7.1.2 Administration

Isoniazid is normally given orally. Parenteral preparation (iv/im) can be used in critically ill patients but currently it is not available in Sri Lanka.

7.1.3 Dosages

For treatment and prevention-

Adults: 5 mg/kg (range 4-6 mg/kg) daily. Children 10 mg/kg (range 7-15 mg/kg) daily maximum 300 mg.

7.1.4 Side-effects

Isoniazid is generally well tolerated at recommended doses.

- Systemic or cutaneous hypersensitivity reactions can occasionally occur during the initial weeks of treatment.
- Peripheral neuropathy may occur in malnourished, chronic alcoholics, pregnant women, breast feeding mothers, patients infected with HIV and diabetics. This can be prevented or minimized by supplementary pyridoxine 10 mg daily for those at risk.
- Other less common forms of neurological disturbances including optic neuritis, toxic psychosis, and generalized convulsions can develop in susceptible individuals,

particularly in the later stages of treatment, which occasionally may necessitate withdrawal of isoniazid.

- Hepatitis is not an uncommon adverse effect that usually needs withdrawal of the treatment (See section on management of anti TB drug induced hepatitis; chapter 7). Monitoring of hepatic transaminases and serum bilirubin should be done in patients with pre-existing chronic liver disease and those who develop deterioration of appetite with or without nausea/vomiting while on treatment.
- Isoniazid tends to raise plasma concentrations of anti-epileptics (phenytoin, carbamazepine and valproate), benzodiazepine, warfarin and theophylline by inhibiting their metabolism in the liver while rifampicin has the opposite effect on such drugs by inducing liver enzymes. Therefore it may be necessary to reduce the dosages of these drugs during treatment with isoniazid. If possible, serum concentrations of phenytoin and carbamazepine should be measured in patients receiving isoniazid and rifampicin. Patients should be monitored closely for the development of fits.
- Patients on treatment with isoniazid should be cautioned against eating 'red fish' such as skipjack and tuna (Balaya, Kelawalla), which contain high concentrations of histamine. Isoniazid is an inhibitor of histaminase, which is normally present in the tissues and is responsible for the inactivation of ingested histamine. As a result, the histamine level in the tissues of the patient tends to rise shortly after a meal containing these varieties of fish, and the patient may experience symptoms of histamine intoxication like erythema, severe headache, red eyes, palpitation, diarrhoea, vomiting and wheezing.

7.2 Rifampicin

Rifampicin has a potent bactericidal action and sterilizing effect against extra cellular dormant tuberculosis bacilli in. It is a semisynthetic derivative of rifamycin which inhibits ribonucleic acid synthesis in a broad range of microbial pathogens. Following oral administration, it is rapidly absorbed and distributed throughout the cellular tissues and body fluids.

Since resistance develops rapidly, Rifampicin must always be administered in combination with other effective anti-mycobacterial agents.

7.2.1 Uses

It is a component of both new and retreatment regimens currently recommended by the WHO.

7.2.2 Administration

Rifampicin is administered orally and should preferably be given at least 30 minutes before meals, since absorption is reduced when it is taken with food. This however may not be clinically significant and food can reduce intolerance to the drugs.

7.2.3 Dosage

Adults: 10 mg/kg (8-12 mg/kg) daily, maximum 600 mg daily.

Children 15 mg/kg (range 10 – 20 mg/kg) daily

It can be given parenterally for critically ill patients but currently parenteral preparation of rifampicin is not available in Sri Lanka.

7.2.4 Side-effects

Rifampicin is well tolerated by most patients at currently recommended doses. Side-effects include:

- Gastro-intestinal - nausea, anorexia, vomiting and abdominal pain.
- Hepatitis is a major adverse effect although it is not very common. Alcohol abusers and those with pre-existing liver disease have increased risk and it is advisable to monitor serum bilirubin and transaminases in such patients. Liver function also should be monitored in patients who develop deterioration of appetite with or without nausea or vomiting while on treatment.
- Skin rashes. Exfoliative dermatitis may occur especially in HIV infected patients.

The following reactions are more likely to occur with intermittent therapy:

- 'Flu' syndrome - consisting of attacks of fever, chills, malaise headache, bone pain
- acute renal failure*
- Thrombocytopenia and purpura*
- Haemolytic anaemia*
- Respiratory symptoms consisting of shortness of breath and rarely associated with collapse and shock*.

* If these reactions occur rifampicin must be stopped immediately and admitted to hospital for management. Rifampicin should not be given again.

7.2.5 Drug interactions

Rifampicin induces hepatic enzymes and may accelerate clearance of drugs metabolized by the liver, and patients may need higher dosages of some drugs.

These include

- corticosteroids,
- oral contraceptives,
- levothyroxin,

- oral hypoglycaemic agents,
- warfarin,
- anti-convulsants (phenytoin, valproate and carbamazepine)
- cyto-toxics/immunosuppressives (cyclosporine)
- cardio-vascular agents (digoxin, calcium channel blockers, beta blockers, ACE inhibitors)
- theophylline
- anti-psychotics and anxiolytics (haloperidol and benzodiazepines)
- anti-microbials (macrolides, doxycycline, chloramphenicol, linezolid, anti-retroviral drugs and anti-fungals)

Since rifampicin reduces the effectiveness of oral contraceptives, female patients of child bearing age should be advised to use an alternative method of contraception.

7.2.6 Other effects

Rifampicin is excreted in urine, tears, sweat and other body fluids and may colour them red or orange. Patients should be made aware of this harmless discoloration of urine and other body fluids. Use of rifampicin during pregnancy is safe. However, because of the risk of postnatal haemorrhage Vitamin K should be administered to neonates at birth if the mother is on rifampicin.

7.3 Pyrazinamide

Pyrazinamide is a synthetic analogue of nicotinamide. It is bactericidal and particularly effective against dormant bacilli in an acid environment inside macrophages. Metabolism of the drug occurs in the liver and is excreted in the urine. It is highly effective during the first two months of treatment, when there is acute inflammation. Introduction of pyrazinamide has enabled to shorten the duration of treatment and also reduced the risk of relapse.

7.3.1 Uses

It is a component of intensive phase of new and retreatment regimens currently recommended by WHO.

7.3.2 Administration and dosage

It is administered orally and is rapidly absorbed from the gastro-intestinal tract and rapidly distributed throughout all tissues and fluids.

Adults – 25 mg/kg (range 20-30 mg/kg) daily

Children – 35 mg/kg (range 30 – 40 mg) daily

7.3.3 Side-effects

- Gastro intestinal symptoms- nausea, anorexia.
- Hypersensitivity skin reactions. Some patients may complain of flushing of the skin.
- Hepatitis is the most important adverse effect. Therefore, serum bilirubin and transaminase should be monitored as in the case of isoniazid and rifampicin.
- Hyperuricaemia may occur due to diminished excretion of uric acid in urine, but this is often asymptomatic. Arthralgia may occur and treatment with simple analgesics is often sufficient. Attacks of acute gout may occur but rare.
- Blood glucose concentration may become labile in diabetics.

7.4 Ethambutol

Ethambutol has a bacteriostatic effect. It is used in combination with other ant-TB drugs to prevent the emergence of drug resistant strains. It is given orally and absorbed readily from the gastro intestinal tract and is excreted by the kidneys.

7.4.1 Uses

It is given during the intensive phase of the treatment of previously untreated (new) and both intensive and continuation phases of retreatment regimen.

7.4.2 Administration and dosage

Ethambutol is given orally.

Adults: 15 mg/kg (15-20 mg/kg) daily

Children: 20 mg/kg (range 15–25 mg/kg daily)

7.4.3 Side-effects

Dose dependant optic neuritis is the most important side effect and can result in impairment of visual acuity and colour vision. Early changes are usually reversible, but blindness can occur if treatment is not discontinued promptly. Therefore patients should be advised to report immediately to a clinician if their vision deteriorates. Impairment of renal function can elevate serum concentration of ethambutol to toxic levels. Hence, ethambutol should be used with caution in the presence of renal function impairment where recommended dose for weight given three days a week or the drug is withdrawn altogether. (See the section on Management of TB in renal disease, chapter 10)

7.5 Streptomycin

Streptomycin is an aminoglycoside which is bactericidal in action. It is not absorbed from the gastrointestinal tract and must be given by intra-muscular injection. Streptomycin is excreted entirely through the kidneys.

7.5.1 Uses

- For treatment of first two months of intensive phase of retreatment regimen specifically when the DST on Xpert MTB/RIF shows sensitive to rifampicin and the Consultant Respiratory Physician considers a risk of having resistance to other first line drug/s.
- Can be used as an alternative to ethambutol in case of neuro TB when meninges are considered to be inflamed.

7.5.2 Administration and dosage

Streptomycin must be administered by deep intra-muscular injection.

Adults and children: 15mg/kg (12-18 mg/kg) daily.

Patients over the age of 60 years, irrespective of their weight should be given only 500 mg daily as they may not be able to tolerate higher doses.

7.5.3 Side-effects

- Nephrotoxicity is the most important adverse effect and is dose related. Auditory nerve (eighth cranial nerve) damage can occur resulting in deafness, ringing in the ear, ataxia, vertigo or giddiness.
- Skin rashes.

It should be used with caution in elderly and in patients with renal insufficiency as dose related ototoxicity and nephrotoxicity can result from accumulation. It should not be given to patients with moderate to severe renal function impairment. Should it be used on patients with mild renal function impairment, recommended dose for age and weight may be given three days a week. If facilities are available plasma concentration should be measured. Plasma concentration when next dose due should not exceed 4 microgram/ml.

Rifampicin, isoniazid, ethambutol and pyrazinamide can safely be used in pregnancy. But Streptomycin should be avoided in pregnancy as it can cause auditory nerve damage and nephrotoxicity in foetus

7.6 Management of side-effects of first-line anti-TB drugs

Side-effects of anti-tuberculosis drugs are of two types.

Major side-effects cause serious health hazards where anti-tuberculosis drugs should be stopped immediately and the patient is referred to hospital for management.

Minor side-effects cause only relatively little discomfort and are often respond to symptomatic treatment. In general, a patient who develops minor side-effects should continue the anti-TB treatment.

Table 7-1 Adverse effects of first line anti-TB drugs

| Drug | Common side-effects | Rare side-effects |
|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Isoniazid | <ul style="list-style-type: none"> • Nausea, vomiting • Peripheral neuropathy • Hepatitis • Histamine Reaction after ingestion of red fish e.g., balaya, kelawalla • Skin rashes | <ul style="list-style-type: none"> • Convulsions, pellagra. • Psychosis • Optic neuritis • Haematological abnormalities (Agranulocytosis, haemolytic anaemia, aplastic anaemia) • SLE like syndrome |
| Rifampicin | <ul style="list-style-type: none"> • Nausea, anorexia, abdominal pain • Hepatitis • Reduced effect of corticosteroids oral contraceptives, antiepileptics, oral hypoglycaemics, warfarin, anti microbials, theophyllines, calcium channel blockers, beta blockers, digoxin, cyto-toxics/immuno-suppressives, anti psychotics, anxyolytics, levothyroxine • Skin rashes • Reddish discoloration of body secretions and urine | <ul style="list-style-type: none"> • Acute renal failure, shock • thrombocytopenia, • Haemolytic anaemia • ‘Flulike syndrome’ (with intermittent doses) • pseudo membranous colitis • adrenal crisis • exfoliative dermatitis |
| Pyrazinamide | <ul style="list-style-type: none"> • Nausea, vomiting • Skin rashes • Joint pains • Hepatitis | <ul style="list-style-type: none"> • Sideroblastic anaemia • thrombocytopenia.. |
| Streptomycin | <ul style="list-style-type: none"> • Auditory and vestibular damage (also to the foetus) • Renal damage • Skin rash | <ul style="list-style-type: none"> • Impairment of neuromuscular transmission |
| Ethambutol | <ul style="list-style-type: none"> • Optic neuritis • Colour blindness | <ul style="list-style-type: none"> • Skin rash, • joint pains, • Peripheral neuropathy. |

Table 7-2 Symptom based management of side-effects of Anti-TB drugs

| Side-effects | Drug(s) responsible | Management |
|-----------------------------------------------------------------------------------------------------------|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MINOR SIDE-EFFECTS - CONTINUE DRUGS | | |
| 1. Itching of the skin without a rash | Rifampicin, Pyrazinamide | INH, Antihistamine |
| 2. Anorexia, nausea, abdominal pain | Rifampicin, INH, Pyrazinamide | Exclude hepatitis. Domperidone/metoclopramide ½ -1 hr before ATT Give drugs with small meals or last thing at night H2 receptor blockers. PPI. |
| 3. Joint pain | Pyrazinamide | Give Paracetamol or Aspirin/NSAIDs |
| 4. Burning, numbness or tingling sensation in the hands or feet without evidence of peripheral neuropathy | Isoniazid | Pyridoxine 50-75 mg daily*. |
| 5. Orange/red urine | Rifampicin | Reassurance |
| 6. Histamine reaction | Isoniazid | Advice not to eat 'red fish' |
| MAJOR SIDE-EFFECTS - STOP DRUGS RESPONSIBLE REFER FOR EVALUATION | | |
| 1. Itching of skin, skin rash | Any drug | Stop anti-TB drugs |
| 2. Deafness | Streptomycin | Stop streptomycin |
| 3. Dizziness, vertigo, nystagmus | Streptomycin | Stop streptomycin |
| 4. Nausea , vomiting, deterioration of appetite +/- Jaundice (other causes of hepatitis excluded) | INH, Rifampicin and Pyrazinamide | Stop anti-TB drugs. Perform liver function test |
| 5. Visual impairment | Ethambutol | Ophthalmology referral. Stop ethambutol if optic neuritis confirmed |
| 6. Shock, purpura, acute renal failure, haemolytic anaemia | Rifampicin | Stop rifampicin (Never give again) |

* Pyridoxine should not be given along with anti-TB drugs at the same time. Give at least 12 hours apart from anti-TB drugs

7.6.1 Management of severe drug reactions

7.6.1.1 Hepatitis

- Most anti-TB drugs can damage the liver. Most commonly Isoniazid, pyrazinamide and rifampicin and rarely ethambutol are responsible.
- When a patient develops hepatitis during anti-TB treatment, it is important to rule out other possible causes of hepatitis before deciding that the hepatitis is drug-induced.

- Mild transient increases in serum transaminases may occur during the initial treatment. This rise is not more than 2-3 folds of the normal. Such rise does not cause symptoms and returns to normal levels despite the continuation of anti-TB drugs. Serum bilirubin level remains normal.
- Ideally, pre-treatment baseline liver function tests (LFTs)⁶ should be done in all patients. Since this may not be practical, it should be done at least on those who are at a higher risk of developing drug-induced hepatitis e.g. known chronic alcoholics, pre-existing liver disease, pregnant mothers, elderly and severely ill patients.
- Liver function tests should be performed when patient is having symptoms & signs suggestive of hepatitis, i.e. nausea, vomiting with or without icterus or hepatomegaly.
- If drug-induced hepatitis is diagnosed, all anti-TB drugs should be stopped and patient may need admission to hospital for supportive treatment. Repeat the liver function tests after 1-2 weeks.
- Anti TB drugs should be re-introduced once liver function tests come back to normal. This should be done sequentially in the order of isoniazid, rifampicin and pyrazinamide with daily monitoring of the patient's clinical condition and at least weekly monitoring of LFT (see below). Re introduction of rifampicin isoniazid and pyrazinamide can be done under streptomycin and ethambutol cover.
- Complete withdrawal of anti TB drugs may be possible in patients with TB lymphadenitis, TB pleural effusion, sputum negative PTB with limited lung involvement who are not very ill. Sometimes tuberculosis disease is so severe that all anti TB drugs cannot be withdrawn. In such situations, patient should be treated with two of the least hepatotoxic drugs i.e., streptomycin and ethambutol (provided the patient is not allergic to these drugs) until the LFTs come back to normal. However, ethambutol and streptomycin is a weak combination which may not be adequate for a severely ill patient. In such a situation alternatives are:
 - a) Streptomycin, INH and ethambutol – when serum bilirubin is high but transaminases are normal.
 - b) Streptomycin, ethambutol and quionolone (ofloxacin/ levofloxacin) when both serum bilirubin and transaminases are high. Consultant Respiratory Physician's advice should be sought in such a situation.
- Once LFTs return to normal, challenge doses of original drugs can be reintroduced sequentially in the order of isoniazid, rifampicin and pyrazinamide with daily monitoring of the patient's clinical condition and at least weekly monitoring of

⁶Includes SGPT and Serum bilirubin

LFTs. If symptoms recur early, LFTs should be repeated before one week. Isoniazid should be introduced initially at 50 mg/day increasing sequentially to reach the maximum dose in 3-4 days. If there are no complains rifampicin is added at 75 mg/ day and increasing the dose sequentially to reach the full dose in 3-4 days. If patient tolerates both drugs, pyrazinamide is added in the same way starting with the dose of 250 mg/day.

- If there is no further reaction, standard chemotherapy can be continued, and any alternative drugs introduced temporarily can then be withdrawn.
- During this procedure, if the patient complains of a recurrence of symptoms suggestive of hepatitis, LFTs should be repeated, and if found to be abnormal the drug added last should be withdrawn. It may not be possible to reintroduce it. In case of standard treatment cannot be recommenced a suitable alternative drug regimen should be used on the advice of and under the supervision of a Consultant Respiratory Physician. If both rifampicin and pyrazinamide are to be excluded from the regimen, the option is to give 2SHE / 10HE. In case of pyrazinamide alone is to be excluded, the option is 2HRE / 7HR. In case of INAH is to be excluded, the option is to give regimen of 2RZE followed by RE for 6-8 months.
- Generally, anti-TB drug induced hepatitis almost always occur during the first 6-8 weeks of treatment but standard treatment can be recommenced in most patients.

N.B. Ideally it is better to get advice from a Consultant Respiratory Physician for the management of drug induced hepatitis especially when it is not possible to recommence standard treatment.

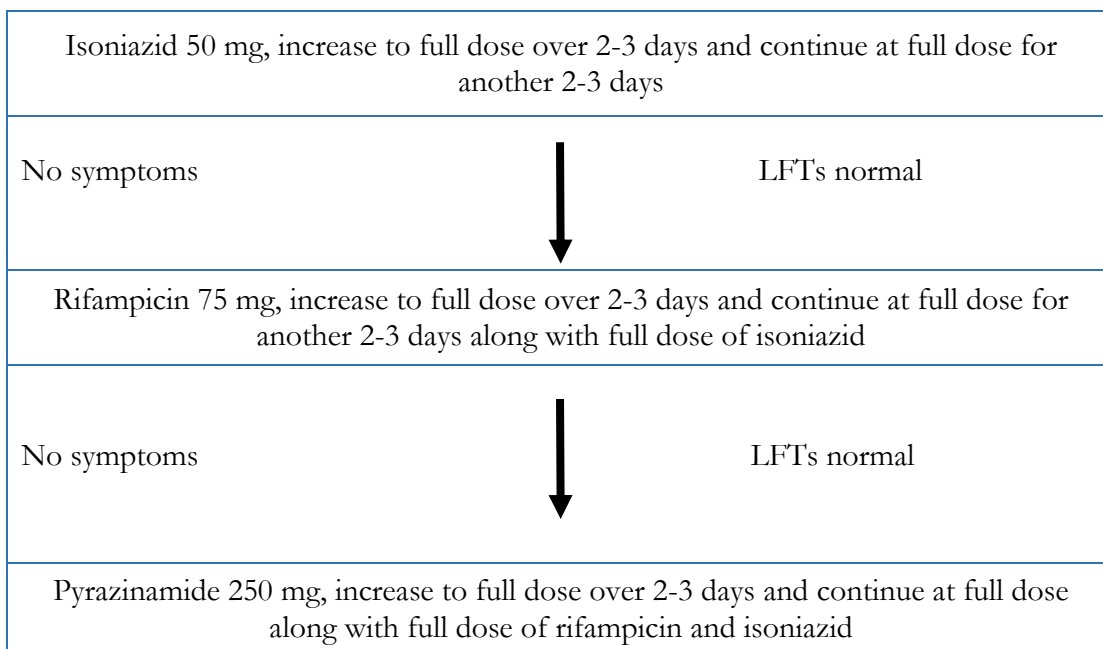



Figure 7-7-1 Method of re-introduction of anti- TB drugs following drug induced hepatitis and after LFTs return to normal

7.6.1.2 Severe cutaneous reactions

- If the reaction is only pruritus and no rash, (and there is no obvious cause e.g. scabies) give symptomatic treatment with anti-histamines, reassure and continue anti-TB treatment and observe the patient closely.
- However, if a skin rash develops, stop all anti-TB drugs.
- Wait till the rash resolves.
- Once the reaction has resolved, anti-TB drugs should be re-introduced. The drug, which was responsible for the reaction, should be identified by drug challenge.
- Drug challenge starts with the most potent anti-TB drug but least likely to be responsible for the reaction (i.e. isoniazid). If a reaction occurs to a small dose it is very likely that to be less severe than that to a full dose. Therefore, start with a small challenge dose (e.g. 50 mg of isoniazid). Then the dose is gradually increased to the full dose over a period of three days. The procedure is repeated, adding one drug at a time in the order of rifampicin, pyrazinamide, ethambutol and streptomycin. A reaction after adding a particular drug indicates the drug responsible for the initial reaction. There is no evidence that this challenge process leads to drug resistance. Referral to Dermatologist is recommended.
- If the drug responsible for the reaction is either pyrazinamide or ethambutol or streptomycin, anti-TB treatment should be resumed without the offending drug. It may be necessary to extend the duration of the treatment regimen. This prolongs the total time of TB treatment, but decreases the risk of relapses. It is best to seek advice of a Consultant Respiratory Physician.
- Rarely, patients develop hypersensitivity reactions to the two most powerful anti-TB drugs- isoniazid and rifampicin which form the cornerstone of Short Course Chemotherapy. If either one or both of them cannot be reintroduced the Consultant Respiratory Physician should be consulted for further advice.

Table 7-3 Re-introduction of anti-TB drugs following severe cutaneous drug reactions

| Drug | Likelihood of causing a reaction | Challenge doses | | |
|--------------|-------------------------------------------------------------------------------------|-----------------|--------|-----------|
| | | Day 1 | Day 2 | Day 3 |
| Isoniazid |  | 50 mg | 100 mg | Full dose |
| Rifampicin | | 75 mg | 150 mg | Full dose |
| Pyrazinamide | | 250 mg | 500mg | Full dose |
| Ethambutol | | 100 mg | 400 mg | Full dose |
| Streptomycin | | 125 mg | 500 mg | Full dose |

8. Preventing Tuberculosis

8.1 Infection control

From the public health point of view, the best way of prevention of TB is by interruption of the chain of transmission. This is achieved by the identification of infectious cases as early as possible and providing effective treatment to cure them. Other measures of prevention are BCG vaccination and chemoprophylaxis. Contact investigation is important not only to improve case detection but also to identify persons who may need chemoprophylaxis.

8.1.1 Importance of infection control for respiratory infections

These guidelines will apply to all health-care facilities from primary level to tertiary level and will include general health facilities, chest clinics, all hospitals and to high-risk areas within these facilities. These high-risk areas include TB bacteriology and culture laboratories, TB and chest clinics, medical clinics, general OPD, STD clinics (HIV treatment facilities), indoor wards, isolation rooms, intensive care units (ICU), DOTS-Plus sites for MDR-TB treatment, bronchoscopy units, and operation theatres (OT) and post-mortem rooms. Beyond health-care facilities, these guidelines offer some limited but practical suggestions on how to minimize the risk of TB transmission in households and other congregate settings.

8.1.2 Overview of transmission and pathogenesis of TB

A person with pulmonary TB or laryngeal TB can release droplet nuclei with *M. Tuberculosis* bacilli into the air by coughing or sneezing; smaller numbers of droplet nuclei are released during normal activities like talking or spontaneously during breathing. These droplet nuclei particles are invisible to the naked eye and are approximately 1 to 5 microns in size. (A micron is approximately one-hundredth the width of a human hair.) Droplet nuclei can remain airborne in room environment for a long period of time, until they are removed by natural or mechanical ventilation.

In order for TB to spread, there must be a source (a patient who has infectious TB disease) and a susceptible host (a person to inhale droplet nuclei containing *M. tuberculosis*). Anyone who shares air with a person with infectious TB disease of the lungs or larynx is at risk, although TB is not usually spread by brief contact. TB is spread when another person inhales one or more of these particles and becomes infected with TB.

8.1.3 Standard precautions

Standard Precautions is the term used for the group of infection control practices to reduce the risk of transmission of pathogens. These are based on the principle that all blood, body fluids, secretions, excretions except sweat, non-intact skin, and mucous membranes may contain transmissible infectious agents. Standard precautions are applicable to all patients

in all health care settings. Standard precautions combine the major features of *Universal Precautions*, *Body Substance Isolation* and *Respiratory Precautions*. Implementation of these precautions requires risk assessment in all health-care activities.

Elements of Standard Precautions

- Hand hygiene
- Selection of personal protective equipment based on assessment of risk
- Respiratory hygiene and cough etiquette
- Prevention of injury from needles and other sharp objects
- Cleaning of the patient care environment
- Cleaning and disinfection of patient-care equipment
- Linen and waste management

8.1.4 Hierarchy of controls to reduce risk of transmission of respiratory pathogens

The selection of the combination of control measures will be based on the infection control assessment and informed by the local epidemiological, climatic and socioeconomic conditions.

❖ Administrative controls

Administrative controls referred to policies and practices which identify persons with respiratory symptoms, separate them in an appropriate environment, fast-track them through the health care facility to reduce exposure time to others, and diagnose/treat them with minimal delay. Hospitalization should be reduced or avoided to the greatest extent possible. At facility level, administrative controls play a major role in reducing the risk of TB transmission and are essential for the implementation of other controls (i.e. environmental controls and personal protective equipment).

❖ Environmental controls

These refer to interventions which minimise the infectious TB particles in the environment. The choice of environmental controls is largely determined by local factors and resources. Ventilation should be prioritized to reduce the number of infectious particles in the air. Effective ventilation may be achieved by natural ventilation where possible. In high-risk settings where optimal ventilation cannot be achieved through natural or mechanically-aided means, properly designed, placed and maintained shielded ultraviolet germicidal irradiation devices should be considered as a complementary control.

❖ Personal protective equipment

Personal protective equipment (e.g. particulate respirators certified as N95 or FFP2) should be available as required in high-risk situations, especially drug-resistant tuberculosis, and during high-risk aerosol-generating procedures such as bronchoscopy or sputum

induction. These should be applied only after addressing the administrative and environmental controls.

8.1.5 Managerial activities for national, state, hospital administration, and local health officials

Managerial activities should ensure political commitment and leadership at all levels (national, province, district and facility level). Airborne infection control committees may be setup at National, Province and District level in order to supervise, monitor and ensure that all health facilities follow these guidelines. These committees are required to play a supportive role and facilitate the implementation of the guidelines.

8.1.6 Role of architects / engineers in health infrastructure design

Professionals responsible for the design, building refurbishment and organization (physical layout) of healthcare facilities need to consider patient flow patterns so that nosocomial transmission is minimized. These professionals need to be engaged in finding affordable solutions to improve the organization of existing and new facilities. To do so, they should also be included in training opportunities that underscore principles of airborne infection control and the role they play to ensure that the elements of airborne infection control are considered. Particular attention is required for facilities that are designed or reorganized to provide integrated or co-located TB and HIV diagnostic and treatment services, and those facilities that deal with drug-resistant TB.

8.1.7 Role of health care facility administration

Hospital administration plays a key role in creating the necessary conditions at the institutional level to prevent spread of health care associated pathogens. The physical separation of TB patients or people suspected of having TB requires rational design, construction or renovation; and use of buildings. Controls aimed at reducing TB transmission in health-care settings include triage, physical separation or isolation of TB patients or people suspected of having TB, cough etiquette and respiratory hygiene and minimize time spent in health care facilities. Facility Infection Control Committee should have a facility infection control / bio-medical waste management plan in place. The airborne infection control plan should be an integral part of this facility plan.

Following are the specific activities for health care facility administration:

❖ Conduct a facility-risk assessment and develop a facility plan for airborne infection control

- Risk assessments to help identify strengths, weaknesses, and opportunities for improvement.
- Health care administration should strengthen facility infection control committees to incorporate airborne and TB infection control as a core responsibility.

- The committees should develop a facility plan for implementation of airborne (including TB) infection control.
 - The facility infection control plan should ensure proper implementation of all recommended controls, and should be aligned with and complement the national guidelines.
- ❖ **Rethink the use of available spaces and consider renovation and/or construction to optimize implementation of controls**
- Consider renovation and/or new construction of physical infrastructure to optimize the implementation of infection control measures.
 - Space for screening of patients should be adequate.
 - Waiting areas should be decompressed and moved out of poorly ventilated corridors.
 - Separate, well-ventilated waiting area for respiratory symptomatic should be made available wherever possible.
 - Consider developing outdoor waiting areas for high-risk settings like chest OPD, respiratory treatment centres, microscopy centres, DOT centres and MDR TB management sites.
 - Ventilation in all areas, especially registration, waiting areas, OPD should meet standards for health care settings.
 - As far as possible, re-circulating air conditioners should be used with great caution, due to the harmful effect on air exchange in most installations.
 - In the event that re-circulating air conditioners have to be used, then it would be desirable to have an exhaust fan installed in the reverse direction forcing fresh air into the room and giving directional control. This would compromise with the comfort to some extent but add value to the safety of the room.
 - Great care should be taken to ensure adequate air exchange regardless of the climate control solution.
- ❖ **Designate focal points for the facility-level activities, and support training of frontline health care workers**
- Facilities should have focal points designated to ensure activities are properly implemented.
 - These focal points should play a key role in sensitization of the front-line health care staff in all aspects of infection control, including standard precautions, patient risk assessments, and airborne infection control considerations.

- Workers should be granted opportunity to participate in trainings.
 - Regular sensitization and reinforcement of policies and practices should be conducted by infection control focal points.
- ❖ **Ensure proper implementation of the administrative controls (listed below)**
- At facility level, administrative controls play a major role in reducing the risk of TB transmission and are essential for the implementation of other controls (i.e. environmental controls and personal protective equipment).
 - Evidence shows that implementation of administrative controls reduces transmission of TB in health care facilities. For this reason, administrative controls should be implemented as first priority.
 - These, however, should be complemented by the environmental controls and personal protective equipment described later.
- ❖ **Budget for maintenance**
- At facility level, a realistic budget should be available for comprehensive maintenance of all controls incorporated in the facility infection control plan.
 - Integrating with other programmes and the general health system at large would be essential to mobilize the requisite funding support to carry out these activities especially for engineering / environmental rectifications recommended in the risk assessment report.
 - Ensure that adequate infection control supplies are provided, i.e. hand hygiene facilities (soap and clean running water, alcohol-based hand rub), PPE – gowns, gloves, eye protection, medical masks and particulate respirators (N 95 masks); additional PPE items for housekeeping purposes should also be made available, e.g. protective footwear, waterproof aprons, rubber gloves, and adequate supply of appropriate cleaning and disinfection materials.
- ❖ **Supervise and monitor infection control activities**
- Facility-level infection control activities frequently involve changes in work practices that tend to weaken over time, hence ongoing supervision and monitoring is essential.
 - Facility administrators are responsible for ensuring that administrative and environmental controls outlined in the facility plan are successfully and consistently implemented.

❖ Address training and communication needs of health workers, patients and visitors

- Human Resource Development (HRD) for TB infection control requires specific planning at all levels.
- Administrators and supervisors should be sensitized in the administrative and environmental controls in greater details while health care workers training should focus more on administrative controls and the appropriate use of personal protective equipment for optimizing patient care.
- Advocacy, communication and social mobilization have to be an essential component of the infection control plan. These activities should include civil society and community involvement, behavioural change campaigns and reinforcement of positive message for health workers, patients and visitors.

8.1.8 Administrative control strategies for health-care facilities

Administrative control measures (policies and work practices) have the greatest impact on preventing TB transmission. They serve as the first line of defence for preventing the spread of TB in health care settings.

Summary of key recommendations on administrative controls

Outpatient settings

- Screen for respiratory symptoms as early as possible upon patient's arrival at the health care facility.
- Provide patient education on respiratory hygiene, cough etiquette and sputum disposal.
- Segregate patients with respiratory symptoms without stigmatising.
- Fast-track patients with respiratory symptoms.
- Well ventilated waiting area - preferably through an open corridor/s

Inpatient settings

- Minimize or no hospitalization of TB patients.
- Establish separate rooms, wards, or areas within wards for patients with infectious respiratory diseases. Such areas should promote minimum mixing with other patients
- Educate inpatients on respiratory hygiene, cough etiquette and provide adequate sputum disposal facilities.
- Establish safe radiology procedures for patients with infectious respiratory disease, including smear-positive TB cases or TB suspects.

8.1.8.1 Administrative controls for outpatient areas

The aim of administrative interventions in the outpatient area of any healthcare facility that manages patients with suspected tuberculosis is two-fold:

- Reduce the total time period that such a patient stays in the healthcare facility, and

- Reduce airborne transmission to other patients and healthcare workers in this limited time period.

Given the heavy patient load at most health care institutions, it is natural that patients of tuberculosis, like any other patient, have to sometimes wait long periods before they are actually examined by the physician. During this period, these patients are a constant source for airborne spread of the disease to others. Reducing the overall stay of such patients in the healthcare facility is likely to prove the single-most effective measure of reducing airborne disease transmission in these settings. This can be achieved by fast tracking these patients, which itself can be accomplished by several measures that are not mutually exclusive. Fast-tracking will also depend upon the type of healthcare facility. The process will be more useful for hospitals and general OPDs.

The implementation of the key administrative interventions (screening, education, segregation, and fast tracking) would vary from facility to facility.

❖ **Screening**

Screening for respiratory symptoms should occur as early as possible upon patient's arrival at the health care facility. Patients can be effectively screened at the registration counter itself by asking simple questions related to chronic respiratory symptoms, and those suspected to have tuberculosis can be given special cards or priority slips. The services of existing staff at the registration counter can be used for this purpose, or a special screening counter can be established prior to the registration process. This screening can be performed by physicians, nurses, paramedical staff and/or volunteers specially deputed for this purpose. Even if screening at registration is not possible, screening can occur when patients are in waiting areas.

❖ **Education on cough etiquette and respiratory hygiene**

Another physical method that can prove useful for reducing airborne transmission is the provision of patient education on cough hygiene and sputum disposal. This education can easily be imparted to patients through posters and other means in the waiting area, as well as through discussions by a paramedical staff or volunteers while patients are waiting for their turn. Cough etiquette should be reinforced by all staff members when poor cough etiquette is observed. Provision of disposable surgical masks to patients attending these facilities with instructions on how and when to use them is also recommended.

❖ **Patient segregation**

Segregation of patients with respiratory symptoms can be achieved by having a separate waiting area for chest symptomatics, within the overall outpatient area. This is particularly important in larger institutions with heavy OPD loads. If feasible, a separate doctor can be deputed to assess these patients in the segregated waiting areas, so that they do not mix with other patients waiting in the outpatient area. Another alternative is to implement a patient flow control mechanism at the entry point of the waiting area, so that chest

symptomatics (who have been screened earlier and are carrying priority slips or other similar identification) are diverted to this special area rather than to the common waiting area. The outpatient area, more so this segregated area, should be well ventilated to reduce overall risk of airborne transmission.

❖ **Fast tracking of patients with respiratory symptoms**

Those identified as patients with respiratory symptoms can be further fast-tracked in both their clinical and laboratory evaluations. One option could be to directly send these patients for sputum smear examination before they see a doctor. The other options are to allow these patients to bypass the routine queue and be seen earlier than other patients, or to have totally segregated physician area. The other important area where these patients can be given priority is while performing chest radiography.

8.1.8.2 Administrative interventions in the inpatient areas

❖ **Minimize hospitalization of TB patients**

One of the most effective means to reduce the risk of transmission of airborne pathogens such as *M. tuberculosis* in hospital settings is to manage such patients in the outpatient setting whenever possible. Many patients can be managed entirely as outpatients, thereby avoiding hospitalization and the risk of exposing other patients and staff. If hospitalized, patients should be re-evaluated frequently for possible discharge with continuation of therapy as outpatients.

❖ **Establish isolation rooms, wards, or areas within wards for patients with infectious respiratory diseases**

When hospitalization is required, patients with infectious respiratory diseases should be physically separated from other patients so that exposure to infectious droplet nuclei by others is minimized. Policies on patient separation inevitably generate concern about stigma, but with appropriate measures, such as training and publicly displaying of separation rules, stigma can be minimized. Administrative procedures should ensure that separation happens promptly and automatically, similar to the automatic separation of men and women during inpatient admission. If sputum-smear microscopy or other relevant diagnostic tests are performed for patients with respiratory symptoms at the time of admission, then those who are most infectious can be quickly identified for separation from other patients.

Suggested priorities for separation of patients are as follows:

- a) Separation of patients with confirmed or suspected diseases of public health concern; such as epidemic influenza, from all other patients.
- b) Separation of sputum-smear positive TB patients from immune-compromised patients.

- c) Separation of patients with known or suspected drug-resistant TB from immune-compromised patients and from drug sensitive TB patients.
- d) Separation of patients with known or suspected TB from all other patients.

The best choice for infectious or potentially-infectious patients is to house and manage them in airborne infection isolation rooms. Where such isolation rooms are not feasible, other options for physical separation include:

- Having a few small ‘airborne precautions rooms’ for patients with infectious respiratory disease patients.
- Having a separate ward designated for patients with infectious respiratory diseases.
- Keep a designated area with better ventilation available for the placement of potentially-infectious patients.
- Where it is not possible to have a designated airborne precaution room, ward, or area of a ward, there can at least be an area designated as a “No Immune-Compromised Patient Area”, where TB inpatients would be preferentially placed.

❖ **Educate inpatients on cough hygiene and provide adequate sputum disposal facilities:**

Wards housing infectious patients should display sign boards in the ward demonstrating cough hygiene. All patients admitted in the ward/area should be issued surgical masks and counselled on their proper use. Adequate measures for safe collection and disposal of sputum should be provided.

❖ **Establish safe radiology and other investigation procedures for patients with infectious respiratory diseases, including smear-positive TB cases or presumptive TB cases**

When caring for an infectious/presumptive TB case, the radiology/ laboratory or other departments should attempt to:

- Schedule inpatient investigations on infectious/presumptive TB patients for non-busy times.
- Provide coughing patients with a surgical mask to wear, or tissues or cloth to cover their mouths.
- Provide priority service to potentially infectious TB patients to minimize the length of time spent in the department.
- Restrict access to the radiology/laboratory suite only to patients and essential personnel.
- Use the room with the best ventilation for taking images of potentially infectious TB patients.

8.1.9 Environmental controls

Environmental control measures are the second line of defence for preventing the spread of TB in health care settings. Environmental controls include ventilation (natural and mechanical), ultraviolet germicidal irradiation (UVGI), filtration and other methods of air cleaning. It is important to recognize that if administrative controls (policies and work practices) are inadequate, environmental controls may not eliminate all the risk. Some environmental control measures are simple and inexpensive while many others are technically complex and expensive.

Environmental controls work on the same basic principle – dilution of infectious particles through real or ‘effective’ air exchange. In case of ventilation, dilution occurs through the introduction of fresh, uninfected air and the removal of infected air. In the case of UVGI or filtration, dilution is ‘effective’ through the creation and re-circulation of ‘cleaned’ air, in which infectious particles have been removed by irradiation or physical extraction.

Certain circumstances may require *directional control of airflow*, so that air containing infectious particles is not introduced into areas with clean air where staff or other patients are located.

Summary of key recommendations on environmental controls

- Health-care facilities should seek to achieve minimum standards for air exchange. High-risk settings should be prioritized for immediate assessment and implementation of improved ventilation.
- In most settings, natural ventilation is the preferred method for ensuring adequate air exchange.
- In existing health-care facilities relying on natural ventilation, ensure effective ventilation at all times and in all climatic conditions through proper operation and maintenance, and by regular checks to ensure fixed, unrestricted openings. If mechanical ventilation is used, the system should be well designed, maintained and operated, to achieve adequate airflow rates and air exchange.
- In high-risk settings where it is not possible to achieve adequate air exchange using natural ventilation, a complementary option is to use upper room or shielded ultraviolet germicidal irradiation (UVGI) devices.
- Optimal workflow and facility arrangement for patients and staff should be implemented in all outpatient departments, DOT treatment centres, microscopy centres, and radiology departments.
- Directional control of air flow is recommended in specific high-risk settings where infectious patients with drug-resistant TB or other acute respiratory diseases of potential concern are likely to be managed – i.e. airborne infection isolation rooms, MDR-TB wards and clinics and bronchoscopy units.

8.1.10 Ventilation

Ventilation can reduce the risk of infection through dilution and removal. When clean or fresh air enters a room; by either natural or mechanical ventilation, it dilutes the concentration of airborne particles, such as droplet nuclei in room air. This is similar to opening of windows and doors to remove foul odours. Dilution reduces the likelihood

that a person in the room will breathe air that may contain infectious droplet nuclei. As room air exchange doubles, the concentration of airborne particles in the room falls by half.

Improved ventilation in health-care facilities is essential in preventing transmission of airborne infections and is strongly recommended. Better ventilation lowers the risk of transmission of TB and other airborne infections.

❖ Natural ventilation

This refers to fresh dilution air that enters and leaves a room or other area through openings such as windows or doors. Natural ventilation is "controlled" when openings are fixed and unrestricted to maintain air flow at all times. Unrestricted openings (i.e. those that cannot be closed) on opposite sides of a room provide the most effective natural ventilation (Figure 8.1). In existing health-care facilities that have natural ventilation, when possible, effective ventilation should be achieved by proper operation and maintenance of openings, and by regular checks to see that openings remain free of obstruction at all times.

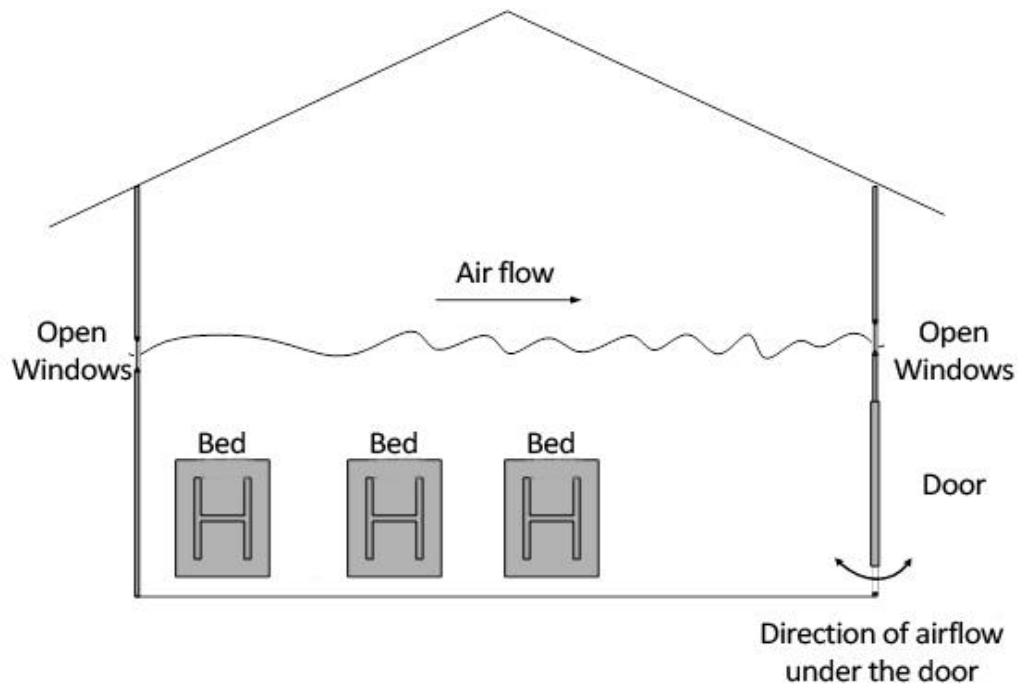


Figure 8-1 Sketch of a room with natural ventilation

Simple natural ventilation may be optimized by maximizing the size of the windows, opening up fixed window panes, by locating windows on opposing walls, and by the use of propeller "mixing fans". Types of mixing fans include ceiling fans, stand/desk mounted fans, or window/exhaust fans located in open windows. Mixing of air can disperse pockets of high concentrations, such as in the vicinity of patients. The total number of infectious particles in the room will not change with mixing; the concentration of particles near the source may be reduced, and the concentration in other parts of the room may increase. In other words, unless adequate ventilation is present the mixing fan will not be useful in reducing infectious particles and the risk of transmission.

A common problem with reliance on natural ventilation is that patients or staff close windows during cold weather or at night. Further, there is likely to be variability of airflow patterns due to varying weather. In colder climates where rooms are closed to keep temperature adequately, natural ventilation can be implemented by airing via windows at frequent intervals. If natural ventilation is inadequate, additional mechanical ventilation or other measures may be needed, especially in areas where risk of *M. tuberculosis* transmission is high.

❖ Mechanical ventilation

Mechanical ventilation uses fans to drive the air flow through a building. Mechanical ventilation can be fully-controlled and combined with air conditioning and filtration systems as is normally done in some office buildings. Mechanical ventilation also includes "Mixed Mode ventilation", in which exhaust and/or supply fans are used in combination with natural ventilation to obtain adequate dilution when sufficient ventilation rate cannot be achieved by natural ventilation alone.

Mechanical ventilation with or without climate control may appropriate where natural ventilation cannot be implemented effectively, or where such systems are inadequate given local conditions (e.g. building structure, climate, regulations, culture, cost and outdoor air quality). If mechanical ventilation is used, the system should be well designed, maintained and operated, to achieve adequate airflow rates and air exchange.

The simplest form of mechanical ventilation is the use of exhaust fans, placed for instance in windows and move air from inside a room to the outdoors. Exhaust fans also may be more acceptable to staff and patients than keeping windows consistently open. If exhaust fans are used, it is important to ensure that airflow is adequate, that air flows across the room (not in and out the same window or vent), and that exhaust fans and air intake (windows or vents) are not located in a way that short-circuiting will occur (Figure 8.2).

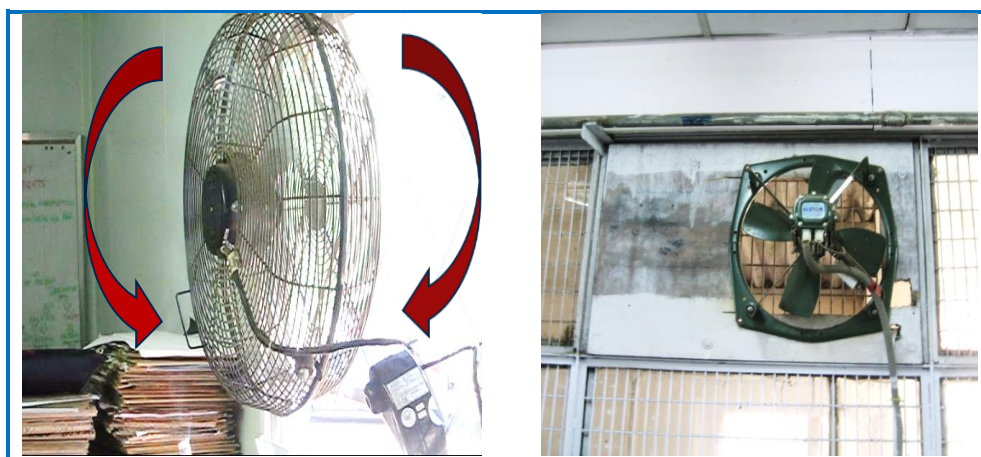


Figure 8-2 Mechanical ventilation

In this installation, the fan adds little to ventilation; removal of the fan was recommended, as natural ventilation was adequate.

An under-utilized form of mechanical ventilation is the use of *air supply fans*, which move air from outside to inside a room. This is usually the same device as a typical exhaust fan, but mounted in reverse. Air supply fans often have particular value when attempting to ventilate a clinical exam room, to ensure that the air flows out of the exam room into the waiting area outside.

❖ Challenges of achieving adequate ventilation and climate control

Effective ventilation is often at odds with efforts to make indoor climate more comfortable. In practice, air cooling or heating is more energy efficient with re-circulation of air. The implication of installing a split A/C and closing the doors and windows is, however, complete lack of air exchange. Careful attention must be paid to ensure adequate ventilation when installing climate control.

It is possible for rooms with air conditioning or heaters to have adequate ventilation. In the example in Figure 8.3, a well-installed exhaust fan has been placed on the other side of the room to achieve adequate air exchange, and air is allowed to enter the room by keeping a larger gap under the door. It is acknowledged that this arrangement leads to less effective cooling than a sealed room, but safety with adequate comfort trumps maximal comfort without safety.

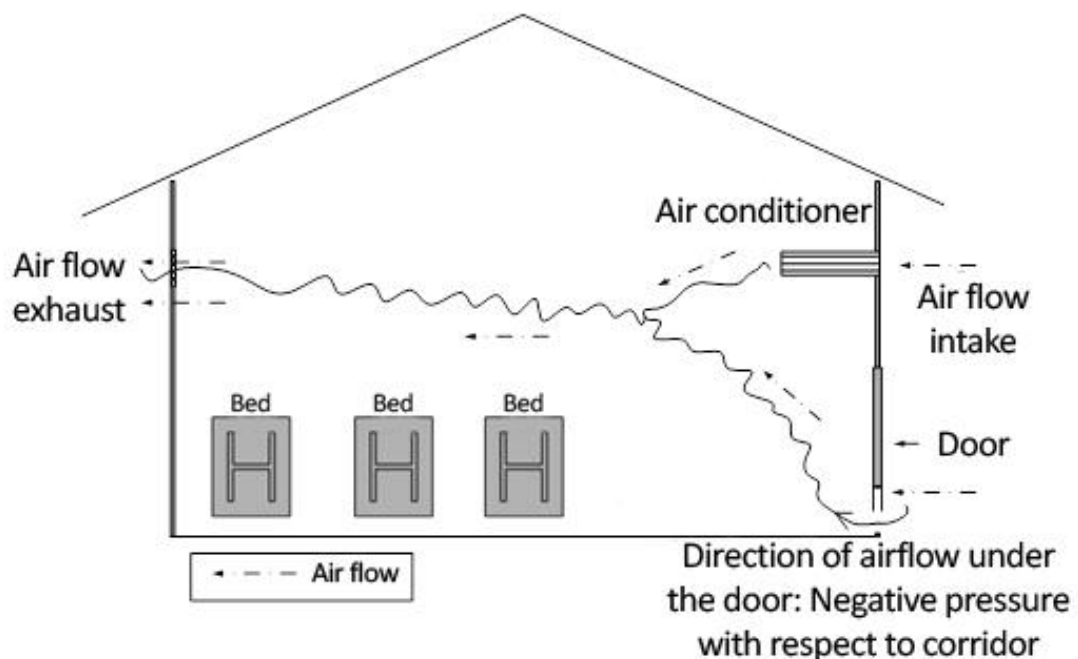


Figure 8-3 Sketch showing how adequate air exchange might be achieved in a room with air-conditioning/heating

The air conditioner is located away from the exhaust, near the door, so that cooled air sweeps across the room. An exhaust fan, adequate to achieve the required air exchange, is installed on the other side. Adequate air intake has been enabled by having enough space under the door (a few inches clearance) for air to freely enter the room.

❖ National standards for minimum ventilation in healthcare settings

Health-care facilities should maintain a minimum amount of ventilation during all climactic conditions (Table 8.1). In settings relying on mechanical ventilation (either fan-assisted or closed systems) this can be calculated with the assistance of local engineers.

Table 8-1 Minimum air-changes per hour required for various health care settings

| Type of healthcare setting | Minimum Air Changes per Hour (ACH) |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| Registration areas | More than 6 ACH |
| Outpatient departments and their waiting areas | More than 6 ACH |
| Inpatients departments | More than 6 ACH |
| High-risk settings and their waiting areas <ul style="list-style-type: none"> • ART centres • TB / respiratory units (outpatient and inpatient) • Bronchoscopy procedure rooms • MDR-TB wards and clinics • Airborne isolation rooms | More than 12 ACH |

Where ACH is not able to be measured, as is usually the case in rooms with natural ventilation, the following standards for ventilation should be followed to ensure that air exchange is safely more than 12 ACH under all climactic conditions.

- Natural ventilation should be "controlled", with fixed, unrestricted openings that are insensitive to climactic conditions.
- Openings should constitute more than 20% of floor area.
- Openings should be on 2 sides, preferably opposite sides. For example, a 100 ft² room should have more than 10 ft² fixed, unrestricted openings on two sites, for a total of 20 ft².

Where these natural ventilation standards cannot be met, the addition of other measures should be considered. Improvements in ventilation should be based on the assessment of the facility and informed by local climatic conditions, building structure, regulations, and cost. If mixed-mode mechanical ventilation is used, the installation should be designed to achieve the minimum ACH standards. Calculation of exhaust fan requirements to achieve a minimum air exchange can be based on the rating of the fan in terms of cubic feet per minute (CFM). Of note, the fan rating should be adjusted downwards depending on estimates of the efficiency of installation, particularly air leakage and resistance from any covering mesh or screen. A typical adjustment to the fan rating would be to assume the fan operates at 75% of rated efficiency.

Optimal arrangement of patient and staff should be implemented in all settings. Health care staff should be mindful of the direction of airflow to ensure that they are closest to

the clean air source, and patients are closest to the exhaust. This involves arranging patients and staff so that contaminated air is not likely to cross directly into staff/patient spaces. The natural direction of air flow should be between patients and staff, and not across patients and staff (Figure 8.4). This is especially important for settings such as DOT centres, OPD examination rooms, and sputum smear microscopy laboratories.

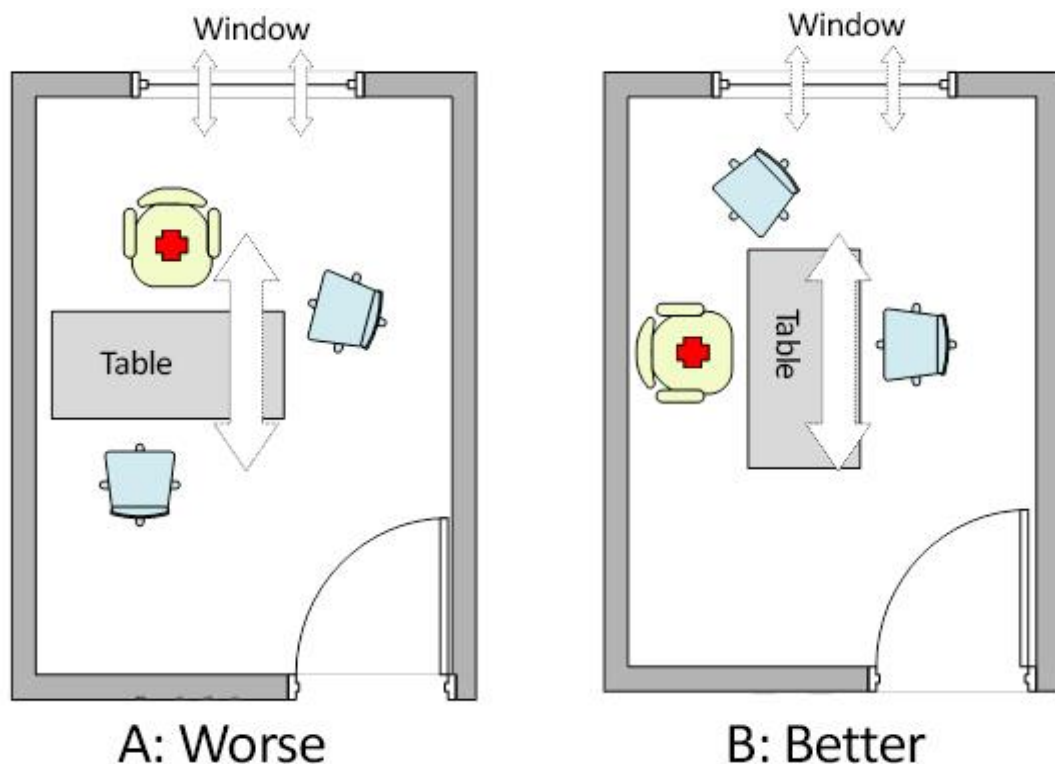


Figure 8-4 Schematic showing seating arrangement for patient and health care worker (red cross)

In A. natural ventilation would allow potentially infected air to cross health care worker. In B. with this seating arrangement the chance of such exposure is lessened somewhat.

Directional control of air flow is recommended in specific high-risk settings where infectious patients with TB or other acute respiratory diseases of potential concern are likely to be managed – i.e. airborne infection isolation rooms, MDR-TB wards and clinics, and bronchoscopy units. This simply means having in place a system to minimize the chance that airflow goes from contaminated to uncontaminated areas. In a room relying on natural ventilation that is situated away from other patient care areas, no additional changes would be required as there would be no area of concern for contaminated air to flow. It is important to keep the doors to corridor or other rooms closed, to prevent escape of infectious aerosols to other parts of the facility. The direction of air movement can be easily assessed using smoke tubes, strips of ribbon, or simply by observing the directionality of dense smoke from incense sticks. Directional control of airflow can be achieved in mixed mode ventilation by proper attention to adequate exhaust and supply ventilation (as in Figure 8.5 below).

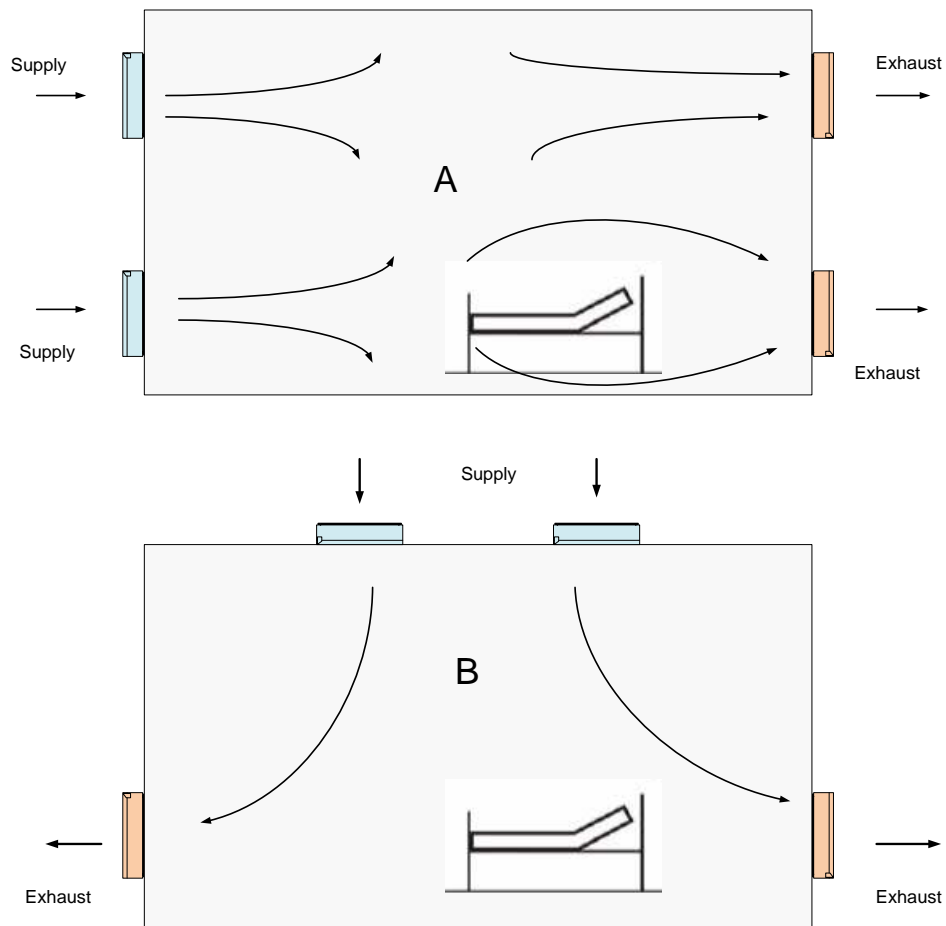


Figure 8-5 Schematic diagrams of mechanical ventilation, with optimal directional control or airflow in the room

In A, supply is on one side, exhaust from the other, so aerosols are not dispersed to other patients or staff. In B, supply is from the top, and again exhaust near the patient's head, for optimal directional control.

8.1.10.1 Ultra-Violet Germicidal Irradiation (UVGI)

Priority should be given to achieving adequate air exchange using ventilation (natural or mechanical). However, in some settings it is not possible to achieve adequate ventilation; for example, because of climatic changes (e.g. in cold climates or during the night), or building structure. In addition, in settings such as MDR-TB wards and HIV wards, transmission of TB poses a high risk of morbidity and mortality. In high-risk settings where adequate ventilation is not possible, a complementary option is to use upper room or shielded ultraviolet germicidal irradiation devices.

Summary of key recommendations on UVGI

- UVGI should only be considered in high-risk areas (defined in Table 8.1) where adequate ventilation is not achievable.
- Installation is critical. If the UVGI is not appropriately installed, it may be ineffective or dangerous to staff and patients.
- Measurement of UV intensity is crucial and required for proper installation.
- Maintenance is critical, and should include cleaning with spirit at least twice-monthly (or more frequently in dusty environments) and periodic bulb replacements. If the UVGI is not maintained, it may become ineffective, providing a false sense of security to staff and patients. If maintenance and prompt bulb replacement with the correct product cannot be guaranteed, then UVGI should not be used.
- Installations should seek to irradiate the maximal air volume with the highest intensity UV, while keeping staff and patient exposure to less than 6.0 mg/cm² over an 8-hour period.
- Avoid installations that directly irradiate patients or have bulbs routinely visible.
- No obstruction should be placed in between the UV bulb and the air that it is supposed to irradiate; e.g. transparent plastic bulb covers will absorb all UV radiation at germicidal wavelengths.

Ultraviolet germicidal irradiation (UVGI) uses a type of radiation that has been shown to kill or inactivate *M. tuberculosis* in air. UVGI is maximally germicidal at a wavelength of 254nm (UV-C, or short-wavelength UV). This sort of UV radiation differs from the longer wavelength UV in sunlight (UV-A and UV-B), in that UV-C penetrates poorly.

UVGI devices of UV-C may be sometimes less expensive than structural alteration of the facility for ventilation purposes. Several studies have shown that a well-designed and maintained UVGI upper room system can disinfect *Mycobacteria* (or surrogate test organisms), with an efficiency of 10–20 equivalent air changes per hour. It has been estimated that when an average UVGI intensity of 10µW/cm² is present, 63% of airborne tuberculosis germs that arrive in that “kill zone” will be killed in 24 seconds, and 99% will be killed in 2 minutes.

UVGI effectiveness is affected by:

- Intensity of the radiation - depends on the wattage, condition, and age of the lamp. The intensity of radiation fades over time as the filament ages and drops sharply as dust accumulates on the lamp.
- Length of exposure time - depends on how quickly air containing infectious particles moves past the lamp.

- Proximity of infectious particles to the UVGI lamp - the placement and number of lamps used should be sufficient to bring radiation of adequate intensity to an adequate air volume.
- Mixing of air - inadequate air mixture has been shown to dramatically reduce the effectiveness of UVGI. Without air mixture in effect, UVGI will sterilize the same volume of air repeatedly and not dilute contaminated air with the sterilized air.
- Relative humidity - UVGI effectiveness decreases with increasing humidity, as water vapour absorbs UVGI at the germicidal wavelength of 254nm. UVGI is not recommended for rooms in which the relative humidity of the air is greater than 70%.

There are a number of limitations to UVGI:

- UVGI only provides an equivalent to air exchange and does not provide fresh air or directional airflow.
- If the UVGI is not installed and maintained properly, it may be ineffective at inactivating *M. tuberculosis* and provide a false sense of security.
- Poorly designed or installed UVGI may cause overexposure injuries to healthcare workers and patients.
- The actual radiation levels of an upper-air UVGI installation are difficult to predict. For a given fixture, final radiation levels will vary for every room and for different parts of the same room.

8.1.10.2 Filtration (HEPA filters)

Filtration is another option to remove infectious particles from the air. It may be considered where sustainable resources for membrane replacement and maintenance are assured, where natural ventilation is not possible, and where the risk of TB transmission and morbidity are high. Filtration devices perform poorly in high-dust conditions, as the effectiveness in terms of equivalent air exchange can rapidly diminish. Situations where it might be considered include small room volume settings like bronchoscopy units, laboratories, or individual TB patient rooms. Careful attention should be given to the equivalent air exchanges per hour the filter requires; most filters clean very little air per hour, and only add marginally to dilution of potentially infectious air with cleaned air.

If filters are chosen, then only true-HEPA membrane filters (rated to remove 99.97% of 1 micron particles) should be entertained. Other filtration mechanisms, such as ionizers, have not been adequately studied.

8.1.11 Personal protective equipment

These include the following:

- Protective clothing
- Gloves – usually not necessary but should be worn when likely to be in contact with respiratory secretions or contaminated articles.
- Plastic aprons and gowns – should be worn at the time of contact with the respiratory secretions or contaminated articles or environment to avoid contamination of clothing.
- Masks
 - Ordinary surgical masks reduce aerosol generation by patients but are not useful for protecting healthcare workers. Accordingly, they could be given to patients with uncontrolled cough to reduce aerosol spread.
 - N-95 Respirators for healthcare workers, in special situations like,
 - during high risk aerosol generating procedures associated with high risk of TB transmission especially in laboratory where sputum needs to be processed for TB culture and,
 - when providing care to infectious or presumptive MDR-TB/ XDR-TB patients.
 - TB wound care too requires the wearing particulate respirators and gloves.
 - Masks should be close fitting and filter particles of 1-5 microns. N95 particulate respirators are usually used which have a filter efficiency of 95%. These masks may be reused a few times (during a session/day) provided they are not damaged and specifically the elastic bands are working well. If this is done, careful labelling is required for a single staff member's use and should be stored without getting contaminated.
 - Fit testing and training on proper use and disposal is essential.

Use of a mask is not a substitute for good infection control management



Figure 8-6 N-95 Respirator

8.1.12 High-risk settings

Using the above principles of infection control, specific guidelines could be made for the high risk areas such as Airborne Infection Isolation Rooms, MDR-TB Wards, HIV wards, sputum collection areas, bronchoscopy units, surgical theatres, intensive care units, TB culture labs and autopsy rooms.

8.1.13 Waste disposal and handling

All infectious waste should be discarded in the clinical waste disposal bin. All infectious solid waste -wipes, swabs, plastic, paper towels, gauze pads, gloves, etc., should be placed inside the double autoclave bags, sealed with autoclave tape and sterilized at 121°C for 30 min in the autoclave and/or sent for incineration.

Liquid waste, in the steel discarding bins, should be disinfected in 5% phenol for at least 1 hour, before sealing the caps and autoclaved at 121°C for 30 minutes.

All reusable material such as glassware should be autoclaved in the autoclave steel trays at 121°C for 30 minutes before being washed and repacked for sterilization.

Colour coded bins and bags are recommended for disposal of various types of bio-medical waste and same should be followed as per National Guidelines for solid waste management.

At least one working incinerator should be available in all laboratories, microscopy centres, hospitals and other places where infectious material is generated and needs to be discarded properly.

8.2 BCG vaccination

BCG (Bacillus Calmette-Guérin) is a live attenuated vaccine made from *Mycobacterium bovis*. It protects young children against developing complications of primary infection, such as TB meningitis and miliary TB. However, it has no impact on the transmission of TB in the community as it does not confer protection against development of post primary disease.

Presentation - BCG vaccine is supplied as lyophilized freeze-dried vaccine with diluent in a separate ampoule.

Schedule -The national policy of Sri Lanka is that a single dose of BCG vaccine should be given to all infants as soon as possible after birth. This protects the young children against developing complications of primary infection, such as TB meningitis and miliary TB.

If children are brought without a BCG scar (after 6 months of the initial dose) despite BCG vaccination could be re-vaccinated with a 2nd dose of BCG after 6 months up to 5 years of age even without doing a mantoux test. Even in the absence of BCG scar following the second dose a further dose is not recommended.

BCG vaccination of adults is not normally recommended but may be considered for tuberculin-negative persons in unavoidable and close contact with cases of multidrug-resistant *Mycobacterium tuberculosis*⁷. Routine BCG vaccination is carried out under the Expanded Programme of Immunisation (EPI).

Storage - BCG vaccine can be stored at room temperature up to one month and in a refrigerator at 4°C up to one year. Nevertheless, BCG vaccine and diluent should be stored and transported between +2 °C to +8 °C. Vaccine should be protected from light as it readily destroyed by sunlight. Once reconstituted, should be used within four hours and any remaining solution should be discarded. If not used immediately after reconstitution, the vaccine should be kept cool (+2 °C to +8 °C) and protected from light.

Dose—Vaccine should be reconstituted according to the instructions in the leaflet supplied with the vaccine ampoule/ vial. The reconstituted vaccine contains a homogenous suspension of BCG vaccine in a concentration of 0.5 mg per ml. The reconstituted vaccine is given intradermally at a dosage of 0.05 ml for children below one year and 0.1 ml for aged one year or above. Expiry date on the label of the ampoule/vial should be checked before use.

Inoculation site -The site of inoculation should be in the deltoid region (i.e. half way down the deltoid muscle) in the left upper arm. It is more likely lead to keloid formation if given at higher sites and the tip of the shoulder should be avoided.

Correct intradermal BCG vaccination results in minor local reactions (erythema, induration, tenderness) followed by a small ulceration at the site of injection which usually heals within 4 – 6 weeks leaving behind a scar. Presence of a scar is used as a marker of previous BCG vaccination. The age and immune status of the vaccinee, the skills of the vaccinator, as well as the strain and dose of the BCG vaccine, may influence the extent of these responses.

8.2.1 Adverse events/complications of BCG vaccination

Adverse events/complications of BCG vaccination are local and may be a result of improper vaccination technique such as subcutaneous/intra muscular injection or inadequate sterile measures taken during vaccination. In older children or adults, local complications result from previous sensitization to mycobacteria,

- a) Non healing ulcer - Ulcer which develops at BCG site usually heals by 6 weeks. Rarely, it fails to heal.
- b) Abscess formation at the site.
- c) Enlargement of regional lymph nodes with or without abscess formation (BCG adenitis). A minor degree of adenitis (1 – 2 cm) in left axilla may occur in the weeks following vaccination and should not be regarded as a

⁷www.epid.gov.lk accessed 11 March 2016

complication. In fact such nodal enlargement is a sign of successful vaccination. However, rarely, enlarged regional nodes become larger and may suppurate.

- d) Disseminated infection with *M. bovis* – BCG is a live vaccine of attenuated *M. bovis*. Therefore systemic or disseminated infection can occur only if there is an impairment of immunity.
- e) Anaphylactic reactions may occur rarely.

8.2.2 Management of adverse events

Since faulty immunization technique can cause local complications, measures should be taken to teach proper immunization technique to nurses.

Local complications are usually self-limiting. However isoniazid may be given for 3- 6-months for non-healing ulcers or sinuses if they do not respond to an initial course of antibiotics such as erythromycin. Enlarged nodes without suppuration are usually resolve spontaneously and are not an indication for treatment with isoniazid. However, large non-suppurative node may need surgical excision. In the case of suppurative lymphadenitis, incision and drainage (not aspiration) should be done before commencing a course of isoniazid. Where there is a discharge or suppuration, it is always better to collect a sample for both AFB and pyogenic culture.

BCG vaccination of infants born to HIV positive mothers

BCG vaccination should be deferred in infants born to HIV positive mothers until their HIV status is known. If they are found to be HIV positive they should not be vaccinated with BCG as disseminated infection with *M. bovis* can occur which is difficult to treat and carries a high mortality. If negative, BCG vaccination should be given.

Other conditions in which BCG should be temporarily withheld

- Acute illness
- Fever
- Local skin sepsis

8.2.3 Absent BCG scar

This is a common occurrence. If children are brought without BCG scar despite BCG vaccination, their revaccination can be done after 6 months of age up to 5 years. Mantoux test needs not to be performed before re-vaccination in this age group.

8.3 Contact investigations

Who is a contact?

Any person who has been exposed to an index case

Who is an index case?

The initially identified patient of any age with new or recurrent TB in a specific household or other comparable setting in which others may have been exposed

Purpose of contact investigation and management

- a) Identify contacts of all ages with undiagnosed TB disease among the contacts of an index case
- b) Provide preventive therapy for contacts without TB disease who are susceptible to developing disease following recent infection. Contacts who were infected recently are at a higher risk of developing TB for 1–2 years after infection. The risk of developing disease after infection is much greater for infants and young children under 5 years of age

Types of contacts

- Close contacts who could be either household or non-household
- Casual contacts

Household contacts - A person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the 3 months before commencement of the current treatment episode

Non household contact - A person who is not in the household but shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods during the day with the index case during the 3 months before commencement of the current treatment episode.

Casual contact – A contact who does not belong to above categories

Close contacts of all TB patients (adults and children above 5 years) irrespective of sputum findings should be screened for symptoms of TB. Those who have symptoms suggestive of TB should be investigated with sputum smears, chest X-ray or other relevant investigation (e.g. in EPTB) irrespective of the duration of the symptoms.

All children under the age of 5 years should be screened for symptoms, examined and whether they have symptoms or not, should be screened with chest X-ray.

The question which contact should be investigated can be looked at from two angles, answers to which actually overlaps

a) Contact investigation from the point of view of index case

House hold and non-household close contacts should be investigated when the index case has any of the following characteristics

- **Sputum smear-positive pulmonary tuberculosis** – Patients with pulmonary TB can transmit *M. tuberculosis*. Patients with sputum smear positive pulmonary TB are more infectious than those with sputum smear negative pulmonary TB. Therefore contact investigation should generally be prioritised to new or recurrent cases with positive sputum smears.
- **Children <5 years of age** - when a child <5 years of age develops TB, it is likely that the infection was acquired from a person in the household. Therefore the rationale of investigating contacts of index cases <5 years of age is to find the source of the infection, not to find secondary cases from the child.
- MDR-TB or XDR-TB (proven or suspected)
- PLHIV

b) Contact investigation from the point of view of contact

House hold and non-household close contacts should be investigated if they have any one of following characteristics

- Contacts of all ages with symptoms suggestive of TB
- Child contacts <5 years of age whether they have symptoms or not
- Contacts with known or suspected immunocompromising conditions (whether they have symptoms or not) especially PLHIV. People with other immunocompromising conditions, such as leukaemia or lymphoma and patients receiving immunosuppressive therapy such as high-dose corticosteroids or TNF α inhibitors are also a high priority for contact investigation
- Contacts of index cases with MDR-TB or XDR-TB (proven or suspected), whether they have symptoms or not

TB control programme would conduct follow-up screening of contacts for up to 2 years at 6 monthly interval, to identify incident cases. The follow-up screening is to be done by the range PHIs

Contact investigation should include

- Detailed medical history
- Clinical examination

- Sputum examination if cough is a symptom or appropriate biological specimen using smear, Xpert MTB/RIF and/or Culture as considered appropriate per the guidelines. This includes samples from extrapulmonary sites for microbiology and pathology investigations
- Chest X-ray
- Mantoux (where indicated)

8.4 Preventive treatment (chemoprophylaxis)

The aim of preventive treatment is to prevent progression of *M. tuberculosis* infection to disease. It means treatment of latent TB infection (LTBI). Most important prerequisite to preventive treatment is to exclude the active disease.

Who should be given prophylactic treatment?

- Children under 5 years who are close contacts sputum smear positive pulmonary TB patients after carefully excluding active TB
- PLHIV who are close contacts of sputum smear positive pulmonary TB patients after carefully excluding active TB
- Other PLHIV who have a Mantoux reaction of ≥ 5 mm after carefully excluding active TB

Other categories of patients who should be considered for chemoprophylaxis

- Transplant recipients
- Patients who are going to be commenced on anti TNF α treatment

Decision to start such patients on chemoprophylaxis has to be taken on an individual basis by a Consultant Respiratory Physician considering contact history, risk of developing active TB, risk of drug toxicity against protection against developing active TB etc.

Before starting chemoprophylaxis it should be ensured that the patient is not suffering from active TB

What chemoprophylactic regimen should be used?

Isoniazid 5mg/kg daily for adults and 10mg/kg daily for children (maximum 300mg) for 6 months. This is referred to as isoniazid prophylactic treatment (IPT). Other prophylactic regimens with rifampicin alone or combination of isoniazid with rifampicin should not be used.

8.5 Intensified case detection

The NPTCCD has already achieved the global targets of case detection and cure rates since 2005 and is also implementing various components of the Stop TB Strategy. However, the case detection under the programme needs to be further enhanced in view of the low incidence rates in the country. Accordingly, the programme proposes to launch the intensified case detection plan as under:-

8.5.1 Investigation of high risk categories

❖ Contacts of TB Patients

All contacts of TB patients should be traced and registered by range PHI or by the PHI of DCC. All symptomatic and asymptomatic contacts mentioned below should be referred to the DCC for investigations.

❖ Investigations of symptomatic contacts

All contacts of TB patients having any symptoms which could be related to tuberculosis (either pulmonary or extrapulmonary) or even having constitutional symptoms irrespective of the duration, need to be investigated for TB. This is described under chapter 3 of the Technical Guidelines.

❖ Screening and investigations of asymptomatic contacts of TB patients

The following categories of TB contacts should be screened in spite of the absence of symptoms.

- Children less than 5years
- Elderly more than 60 years
- Patients with diabetes
- Immuno compromised individuals
- Patients on immuno suppressive drugs such as long term steroid therapy
- Cancer patients on anti-cancer treatment
- Patients who have undergone transplant surgery
- People living under risk environments (eg. slums, estates, internally displaced, migrants)

All the other asymptomatic contacts should be followed up by the range PHIs for appearance of symptoms for two years at six-month intervals. In addition, contacts should be advised to attend the DCC if symptoms suggestive of TB appear at any time.

❖ **Screening of inmates of institutions in congregate settings**

The following categories of institutionalised persons are at high risk of TB due to their life style and social and environmental conditions. Therefore they should be screened regularly.

- Prisoners
- Inmates of elderly homes
- Inmates of destitute homes
- Inmates of rehabilitation centres for drug addiction.
- Healthcare workers in high risk settings such as MDR-TB wards and laboratories

❖ **Screening of all HIV positive patients**

HIV infected persons are having high susceptibility to TB infection and those who are already infected with Mycobacterium tuberculosis have high risk of developing active TB. Therefore all the persons infected with HIV should be referred to the DCC for examination for TB.

❖ **Other priority groups**

- Current and former workers in workplaces with silica exposure
- Migrant population and returning refugees
- People with diabetes
- Subpopulations that have very poor access to health care, such as people living in urban slums, homeless people, people living in remote areas especially tea estates with poor access to health care, and other vulnerable or marginalized groups

Sub-populations needing to be screened may vary from district to district. Hence the decision on selection of subpopulations to be screened should be taken at local level by DTCO in consultation with national and provincial level technical experts and programme managers that include NPTCCD Director, Provincial and Regional Directors, Consultant Community Physicians, Consultant Respiratory Physicians etc).

8.5.1 Method of screening

The screening in the intensified case detection plan would include:

- Clinical-screening (history and examination/symptoms and signs)
- Sputum examination
- Chest X-ray

Key principles when planning a TB screening strategy

- a) Before screening is initiated, high-quality TB diagnosis, treatment, care, management and support for patients should be in place, and there should be the capacity to scale these up further to match the anticipated rise in case detection that may occur as a result of screening. In addition, a baseline analysis should be completed in order to demonstrate that the potential benefits of screening clearly outweigh the risks of doing harm, and that the required investments in screening are reasonable in relation to the expected benefits.
- b) Indiscriminate mass screening should be avoided. The prioritization of risk groups for screening should be based on assessments made for each risk group of the potential benefits and harms, the feasibility of the initiative, the acceptability of the approach, the number needed to screen, and the cost effectiveness of screening.
- c) The choice of algorithm for screening and diagnosis should be based on an assessment of the accuracy of the algorithm for each risk group considered, as well as the availability, feasibility and cost of the tests.
- d) TB screening should follow established ethical principles for screening for infectious diseases, observe human rights, and be designed to minimize the risk of discomfort, pain, stigma and discrimination.
- e) The TB screening approach should be developed and implemented in a way that optimizes synergies with the delivery of other health services and social services.
- f) A screening strategy should be monitored and reassessed continually to inform re-prioritization of risk groups, re-adaptation of screening approaches when necessary and discontinuation of screening at an appropriate time.

Sub-populations needing to be screened may vary from district to district. Hence the decision on selection of subpopulations to be screened should be taken at local level by DTCCO in consultation with various stakeholders.

9. TB in Special Situations

9.1 Pregnancy with TB

In all cases of special situations, Consultant Respiratory Physician and experts of respective speciality should be consulted at the time of initiation of TB treatment and reviewed jointly on monthly basis during the treatment or as advised by experts.

9.1.1 Diagnosis

In pregnancy, chest X-rays should be avoided as far as possible, especially during the first trimester. Therefore, diagnosis will depend more on bacteriological /sputum examination and clinical grounds when a pregnant mother is presented with symptoms suggestive of tuberculosis. However, if an X-ray is absolutely necessary, this may be taken with the abdomen is covered with a lead apron.

9.1.2 Treatment during pregnancy

Anti-TB treatment should be started as soon as the diagnosis is made, and the full course of treatment is given. The basic principles of treatment in pregnancy do not differ. Most anti-TB drugs are safe to use during pregnancy. The exception is streptomycin which should not be prescribed because it can cause ototoxicity in the foetus.

Pregnant mothers should be treated with pyridoxine 10 mg daily along with INH. Neonates born to mothers on rifampicin should be administered Vitamin K at birth to prevent the risk of post-natal haemorrhage. Recently diagnosed sputum smear positive mothers should be advised to wear a face mask during breast feeding and avoid coughing on to infant's face. They should breast feed in an adequately ventilated place and minimise sharing common breathing space with the infant.

9.2 Treatment during breast-feeding

Breast feeding mothers with TB should receive the full course of anti-TB treatment. Proper treatment is the best way of preventing transmission of TB to the baby. All anti-TB drugs are compatible with breast-feeding. Breast feeding can be continued in the normal manner while the mother is taking anti-TB treatments. Breastfeeding should be avoided only in cases where the mother has TB/HIV co-infection.

9.3 Management of a new-born child of a mother with active TB

- Do not separate the child from the mother unless she is acutely ill.
- If the mother is sputum smear negative, and if the infant has no evidence of congenital TB, BCG is given to the infant.

- If the mother is sputum smear-positive at the time of delivery, infant should be carefully examined for evidence of active disease.
 - If the infant is ill at birth and congenital TB is suspected, a full course of anti-TB treatment should be given.
 - If the child is well, give prophylactic treatment of INH 10 mg/kg body weight, daily for three months. BCG is withheld.
- The Mantoux skin test is done after three months.
 - If the Mantoux test is negative and the child is well, prophylactic treatment with INH is stopped and child is given BCG.
 - If the Mantoux test is positive, careful examination of the child for active TB is done including a chest X-ray.
 - If active disease is diagnosed, a full course of anti-TB treatment should be commenced.
 - If the physical examination and the chest X-ray are normal, INH chemoprophylaxis is continued up to six months.

10. Management of Co-Morbidities

10.1 HIV infection

For further details reader is advised to refer to NPTCCD Guidelines for Management of TB/HIV Co-infection

The Human Immunodeficiency Virus (HIV) damages the immune system of an individual and increases his susceptibility to many infections including TB. HIV is the most potent factor known to increase the risk of progression of latent tuberculous infection to tuberculous disease. In a HIV negative patient who is infected with *M. tuberculosis*, the lifetime risk of developing tuberculosis is only 10%, whereas in a person infected HIV, it is 50%. Tuberculosis is one of the most important life threatening infections associated with HIV infection. It is the leading cause of death among people who are HIV positive and accounts for more than one third of AIDS deaths worldwide.

10.1.1 Features of HIV related TB

TB usually occurs earlier in the course of HIV infection than other opportunistic infections associated with HIV, but it may occur at any stage of HIV infection as a result of rapid progression of a recently acquired or latent infection. Among HIV infected people, TB infection results in a transient drop of CD4 count and progression of the HIV infection.

As HIV infection progresses, the CD4 lymphocyte count declines and the immune system is less efficient in preventing the growth and spread of *M. tuberculosis*. As a result, disseminated and extrapulmonary disease is more common in HIV positive patients than in HIV negative patients. Nevertheless, pulmonary TB is still the most common form of TB seen in HIV infected patients, with or without concomitant extrapulmonary TB.

10.1.2 Pulmonary TB

The presentation of pulmonary TB in HIV infected individuals depend on the stage of the degree of immune-suppression. The clinical picture, sputum result, and chest X-ray appearance often differ in early and late HIV infection (Table 10.1).

10.1.3 Diagnosis

The diagnosis of TB in HIV infected patients is often difficult because:

- The sputum smear examinations tend to be negative more often, particularly in the late stages of HIV infection.
- X-ray abnormalities are often atypical.
- The Tuberculin skin test is often negative due to immune-suppression.

Table 10-1 How PTB differs in early and late HIV infection

| Features of PTB | Stages of HIV infection | |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | Early (CD4 > 350) | Late (CD4 < 350) |
| Clinical picture | Often resembles post primary PTB | Often resembles primary TB |
| Sputum smear result | Often positive | Often negative |
| Chest X-ray | <ul style="list-style-type: none"> • Often cavities • Lymphadenopathy usually absent • Pleural effusions rare | <ul style="list-style-type: none"> • Often infiltrates • Cavitation (uncommon) • Lymphadenopathy and pleural effusions often present |

If TB is suspected in HIV infected people, their sputum for direct smear (three samples) culture (two samples) for *Mycobacteria* and Xpert MTB/RIF should be done. Other investigations include chest-x ray, Mantoux, tissue biopsy, aspirations from suspected extrapulmonary sites for cytology, histology, direct smear, and culture for *mycobacteria*.

10.1.4 Important points to remember in the treatment of HIV associated TB

- In TB/HIV co-infection, priority is to treat TB. Current WHO guidelines recommend that TB treatment should be commenced first and ART commenced subsequently as soon as possible but within the first 8 weeks of starting anti-TB treatment. In case of severe immunosuppression (CD4<50) and in very ill patients, ART should be commenced within two weeks.
- Generally, anti-TB treatment in HIV positive patients is same as for that of HIV negative TB patients.
- It is important that these patients should receive Directly Observed Treatment. (DOT). To maintain confidentiality, HIV status need not be divulged to the DOT provider. Effective treatment using quality drugs under observation can cure TB, prevent the spread of the disease and prolong the life of HIV patients.
- Adverse reactions to anti-TB drugs are more common in HIV positive patients and drug interactions occur between anti-TB and anti-retroviral drugs.
- Paradoxical exacerbation of symptoms, signs and radiographic manifestations of TB may be seen in patients on anti-TB drugs when they are started on anti-retroviral drugs. This is known as Immune Reconstitution Inflammatory Syndrome (IRIS).
- The rate of recurrence of TB after completion of treatment is higher in HIV positive patients than in HIV negative TB patients.

- The case fatality rate is higher in HIV positive TB patients than in HIV negative TB patients. The excess deaths in TB/HIV patients are partly due to the tuberculosis itself and partly due to other HIV related problems.
- Considering the higher rates of morbidity and mortality in case of co-infection, all HIV positive cases, subjected to availability, should undergo Xpert MTB/RIF for detection of TB disease as well as resistance to Rifampicin on relevant biological specimens.

10.1.5 Screening of TB patients for HIV

All TB patients should be screened for HIV at the time of diagnosis or at a subsequent visit if not screened at the initial visit. Screening should be done as provider initiated counselling and testing.

Counselling should be done by the Medical Officer or by the Nursing Officer or Public Health Inspector. Blood should be drawn at the Chest Clinic (or Chest Ward, if the patient is admitted) and sent to the Sexually Transmitted Disease (STD) Clinic for the HIV screening test. A coding system should be used to record the test results.

In case where, a patient is required to be referred to the STD Clinic for a confirmatory test or for HIV care services, it should be done with a duly filled referral form. This also should be recorded in the Standard Treatment Card that is kept in the patient's file.

10.1.6 Screening of HIV patients for TB

All HIV infected patients should be screened for TB at the time of the diagnosis and subsequently whenever it is suspected. Patients are referred from STD Clinics to the District Chest Clinics for this purpose using the standard referral form. For those patients who are found to have tuberculous disease anti-TB treatment should be commenced immediately. All HIV positive cases, subject to the availability, should undergo Xpert MTB/RIF as initial test for detection of TB disease as well as resistance to Rifampicin.

HIV patients who are already on ART and diagnosed subsequently with TB may need a change in ART regimen while starting on anti-TB drugs. Close consultation between STD clinic and DCC should take place when such a situation arises.

10.1.7 Isoniazid prophylactic treatment (IPT)

In the case of HIV infection without active TB, IPT is recommended in the following:

- All HIV infected adult /children who are close contacts of smear positive TB patients
- HIV infected Adults/ children with a tuberculin test > 5mm

Isoniazid 5mg/kg in adults and 10 mg/kg in children with a maximum of 300mg per day for 6 months is recommended for preventive TB treatment. This should be commenced after carefully excluding active TB.

IPT is not recommended for HIV infected who do not belong to above categories. They should be monitored closely and if symptoms develop at any time after the initial screening, they should be reinvestigated to exclude active TB.

10.1.8 TB treatment and anti-retroviral therapy (ART)

As mentioned in section 8.1.3, HIV infected patients with active tuberculosis should be commenced on tuberculosis treatment immediately. ART should be started in all TB patients living with HIV regardless of CD4 count. TB treatment should be initiated first, followed by ART as soon as possible but within the first 8 weeks of treatment. HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm³) should receive ART within the first two weeks of initiating TB treatment. ART should be started in any child with active TB disease as soon as possible but within eight weeks following the initiation of anti-tuberculosis treatment regardless of the CD4 count.

Rifampicin stimulates the activity of cytochrome P450 that metabolizes protease inhibitors (PI) e.g. saquinavir, ritonavir, indinavir, nelfinavir, amprenavir) and non-nucleoside reverse transcriptase inhibitors (NNRTI), except efavirenz (EFV). PIs and NNRTIs also enhance or inhibit the same enzyme system and this may result in altered blood levels of rifampicin and the anti-retrovirals resulting in ineffectiveness of both. The preferred ART regimen is Tenofovir + Lamivudine or Emtricitabine + Efavirenz (TDF + 3TC (or FTC) + EFV). In case of suspected drug interaction or a special situation, the case should be jointly reviewed by TB and HIV programmes.

10.1.9 Linkages between TB and HIV programmes

In view of the close association between TB and HIV, both fuelling each other, it is imperative that the two programmes should be linked for certain activities. Efforts are being strengthened in the following components:

- Joint trainings on TB and HIV
- Intensified TB detection amongst HIV patients
- HIV detection amongst TB patients
- Joint monitoring and supervision of the programmes

To strengthen collaborations, the following activities will be undertaken

- Joint review of the programmes at National and sub-national level every quarter
- TB training modules will have a section on TB-HIV co-infection and vice-versa. The training on relevant section will be held in coordination with both programmes
- Both programme will plan joint supervisory visits, at least once a year from the national level and at least twice a year at district level

10.2 Tuberculosis and diabetes

Patients with diabetes are more vulnerable to develop TB. TB and diabetes comorbidity make each other worse. Studies have shown that there is increased morbidity and mortality in patients who have TB diabetes co-morbidity. Therefore early diagnosis of TB in diabetics, exclusion of diabetes and proper control of diabetes in patients with TB is important to improve outcome of TB treatment.

Treatment of TB is as same as for non-diabetics. It is important to assess renal function and patients with renal function impairment should be managed as described below.

10.3 Tuberculosis and liver disease

This section covers TB treatment in patients with pre-existing liver disease. For detection and management of TB drug induced hepatitis, refer chapter 7.

LFT (serum bilirubin, ALT) should be done on all patients with a history of liver disease (includes patients who abuse alcohol, carriers of hepatitis virus, past history of acute/chronic hepatitis, alcoholic/non-alcoholic cirrhosis and fatty liver) prior to commencement of ATT. Patients can receive the usual TB regimens provided there is no clinical and bio chemical evidence of liver function impairment. However, hepatotoxicity to anti-tuberculosis drugs may be more common among these patients and should therefore be anticipated.

If pre-treatment serum bilirubin and ALT are abnormal, such patients should be managed as per guidelines for anti TB drug induced hepatotoxicity (See chapter 7)

10.4 Tuberculosis and renal insufficiency

The recommended initial TB treatment regimen for patients with renal failure or severe renal insufficiency is two months of isoniazid, rifampicin, pyrazinamide and ethambutol, followed by 4 months of isoniazid and rifampicin. Isoniazid and rifampicin are eliminated by biliary excretion, so no change in dosing is necessary. Ethambutol and metabolites of pyrazinamide have significant renal excretion and thus, dosing adjustments are required. Three times per week administration of these two drugs at the following doses is recommended: pyrazinamide (25mg/kg), and ethambutol (15 mg/kg) specifically in late stages of renal disease (Stage 4 and Stage 5). While receiving isoniazid, patients with severe renal insufficiency or failure should receive pyridoxine in order to prevent peripheral neuropathy.

Because of an increased risk of nephrotoxicity and ototoxicity, streptomycin should be avoided in patients with renal failure. If streptomycin is essential to use, the recommended dosage is 15 mg/kg, two or three times per week, with a maximum of 1 g per dose. Ideally, serum levels of streptomycin should be monitored during treatment.

Treatment can be given immediately after haemodialysis to avoid premature drug removal. With this strategy there is a possible risk of raised drug levels of ethambutol and pyrazinamide between dialysis sessions. Alternatively, treatment can be given 4–6 h before dialysis, increasing the possibility of premature drug removal but reducing possible ethambutol or pyrazinamide toxicity. The choice of strategy may be influenced by a need to ensure adherence (when post dialysis offers the opportunity for directly observed therapy), practical issues (post dialysis for morning shift patients) and expected pharmacokinetics or drug interactions.

Rifampicin in particular can interact with immunosuppressive regimens, increasing the chance of graft rejection, and doses of mycophenolatemofetil, tacrolimus and cyclosporine may need adjustment. Corticosteroid doses should be doubled in patients receiving rifampicin.

10.5 Important drug interactions

Many TB patients have concomitant illnesses. At the start of TB treatment, all patients should be asked about medicines they are currently taking. The most important interactions with anti-TB drugs are due to rifampicin. Rifampicin induces pathways that metabolize other drugs, thereby decreasing the concentration and effect of the other drugs. To maintain a therapeutic effect, dosages of the other drug may need to be increased. When rifampicin is discontinued, its metabolism-inducing effect resolves within about two weeks, and dosages of the other drug will need to be decreased again.

10.5.1 Commonly used drugs affected by rifampicin

Rifampicin substantially decreases the concentrations of certain drugs. They are:

- antimicrobials
 - antibacterials – clarithromycin, doxycycline, chloramphenicol, linezolid.
 - antifungals – fluconazole, itraconazole, ketoconazole
 - antiretrovirals
- hormones – oestrogens progestogens, levothyroxine
- corticosteroids
- tamoxifen
- methadone
- anticoagulants – warfarin, apixaban, rivaroxaban
- immuno suppressives – cyclosporin, mycophenolate, tacrolimus
- anticonvulsants – carbamazepine, phenytoin

- cardiovascular agents - digoxin, calcium channel blockers (verapamil, nifedipine, diltiazem), beta blockers (propranolol, metoprolol)
- theophylline
- hypoglycaemics – sulfonylureas
- lipid lowering drugs – atorvastatin, simvastatin
- antipsychotics – haloperidol
- anxiolytics – benzodiazepines
- cytotoxics – gefitinib, imatinib
- bosentan

11. Drug-Resistant Tuberculosis

For additional details, the reader is advised to refer Programmatic Management of Drug Resistant TB in Sri Lanka

11.1 Background information

Multi Drug Resistant Tuberculosis (MDR-TB), which is defined as resistance to both isoniazid and rifampicin, is emerging as a major threat to global tuberculosis control. According to the 2015 Global Report on TB⁸, an estimated 480 000 people developed multidrug-resistant TB (MDR-TB) and an estimated 190 000 deaths from MDR-TB occurred globally in 2014. If all TB cases notified in 2014 had been tested for drug resistance, an estimated 300 000 would have been found to have MDR-TB. Thirty countries in the world have been identified as high burden countries for MDR - TB. The highest levels of MDR-TB were found in Eastern Europe and Central Asia. .

The current recommendation using first line drug combinations and the regimen (H, R, Z, E) are ineffective in drug resistant TB specifically the RR/MDR-TB which implies that MDR-TB strains would continue to be transmitted and in areas of high transmission such strains may lead to epidemics (hot spots) of MDR-TB. Hence, special strategies are required in addition to the usual TB control strategy and this community based strategy is now referred to as 'Programmatic Management of Drug Resistant TB (PMDT)'.

A new threat to TB control is emerging in the form of extensively drug resistant TB (XDR-TB) defined as resistance to Isoniazid and Rifampicin along with resistance to any of the quinolones and one of the second line injectable anti-TB drugs. XDR-TB has been identified in 105 countries. The average proportion of MDR-TB cases with XDR-TB is 9.6%. Strains of XDR-TB are readily transmissible and outbreaks have been reported. HIV-TB co-infection compounds the problem. Therefore, there is an urgent need to strengthen NTP to prevent the emergence of MDR/ XDR-TB cases.

Prevalence of MDR-TB is not available on a countrywide basis. Sri Lanka had undertaken a *Mycobacterium tuberculosis* drug resistance survey in 2005-2006 amongst 1036 patients enrolled for treatment at all chest clinics (905 newly diagnosed and 93 previously treated cases). Culture positivity was 57.4% (62% for new and 36.6% for previously treated cases). The drug resistance to any drug was 1.4% in new and 8.8% for previously treated cases. Only one case (1/595) was reported to have MDR-TB.

The country has developed the guidelines and the manual for the Programmatic Management of DR-TB. The framework for management presented in these guidelines is integrated into the basic TB control strategy of NTP as MDR-TB prevention and control is an integral part of the Sri Lankan TB control programme.

⁸Global tuberculosis report 2015, World Health Organization, Geneva 2015. ISBN 978 92 4 156505 9

Management of MDR-TB is integrated PMDT programme into the basic TB control strategy of NTP as MDR-TB prevention and control is an integral part of the national TB control programme. The five essential components of the framework approach for MDR-TB management that are integrated into the national TB control programme in Sri Lanka are described below.

TB control framework as applied to the drug-resistant TB – PMDT Strategy:

- Sustained political and administrative commitment
- Appropriate case-finding and diagnosis strategy using quality assured rapid molecular tests and, culture and drug susceptibility testing (DST)
- Appropriate treatment strategies that use second-line drugs under proper case management conditions in alignment with globally accepted standards.
- Uninterrupted supply of quality assured second-line anti-TB drugs
- Recording and reporting system designed for MDR-TB control programme that enables performance monitoring and evaluation of treatment outcomes

Sustained political and administrative commitment

- ❖ Essential to establish and maintain other four components
- ❖ Administrative support for National Tuberculosis Programme to implement effective TB control policies
- ❖ Address the factors leading to the emergence of drug resistance
- ❖ Long term investment of staff and resources
- ❖ Coordination between government institutions, local and international agencies, and non-governmental sector
- ❖ Long term financial support
- ❖ Central level and provincial level commitment

Appropriate case finding and diagnosis strategy using quality assured rapid molecular tests and, culture and drug susceptibility testing (DST)

- ❖ Rational triage of patients for testing drug resistance
- ❖ Appropriate use of WHO endorsed rapid tests as well as Quality assured culture and DST with internal quality control and external quality assurance
- ❖ Close relationship with supranational TB reference laboratory for proficiency testing
- ❖ Linking of all sectors treating TB patients

Appropriate treatment strategies that use second-line drugs under proper case management conditions in alignment with globally accepted standards

- ❖ Rational treatment design

- ❖ Ensure DOT throughout the whole treatment duration
- ❖ Active monitoring and management of adverse effects
- ❖ Properly trained human resources
- ❖ Treatment adherence through patient centric approach and psycho- social support

Uninterrupted supply of quality assured second-line anti-TB drugs

- ❖ Ensure availability of quality assured second-line drugs without interruptions
- ❖ Drug management should take into consideration the short shelf life of second-line drugs and the storage conditions required to maintain proper shelf life
- ❖ Procurement process must take into account the limited suppliers of quality assured second-line drugs
- ❖ Strengthening the inventory management capacity at sub national level

Recording and reporting system designed to enable the performance monitoring and evaluation of treatment outcomes

- ❖ Effective recording and reporting system
- ❖ Documentation of laboratory results
- ❖ Monitoring treatment delivery and treatment response for the whole duration of treatment
- ❖ Introduction of electronic recording and reporting system
- ❖ Effective functioning of PMDT committee at national level and the PMDT implementing sites for regular review of performance.

11.2 Definitions and classifications

This section describes types of drug resistance, bacteriological definitions for drug resistance, case definitions, patient registration categories, treatment outcome definitions which are important in cohort analysis procedures for MDR-TB patients who are treated under PMDT strategy.

11.2.1 Types of drug resistance

- **Drug resistance among previously treated cases (acquired resistance)** is that found in a patient who has previously received at least one month of anti-TB therapy. Inadequate dosage or duration/erratic treatment and /or treatment with substandard drugs lead to proliferation of drug resistant organisms or acquisition of drug resistance by organisms which are previously sensitive.
- **Drug resistance among new cases (primary resistance)** is the presence of resistant strains of *M. tuberculosis* in a newly diagnosed TB patient who has never received anti-TB drugs or has received for a period less than one month. This means that the patient has been infected with organisms which are already drug resistant, likely from exposure to a person who harbours drug resistant bacillus.

- **Wild type resistance.** In a colony of *M. tuberculosis* there can be few organisms which are resistant to a given anti-TB drug not because of previous exposure to that drug but due to spontaneous genetic mutations. Such drug resistance is known as wild type resistance. When anti-TB drugs are used in combination, the organisms which are wildly resistant to one drug are killed by another drug in the combination. Monotherapy leads to selection of drug resistant organisms and their proliferation.

11.2.2 Causes of drug resistance

MDR-TB/other types of DR TB is entirely a man-made phenomenon and is an indicator of poor management of TB patients by the entire health system. The common causes of DR-TB are:

Service factors

- Prescribing incorrect chemotherapy (wrong combination of drugs, dosages and duration).
- Failure to ensure a regular and uninterrupted drug supply.
- Poor case management – incomplete and irregular treatment, where patients are not directly observed taking their drugs.
- Use of drugs of unproven bioavailability/unsure quality.
- Adding one new drug at a time to a failing (or failed) anti-TB drug regimen.
- Inappropriate treatment regimen in patient with history of previous TB treatment including irrational use of second line drugs (SLD).
- Not referring TB patients to the state health sector for treatment and patients being forced to purchase drugs which they cannot afford.
- Regular services not being accessible in terms of distance or timing of operation
- Failure to educate patient and the family about the disease, treatment approach and failure to stress the importance of adhering to treatment throughout the prescribed period

Patient factors

- Not taking the full prescribed number of drugs.
- Taking lesser than the prescribed dose.
- Taking drugs irregularly or discontinuing treatment before the prescribed period.
- Adverse effects to anti-TB drugs
- Social, psychological and economic barriers preventing proper treatment
- Malabsorption or other concomitant illness
- Alcoholism and substance abuse leading to non-adherence
- Lack of family support.
- Lack of knowledge about the disease and its treatment

11.2.3 Significance of MDR-TB

- Commonly used first-line anti-TB drugs are no longer effective.
- MDR-TB is more difficult to treat and it requires treatment with ‘reserve’ or second-line anti-TB drugs which are not as potent as first-line drugs (FLD) and have to be given for at least twenty months.
- These drugs are very toxic to the patients and sometimes have severe adverse reactions (ADR).
- The reserve drugs are more expensive than the standard first-line drugs.
- The results of treatment are poor and the mortality rate is high.

11.2.4 General definitions of resistance

- **Mono-resistance:** TB in a patient, whose infecting isolates of *M. tuberculosis* are resistant in vitro to one of first line anti-tuberculosis drug.
- **Poly-resistance:** TB in a patient, whose infecting isolates of *M. tuberculosis* are resistant in vitro to more than one first-line anti-tuberculosis drug, other than to both isoniazid and rifampicin.
- **Multi Drug Resistant TB (MDR-TB):** Tuberculosis in a patient, whose infecting isolates are resistant in vitro to both isoniazid and rifampicin with or without resistance to other first-line drugs.
- **Extensively Drug Resistant (XDR-TB):** TB in a patient, whose infecting isolates of *M. tuberculosis* are resistant in vitro to both rifampicin and isoniazid along with resistance to any quinolone and one of the second-line injectable anti-TB drugs.
- **Rifampicin resistance (RR):** Resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti TB drugs. This includes any resistance to rifampicin in the form of mono-resistance, poly-resistance, MDR or XDR

11.2.5 Classification according to the site affected

11.2.5.1 Pulmonary Tuberculosis

Pulmonary tuberculosis (PTB) is TB involving the lung parenchyma. A patient with both pulmonary and extrapulmonary TB will be classified as pulmonary TB. Miliary TB is classified as pulmonary TB because there are lesions in the lung parenchyma as well.

11.2.5.2 Extrapulmonary Tuberculosis

TB of organs other than the lung paranchyma and tracheobronchial tree.

11.2.6 Classification based on history of previous anti-TB treatment

Each RR/ MDR-TB patient commenced on second-line drug regimen should be classified in two different ways:

Classification according to history of previous drug use, mainly to assign the appropriate treatment regimen

- **New:** A patient who has received no or less than one month of anti-TB treatment. Patients are placed in this group if they had sputum collected for DST at the start of a new treatment regimen with first line drugs (FLD) and were then switched to a Second line treatment regimen because MDR-TB was later confirmed. They should be considered “new” if DST was performed within one month of the start of treatment (even if they had received more than one month of new treatment regimen with FLD by the time the results of DST returned and they were started with second line treatment).
- **Previously treated with FLD only:** A patient who has been treated for one month or more for TB with only first-line drugs.
- **Previously treated with SLD:** A patient who has been treated for one month or more for TB with one or more SLD, with or without FLD.

Classification according to the history of their previous treatment (Commonly referred to as patient’s “registration group”)

The registration groups are the established groups used in the DOTS recording and reporting system, with additional sub grouping of patients treated after failure.

The groups are as follows:

- **New:** (Same definition as in classification according to previous drug use). A patient who has received no or less than one month of anti-TB treatment.
- **Relapse:** A patient whose most recent treatment outcome was “cured” or “treatment completed”, and who is subsequently diagnosed with bacteriologically positive TB by sputum smear microscopy, molecular tests or culture.
- **Treatment after loss to follow-up:** A patient who had previously been treated for TB and was declared ‘Lost to follow-up’ at the end of the most recent course of treatment. (This was previously known as treatment after default.).
- **Treatment after failure of first line regimen for new cases:** A patient who has received treatment for TB (with first line drugs for a new case) and in whom treatment has failed. Failure is defined as sputum smear positive at five months or later during treatment.
- **Treatment after failure first line regimen for retreatment cases:** A patient who has received retreatment for TB with first line drugs and in whom treatment has failed. Failure is defined as sputum smear positive at five months or later during treatment.
- **Other previously treated:** A previously treated TB patient whose outcome after the most recent course of treatment is unknown or undocumented

Patients placed on second-line anti-TB medications usually belong to one of the following groups:

- Confirmed RR-TB or MDR-TB.
- Presumptive RR-TB or MDR-TB. Patients may be registered and started on second-line anti-TB treatment on the basis of significant risk for drug resistance and before laboratory confirmation of resistance, or on the basis of a rapid molecular result. All attempts should be made to confirm microbiologically the status of resistance in such cases at the earliest possible.
- Poly-/mono-resistant TB without rifampicin resistance. Some of these cases may have second-line anti-TB drugs added to their treatment.
- XDR-TB (confirmed or presumptive). Patients may be started on XDR-TB treatment on the basis of a laboratory diagnosis or, in its absence, because of significant risk.

11.2.7 Treatment outcome definitions of MDR-TB patients

Sputum culture conversion is defined as two sets of consecutive negative cultures taken 30 days apart. The specimen collection date of the first negative Culture is used as the date of conversion.

- **Cured:** An MDR-TB patient who has completed treatment according to the programme protocol and has at least three or more consecutive negative cultures from samples collected at least 30 days apart in the final 12 months of treatment. If only one positive culture is reported during that time, and there is no concomitant clinical evidence of deterioration, a patient will be considered cured, only if this positive culture is followed by a minimum of three consecutive negative cultures taken at least 30 days apart.
- **Treatment completed:** An MDR-TB patient who has completed treatment according to the programme protocol but does not meet the definition for cure because of lack of bacteriological results; i.e. fewer than three or more cultures were performed in the final 12 months of treatment.
- **Died:** An MDR-TB patient who dies for any reason during the course of MDR-TB treatment.
- **Failed:** Treatment will be considered to have failed if treatment is terminated or need for permanent regimen change of at least two anti-TB drugs because of
 - Lack of conversion by the end of the intensive phase or
 - Bacteriological reversion⁹ in the continuation phase after conversion to negative; or

⁹Culture is considered to have reverted to positive when, after an initial conversion, two consecutive cultures, taken at least 30 days apart, are found to be positive. For the purpose of defining Treatment failure, reversion is considered only when it occurs in the continuation phase. Only single culture positive with improving clinical picture may be due to errors.

- Evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs; or
 - Adverse drug reactions.
- **Lost to follow-up:** A patient on second line drugs whose treatment was interrupted for two or more consecutive months for any reason.
 - **Not evaluated:** A patient for whom no treatment outcome is assigned due to any reason.
 - **Treatment success:** The sum of Cured and Treatment completed.

11.3 Strategies for case finding and diagnosis of DR-TB

The diagnosis of DR-TB is essentially laboratory based. Therefore quality assured laboratory plays a key role in the management of DR-TB patients. This chapter describes identification of probable MDR-TB patients, bacteriological tests that will be used in confirming the diagnosis of MDR-TB.

11.3.1 Strategy for case finding of DR-TB patients

The first step in case finding begins with identification of presumptive DR-TB cases. DR-TB should be suspected in the following categories of patients and their sputum should be sent for rapid molecular tests Xpert MTB/RIF (GeneXpert), and culture and DST in order of priority.

Category A¹⁰: High risk cases for drug resistance

- a. Symptomatic contacts of MDR-TB patients or those asymptomatic contacts screened with chest X-ray and found to have changes suggestive of TB
- b. First line regimen failures and non-converters/ delayed sputum conversion
Patients who continue to remain sputum smear positive after 3 months of retreatment with FLD or failures of retreatment with FLD Patients who continue to remain sputum smear positive after 2 months of new treatment regimen with FLD or failures of new treatment regimen with FLD
- c. Patients with history of repeated treatment interruptions
- d. All other previously treated TB patients

Category B: Patients with moderate or low risk of drug resistance but in whom the risk of mortality or chance of spread of resistant bacillus to contacts is high

- e. Patients with TB/HIV co-infection,
- f. Institutionalized patients e.g.: prisoners
- g. Drug addicts
- h. Healthcare workers

¹⁰The categorisation of risk cases is temporary and only for prioritisation for using Xpert MTB/RIF (GeneXpert) tests. The categories will be used only till such time the country has enough capacity to test all cases at risk of drug resistance

- i. Those who return from abroad with active TB.
- j. TB patients treated outside the NTP.

In some cases classified as low risk, clinical judgement would have to be used to determine if they could be high risk e.g. a health care worker working in a facility where MDR-TB is being treated will be considered high risk for drug-resistance.

Xpert MTB/RIF (GeneXpert) tests will also be used in addition to AFB culture when adequate and suitable samples are sent from smear negative patients (including paediatric cases) and extrapulmonary cases (except pleural fluid which is considered sub-optimal sample. The current WHO recommendations also do not cover blood, stool or urine samples). However this testing policy comes into effect from 2016, when additional machines are available and installed. Till such time, priority is being given to high risk DR-TB cases.

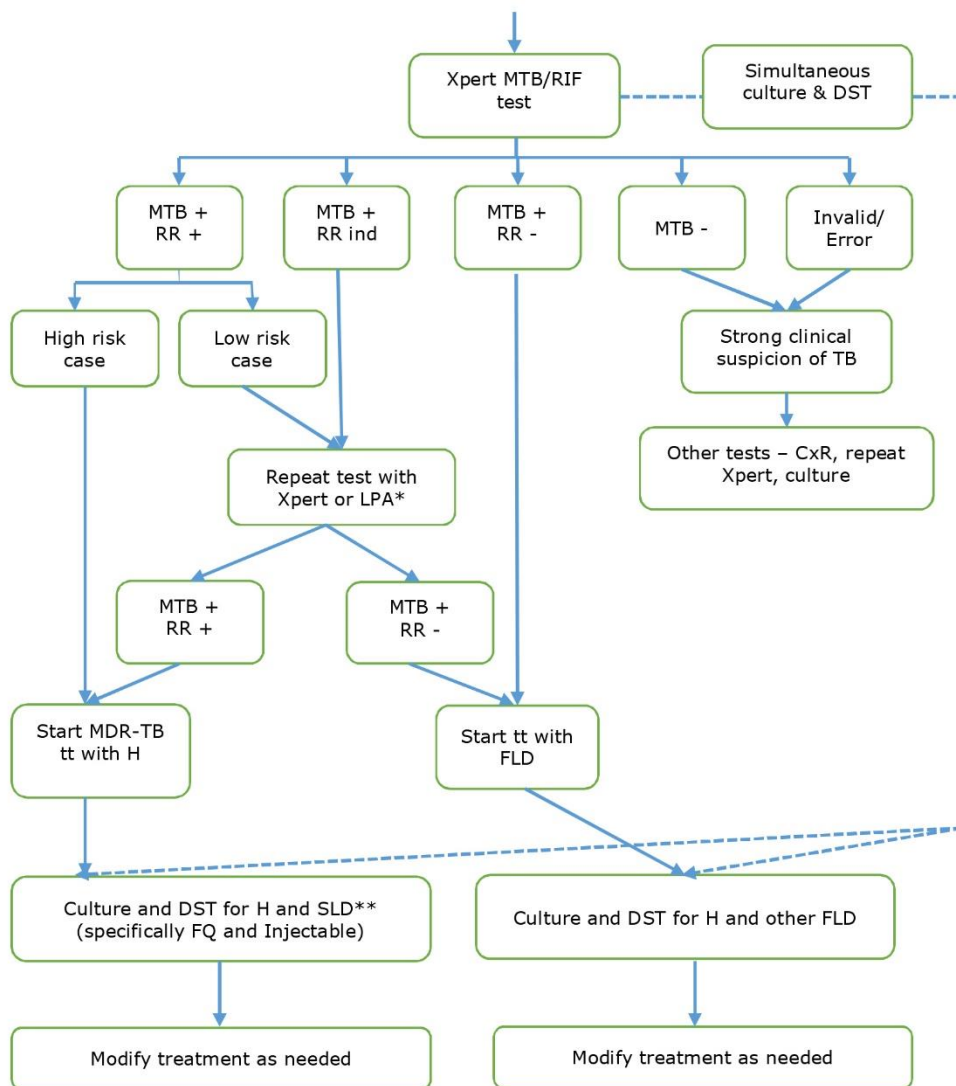
From presumptive DR-TB cases, collect two sputum specimens in sterile universal bottles. One sample should be sent to the nearest facility where Xpert MTB/RIF (GeneXpert) test is available (NTRL at Welisara for now and from 2017 other facilities). The other sample should be sent to the nearest culture facility which could be NTRL at Welisara or a Intermediate Tuberculosis Laboratory. Such specimens can originate from the DCCs, other government health institutions or the private sector health institutions. Patients will be continued on first line treatment till the Xpert MTB/RIF, LPA (results of which will be ready early if done) and DST results of culture are available. If the sample is found to be contaminated, the sender should be informed by the laboratory to send two further sputum specimens. DST results indicating RR/ MDR-TB should be sent as soon as possible to the sender, the DTCCO of the relevant district and to the PMDT Coordinator. Results should be communicated over the telephone which should be followed by a written report by post and by e-mail.

Sputum collection and transport system

At all DCCs a **Register of Referral for bacteriological examination** from which presumptive DR-TB patients can be identified should be maintained. Patients will be advised to provide 2 sputum samples (preferably consecutive early morning sputum samples). The specimens will be collected in sterile universal bottles and transported to the laboratory, as above, through a messenger with a request form for bacteriological examination.

Other government health institutions and private sector health institutions are also free to send samples for bacteriological examination on presumptive MDR-TB patients. However, in such situations it is advisable to send such samples through the respective DCC or with a copy of request form being shared with respective DCC.

High risk^{\$} cases – Priority till such time there is only one GeneXpert machine in the country. Other groups will have culture and DST on liquid or solid culture
 Moderate or low risk cases – To be included when there are at least three functioning machines in the country
 When there are five functioning machines then all smear negative (including paediatric cases) as well as eligible EP cases will be screened



MTB – Mycobacterium tuberculosis; RR – Rifampicin resistance; FLD – First line drugs; DST – Drug susceptibility testing; tt – treatment; MDR – Multi drug resistance; FQ – fluoroquinolones; H - Isoniazid

^{\$} as defined in PMDT guidelines

* Depending on the availability, either of the two tests may be used on a fresh sample of the sputum

** Till such time SL DST is available in the country, the samples will be sent to SNRL

Figure 11-1 Algorithm for detection of DR-TB using molecular diagnostic techniques

Procedures for bacteriological examination

Xpert MTB/RIF (GeneXpert) tests will be done at the respective centres for detecting TB as well as resistance to rifampicin. It is expected that the results of test will be available within 2 days of receiving the sputum sample at the laboratory.

Cultures will be done at NTRL or Intermediate Tuberculosis Laboratories. The DST will be done only at NTRL. All procedures of smear, molecular testing, culture and DST of these presumptive cases should be handled with appropriate bio-safety measures.

Smear microscopy will be done on sputum samples and reported with grading.

The country policy as of now recommends that the Xpert MTB/RIF (GeneXpert) test needs to be backed up with Culture and DST test.

11.4 Treatment of MDR-TB

Any patient in whom drug-resistant TB is diagnosed and treatment indicated with second-line drugs will need carefully formulated regimens. This section describes the standardized approach to treat patients with MDR-TB, the rationale and the role of counselling in ensuring patient compliance while on treatment. Standard treatment regimen for MDR-TB should always be backed up by the DST results.

If a case is found to be Rifampicin resistant using Xpert MTB/RIF (GeneXpert) test among any of the high risk categories (Close contact of MDR-TB, treatment failure of new or retreatment,, non-converters of first line treatment or a case of repeated treatment interruption of first line drugs), such cases will be immediately started on second line treatment including isoniazid while waiting for results of DST. However if a case from low risk category is found to be RR on Xpert MTB/RIF (GeneXpert), then the clinician may decide to get another test done on Xpert MTB/RIF (GeneXpert) or LPA using another sputum sample. Upon confirmed diagnosis of RR/ MDR-TB, patients are admitted to NHRD or another designated treatment centre (it is planned that there will be at least 2-3 additional treatment centres for initiation of treatment in future) for the initiation of treatment. NHRD and all such facilities will have an isolation ward with proper infection control measures in place for treatment of MDR-TB patients.

Patients are registered in the RR/ MDR-TB register maintained by the PMDT Coordinator and a MDR-TB number is given. The same number is allotted to the patient throughout treatment. Patients are commenced on a standardized regimen of second line anti-TB drugs. On completion of inward phase, patients are referred to respective DCC for continuation of remaining treatment. The treatment should be directly observed for the whole duration of treatment.

11.4.1 Referral for MDR-TB management

The DTCO will trace the MDR-TB patient and after counselling, refer to NHRD or to the nearest treatment initiation centre. A copy of the TB treatment card, DST result and Second line Referral for Treatment form should be sent with the patient. Patient referred to the MDR-TB treatment initiation centre will be admitted to the hospital and the Consultant Respiratory Physician and the PMDT Coordinator are informed regarding the admission. The DTCO will also send a copy of the request for MDR-TB treatment by post

to the PMDT Coordinator. The PMDT Coordinator informs the DTCCO about receipt of patient and treatment initiation in ward.

11.4.2 Pre-treatment evaluation

All confirmed MDR-TB patients will be subjected to pre-treatment evaluation prior to start of the second line treatment regimen. Pre-treatment evaluation will include a thorough clinical evaluation by a physician, chest radiograph, and relevant haematological and bio-chemical tests.

Since the drugs used for the treatment of MDR-TB are known to produce adverse effects, a proper pre-treatment evaluation is essential to

- a) Identify already existing co morbidities
- b) Have baseline levels of screening parameters for future reference.
- c) Identify patients who are at increased risk of developing such adverse effects

These include screening for diabetes mellitus, liver disease, drug or alcohol abuse, mental illness, renal insufficiency, thyroid function, pregnancy and lactation. All presumptive DR-TB cases will be offered HIV counselling and testing. If not tested for HIV already, all patients on MDR-TB treatment should be counselled and tested for HIV. If they are found to be HIV positive, then they are referred for further counselling, ART and CD4 counts.

Management of patients with any of these conditions is likely to vary from the standard practice depending on the condition and may require more intense monitoring.

11.4.3 Treatment regimen

The basic principle in the treatment of MDR-TB is to give at least four drugs to which the organisms are most likely to be susceptible (drugs which have not been used on that patient before) along with Pyrazinamide. While there could be many possible regimens for MDR-TB, all fall into two broad groups:

- (a) **Standardized treatment regimen (STR)** - Drug resistant survey (DRS) data from representative patient populations are used to base the regimen design in the absence of individual DST. All patients with a confirmed diagnosis receive the same regimen in the beginning unless there is a known hypersensitivity to any of the second-line drugs.
- (b) **Individualized treatment regimen (ITR)** - The treatment regimen is individualized for each patient depending upon the second-line drug sensitivity profile. To start with, patients are started on standardised regimen and subsequently this is modified when DST results for second line drugs are available.

11.4.3.1 MDR-TB treatment regimen for Sri Lanka

DST to second line drugs is not currently available in Sri Lanka. Therefore, NTP of Sri Lanka will be using a standardized treatment regimen for the treatment of MDR-TB cases under the programme. Standardized regimens are simpler to operate, to order drugs and easy for the health workers to understand and apply DOT.

11.4.4 Classes of anti-tuberculosis drugs

The classes of anti-tuberculosis drugs have traditionally been divided into first and second-line drugs, with isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin being the first-line drugs. An alternative method of grouping the anti-TB drugs has been suggested by WHO as given in the Table 11.1 below.

Table 11-1 Grouping anti-tuberculosis drugs

| Group | Description | Drug | Abbreviation |
|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|--------------|
| 1 | First-line oral anti-TB drugs | Isoniazid | H |
| | | Rifampicin | R |
| | | Ethambutol | E |
| | | Pyrazinamide | Z |
| | | Rifabutin | Rfb |
| | | Rifapentine | Rpt |
| 2 | Injectable anti-TB drugs (injectable agents or parenteral agents) | Streptomycin | S |
| | | Kanamycin | Km |
| | | Amikacin | Am |
| | | Capreomycin | Cm |
| 3 | Fluoroquinolones (FQs) | Levofloxacin | Lfx |
| | | Moxifloxacin | Mfx |
| | | Gatifloxacin | Gfx |
| | | Ofloxacin | Ofx |
| 4 | Oral bacteriostatic second-line anti-TB drugs | Ethionamide | Eto |
| | | Prothionamide | Pto |
| | | Cycloserine | Cs |
| | | Terizidone | Trd |
| | | p-aminosalicylic acid | PAS |
| | | p-a inosalicylate sodium | PAS-Na |
| 5 | Anti-TB drugs with limited data on efficacy and/or long-term safety in the treatment of drug-resistant TB (This group includes new anti-TB agents) | Bedaquiline | Bdq |
| | | Delamanid | Dlm |
| | | Linezolid | Lzd |
| | | Clofazimine | Cfz |
| | | Amoxicillin/Clavulanate | Amx/Clv |
| | | Imipenem/Cilastatin | Ipm/Cln |
| | | Meropenem | Mpm |
| | | High-dose isoniazid | High dose H |
| | | Thioacetazone | T |
| Clarithromycin | Clr | | |

11.4.5 Regimen design

The following basic principles are involved in designing the regimen.

- Detailed history of anti-TB drugs taken by the patient in the past should be taken.
- Drugs and regimens commonly used in the country and the prevalence of resistance to first-line drugs should be taken into consideration.
- Regimens should consist of at least four second line drugs which are likely to be effective (including an injectable agent).
- Pyrazinamide should be added in spite of its previous use during the intensive phase of treatment and can be extended for the entire treatment duration if it is judged to be effective. Sensitivity to pyrazinamide is not currently available in the NTRL and many MDR-TB patients have chronically inflamed lungs, which theoretically produce the acidic environment where pyrazinamide remains active. Furthermore it is said that *M. tuberculosis* cannot acquire resistance to pyrazinamide easily.
- Where DST shows sensitivity to ethambutol, it should be added. However streptomycin should be replaced with kanamycin or amikacin even if DST shows sensitivity to streptomycin.
- Oral drugs are administered for seven days a week throughout the treatment duration while injectables will be administered six days in a week during the intensive phase. All drugs should be given in a single dose. In the event of patient is not tolerating all drugs as a single dose, the dosage may be split and given twice-a-day for ethionamide, cycloserine and PAS.
- The drug dosage should be determined by body weight.
- The total duration of treatment is at least 20 months.
- An injectable agent (an aminoglycoside or capreomycin) is used for a minimum of 8 months and 4 months after culture conversion (intensive phase) whichever is longer.
- Treatment should be continued for at least 12 months after culture conversion (conversion is defined as two consecutive sputum samples taken 30 days apart are negative for direct smear and culture. Of the two consecutive negative samples the date of collection of the first sample is taken as the date of conversion).
- Each dose is administered as DOT throughout the treatment. A treatment card is marked for each observed dose
- Early MDR-TB detection and prompt initiation of treatment are important factors in achieving successful outcomes.

Standardized treatment regimen (STR) used in Sri Lanka

Intensive phase At least 8 Km + Lfx + Eto + Cs + Z +/- E

Continuation phase At least 12 Lfx + Eto + Cs + Z / +-E

Km-Kanamycin; Cs- Cycloserine; E-Ethambutol; Lfx- Levofloxacin; Eto- Ethionamide; Z- Pyrazinamide

Cm and NaPAS will be kept as reserve drugs to be used in the event of intolerance to any of the drugs used in the regimen. Generally reserves drugs would be made available at Central level for 10% of cases expected to be on treatment.

11.4.5.1 Drug dosages and administration

Drug dosages for MDR-TB cases are decided according to the weight band as recommended in the 2015 Companion Handbook to the WHO guidelines for programmatic management of drug-resistant tuberculosis (WHO, 2015). Monthly monitoring of weight and changing dose to the next weight band according to the weight gain is necessary.

All the oral drugs will be given in a single daily dosage on all 7 days of the week throughout the treatment while injectables will be given six days a week during the intensive phase. If intolerance occurs to ethionamide, cycloserine and/or PAS, these may be split into two dosages and the morning dose is administered as DOT. The evening dose will be self-administered. The empty strip of the self-administered dose will be checked the next morning during DOT. Pyridoxine (vitamin B6) at a dose of 50 mg for every 250 mg of cycloserine should be administered to all patients on MDR-TB regimen.

11.4.6 XDR-TB regimen

As per the Companion Handbook to WHO guidelines for PMDT, there is very limited data on the different clinical approaches to XDR-TB. Analysis of available data did indicate that treatment success in XDR-TB patients was highest if at least six drugs were used in the intensive phase and four in the continuation phase. The following steps are recommended for constitution of an XDR-TB regimen:

- Use pyrazinamide and any other Group 1 agent that may be effective.
- Use an injectable agent to which the strain is susceptible and consider an extended duration of use. If resistant to all injectable agents consider designing the regimen with an injectable agent that the patient has never used before or consider designing the regimen without an injectable agent.
- Use a higher-generation fluoroquinolone such as moxifloxacin or gatifloxacin.
- Use all Group 4 agents that have not been used extensively in a previous regimen or any that are likely to be effective.
- Add two or more Group 5 drugs (consider adding bedaquiline or delamanid).

In the absence of second line DRS and based on the current recommended MDR-TB regimen, the following regimen will be used for diagnosed or presumed MDR-TB cases:

- Intensive phase 12 Z+Cm+Mfx+Cfz+Lzd+NaPAS+Amx/Clv
- Continuation phase 12 Z+Mfx+Cfz+Lzd+Amx/Clv

Z – Pyrazinamide; Cm – Capreomycin; Mfx – Moxifloxacin; Cfz - Clofazimine; Lzd – Linezolid; PAS – Para-amino Salicylic acid; Amx/ Clv - Amoxicillin/Clavulanate

It is expected that the programme may need XDR-TB regimen for 1-2 patients annually.

11.4.7 Treatment of MDR-TB under special situations

The management of drug-resistant TB in special conditions and situations such as pregnancy and breastfeeding, children with MDR-TB and people with co-morbid conditions such as diabetes, renal insufficiency, liver disorders, substance dependence, seizures and psychiatric disorders has been extensively dealt with in the Manual on Programmatic Management of MDR-TB.

11.4.8 Management of contacts of MDR-TB

Close contacts of MDR-TB patients should receive careful clinical follow-up for a period of at least two years. Symptom screening is done for all contacts initially, and at 6-monthly intervals for at least 24 months. If symptomatic, the diagnostic algorithm for symptomatics is followed irrespective of the duration of symptoms. If diagnosed to have TB, further management will be as per probable MDR-TB case.

There are no definite chemo-prophylactic recommendations for contacts of MDR-TB patients. New born children of MDR-TB mothers should be vaccinated with BCG after excluding congenital TB.

11.4.9 Monitoring and supervision

Patients should be monitored closely for regularity of drug intake, development of adverse drug reactions and signs of treatment failure. Clinically, the most important way to monitor response to treatment is through regular history-taking, physical examination and reviewing with periodical sputum and blood tests.

Each MDR-TB patient should be closely monitored according to the following standardized parameters. The success of the programme depends on the intensity and quality of monitoring and supervision activities.

Table 11-2 Monitoring treatment of MDR-TB patients

| Month | Clinical Consultation | Weight | Smear | Culture | DST | CXR | LFT ^s | CR, K | TSH | Audiometry* | HIV Testing |
|------------------|-----------------------|-----------------|---------|------------------|----------------------------|-----------|------------------|-------|-----|-------------|---------------------|
| 0 (baseline) | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| 1 | Every two weeks | Every two weeks | √ | √ | | | | √ | | | |
| 2 | | | √ | √ | | | | √ | | √ | |
| 3 | | | √ | √ | | | | √ | | | |
| 4 | √ | √ | √ | √ | | | | √ | | √ | |
| 5 | √ | √ | √ | √ | | | | √ | | | |
| 6 | √ | √ | √ | √ | | √ | | √ | √ | √ | |
| 7 | √ | √ | √ | √ | | | | √ | | | |
| 8 | √ | √ | √ | √ | | | | √ | | √ | repeat if indicated |
| 9 | √ | √ | √ | | Repeat if culture positive | | | | | | |
| 10 | √ | √ | √ | | | | | | | | |
| 11 | √ | √ | √ | Every two months | | | | | | | |
| 12 | √ | √ | √ | | | | √ | | | √ | |
| until completion | Every two months | monthly | Monthly | | | 6 monthly | | | | | |

Linkages should be developed to ensure that specialist consultations are available from Endocrinologist, Neurologist, Dermatologist and Nephrologists as and when required.

11.4.10 Adverse reactions (ADRs) and management

The second-line Anti TB Drug are more toxic than the first-line drugs and the health workers involved in the management of MDR-TB patients need to be specifically trained for identifying these adverse drug reactions and managing them. DOT worker, nurses in the hospital and clinician should monitor and record all the adverse events routinely and laboratory screening tests will be done on a routine basis as per the National Guidelines. The initial evaluation serves to establish a baseline and may identify patients who are at increased risk for adverse effects or poor treatment outcomes. It is rarely necessary to suspend anti-TB drugs completely. Ancillary drugs for the management of adverse effects should be available to the patient free of charge. The details of the second-line drugs and management of ADRs is available in the Guidelines for Programmatic Management of MDR-TB patients.

11.4.11 NPTCCD policy of treating MDR-TB in Sri Lanka

Decisions pertaining to management of MDR-TB are taken by the PMDT Committee appointed and chaired by the Director/NPTCCD. The other members of the committee include PMDT Coordinator, Consultant Respiratory Physicians of NHRD, Director of NHRD, Consultant Microbiologist of the NTRL, Consultant Community Physicians of NPTCCD and the Chief Pharmacist of the Central Drug Store. The committee will seek the opinion/advice of other Consultant Respiratory Physicians and experts in other fields as and when necessary.

Upon confirmed diagnosis of MDR-TB, patients are admitted to NHRD for the intensive phase of treatment. NHRD has an isolation ward for MDR-TB patients. Patients are registered in the MDR-TB Register maintained by the PMDT Coordinator and a MDR-TB number will be issued. The same number is allotted to the patient throughout treatment. On completion of inward intensive phase, patients are referred to respective DCC for continuation phase of treatment. Ideally treatment should be supervised throughout the course of treatment.

**OPERATIONAL GUIDELINES
FOR
TUBERCULOSIS CONTROL**

12. Epidemiology of Tuberculosis in Sri Lanka

Tuberculosis is still a significant public health problem in Sri Lanka. WHO estimates that there were 13,000 incidence cases of all forms of TB in Sri Lanka in year 2015¹¹.

There are about 9,000 - 10,000 cases of TB notified to the NPTCCD each year. According to the annual statistics, a total of 9,575 cases of all forms of TB cases were notified to the NPTCCD in 2015. Out of this, 9,293 were incidence cases (new and relapse), 270 were previously treated excluding relapse cases and 12 were other cases.

A total of 2,699 extrapulmonary TB out of the all TB cases were notified in year 2015. The commonest form of EPTB is TB lymphadenitis.

It was also noted that there is a shift in incidence of new cases towards the older age groups. The highest number (1808) of new TB cases was in 45-54 age group. The lowest number was in 0-14 age group (307 cases, 3.4 %) out of 8,990 all new cases. Of the new cases, 59.3% (5,328) were in the productive age group of 15-54.

Most of the TB cases are reported from the Western, Central and Sabaragamuwa Provinces. Western province accounts for nearly 41 % of all cases of TB in the country and 2,264 (23.6%) cases are from the Colombo District alone.

The treatment success rate was 83.9% for the new smear positive pulmonary TB patients in 2014 and the loss to follow-up rate was 5% in the same year.

It is estimated that annually around 5-6% of TB patients die whilst on treatment in the country and most of the deaths among TB patients occur during the first month of treatment. The total number of deaths among the TB patients notified to the NPTCCD was 657 and death rate was 6.9 % for the 2014 cohort.

TB/ HIV confection is not a major threat to the country as Sri Lanka remains as a low burden country for both HIV and TB. HIV co-infection rates among TB patients are currently estimated as less than 0.1%.

Multidrug resistant forms of TB that has been detected in Sri Lanka also remains low during the past few years. Only 13 cases of RR/ MDR TB were reported in 2015.

¹¹www.who.int/tb/data accessed 15 January 2016

Table 12-1 Estimates of disease burden for 2015

| Parameter | Estimate |
|-----------------------------------------------------------------------------------|-----------------------|
| Incidence of all forms of TB | 13,000 (9,700–18,000) |
| Incidence rate of all forms of TB (per 100 000 population per year) | 65 (47–86) |
| Incidence rate HIV+TB only (per 100 000 population per year) | 0.043 (0.028–0.062) |
| TB death rate (of all forms of TB, excluding HIV per 100 000 population per year) | 5.6 (4.5–6.9) |
| % of MDR-TB cases among new TB cases | 0.54 (0–1.3) |
| % of MDR-TB cases among retreatment TB cases | 1.7 (0.64–3.7) |
| Estimated number of MDR-TB cases among notified pulmonary TB cases | 43 (0–93) |

13. Administration and Planning

13.1 WHO End TB strategy for global TB control¹²

In May 2014, the World Health Assembly in its resolution WHA67.1 adopted the global strategy and targets for tuberculosis prevention, care and control after 2015 based on a bold vision of a world without tuberculosis and targets of ending the global tuberculosis epidemic, elimination of associated catastrophic costs for tuberculosis-affected households. The three pillars of the strategy include – integrated, patient-centred care and prevention; bold policies and supportive systems; and intensified research and innovation. The strategy is based on principles of government stewardship and accountability, with monitoring and evaluation; strong coalition with civil society organizations and community; protection and promotion of human rights, ethics, and equity; and adaptation of the strategy and targets at the country level, with global collaboration.

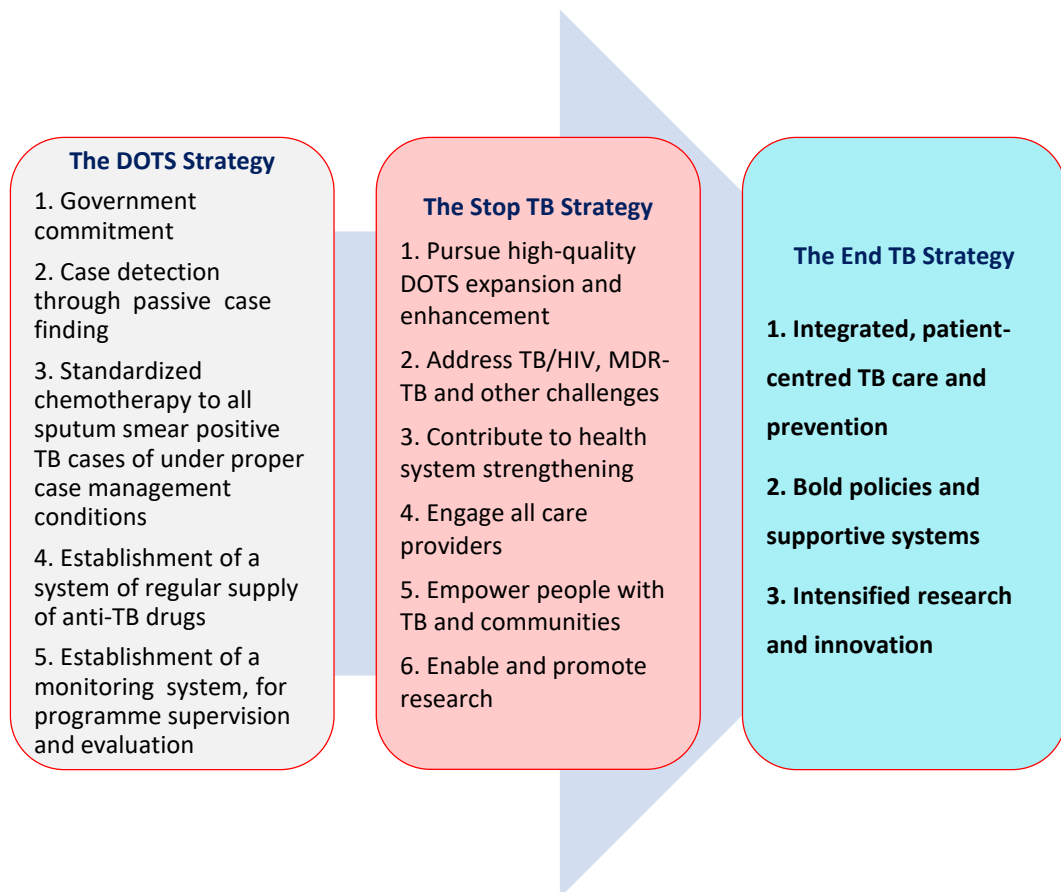


Figure 13-1 Evolution of the end TB strategy

¹²<http://www.who.int/tb/strategy/en/> accessed 15 January 2016

13.2 National strategic plan 2015- 2020

The previous National Strategic Plan for TB control in Sri Lanka covered the period 2012-2016. It was based on the Stop TB Strategy Framework and the Global Plan to Stop TB 2011-2015. Its central aim was the enhancement of access to TB diagnostic and treatment services. Six strategic directions were identified to support the achievement of the overall goals. Key components of the plan included improving access and quality services to enhance case finding and further improve the treatment outcome, engaging all care providers in TB control, strengthening the health system, and implementing a comprehensive advocacy and communication strategy.

Several recent developments have necessitated the development of a revised National Strategic Plan even before the completion of the previous plan in 2016. Foremost is the addressing gaps identified by the fifth Joint Monitoring Mission of the National Programme for TB Control that was held in June 2014. The Mission has recommended several key interventions targeting at decentralization of TB diagnosis and treatment services, strengthening case finding, improving treatment adherence, management of human resources for TB control, and promoting and contributing to research. Second, WHO has recently issued a new End TB strategy for global TB control focusing on the post-2015 era. The strategy includes important modifications and updates to the earlier Stop TB strategy, which should be rapidly translated into revised national strategic plans. Adaption and quick roll out of new technologies like the Xpert MTB/RIF is becoming pivotal for TB control. The technology allows for highly sensitive detection of smear negative cases and also resistance to Rifampicin, one of the important first line drugs. Sri Lanka has successfully introduced this new methodology at the NTRL. Due to its strategic potential, a revision of the National Strategic Plan including the rapid expansion of the Xpert MTB/Rif methodology is required.

The National Strategic Plan 2015-2020 therefore seeks to re-structure TB control activities, incorporate recent technological advances in TB control as well as new strategic directions developed by the World Health Organization in order to lay a sound foundation for the future development of the NPTCCD and its continued collaboration with NGOs, technical partners and donor organizations.

Goal of the National Strategic Plan 2015-2020

Decrease the prevalence of TB by 10 % by 2020 based on TB burden figures of 2014 as per the WHO estimates

Objectives of the National Strategic Plan 2015-2020

PILLAR 1: INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION

Objective 1:

To improve the TB control by detecting at least 80% of incident TB cases (all forms) by 2017 and 90% of incident cases by 2020

Objective 2:

To improve the outcome of enrolled TB patients

- a) By achieving 90% treatment success rate of all forms of non MDR-TB patients and;
- b) To maintain at least 75% of treatment success rate among MDR-TB cases by 2017

PILLAR 2: BOLD POLICIES AND SUPPORTIVE SYSTEMS

Objective 3:

To integrate TB control activities in to general healthcare system by establishing TB diagnostic and treatment services in 40% of all hospitals up to the level of Divisional Hospitals Type B or above by 2017 and in 80% -by 2020

Objective 4:

To improve the accessibility to TB treatment and care by engaging 30% of all private health care providers (hospitals and General Practitioners) in TB control by 2017, and 50% by 2020

Objective 5:

Ensure that quality TB services in line with current international standards are provided by qualified and regularly supervised personnel at 100% of all implementation sites by 2017

PILLAR 3: INTENSIFIED RESEARCH AND INNOVATION

Activities related to this Pillar are included under strategic interventions related to Objective 1 (implementation of Xpert MTB/RIF as an innovative method for the diagnosis of smear-negative cases), Objective 3 (implementation of Xpert MTB/RIF as an innovative method for the diagnosis of drug-resistant cases), and Objective 5 (establishment of an operational research committee and implementation of an annual grant program).

13.3 National Programme for Tuberculosis Control and Chest Diseases (NPTCCD)

TB control activities in Sri Lanka were initiated in a planned manner along with the establishment of the TB Commission in 1910. As a pioneer step, Tuberculosis Detection centre was established in Colombo Petah in 1916. Inward facilities for TB patients were established in 1917 at Ragama hospital and later on at Kandana (1919) and Kankasanturai (1930) hospitals. In 1949, Welisara Hospital, which was used as a hospital for soldiers during the World War II, was converted to a Chest Hospital with out-patient facilities. The Anti-TB Campaign was established as a vertical programme in 1945 and functioned under the Deputy Director General of Medical Services. It functioned through two chest hospitals, a network of chest wards and nine provincial chest clinics. It was renamed as Respiratory Disease Control Programme (RDCP) in 1989. At the same time the chest clinics (with the exception of Colombo and Gampaha) were brought under the administrative and financial control of the provinces while technical support continued to be provided by RDCP. The RDCP was renamed National Programme for Tuberculosis Control and Chest Diseases (NPTCCD) in 2002 after being transferred from the Deputy Director General (DDG), Medical Services to the DDG, Public Health Services in 2001.

The National Programme for Tuberculosis Control and Chest Diseases is one of the key institutions in the national health system. The programme is headed by the Director and is responsible for the tuberculosis and other respiratory disease control activities of the entire country and is in close co-ordination with the general health services and other governmental and non-governmental stakeholders. At present, there are 26 DCCs functioning in 25 Administrative Districts in the country. Inward facilities are provided through National Hospital for Respiratory Diseases and chest wards in 13 district Hospitals. Diagnostic services are carried out through the NTRL, Intermediate Tuberculosis Laboratories, DCC Laboratories and Microscopic Centres. Central Drug Stores of the NPTCCD is responsible for the estimation, procurement, supply and distribution of anti TB Drugs to chest clinics.

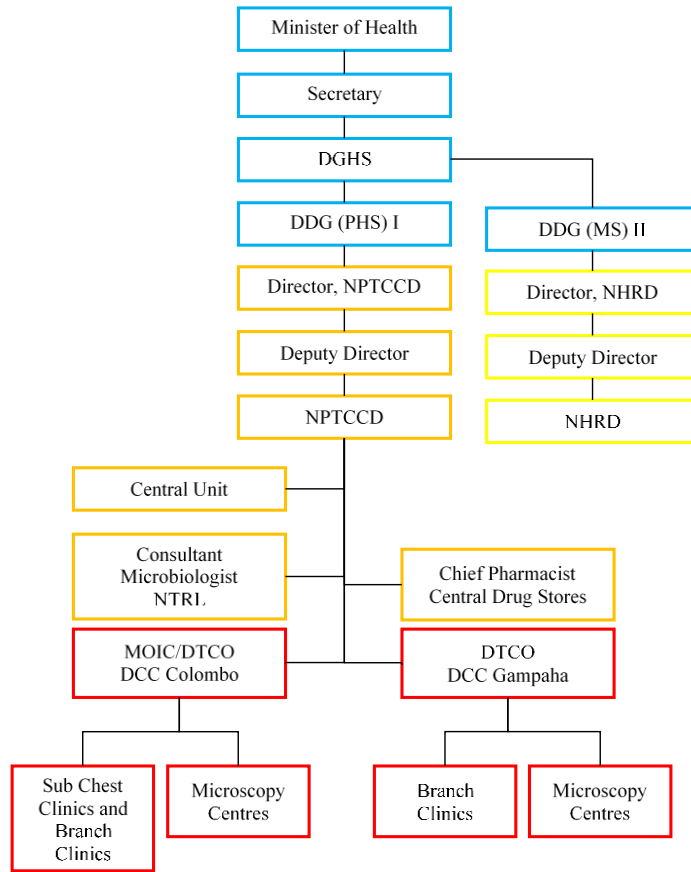


Figure 13-2 Organizational structure of the NPTCCD at central level

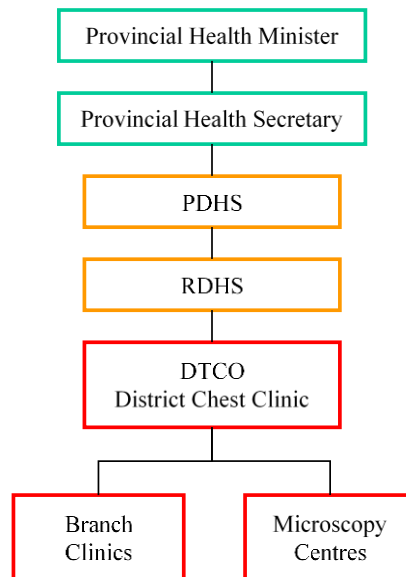


Figure 13-3 Organizational structure of national TB control programme at the provincial level*

*The flow chart includes only administrative positions

13.4 The central level

The NPTCCD consists of several institutions which functions at the national level. These include the central unit, NTRL, Central Drug Stores, Central Chest Clinic Colombo and District Chest Clinic Gampaha.

13.4.1 Main responsibilities of the NPTCCD

- Formulation of policies and guidelines for control of TB and other respiratory diseases in the country.
- Planning, organization, implementation, coordination, supervision, monitoring and evaluation of tuberculosis and other respiratory disease control activities throughout the country.
- Co-ordination within the Ministry of Health with other programmes and with other national and international stakeholders.
- Quantification and forecasting for uninterrupted drug supply and other logistics for the programme activities in the country.
- Technical guidance in consultation with concerned specialists.
- Human resource planning and development.
- Mobilising financial resources through domestic and international sources.
- Planning and organization of diagnostic services.
- Advocacy, communication and social mobilization in tuberculosis and other respiratory diseases.
- Surveillance and management of information system on tuberculosis and other respiratory diseases.
- Infrastructure planning and development.
- Operational research on tuberculosis and other respiratory diseases.
- Management of institutions under its direct administrative purview.

13.5 Provincial & regional level

With the introduction of the Provincial Councils Act to the Constitution of Sri Lanka in 1987, some health care services were devolved in to the Provincial Councils. Accordingly there are line Ministry of Health at central level headed by a Cabinet Minister and Provincial Ministries of Health in the nine provinces. The Provincial Directors of Health Services (PDHSs) and Regional Directors of Health Services (RDHSs) are responsible for the management and effective implementation of health services including TB control activities in their respective provinces and districts. These activities are carried out through a network of DCCs in accordance with the policy and technical guidance provided by the NPTCCD. All the chest clinics except chest clinics in Colombo & Gampaha districts (which directly function under the purview of the Director, NPTCCD) function under the administrative control of Provincial Health Ministries.

13.5.1 Main responsibilities at provincial and regional levels

- Implementation and maintenance of TB control activities in their respective provinces/regions.
- Coordination with the central unit for technical guidance and other related matters to maintain the uniformity of the services provided.
- Coordination with Health Institutions and other relevant governmental and non- governmental organizations in the respective provinces and districts.
- Provision of financial assistance for programme activities.
- Capacity building of the health staff in respective provinces /regions in collaboration with the Central Unit.
- Provision of medical supplies to the DCCs under their jurisdiction.
- Review of TB and respiratory disease control activities and implementation of remedial and promotional measures.

13.6 District level

The District Chest Clinic (DCC) is the key organizational unit of the National Tuberculosis programme at district level. It is the focal point of the NTPCCD for all TB control activities in the district. DCC is the coordinating centre and DTCCO is the focal point for the tuberculosis and respiratory disease control activities in the district. DTCCO is responsible administratively to the Provincial Director and Regional Director of Health Services and is technically guided by the Director, NTPCCD.

The DCC is under the administrative control of the District Tuberculosis Control Officer.

Other staff of the DCC includes:

- Medical Officer/s
- Nursing Officer/s
- Radiographer
- MLT/PHLT
- PHI
- Pharmacist / Dispenser
- Management assistants/PPO/Development Officer
- Laboratory orderly/Labourers
- Driver

Due to service needs, TB assistants for sputum microscopy and data entry officers for data management were recruited to the chest clinic staff on contract basis and will be in service until permanent officers are recruited.

13.6.1 Structure of DCC

Basically the Chest Clinic consists of the following sections:

- Reception and Registration
- Clinical section including adequate space and facilities for Consultant Respiratory Physicians visiting the DCC
- Laboratory
- X-ray department
- Pharmacy & Drug store
- Health Education and Counselling section
- Statistical section
- General Office/Administrative section
- Stores

13.6.2 Records and registers are to be maintained at the DCC

- District TB Register
- Laboratory register at the DCC laboratory
- Xpert MTB/RIF and Culture register
- TB symptomatics register
- Contact tracing and investigations register
- Treatment interruption and follow-up record
- INH prophylaxis register
- Inventory register
- Drugs issuing registers for stores and dispensaries
- Maps
 - Health institutions providing TB services
 - Spot map of TB notification
- Charts
 - Disease notification and programme performance trends

13.6.3 Roles and responsibilities of consultant respiratory physicians in relation to TB control

Consultant respiratory physicians are experts who hold necessary experience and technical expertise to provide higher level inputs as and when required. Except for Colombo Chest Clinic, CRPs are attached to hospitals, but play an important role in chest clinics. Their roles include:

Advisory tasks

- At national level, provide technical advice to the programme on policy issues specifically those related to clinical aspects of TB control
- At district level, advise on clinical aspects of national policy implementation

Clinical tasks

- Guide on diagnosis and decide on treatment of clinically diagnosed new TB (both pulmonary and extrapulmonary) cases and retreatment cases
- Expert opinion on management of comorbidities in consultation with relevant experts from respective field, as and when required e.g. in case pregnant females with TB, coordinate with Obstetrician.
- Management of complex situations like TB with renal insufficiency, hepatic disorders etc. and complications arising during the course of TB treatment
- Initiation of treatment, management of drug resistant cases during hospitalisation and oversight during ambulatory care. Consultant Respiratory Physicians will also head the PMDT site committees.

Capacity building

- Facilitate training activities as and when required

13.6.4 Roles and responsibilities of DTCOs

The overall responsibility of DTCO is implementation and management of the National TB Control Programme activities through the staff of the chest clinic and other health institutions, as well as coordination with various stakeholders in the district while providing necessary oversight. DTCO is technically responsible to the NPTCCD and administratively responsible to respective provincial authorities except in Colombo and Gampaha where they are both administratively and technically responsible directly to NPTCCD.

To achieve this, the DTCO will undertake following activities.

Managerial tasks

- Prepare the annual district activity plan with budget keeping in mind national and sub-national targets and strategic interventions as outlined in the National Strategic Plan for TB Control, in consultation with all relevant stakeholders.
- Ensure maintenance of a district map of all health facilities providing TB control services and a register of staff available at these places for TB control activities.
- Ensure establishment of microscopy centres and DOT centres at suitable places and identification of the staff responsible for DOT provision in consultation with the officers in charge of these health institutions.
- Ensure that case screening and diagnostic activities are in accordance with the national guidelines
- Ensure that all TB patients are receiving appropriate treatment regimen using quality assured drugs in accordance with the national guidelines at all participating facilities.

- Ensure maintenance of records and preparation of reports by district staff and other institutions participating in national programme as per national guidelines
- Ensure successful implementation of patient centred DOT throughout the district including community involvement in DOT provision
- Inventory management as well as maintain an uninterrupted supply of anti-TB drugs, laboratory materials, equipment, and forms and registers for the entire district and the distribution of those to the treatment and microscopy centres.
- Carry out administration and financial management of the Chest Clinic.

Supervisory, monitoring and evaluation tasks

- Conduct supervisory visits to health facilities providing TB care as per guidelines.
- Evaluate the TB control activities against the established performance indicators
- Ensure availability of updated spot maps of TB cases notified in the DTCCO office
- Organise monthly meeting at DCC level participation of all relevant staff to review clinical progress of all TB patients on treatment. Where Consultant Respiratory Physician is available for the meeting, he/ she should chair the proceedings.
- Organise quarterly district review meetings to discuss programmatic management, participate in provincial and national review meetings, and monthly conference of Medical Officer of Health (MOH) officers
- Ensure accurate and timely reporting of data (including quarterly reports) to centre and others concerned, including MOH of respective area.

Coordination tasks

- Ensure organization and coordination of case finding in all public and private health institutions in the district including proper identification and referral of all TB symptomatics for diagnosis.
- Coordinate with other district level programmes specifically the HIV control programme and social services departments
- Liaise with the general practitioners, other governmental and non-governmental organizations (NGOs) to improve TB control in the district.
- Organise a MoU with participating NGO's and private physicians as per the national guidelines defining roles and responsibilities of each partner specifically when the other party is receiving funding for activities

Capacity building and sensitisation tasks

- Organise and facilitate capacity building of district level staff in TB control activities as and when needed

- Participate in relevant trainings at district and national level as and when needed
- Organise and facilitate sensitisation of existing and potential stakeholders in the district.
- Organize and facilitate capacity building for stakeholders providing TB services within the district.
- Organize awareness activities for the public in close coordination with other clinicians and stakeholders.

Prevention of Tuberculosis tasks

- Ensure implementation of the infection control plan in the DCC and decentralised units in the district
- Organise contact tracing and locally appropriate screening activities

Other technical activities as requested by NPTCCD need to be coordinated by DTCO within the respective district.

13.6.5 Roles and responsibilities of medical officer (MO) at DCC:

The overall responsibility of the MO is to implement all aspects of clinical management of Tuberculosis and support DTCO in implementation and management of national TB control programme.

To achieve this the MO shall undertake the following tasks:

Clinical tasks:

- Screen and detect cases of TB and other respiratory diseases
- Manage patients with TB and other respiratory diseases, and follow them up
- Undertake clinical work delegated by consultant respiratory physician
- Provide counselling to patients and family members of patients.
- Conduct branch clinics
- Participate in screening programmes and in other preventive activities organised by the DTCO/ RDHS/ PDHS

Managerial tasks

- Support preparation of the annual district activity plan with budget
- Support maintenance of records and preparation of reports as per national guidelines
- Carry out administration and financial management duties delegated by DTCO of the Chest Clinic.

Supervisory, monitoring and evaluation tasks

- Conduct supervisory visits to health facilities providing TB care including microscopy centres in the district.

Coordination tasks

- Support DTCO in liaising with the general practitioners and the non-governmental organizations (NGOs) to improve TB control in the district.

Capacity building and sensitisation tasks

- Facilitate capacity building of district level staff in TB control activities as and when needed

MO-DCC will also carry out other functions delegated by DTCO

13.6.6 Roles and responsibilities of chest clinic public health inspector (PHI)

Recording and reporting tasks

- Ensure notification of TB cases by form H816 to central unit of the NPTCCD and relevant MOH officers
- Review information received from MOH offices after investigation by H816 B and inserting it to relevant patient files.
- Prepare quarterly reports.
- Update treatment cards.
- Maintain and update District TB Register and electronic Patient Information Management system (PIMS).
- Monitor the TB screening register maintained at the health institutions regularly and referring patients to chest clinic who had not yet registered at the chest clinic
- Ensure notification of TB deaths by H 814
- Assist DTCO in disease surveillance and TB control activities including preparation of a spot map of notified cases

Logistics management tasks

- Maintain an adequate uninterrupted anti-TB drug supply to the DOT centres by ensuring adequate stocks at all levels. This includes timely distribution of anti-TB drugs to DOT centres, Supervision of DOT centres and maintaining records and reports pertaining to ongoing treatments.

Tasks to ensure treatment adherence

- Provide DOT whenever necessary
- Trace the patients who do not start on treatment (primary lost to follow up cases)
- Take actions to retrieve, counsel and support treatment interrupters. The actions include informing relevant Medical Officers of Health regarding

interrupters in their respective MOH areas in view of getting their support to trace patients.

- Impart health education to the patient and their family.
- Review the TB register maintained at the microscopy centres and refer patients to chest clinic who had not yet registered at the chest clinic

TB prevention tasks

- Ensure the preparation and implementation of the (updated) infection control plan of the DCC
- Participate in the District Infection Control Committee.
- Support organisation of infection control meetings and preparation of an infection control plan for health facilities in the district
- Ensure contact tracing and investigation including maintenance of a contact register. Liaising with Range PHIs to trace the contacts of TB patients who did not appear for the investigations at chest clinic.
- Organize mobile clinics, screening programmes.
- Carry out health education programmes and public awareness
- Carry out BCG vaccination and Mantoux testing whenever necessary.

Other than the above mentioned duties PHI should carry out all the activities designated by the DTCO.

13.6.7 Roles and responsibilities of nursing officers attached to chest clinic

Several activities listed below overlap with those of PHI and hence depending on the workload, the DTCO should divide the responsibilities among both staff. However in absence of one staff the other should be able to undertake all activities. In case of a non-availability of PHIs or Nursing officers in the chest clinic duties indicated in PHI, and nurses duty lists should be allocated to a suitable officer to carryout uninterrupted services.

Recording and reporting tasks

- Ensure patients registration
- Maintenance of the District TB register
- Update records returns and other relevant documents as per delegation of the DTCO

Clinical tasks

- Providing nursing assistance to consultants and medical officers when they are examining patients
- Carry out BCG vaccination and Mantoux testing

Tasks to ensure treatment adherence

- Provide DOT
- Carry out counselling and health education to patients and family members
- Infection control
- Attend meetings of the District Infection Control Committee.
- Ensure implementation of the infection control plan of the DCC
- Other than the above mentioned duties, Nursing Officers should carry out all other activities assigned by the DTCCO

13.6.8 Roles and responsibilities of Medical Laboratory Technician (MLT)/ Public Health Laboratory Technician (PHLT) at DCC

Laboratories play a pivotal role in TB case management as diagnosis of Tuberculosis is based on bacteriological tests. The role of MLT/PHLT at DCC is crucial in this regards

Diagnostic tasks

- Collect requisite number of sputum specimens with proper guidance to the patient
- Examine sputum specimens of all TB symptomatics referred from the same institution, other health institutions in the area, by General Practitioners or self-referrals.
- Examine follow up sputum samples of TB patients referred to the centre.
- Ensure that three sputa are examined for diagnosis and two for follow up.
- Positive results should be entered in red ink.
- Report test results to DTCCO. Positive results to be reported on priority over telephone
- Ensure availability of sufficient quantity of unexpired lab consumables

Referral tasks

- Ensure transport of sputum with proper packing and under appropriate conditions to intermediate or national lab for Xpert (MTB/RIF) or TB culture.
- Proper storage of samples in case of any delay in transportation
- Coordinate with laboratory staff at the referred lab to verify receipt of samples as well as timely collection of results.

Quality assurance

- Maintain microscopes and ensure proper storage of lab consumables
- Maintain sputum smear slides as per the EQA protocol and participate in quality assurance and quality improvement activities
- Maintain records and registers according to the TB laboratory manual

Coordination tasks

- Assist the DTCCO to conduct EQA in the microscopy centers

Role of microscopists working at other microscopy centres within the district are similar except for undertaking quality assurance of other microscopy centres.

These are only some of the key staff at DCC. There are other staff also working at DCC whose tasks are determined as per the official job description of the post and duties delegated by the DTCO

13.6.9 Branch chest clinics

In every district, one or more branch chest clinics are held in selected general health institutions. These are conducted once a month or more frequently depending on the case load and other important parameters. DTCO should ensure that these clinics are conducted by the DTCO him or herself and MOs on rotational basis. At these branch chest clinics, diagnosis of new patients, provision of treatment and follow up of patients through the treatment regimen are carried out.

13.7 Health institutions

All general health institutions including National Hospital, teaching hospitals, provincial and district general hospitals, base hospitals, district hospitals, divisional hospitals and primary medical care units (PMCU) should take part in TB control activities particularly in case finding.

Medical Officers of Health and their staff also should play an active role in TB control in their respective areas.

13.7.1 Main responsibilities at the health institutional level

Medical Officers, Registered or Assistant Medical officers at these health institutions are responsible for the TB control activities in addition to other duties.

The main functions are:

- To identify tuberculosis symptomatics and refer them to the chest clinic or to a microscopy centre for sputum examination. All such cases should also be screened for possible drug resistance or other risk factors such as HIV co-infection.
- Maintain the Register of TB symptomatics. Name, complete address and contact telephone numbers of all TB symptomatics referred should be entered in this register. When the results of sputum examinations are received from the laboratory, they also should be entered in the appropriate column of the Register of TB symptomatics.
- Cases diagnosed as tuberculosis should be referred to the DCC or Branch Chest Clinic for registration, notification and commencement of treatment.
- Should act as a DOT provider when a necessity arises (MO/RMO/AMO/ Nurse/ Pharmacist/ Dispenser/ PHI/ Family Health Worker, etc can be chosen as a DOT provider) and they should be trained by the DTCO.
- DOT should be strictly implemented for the patients referred from the DCC after registration and commencement of treatment.

- Should ensure that patients complete the full course of treatment.
- Those who interrupt treatment should be contacted promptly and failing so, should be informed to the DCC.
- Follow triage and other infection control practices

13.8 Duties of DOT provider

- Observe the patient while swallowing drugs daily during the intensive phase of treatment and mark the Treatment Card accordingly.
- Provide health education to the patients and family member, explaining them the importance of taking the drugs regularly without interruption for prescribed duration. This should be done on a continuous basis.
- Refer the patients at correct intervals for follow up sputum examination.
- If the patient develops any side-effects due to the drugs, or any other complication refer the patient to a Medical Officer in the particular health institution or to the DCC or Branch Chest Clinic.
- If the patient interrupts treatment even for a single day, take action to trace him and to continue treatment. Accordingly,
 - Get the help of a nominated contact person of the patient (available in the TB Treatment Card – TB 01) to retrieve him/her.
 - Inform DTCO and through him relevant Medical Officer of Health (MOH) in order to trace the patient by the range PHI
 - If the patient cannot be traced inform the DTCO.
- All TB Treatment Cards should be kept in a separate file and numbered serially.
- Keep the Treatment Cards updated for inspection by the DTCO on his supervisory visits.
- Once the intensive phase of treatment is completed, refer back the patient to the DCC for evaluation and continuation of treatment. This is better done 3 days before the end of the intensive phase treatments so that results will be available on time to decide on commencing the continuation phase or extension of the intensive phase.

14. Organising Diagnostic Network

14.1 Network of laboratories

The National Reference Tuberculosis Laboratory (NTRL) is located at Welisara. At present, the NRTL has the capacity to perform sputum microscopy, Xpert (MTB/RIF) test, Line Probe Assay, TB culture (solid and liquid) and drug sensitivity testing (DST) for first-line drugs. It is in the process of acquiring, DST capacity for second-line drugs and other advanced technologies in TB diagnosis. In addition, a network of intermediate TB culture laboratories is under development. The network of laboratories of NTP also consists of District Chest Clinic Laboratories (DCCL) and Microscopy Centres (MC) located in certain hospitals / health institutions. There are private laboratories and state sector hospital laboratories which perform sputum microscopy, and some of them are linked to the NTRL through the quality assurance network. The NPTCCD is in the process of integrating other laboratories into the national quality assurance system. The quality assurance of microscopy centres is performed by the DCCL which in turn is quality assured by the NTRL. The quality assurance of NTRL is done by the Supra National Reference TB Laboratory in Belgium.

Table 14-1 Proposed laboratory expansion for PMDT activities

| | Baseline (end of 2014) | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 |
|---------------------------------------------------------------------------|------------------------------|------|------|------|------|------|------|
| Number of Solid culture facilities- central and intermediate ¹ | 3 | 3 | 5 | 7 | 7 | 7 | 7 |
| Conventional DST facilities- at NTRL | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Liquid culture facility- central and intermediate ² | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
| Xpert MTB/Rif 16 module instruments at NTRL | - | - | 1 | 1 | 1 | 1 | 1 |
| Xpert MTB/Rif 4 module instruments- provinces and districts ³ | 1 | 1 | 4 | 10 | 10 | 10 | 10 |
| Line probe assay for first line DST at NTRL | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Line probe assay for second line DST at NTRL | - | | ✓ | ✓ | ✓ | ✓ | ✓ |

¹ Solid culture facilities: currently at NTRL, Kandy and Ratnapura districts; 2016- Jaffna and Galle; 2015- Batticaloa; 2016- Anuradhapura

² Liquid culture facility: MGIT 960 and BacTAlert systems are currently available at NTRL. A new MGIT 320 system will be established at the TB culture lab in DCC Kandy.

³ One unit of 4 module Xpert MTB/Rif instrument was available since 2013 and a 16 module unit has been recently established at the NTRL. Ten more 4 module Xpert machines will be installed at provincial centres and currently functioning Intermediate Culture Laboratories in future.

14.2 Laboratory quality assurance

Sputum examination is one of the key components of diagnosis and monitoring of the treatment of Tuberculosis. Accordingly, it is very essential that all laboratories performing AFB are adhered to the uniform standards so that the quality assured results are comparable. The quality assurance procedures are described in the Laboratory Manual in detail.

An effective quality assurance (QA) system of sputum smear microscopy network is crucial for reliability of data generated under NPTCCD. QA is a comprehensive system consist of Internal Quality Control (IQC), assessment of performance using External Quality Assessment (EQA) methods and continuous Quality Improvement (QI) of laboratory services.

Quality Assurance:

Internal Quality Control + External Quality Assessment + Quality improvement

External Quality Assessment (EQA):

On-Site Evaluation (OSE) + Random Blinded Re-checking (RBRC) + Panel testing (PT)

14.2.1 Internal quality control

The following procedures are adopted to assure the internal quality of laboratories which conduct sputum microscopy for TB:

- Ensure adequate training of laboratory technicians before recruitment and re-training to maintain required level of competency
- Adhering to Standard Operating Procedures (SOPs)
- Proper documentation of all activities carried out in laboratories
- Quality control of stains
- Quality control of staining procedure on daily basis
- Training of laboratory technicians for equipment maintenance
- Training in infection control and waste management
- Infrastructure development
- Uninterrupted supply of good quality equipment, reagents and all other consumables required for sputum smear microscopy

14.2.2 External quality assessment (EQA)

The EQA process for DCCL/MCs involves the following:

- On-site Evaluation of DCCL/MCs,
- Random Blinded Re-checking (RBRC) of slides at DCCLs or NTRL,
- Panel testing

All the relevant data from DCCLs are regularly transmitted to the NTRL. These reports also include data from Microscopy Centres in each district.

14.2.2.1 Random blinded rechecking of routine slides (RBRC)

This is one of the important components of EQA. This method provides reliable assurance that a district has an efficient sputum microscopy laboratory network supporting NTP. Blinded rechecking is a process of re-reading a statistically valid sample of slides from a laboratory to assess whether that laboratory has an acceptable level of performance.

The quality assurance is done through the Lot Quality Assurance Sampling method (LQAS) wherein the number of slides for RBRC is calculated and given at the beginning of the year from the NTRL to each DTCCO. This number is calculated based on the number of sputum smears examined in the previous year and the sputum positivity at the specific laboratory. The DTCCO should send a copy of this document to microscopy centres along with reporting formats.

The LQAS involves selection of a random sample of slides, which is representative of all slides of the laboratory (both positive and negative). Every month samples are sent to the NTRL by DCCLs and microscopy centres send samples to the DCCL. The samples are blinded and rechecked. If a discrepancy is found a second controller examine the slides before issuing the report. A timely feedback is provided every month to the laboratory.

The DCC staff including DTCCO, MLT and PHLT should make supervisory visits to the microscopy centres regularly. If corrective actions are needed, DTCCO should give a report to head of the institution.

The frequency of on-site evaluation of any microscopy centre is decided on the basis of its performance. On-site evaluation of every MC is conducted at least once a quarter by the Laboratory Technician and the DTCCO. When poor performance is identified through any of the above-mentioned activities, additional visits by DTCCO are mandatory for evaluation of all laboratory procedures.

14.2.2.2 On-site evaluation of laboratories

DCC laboratories are paid an on-site evaluation visit once a year by the NTRL. MCs are paid an on-site visit once in every quarter by the DTCCO and MLT/ PHLT. (DTCCO and the Laboratory Technician usually go as a team). This includes a comprehensive assessment of laboratory infrastructure, layout, adequacy of supplies, laboratory safety and waste disposal, maintenance of equipment for example, condition of the binocular microscope, staff training, proper documentation as well as the technical components of sputum smear microscopy, including preparation, staining and reading of smears. On-site evaluation should always include all steps of microscopy procedure including specimen collection, smear preparation, staining, examination of positive and negative control smears, recording and reporting. A set of slides (a panel consisting of positive and negative) is taken during on site evaluation visit to check the proficiency of the technicians of the laboratories.

Checklists have been developed by the NTRL to assist supervisors during the field visit and to allow the collection and analysis of standard data for subsequent remedial action. This will provide written documentation of the visit and findings and also proposed corrective actions to monitor improvements. The feedback of the on-site evaluation is given to the MC and the NTRL is informed along with the comments of the DTCCO. Copies of all evaluation reports are maintained at the DCC and a quarterly summary report is sent for review by the NTRL.

❖ **Panel checking**

Panel checking has been incorporated in to the on-site evaluation. Routine panel slide is not sent separately.

Ensure that the quality assurance network for sputum smear microscopy is in place and functioning

The EQA activities that need to be conducted by the laboratory technician and DTCCO are illustrated below

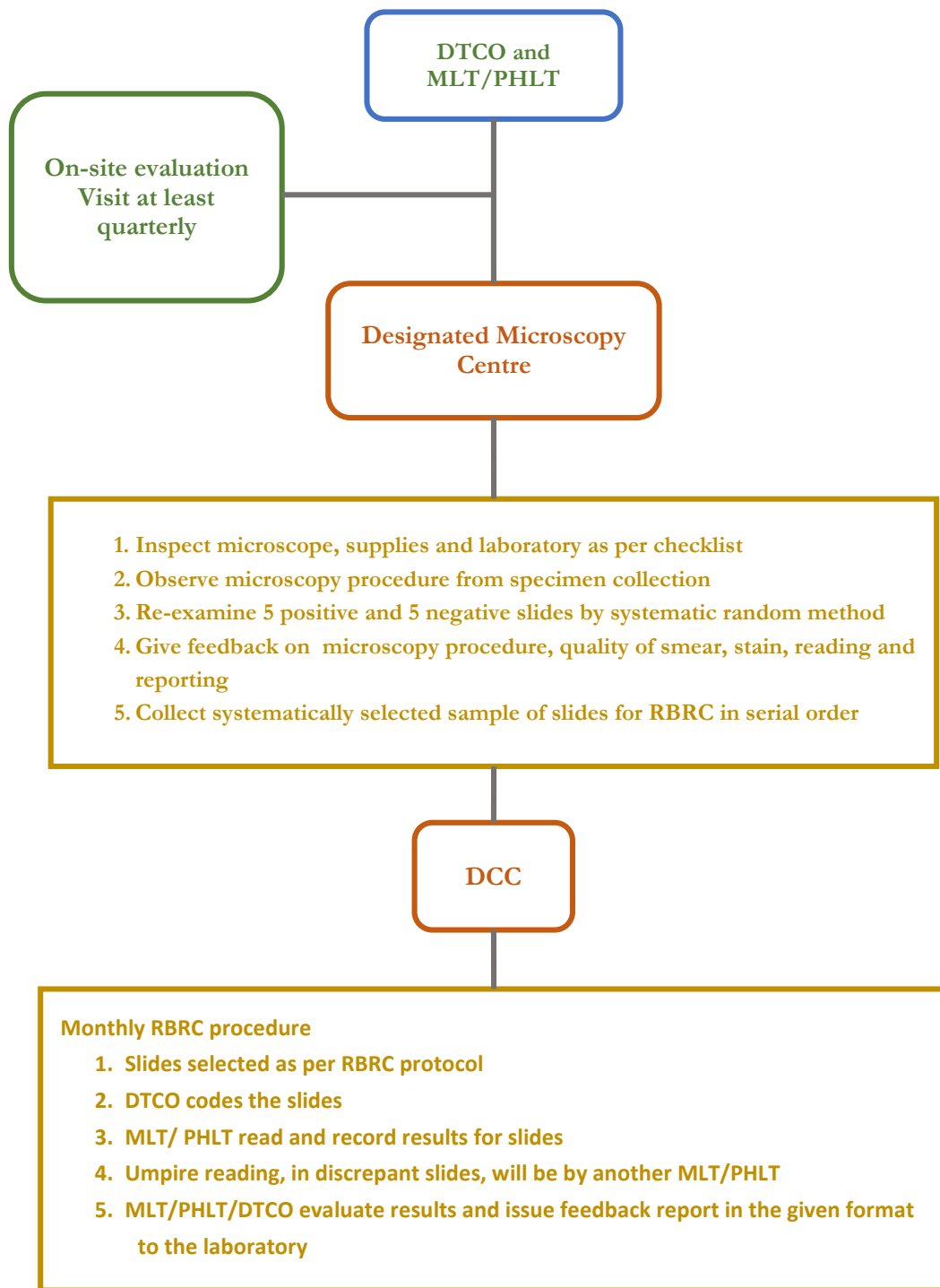


Figure 14-1 Quality assurance network in sputum smear microscopy

The DCC Laboratory Technician should:

- Visit MCs at least once a month
- Test the quality of smear preparation, staining, reading and recording done by the laboratory technician of the MC

Collect sample of slides for blinded rechecking at the district level

14.3 Maintenance of adequate supply of quality laboratory consumables

The DTCCO is responsible for coordinating with lab technician/ microscopist to determine the amount of reagents and other materials the DCC and MC needs. The NTRL should be provided with this information annually in the given format to prepare the yearly estimates for the DCCs and MCs.

It is very important for the laboratory to maintain an adequate stocks of reagents and other laboratory materials. If the laboratory has lower levels of stocks of any items, it should be ensured that supplies are provided to the laboratory from the district stock. Laboratory technicians are reminded to exhaust the old supplies before the use of the new supplies. Old reagents should not be mixed with the new supplies. They should be kept in separate containers.

It is ensured that the reagents are of good quality. It should be freshly prepared at the DCC laboratory and supplied to the MCs on monthly basis. The laboratory technicians should quality control the reagents after preparation. They should be labelled properly to be dispatched to MCs. When a fresh batch of reagents is prepared by the DCC, its quality is checked by the laboratory technician. Reagent QC is performed each time on preparing new batches before distribution

Reagents should not be used beyond 6 months from the date of its preparation. Maintenance of microscopes by a qualified technician on annual basis is essential for the proper functioning of the microscope.

15. Organising Treatment

15.1 Roles and responsibilities of the patient, TB programme staff, community and other providers

Cure from TB can only be achieved if the patient and the health service staff work together. Other health care providers and the community also have important roles to play.

15.1.1 Patient as partner

According to the Patient's Charter for TB Care¹³, patients are not passive recipients of services, but active partners. Patients have the right to quality care, dignity, information, privacy, and/or other types of support and incentives, if needed. They also have the right to participate in TB programme development, implementation and evaluation. Patients have the responsibility to share information with the health provider, follow treatment, contribute to community health, and show solidarity by passing the expertise gained during treatment to others in the community. Because of their first-hand TB experience, their involvement in stigma-reduction activities in the community and supporting treatment completion of other patients can be very effective.

15.1.2 NTP and health staff

TB is a public health as well as a social problem and its transmission poses a risk to the community. Therefore, ensuring regular intake of all the drugs by the patient is a responsibility of the healthcare staff and of the NTP. To facilitate patient adherence, the NTP needs to set up and maintain systems to maximize patient access to care, and train and supervise healthcare workers to provide patient centred care. Factors such as category of treatment, social circumstances (example: family support, family income, distance to DOT centre) and habits of the patient (smoking, alcohol and substance abuse) should be considered in organizing patient supervision.

15.2 Organisation of DOT

15.2.1 New TB cases - bacteriologically confirmed as well as clinically diagnosed

Intensive phase of treatment

- During the intensive phase of treatment, each and every dose of medicine should be given under the direct observation of the identified treatment observer (DOT provider).
- Discuss with the patient to identify a DOT provider, easily and conveniently accessible to the patient.

¹³http://www.who.int/tb/publications/2006/patients_charter.pdf?ua=1 accessed 11 February 2016

- If the patient is too ill for outdoor treatment or if he/she is unable to come for daily-observed treatment, he/she may be admitted to hospital for indoor treatment. In this situation patients should swallow drugs under the direct observation of the nursing staff.
- One copy of the Treatment Card and the drugs are dispatched to the appropriate treatment centre through a staff of the chest clinic (usually PHI).

At the treatment centre

- The DOT Provider should receive the Treatment Card and the drugs (one month supply) which is sent by the Chest Clinic.
- Once patient comes to the DOT Provider, He should talk with the patient and establish a good rapport with him.
- The patient should be informed on the importance of taking the drugs daily for the entire period without interruption.
- The DOT Provider should select a time convenient for the patient and advise the patient to adhere to the time schedule as far as possible.
- Once the patient arrives drugs should be given promptly avoiding any delays to the patient.
- DOT provider should observe the patient swallowing drugs.
- Treatment Card should be ticked off daily after the patient swallowed drugs.
- If the patient develops any side-effects, DOT provider should take action according to the instructions given. For most minor-side effects, reassurance is adequate. In case of a doubt or if there are any major side effects, the patient should be referred to the chest clinic/hospital.
- At the end of the intensive phase of treatment, the patient should be referred back to the Chest Clinic with the Treatment Card and advise the patient to take an early morning sputum sample for examination.

Continuation phase of treatment

- At the end of the intensive phase the patient should visit the Chest Clinic with an early morning sample of sputum.
- Another spot sample should be collected at the clinic.
- If the sputum smear is positive, the patient should be directed to the treatment centre with the Treatment Card for continuation of DOT for another one month.
- After one month, the patient has to be referred back to the clinic with the treatment card and another early morning sputum sample.
- When the sputum smear is negative at the end of intensive phase, the continuation phase of the treatment will be commenced.
- Since the continuation phase also contains Rifampicin, every effort should be made to give each dose under observation. Wherever this is not possible patients should be advised to attend the DOT centre/chest clinic once a week, and the first dose will be given under direct observation and the remaining six

doses are issued for self-administration at home. The DTCO should ensure that a household member observes the patient taking the drugs daily and should make arrangements for supervisory visits by PHI to check drug intake (including pill counts). Each time, when the patient comes to collect drugs, he/she is advised to bring the empty drug foils/ wrappers which is counted as surrogate for pill intake.

- Until the treatment is completed, sputum should be examined at the required intervals.
- At the end of the treatment, the treatment outcome is entered in the TB Follow up Card (TB 02) and the District TB Register (TB 03). Then, the patient is advised to keep the TB Follow up Card as a diagnosis card.

15.2.2 Re-treatment cases

- All Re-treatment cases should be provided DOT throughout the entire period of treatment. Admission to hospital is recommended whenever necessary.
- During the first two months of intensive phase DOT should be provided essentially in a health institution with injection facility since daily streptomycin injections are included in the treatment regimen.

Note:

- **As weight of the patient increases during treatment, the dosage should be modified accordingly.**
- **Extension of treatment should be based on the situations given in the Technical Guidelines under section 4.7. Treatment should not be extended based on clinical and radiological findings alone.**

15.3 Loss to follow-up retrieval action

If the patient does not come for treatment even for one day, prompt action should be taken to trace the patient

- DOT provider should contact the patient through telephone
- Failing that, send a message through a volunteer or any other patient or staff member who lives close to the patient's residence.
- DTCO should be informed within two days
- DTCO should send a letter to the patient as soon as he received the information (and a second reminder after one week in case the patient cannot be retrieved.)
- At the same time, MOH should be informed and his help should be sought in tracing defaulters.

- If the patient is not retrieved, the PHI of the DCC should visit the patient's residence.
- Action that has been taken in retrieving treatment interrupters should be recorded promptly.

After the patient is traced, a non-confrontational attitude should be used to enquire reasons for treatment interruption. All efforts should be made to provide psycho-social support to the patient to overcome any barriers to treatment.

Early loss to follow-up: These are the patients who have been diagnosed as having TB but do not report for treatment. Every effort should be made to identify and retrieve these patients especially sputum smear positive TB patients. The following procedure should be followed:

- At the microscopy centre, on the weekly basis, the laboratory technician should inform over the phone details of all the sputum smear positive patients to the DCC. In the event where there is no telephone facility, details should be sent by post.
- Similarly, the supervisory staff from the DCC (DTCO/MLT/PHLT) on their monthly visits to the MC, should list out all the sputum positive patients from the Laboratory Register.
- These patients are then traced in the District TB Register. If such patients are not registered in the District TB Register, they should be traced.
- At the DCC, the assigned Laboratory Technician, on a weekly basis should ensure that District TB number is entered against all sputum smear positive patients in the Laboratory Register. If not, they should be traced in the District TB Register and the Laboratory Register should be updated. If any sputum smear positive patient in the Laboratory Register has not been registered for treatment, they should be treated as primary defaulters unless they were referred to another Chest Clinic for treatment. Such patients should be informed to DTCO/ PHI for tracing.

15.4 Transfer of patients

Some patients before completing treatment may be transferred out to another district where they will continue treatment. However, the district that initiated treatment is responsible for reporting the treatment outcome of such patients.

If the patient is transferred to another district after starting treatment

- Fill up the Referral /Transfer Form (TB 07) in triplicate
- A feedback should be sent to the referring clinic using the duly filled relevant part of the Transfer form which brings by the patient.
- At the end of treatment, treatment outcome of the patient should be informed to the referring chest clinic using the copy of the Transfer Form sent by the post.

If the patient is transferred to another district before starting treatment

- Information regarding the patient's residential area should be obtained from the patient and District TB number should be obtained from the relevant CC and then patient should be instructed to go the relevant chest clinic with duly filled transfer form.
The patient should be issued with 5-7 day's supply of drugs to cover the period of travel.

15.5 Integration of TB services to general healthcare system for improved access to TB care

Integration of TB services will be implemented in a phased out manner in Sri Lanka to ensure ease of access by TB patients. One year after initiation of the first phase, evaluation will be carried out and rolled out further accordingly. In the model, while the administrative and reporting unit for TB services from a district will be retained at the DCC, there will be at least one more centre within the district working at par with the chest clinic.

The first phase will be limited to 13 selected districts. An institution that is already having a successful branch clinic and microscopy facilities in respective district will be selected for this purpose.

Before initiation, Regional Health administrators of respective districts, heads and key persons in the selected Institutions will be briefed on the new strategy to obtain their maximum support. The staff of chest clinics and selected institutions will be trained and training material will be provided for their easy reference.

Regular monitoring will be carried out from central Unit and respective DCC. The existing reporting and recoding formats will be modified to gather information from newly integrated TB units.

Documents to be kept at the Unit

- District TB register. This is to be maintained by the nursing officer. For providing the numbers, the officer in charge should get the district TB number from the chest clinic over the telephone.
- DOT register
- Contact register
- Patient referral Register

Anti TB Drugs

Total stock of drugs available at the centre should be sufficient for the number of patients already on treatment and possible new patients to be enrolled before the next drug distribution schedule. Therefore Buffer Stock of drugs to be kept considering average number of patients. The stock needs to be replaced on patient basis. The Dispenser or

Pharmacist will be responsible for maintaining the records of drug stocks available and dispensed.

The other responsibilities of the institution are similar to the institutional level responsibilities, as mentioned in Chapter 13.

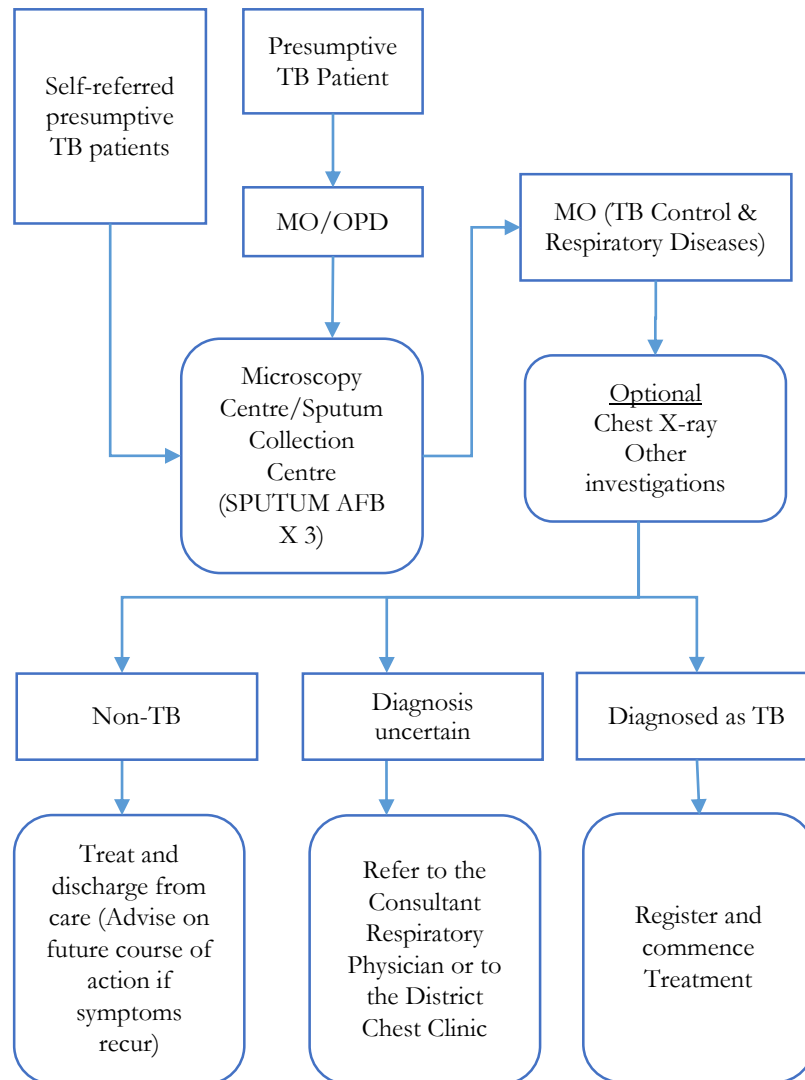


Figure 15-1 Algorithm for presumptive TB patients attending OPD in institutions with integrated care for TB

16. Logistics Management

16.1 Management of drugs and supplies

Uninterrupted supply of quality assured anti TB drugs in adequate amounts, supportive drugs and consumables is mandatory for a smooth functioning of tuberculosis control activities in the country. Estimates of the drugs and other items should be made taking into account the current requirement, future needs and availability of stocks. A buffer stock is managed at all levels to take into account unforeseen delay/ disruption in supply as well as increase in number of patients. Process of drug management has several components, which are interlinked and has to be carried out in a specific order. The components of this management cycle are given below.

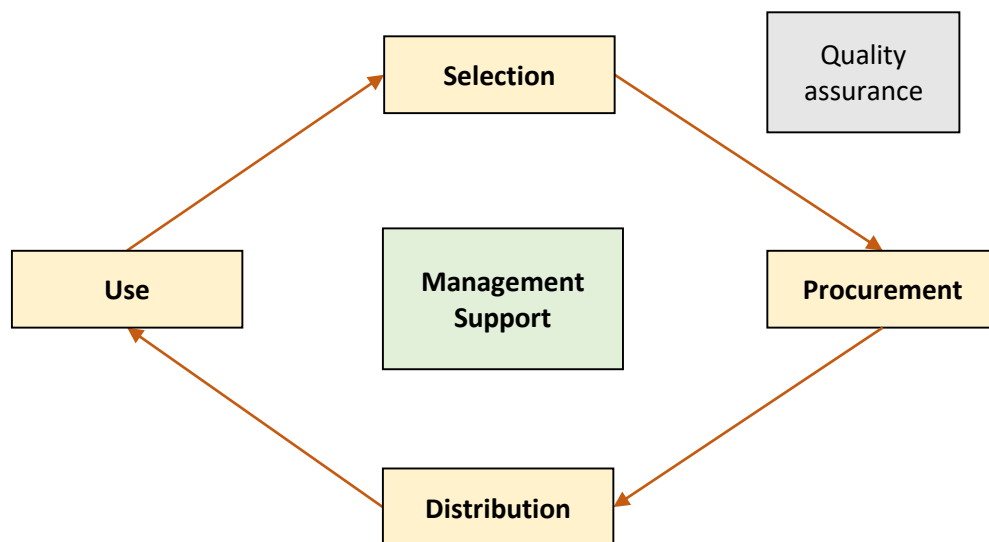


Figure 16-1 Drug management cycle

Management support is an integral part of each of these components. A viable drug management information system (DMIS) must be in place in order to ensure adequate drug supply. In NTP, the quarterly reporting system helps to identify requirements of each item and based on these requirements, drugs are procured.

16.2 Selection of drugs and consumables

Usually selection of drugs and consumables are carried out using a tender procedure and should be based on, quality, efficacy safety and cost of the items. After introduction of the Fixed Dose Combination (FDCs) of Anti TB drugs in 2005, as recommended by the WHO, first and second line drugs are procured through the Global Drug Facility (GDF). Individual anti TB drugs will be procured through GDF from 2017 and other supportive drugs and consumables are supplied through the Medical Supplies Division (MSD) of the Ministry of Health.

16.3 Process of indent and supply

The estimation of the annual requirement of drugs is carried out on the basis of the following.

- Expected number of patients for the year being requisitioned – This is calculated based on the trend of patients treated with anti TB drugs during the previous years.
- The total doses for each treatment regimens- This figure is calculated by multiplying the number of expected patients by the number of tablets needed to treat a patient in each regimen for one year.
- Buffer stock- a 50% buffer stock is added for the national level.
- Available stocks of drugs that will be used before expiry date/s – This needs to be subtracted from the amount being ordered
- Any other supplies in pipeline – This should also be subtracted

The Chief Pharmacist at the Central Drug Store, Welisara is responsible for the annual estimation of drug requirement in consultation with the programme manager and consultants. The requirement is sent to the Director, NPTCCD for ordering the same from the Global Drug Facility (first line drugs and second line drugs). The procured drugs are supplied to the Central Drug Store and from there, it is distributed to the DCCs on a quarterly basis on their request. A three-month buffer stock at the DCC and a six-month buffer stock at the Central Drug Store should be maintained. Proper record of all drugs received, stock in hand and those distributed should be maintained at all levels

It is essential that all drugs are stored in proper conditions, away from heat, sunlight and moisture. The following precautions are important during the storage:

- Preventing Damage and Contamination
- Protecting Against Fire
- Protecting Against Pests
- Controlling Temperature
- Protecting Against Theft

All stores should follow the principle of First Expiry First Out (FEFO). The drugs should be arranged in a manner that the early expiry drugs are more easily accessible and hence FEFO can be implemented.

16.4 Consumables supply at the district level

The District TB control Officer should calculate the requirements of the drugs, treatment related supplies and specimen containers for smear microscopy needed for the district for the relevant quarter and send the estimates to the D/NPTCCD with a copy to the Chief pharmacist. The requirements will be issued to the DCC quarterly from the Central Drug Stores. Supply of some requirements such as non TB drugs are issued through RMSD.

The requirements for sputum containers, tuberculin and Tuberculosis forms and registers should be sent to the Central Unit of the NTP. The DCC should have a reserve stock of drugs for a three-month period.

The DTCCO must work closely with the treatment units and the Microscopy centres to make sure that they receive drug supplies and other materials regularly. It is essential that patients receive the drugs promptly after diagnosis. Keeping large stocks of drug supplies is not always practical for peripheral health units because they may have a limited number of patients in a given year. Arrangements should be made to deliver the drugs to the treatment centres immediately, when a patient is referred to a health centre for DOTS.

16.5 Estimation of anti-TB drug requirements at DCC level.

Calculation of the amount of drugs needed for the current quarter is based on the average monthly consumption (AMC).

Calculate as follows:

- a) Calculate the average monthly consumption of the drug by dividing the total consumption of the previous year by 12.
- b) Calculate the total number of tablets of each drug needed for the entire quarter by multiplying AMC by 3 and add buffer stock for a quarter by multiplying the AMC by 3 (for the quarter + one quarter buffer stock).
- c) Check the stocks available in the stores. Subtract the amount of tablets in the drug store from the total amount of each drug needed.
- d) Calculate the number of syringes and needles required for administering streptomycin injections for the quarter.
- e) Add the number of drugs for the paediatric patients calculated in the same manner.

After calculating the amount of drugs and other supplies needed for the year, the quarterly requirement should be sent to the D/NPTCCD with a copy to the Chief Pharmacist of the Central Drug stores.

16.6 Storage of drugs

- Drugs should be stored in a secured store room and protected from unauthorized access
- Should be protected from heat, light, moisture/rain, dust, pests and fire
- Store the drugs according to their expiry dates with each drug clearly marked.
- Use the FEFO (First –Expired –First–Out) rule: First drugs to expire are the first drugs out (i.e., issue the oldest drug s first).
- The Chief Pharmacist should be informed three months prior to expiry of any drug and efforts should be made to re-distribute these drugs to other sites. If however, these drugs expire on shelf, then they are returned to the Chief Pharmacist by an issue order. The Chief Pharmacist request for condemnation and after due

ministerial approval, the drugs are destroyed by incineration at the Cement Corporation or any other properly approved procedure.

- Expired drugs are to be accounted for in the Stock Register.

17. Recording and Reporting

Recording and Reporting is an essential part of the National Tuberculosis Programme.

- Careful recording of information helps to monitor the treatment and the progress of each patient.
- Periodic reporting on NTP activities helps to evaluate the performance of the control programme and proper planning.
- The NPTCCD is in the process of developing a new Patient Information Management System (PIMS) so that computerized patient data at the district level can be transmitted to a central database in order to facilitate monitoring and evaluation more efficiently and effectively.

17.1 Registration and notification process

- ❖ Once diagnosed, the patient should be classified depending on the site and history of previous treatment for TB
- ❖ Correct category of treatment should be identified for,
 - New cases
 - Previously treated cases (relapse, treatment after failure, treatment after loss to follow-up, other previously treated and unknown previous treatment history).
- ❖ The patient should be registered in the District TB Register (TB 03) and allotted a district TB number. If the patient's district of residence is elsewhere, the district TB number should be obtained over the phone from the particular district.
- ❖ The TB Treatment Card (TB 01) should be filled in duplicate. One copy should be kept in the file and the second copy should be sent to the DOT provider.
- ❖ Patient Follow-up Card (TB 02) should be prepared and handed over to the patient.
- ❖ **Notification** - The TB Notification Form (H 816) should be filled in triplicate and one copy should be sent to the central unit of the NPTCCD, one copy to the MOH of the area of residence of the patient and the remaining copy should be kept in the clinic.
If a patient is diagnosed at a hospital, two copies should be sent to the central unit and one copy should be maintained at the relevant health institution

17.2 Recording and reporting formats used in the NTP

Records

17.2.1 Tuberculosis Treatment Card (TB 01)

As soon as the diagnosis is made, this card should be filled for each patient who was put on treatment. If the DOT provision is not done at the chest clinic, Tuberculosis Treatment Card should be filled in duplicate. The original card is retained in the clinic and the

duplicate is sent to the treatment centre where patient is provided with DOTS. When patient comes for DOT, the DOT provider should mark it each time in the relevant spaces in the Tuberculosis Treatment Card.

The information on the duplicate treatment card should be transferred to the original Treatment Card during supervisory visits or when the PHI/health worker deliver drugs to the DOT centre.

The relevant information, particularly the sputum results should be transferred from the Tuberculosis Treatment Card to the District TB Register kept at the DCC.

If the patient is transferred to another district, the original is kept at the clinic and the updated duplicate Tuberculosis Treatment Card should be given to the patient to be taken to the new district along with the Transfer Form.

17.2.2 Tuberculosis Follow-up Card (TB 02)

This should be filled as soon as a patient is diagnosed and is kept by the patient. Information regarding disease type, treatment category, drugs regimen, sputum follow-up results, x-ray findings and treatment outcome should be recorded in the Tuberculosis Follow-up Card. Dates for follow up appointments are also entered in this card. At the end of treatment this card is given to the patient to use as a diagnosis card.

17.2.3 District Tuberculosis Register (TB 03)

This register is maintained at the DCC. All tuberculosis patients receiving treatment in the district are entered in this register. It contains patient's personal and contact details, disease type, disease site, treatment category, date of commencing the treatment and DOT centre, results of sputum examination and treatment outcome. This register should be updated regularly according to the Tuberculosis Treatment Card of the patient. It is the responsibility of the DTCO to maintain and update the District TB Register. He may entrust this work to the PHI (preferably) or the nursing officer or any other health staff at the DCC. The information in this register is used to prepare the Quarterly Reports on Case Finding, Sputum Conversion and the Treatment Outcome.

17.2.4 Tuberculosis Laboratory Register (TB 04)

This is maintained at all laboratories and microscopy centres where sputum smear examination is carried out. It is a responsibility of the laboratory technician to maintain and timely update this.

17.2.5 Request forms for Bacteriological Examination (TB 05 & TB 06)

These should be available at all health institutions. The medical officer should complete this for every patient referred for sputum or a biological specimen examination. TB 05 form should be filled for sputum microscopy requests from each patient. TB 06 form should be filled for all sputum/other respiratory samples sent for TB culture and Xpert

MTB/RIF and all extrapulmonary specimens collected. The form has space for requesting both culture & DST and Xpert MTB/RIF test. It should be ensured that the form is completely filled. Specifically, the reasons for requesting culture & DST and Xpert MTB/RIF test should be clearly mentioned, indicating the risk group. In case smear examination is not required, the specimen along with form should be directly sent to a laboratory where the requisite tests are available.

Soon after the sputum microscopy is completed, the laboratory technician should complete the same TB 05 form with results and send it to the referring medical officer.

Results of culture, DST and Xpert MTB/RIF will be issued on different formats designed by the NTRL.

In case of a self-referral or referral without duly filled form, the laboratory technician should complete a form for the patient. Once the results are available, he/she should refer the patient appropriately for further management.

17.2.6 Transfer / Referral Form for TB Patients (TB 07)

When a patient is transferred to another district, this form should be filled in triplicate.

- Original form is given to the patient to be taken to the new district
- Second copy is sent directly to the new district by post
- The remaining copy is retained in the clinic

The receiving Chest Clinic should fill the bottom part of the copy brought by the patient and return it to the referring clinic as soon as the patient has been registered in the new district as a ‘**Transfer in**’, in a separate register. At the end of treatment, the bottom part of the copy sent by post, should be completed and returned to the referred unit informing the treatment outcome of the patient. The treatment outcome is reported from the original institution of the transfer.

In case of a treating TB patient is discharged from the ward, this form should be used to refer back to the chest clinic to continue treatment.

17.2.7 Register of Tuberculosis Symptomatics (TB 16)

This is maintained at all health institutions in the district which are involved in detecting TB symptomatics. This register is useful to ensure that TB suspects are subjected to proper investigation and management. In addition, it helps to monitor the performance of health institutions in TB case finding.

17.2.8 Tuberculosis Death Investigation Form

This form should be filled by DTCO for each TB deaths after thorough investigation. It includes details on cause of death, hospitalization details (if relevant), TB history, co-morbidities and adverse drug reactions. These records will be used in TB death reviews.

17.2.9 TB Notification Register (TB 18)

This register is maintained at MOH offices. All TB patients notified by H816A are entered in this register.

17.2.10 TB Investigation Register (TB 19)

This register is maintained by PHIs at MOH offices. All TB patients notified to them are further investigated and details are recorded here.

Reports

The DTICO should submit the following quarterly reports to the central unit within the first two weeks of the next quarter. The reports should be completed in duplicate. The original should be sent to the Central Unit and the duplicate is retained at the clinic for recording purposes.

17.2.11 Quarterly Report on Case Finding (TB 08)

This report is prepared on all TB patients registered during the quarter. The dates for submitting the report is as follows:

| Quarter | Date of completion |
|----------------------------------------------|-----------------------------------------------------------|
| 1 st Quarter (January - March) | Before 14 th of April of the same year |
| 2 nd Quarter (April –June) | Before 14 th of July of the same year |
| 3 rd Quarter (July – September) | Before 14 th of October of the same year |
| 4 th Quarter (October – December) | Before 14 th of January of the succeeding year |

17.2.12 Quarterly Report on Sputum Conversion (TB 09)

This report is prepared on sputum positive patients (new and retreatment) registered during the quarter ended three months ago. Sputum results are collected in the following manner in this report:

- At the end of second month
 - New patients
- At the end of third month
 - New patients if sputum smear is positive at the end of second month
 - New patients if sputum smear is not available at the end of second month
 - Re-treatment patients

The reports should be submitted as follows:

| Quarter | Date of completion |
|----------------------------------------------|---------------------------------------------------------|
| 1 st Quarter (January - March) | Before 14 th of October of the same year |
| 2 nd Quarter (April –June) | Before 14 th of January of the next year |
| 3 rd Quarter (July – September) | Before 14 th of April of the succeeding year |
| 4 th Quarter (October – December) | Before 14 th of July of the succeeding year |

17.2.13 Quarterly Report on Treatment Outcome (TB 10)

This report is completed on the treatment outcome of patients registered 12-15 months earlier.

The report provides information needed to analyse the treatment indicators of the NTP. Regular monitoring of treatment results will enable to assess the adequacy of treatment regimens as well as quality of case management.

Example: Dates for submitting the report on treatment outcome of patients who started treatment in 2016 will be as follows:

| Quarter | Date of completion |
|----------------------------------------------|-----------------------------------------|
| 1 st January - 31st March 2016 | Before 14 th of April 2017 |
| 1 st April - 30th June 2016 | Before 14 th of July 2017 |
| 1 st July - 30th September 2016 | Before 14 th of October 2017 |
| 1 st October - 31st December 2016 | Before 14 th of January 2018 |

The above mentioned quarterly reports are made so as to permit cohort analysis of TB patients. They are prepared using the information in the district TB register. Information derived from these reports are important for planning and monitoring of the programme implementation, disease trends and treatment outcome.

17.2.14 Quarterly Report on Microscopy Activities and Logistics (District Level) (TB 11)

This report has two parts. Part A provides information regarding case finding activities and has to be filled by all health institutions in the district. Part B has to be filled by the health institutions where Microscopy Centres are located. This should be sent to the DTCCO during the first two weeks of the next quarter.

17.2.15 Quarterly Report on Programme Management (District Level) (TB12)

This should be completed by the DTCCO and sent to the Central Unit before end of the third week of next quarter. This report provides information on case finding and microscopy activities, supervisory activities, availability and training of health staff,

involvement of other stakeholders for TB control and advocacy programmes conducted in the district. It also provides information on drug consumption and other supplies.

17.2.16 Quarterly Report - TB & Non TB Wards (TB 13)

This report should be completed by the DTTCO for all TB wards and for Non TB wards managed by a Consultant Respiratory Physician in the district. It provides information regarding admissions and discharges, microscopy, culture and other investigations carried out. Duly completed reports should be sent to the Central Unit during the first two weeks of the next quarter.

17.2.17 Quarterly Report – National Hospital for Respiratory Diseases (TB 14)

This report is compiled quarterly by NHRD. It contains information on OPD services, beds and admissions, deaths, lab services and radiology services of NHRD.

17.2.18 Quarterly Report - National Tuberculosis Reference Laboratory (TB 15)

This report provides information on culture examinations, and quality assessment of DCCs conducted in the NTRL during the quarter. This report should be sent to the Central Unit before end of the second week of the next quarter.

17.3 Compilation and analysis

The quarterly reports are compiled at the district level during the first two or three weeks of the next quarter and sent to the central level. The DTTCO should initiate remedial actions if technical and managerial indicators have not been met or any other deficiencies are identified. Actions taken and further remedial actions proposed should be communicated to the central unit.

The central unit compiles and analyses reports from all the districts and should provide a feed back to the DTTCO within 6 weeks of receipt of the reports. In addition, these data are periodically transmitted locally and internationally to relevant institutions.

18. Supervision and Monitoring TB Control Programme

Supervision is an essential part of any programme. Supervision can be defined as a relationship between different levels of the staff which is evaluative, serving to enhance the skills of the staff and monitor the quality of the services provided by them at various levels of functioning. Supervision is not a one-time activity but a continuous process that extends over time.

Supervisions can be carried out in several ways. They include on-site supervision, review meetings and analysis of data derived from routine information system.

18.1 Supervisory visits

Supervisory visits give an opportunity to assess their performance and provide technical advice and guidance so that the staff can correctly perform their activities as stipulated in the programme. The crux of the supervisory visits should be on education and guidance to perform as per guidelines.

Supervisory visits should be carried out on a regular basis at all levels.

- Supervision from the Central level to the District level. This include supervisory visits by the Director of the National Programme and the staff of the central unit including Consultant Community Physicians, Deputy Director, Medical Officers, Medical Records Officer etc., Consultant Microbiologist of the NTRL and the staff, and supervisory visits by the Chief Pharmacist/ Pharmacist. Efforts should be made to visit each district at least once in a year and underperforming districts more frequently.
- Supervision done by the District level officers. This includes supervisory visits by the DTCO, PHI and MLT/PHLT that are carried out to Branch Clinics, health institutions (including decentralised units), DOT centres, and microscopy centres in their respective districts. DTCO should be able to visit all DOT centres at least on a quarterly basis. The Microscopy centre would be visited by DTCO each month.

The frequency and the number of the visits should be carefully planned and prepared on a schedule based on the priority needs and available performance indicators of each unit. Adequate time should be allocated to each supervisory visit.

18.2 For the supervisory visit to be productive and effective

- Plan and prepare for the visit
- A supervisory check list should be used. Check list should include activities in relation to
 - Administrative functions (staff, logistics and finance)
 - Information system (PIMS, records and returns)
 - Referral system (referral, back referral and feedback)
 - Quality of care (case finding, treatment, microscopy, and drugs)

- Community involvement (patient awareness and community based activities).
- Training needs (in-service training, local and international)
- Staff concerned should be informed in advance about the visit so that they can be prepared and be available at the time of the visit. Occasionally, surprise visits may also be necessary.
- Some ways to collect information during supervisory visits are:
 - Review of documents (Tuberculosis treatment card, Laboratory register, District TB Register, etc.)
 - Observation (activities of the staff, procedures, other resources, etc.)
 - Communication (Talking with the staff, patients and bystanders)
 - Verification (stock position of drugs and other consumables, equipment)

In review of documents emphasis should be given on¹⁴:

- **Accuracy:** Also known as validity. Accurate data are considered correct: the data measure what they are intended to measure. Accurate data minimize errors (e.g., recording or interviewer bias, transcription error, sampling error) to a point of being negligible.
- **Reliability:** The data generated by a programme's information system are based on protocols and procedures that do not change according to who is using them and when or how often they are used.
- **Precision:** This means that the data have sufficient detail. For example, an indicator requires the number of TB patients who received HIV counselling & testing and received their test results, by sex of the individual. An information system lacks precision if it is not designed to record the sex of the individual who received counselling and testing.
- **Completeness:** Completeness means that an information system from which the results are derived is appropriately inclusive: it represents the complete list of eligible persons or units and not just a fraction of the list.
- **Timeliness:** Data are timely when they are up-to-date (current), and when the information is available on time. Timeliness is affected by: (1) the rate at which the programme's information system is updated; (2) the rate of change of actual program activities; and (3) when the information is actually used or required.
- **Integrity:** Data have integrity when the system used to generate them is protected from deliberate bias or manipulation for political or personal reasons.
- **Confidentiality:** Confidentiality means that clients are assured that their data will be maintained according to national and/or international standards for data. This means that personal data are not disclosed inappropriately, and that data in hard copy and electronic form are treated with appropriate levels of security (e.g. kept in locked cabinets and in password protected files).

¹⁴Data Quality Audit Tool. Guidelines for implementation. MS-08-29. September 2008

Observation of staff and procedures may include:

- Interaction with patients
- Personal safety and infection control
- Quality of care
- Accuracy of procedures
- Measures to minimize wastage
- Waste disposal
- Cleanliness
- Status/condition of buildings and other resources

Communication with staff, patients and bystanders should be done in order to get information on:

- Views and attitudes on services provided
- Patients' satisfaction
- Staff satisfaction
- Records verification - triangulation
- Service improvement needs

Supervising officer should verify:

- Stocks of drugs (maintenance of bin card system)
- Drugs balance of each patient provided with DOT
- Stocks of other consumables
- Functionality and maintenance of equipment
- Physical inspection of drugs and consumables

Frequency of Supervisory Visits

- **DTCO**
Each Microscopy Centre and decentralised unit at least once a month and DOT Centre at least once a quarter
- **DCC – PHI**
Each DOT Centre at least once a month
- **DCC -MLT/PHLT**
Each Microscopy Centre at least once a month

18.3 Monitoring and evaluation

Monitoring and evaluation are essential tools to identify and measure the results of any programme or project. Monitoring provides regular information on how things are working while evaluation can only be done after a certain time and requires more thorough investigations.

- Monitoring can be defined as a continuous process of data collection and analysis to assess a programme (or a project) and comparison it with the expected performance.
- Evaluation is defined as a systematic and objective measurement of the results achieved by a programme, or a project, in order to assess its relevance, its coherence, the efficiency of its implementation, its effectiveness and its impact, as well as the sustainability.

Monitoring and evaluation can be performed at various levels from the individual level through the unit level, district level, provincial level to the national level. For a successful monitoring and evaluation, every aspect of the programme should be covered. This includes:

- Resources: human resources, financial resources and logistics
- Activities: case finding, case holding, treatment, public and private mix (PPM), ACSM, etc.
- Achievements: meeting set targets
- Services provided: adequacy, quality of service, sustainability, infection control

TB control measures implemented is one of the most important areas that should be continuously monitored and evaluated at regular intervals. It is carried out by reviewing and analysing the following reports:

- Quarterly Report of Case Finding
- Quarterly Report of Sputum Conversion of smear-positive cases
- Quarterly Report on Treatment Outcome

Indicators can be used to measure the achievement of activities of a programme. There are certain indicators, which is useful to be examined regularly by the NTP.

18.4 Monitoring indicators

18.4.1 Notification indicators

i) Notification rate of new and relapse TB cases

$$\frac{\text{No of new and relapse TB cases notified during the year}}{\text{Mid-year population for the same year}} \times \frac{100,000}{\text{population}}$$

If all new and relapse cases were to be notified, this would be an indicator for incidence rates. Notification of new cases is indicator of spread of the disease

ii) Notification rate of bacteriologically confirmed TB cases

$$\frac{\text{No of new bacteriologically confirmed cases reported for a specified year}}{\text{Mid-year population for the same year}} \times 100,000 \text{ population}$$

Both these indicators are important for observing trends in case notification over several years. This is usually calculated annually. This should be analysed by age and sex at national level (age group/ sex specific rates per 100,000 population). It provides information on the trend of TB.

iii) TB mortality rate- All TB cases

$$\frac{\text{No of deaths caused by TB excluding deaths occurring in HIV positive TB cases in a specified year}}{\text{Mid-year population for the same year}} \times 100,000 \text{ population}$$

Estimates of deaths caused by TB in HIV positive cases are presented separately. Since prevalence of HIV is very low in Sri Lanka, this is negligible.

18.4.2 Programme outcome indicators

Indicators of Case Finding

i) Case detection rate for all forms of TB

$$\frac{\text{No of all forms of cases (new and relapse) detected during the specified year}}{\text{Estimated incidence of all forms of TB cases for the same year}} \times 100$$

ii) Bacteriologically confirmed rate among all new TB cases

$$\frac{\text{No of new bacteriologically confirmed cases detected}}{\text{No of all new TB cases detected}} \times 100$$

iii) Proportion of bacteriologically confirmed cases among TB symptomatics tested

$$\frac{\text{No of bacteriologically confirmed cases detected}}{\text{Total number of TB symptomatics examined}} \times 100$$

When the prevalence of TB decreases in the community this rate also decreases. However in certain instances, the rate may increase initially if there are intensified case finding activities and with introduction and greater use of highly sensitive molecular tests like Xpert MTB/RIF

iv) Re treatment TB cases

$$\frac{\text{Number of re treatment TB cases registered during specified time period}}{\text{Total number of TB cases registered in the same period}} \times 100$$

Generally retreatment cases are a small proportion of TB cases – around 5% in Sri Lanka (globally 11% in 2014). A high proportion of retreatment cases could be due to cases not being given appropriate treatment in the first course of treatment, adherence problems or poor quality of drugs. This should decline with time with proper implementation of quality assured services. However a very low proportion of retreatment cases may also point to the fact that history of previous treatment is not being properly taken.

v) New extrapulmonary TB cases

$$\frac{\text{No of new extrapulmonary TB cases registered during a specified time period}}{\text{Total No of new TB cases registered in the same period}} \times 100$$

High proportions of EPTB cases may indicate an improved access to diagnostics specifically WHO approved rapid diagnostics (like Xpert MTB/RIF), imaging diagnostics detecting occult TB or a higher proportion of HIV co-infection. The data needs to be analysed taking into account local epidemiology.

vi) Diagnosis of childhood TB

$$\frac{\text{No of childhood TB cases registered during a specified time period}}{\text{Total No of all TB cases registered in the same period}} \times 100$$

The proportion is targeted to be at least 8% by 2020

vii) Detection rate of RR/MDR-TB cases

$$\frac{\text{No of laboratory confirmed RR/MDR-TB cases registered during a specified time period}}{\text{Estimated MDR-TB cases among notified TB cases in the same period}} \times 100$$

The proportion is targeted to be 100% by 2020

viii) Proportion of HIV TB co-infected cases started on ART

$$\frac{\text{No of HIV-TB co-infected cases started on ART}}{\text{Number of TB cases found HIV positive in the same period}} \times 100$$

The proportion is targeted to be 100% by 2020

Indicators of case holding

i) Sputum conversion rate at the end of the initial phase of treatment for new TB cases

$$\frac{\text{No of new bacteriologically confirmed pulmonary TB cases registered in a specified time period that are smear negative at the end of initial phase of treatment}}{\text{Total No of new bacteriologically confirmed pulmonary TB cases registered for the treatment in the same period}} \times 100$$

The proportion of new cases showing negative sputum smear at the end of 2 months is at least 80% and at the end of 3 months is at least 90%

- ii) **Cure rate of new TB cases**
- $$\frac{\text{No of new bacteriologically confirmed TB cases registered in a specified time period that were declared cured}}{\text{Total number of new bacteriologically confirmed TB cases registered in the same period}} \times 100$$
- iii) **Cure rate of patients started on second line treatment**
- $$\frac{\text{No of RR/MDR- TB cases registered in a specified time period that were declared cured}}{\text{Total number of RR/MDR- TB cases registered in the same period}} \times 100$$
- iv) **Treatment completion rate for new bacteriologically confirmed TB cases**
- $$\frac{\text{No of new bacteriologically confirmed TB cases registered in a specified time period that completed treatment and did not meet the criteria for cure or failure}}{\text{Total No of new bacteriologically confirmed TB cases registered in the same period}} \times 100$$
- v) **Treatment completion rate for all TB cases**
- $$\frac{\text{No of TB cases registered in a specified time period that completed treatment and did not meet the criteria for cure or failure}}{\text{Total No of TB cases registered in the same period}} \times 100$$
- vi) **Treatment completion rate of RR/MDR-TB cases**
- $$\frac{\text{No of RR/MDR-TB cases registered in a specified time period that completed treatment and did not meet the criteria for cure or failure}}{\text{Total No of RR/MDR-TB cases registered in the same period}} \times 100$$

vii) Treatment Failure Rate

$$\frac{\text{No of new bacteriologically confirmed pulmonary TB cases registered in a specified time period that are sputum positive at five months or later after initiating treatment}}{\text{Total No of new bacteriologically confirmed pulmonary TB cases registered in the same period}} \times 100$$

Ideally this should be less than 5%

viii) Loss to follow-up Rate

$$\frac{\text{No of all TB cases registered in a specified time period that interrupted treatment for more than two consecutive months}}{\text{Total No of TB cases registered in the same period}} \times 100$$

Ideally this should be less than 5%

ix) Death rate

$$\frac{\text{No of deaths occurred among TB cases registered in a specified time period, due to any reason during course of treatment}}{\text{Total No of TB cases registered in the same period}} \times 100$$

This is usually between 3-5%. All deaths among TB patients that occurred due to any cause are accounted here.

x) Treatment Success Rate*

Treatment Success Rate = Cure rate + Treatment Completion rate

The target for treatment success rate is at least 90% for all TB cases.

** Can be used to measure treatment success rate of RR/MDR-TB cases as well. The country target of success rate among RR/MDR-TB cases is 75%*

Cohort analysis of re-treatment cases, clinically diagnosed cases and extrapulmonary cases also should be done in the same way as of the analysis carried out for bacteriologically confirmed TB cases.

The central unit will give feed back to the DTCO regarding the performance of their district for the quarter and suggest corrective actions, if any.

The NPTCCD conducts review meetings at the central level for all DTCOs and consultants once in every two months to review the performance indicators and discuss on the problems / solutions at the district and peripheral level.

In addition, review meetings are conducted annually at district level with the participation of all stakeholders in TB control in the respective district.

There are other indicators that also need to be monitored at national level and have been included in the M&E plan of the national TB control Programme.

19. Capacity Building

The ultimate goal of Human Resource Development (HRD) for comprehensive TB control is to have the right number of people, with the right skills, in the right place, at the right time, who are motivated and supported to provide the right services to the right people. The HRD vision and goal for comprehensive TB control contribute to reaching the vision and the goal for overall TB control. The result of having a sufficient number of staff in all categories who are competent should be responsiveness, productivity, and client satisfaction. Specifically, responsiveness ensures that the patients being served are treated appropriately, regardless of whether or not their health improves or who they are; productivity ensures the maximum effective health services and health outcomes possible; and client satisfaction ensures there is demand for these services¹⁵.

19.1 Capacity building activities

Continuing capacity building of staff is imperative to meet the HRD vision as described above. Capacity building activities include, but are not limited to:

- Formal training courses
- Follow up visits after training
- Regular supervision
- Workshops
- Seminars
- Conferences
- Regular review meetings

Formal, high quality training of all the staff involved in the programme as per the national TB control strategy is the most important component of the capacity building activities. All staff should be trained on technical and operational aspects of TB control and be familiarized with the policies and guidelines pertaining to TB control. Trainings are conducted at different levels and include Central, District and International levels. Training of DTCOs and chest clinic MOs is conducted at the central level and they in turn train other Medical Officers, paramedical staff and DOT providers in the district. In addition, Nursing Officers, Pharmacists, PHIs and Data Entry Officers are also trained at the central level. MLTs, PHLTs, and TB Assistants receive training at the central level at the NTRL. All training programmes are guided by standardized training modules which include practical exercises and field visits.

Training programmes whose purpose it is to improve the task related skills of staff members should be competency-based. Competency based training is a systematic way of

¹⁵Planning the development of human resources for health for implementation of the Stop TB Strategy: a handbook. WHO/HTM/TB/2008.407

designing and implementing an instructional programme that prepares the participants to demonstrate job-related competencies by achieving specific learning objectives.

The training schedule for operational staff of the NPTCCD – initial training, is illustrated in table 19:1 and training schedule for staff at health facilities than DCC, private providers and NGOS initial training is found in table 19:2 below.

In addition to the training schedules listed in tables 19.1 and 19.2, trainings are organized as follows:

- Training on TB-HIV
- Training on TB in children
- Training on management of MDR-TB
- Training of Private providers on management of TB
- Pharmacists

19.2 Follow up after training

A major challenges for trainers and programme managers is the “learning transfer”, that is, making sure that performance on the job is actually improved after the capacity building activities.

Trainers are responsible for the quality of training and should follow up on course participants to make sure that course objectives, content, methods, and materials were appropriate and to help participants apply their learning to the challenges they face on the job.

Table 19-1 Current Training schedule for operational staff of the NTP

| Officials to be trained | Duration | Methodology | Place of training |
|-------------------------------------------------------|----------|--------------------------------------------------------|-----------------------------------|
| Post Graduate trainees/DTCOs/ MO chest clinics | 9 days | Training modules, and field visits, practical exercise | Central unit |
| Nurses/PHIs of District Chest Clinic | 5 days | Training modules, practical exercise, field visits | Central unit |
| MLTs/ PHLTs/Microscopists of District Chest Clinic | 5 days | Training modules and practical exercise | Central unit (NTRL) |
| Pharmacists and Dispensers of Chest Clinics | 3 days | Training modules and practical exercise | Central Unit (CDS) |
| MOs of other health institutions of the district | 3 days | Training modules and practical exercise | District chest clinic |
| DOT providers | 2 days | Training modules and practical exercise | District chest clinic/DOT centers |
| Field Health Workers | ½-1 day | Training Guidelines | RDHS, District Chest Clinic, MOH |

In addition based on requirements training programmes for other categories of healthcare providers are also conducted by the NPTCCD. This may include training of ayurvedic physicians, pharmacists, nurses and PHIs in non TB units etc.

At the end of each course, participants are expected to effectively manage and/or implement the programme at their respective levels. Each training course is designed as per the learning objectives for each category of staff.

Special training for both public and private health care staff for example training on BCG and Mantoux techniques are conducted by the NPTCCD whenever such requirement is identified.

20. Inter-Sectoral Coordination

Patients with symptoms suggestive of TB seek care not only from government health services but also from other government institutions such as police, armed forces, prisons, transport, tea estates, universities and local government institutions where their own medical services exist and from private sector health institutions. Diagnosed TB patients are managed at all these levels.

A proper coordination between these institutions is very much essential for the effective control of TB. It is also necessary to have a proper linkage within the health sector, between preventive and curative care services.

All these institutions should adhere to the National guidelines of the NTP in managing patients and should follow proper notification procedures in order to maintain a single National Tuberculosis Programme through all health care providers as described in the National Strategic Plan.

Following activities will be undertaken to promote inter-sectoral coordination:

- 1) Formation of a taskforce with representation from all relevant sectors
- 2) Review meetings every 6 months to assess progress in implementation of the national programme in these sectors, identify hurdles and agree on measures to overcome the hurdles in implementation
- 3) Joint monitoring and review of the programme with representatives from the task force

The national programme will offer to supply lab consumables and drugs to all the sectors participating in the programme and undertake necessary quality assurance and supervisory activities. For sectors willing to participate but having their own procurement mechanisms, the Programme will share the quality assurance protocols as well as provide technical guidance on purchase of appropriate drugs and administration of regimen as per the national guidelines.

The different sectors involved are given in Figure 20-1 as below:

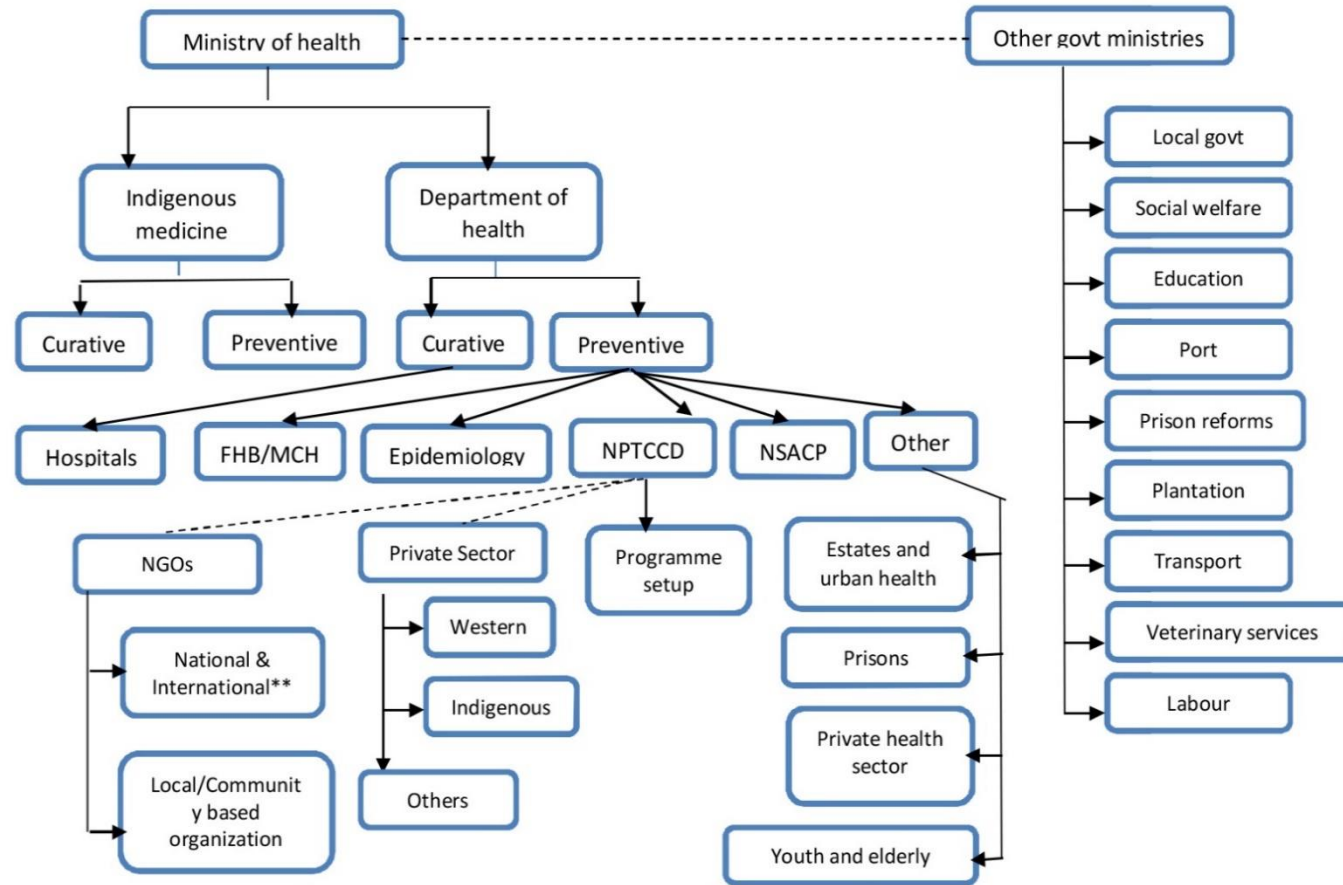


Figure 20-1 Inter-sectoral coordination

* Dashed line shows only coordination role but no direct administrative authority

** Includes technical and funding agencies like the GF, IOM, SAARC TB and HIV Centre, WHO and World Bank

20.1 Engage providers outside the TB programme in providing DOT

WHO has developed guidance on engaging all health care providers to take on TB tasks according to their capacity. For example, public and private practitioners can successfully provide DOT in collaboration with the NTP. They should be capable of:

- Discussing the condition and the treatment being given to the patient.
- Recognizing and managing adverse effects of medications, and making referrals if necessary.
- Assessing the adherence of the patient to the regimen and addressing poor adherence when it occurs.
- Completing the appropriate documentation.
- Collaborating with the local public health services.
- Ensuring that the patient accepts the proposed care.

20.2 NGOs and community involvement in TB care

Engagement of communities, civil society organizations, and public and private care providers is a component of pillar 2 of the End TB strategy. Community involvement refers to partnership and shared responsibility with health services. Social mobilization can create demand for quality assured TB services, and help the community to avail itself of these services.

In community-based care, a TB treatment supporter shares the responsibility for the successful completion of treatment with the TB patient, and provides therapy under supervision as well as social and psychological support. Community-based care can help expand access to care, but requires a strong reporting system, access to laboratory facilities, and a secure drug supply. Treatment supporters need regular contact with NTP staff to ensure that motivation and quality outcomes are maintained. This is a sign of commitment by the NTP to this partnership with the community.

Following roles for NGOs are envisaged under the TB control programme:

- TB symptomatic identification and referral – NGOs and CSOs being grassroots organisations work close to the community. Hence trained volunteers could identify TB symptomatics early and refer them to appropriate health institutions for diagnosis. Community workers can also help in screening contacts of known TB patients and referring the symptomatics.
- Treatment adherence through psychosocial support – Trained NGO personnel can administer DOT at a time and place convenient for the patients. Counselling of patients through peer groups, family members and community around the patients can also effectively be carried out by people working at grassroots. Counselling support will also become important in case of treatment interruption where the community organisations can support patient in overcoming barriers to treatment adherence.

- Rehabilitation services – Some of the patients on TB treatment lose jobs or face reduced earnings. Such patients will need support to enter back in similar job or develop new skills to start earning again. NGOs can coordinate with the employers to advocate for jobs where possible. They can also organise skill development workshops for such patients along with other members of the society that can help them tide over any financial crisis that they may face because of the disease.
- Domestic fund mobilisation with targeted advocacy – Some of the NGOs working in the country have a good history of contributing to the national programme by mobilising domestic resources and providing support for infrastructure renovation.
- Advocacy/ education campaign with chest physicians (registrars), private physicians, nursing associations and pharmacists. The NGOs and CBOs which have members with technical background can organise themselves or collaborate with other agencies in organising awareness campaign for various associations so as to sensitise them to TB screening as well as proper treatment of TB.
- As members of the programme review committees at various levels, NGOs and CSOs can provide independent views on the operational aspects of the programme for making the services more accessible and convenient for the patients.

NGOs can have presence across several districts or may have local activities confined to a single district. Depending on the presence and ability to offer services, the NGOs could liaise with central or district level. At respective level, specifically where NGOs are getting funded for their activities, an MoU will be organised defining roles and responsibilities of each partner and indicators that will be used to measure their outcome and contribution to the programme. However it is not always possible to measure contributions from activities undertaken. In such cases direct output of the activities will be measured and programme performance will be compared with performance before the initiation of the activities or with those of the neighbouring district to make an objective assessment of the activities.

21. Awareness Generation

Community and civil society engagement through advocacy, communication and social mobilization is part of the National TB control activities and District TB Control Officers are responsible for activities for awareness among the General public. DTICO needs to engage with NGOs, private practitioners and private hospitals and plan for their involvement in TB care services. Involving community volunteers, community leaders and civil society is part of role of the DTICO for providing patient support services.

Awareness generation regarding TB is a critical component of tuberculosis control. The target groups, which need to be addressed, are the patients and their families, health personnel, and the community.

The health staff should educate the patients and their families regarding the disease, how it is spread, and the duration of treatment. It must be emphasized that TB is curable if the treatment is taken fully and should stress the importance of directly observed treatment. Patients should be made aware of the risks of irregular and incomplete treatment. Health workers should also teach them simple ways of decreasing the risk of transmitting the disease, like covering the mouth with the hand when coughing and using a pot with a lid to collect sputum and disposing of sputum by burning.

The general public should be educated regarding the disease and the symptoms and the importance of seeking medical advice early if they have any symptoms suggestive of TB. They should be made aware of the locations and the facilities available for the management of TB. Also, education should be aimed at removing the social stigma attached to TB, so that symptomatic patients will seek treatment early.

Health personnel should also be made aware of the importance of identifying TB symptomatics early and referring them for investigation. It is frequently observed that at first contact physicians are not vigilant enough to identify symptomatic patients as 'TB presumptive cases' to carry out necessary investigations especially sputum smear examination. This delays the diagnosis which damages patient's health as well as places the community at risk.

The key messages to be disseminated include:

- Patients with cough for two weeks or more should get screened for TB
- TB is curable with appropriate treatment
- TB patients become non-infectious within two weeks of start of appropriate treatment
- TB treatment should always be taken regularly and for prescribed duration
- Cough etiquettes should be maintained at home for any type of cough. However there is no need to discriminate TB patients

Various awareness generation activities that could be carried out are:

- Mass awareness programs and local awareness meetings with community
- Events around the World TB Day each year for both advocacy with higher level politicians as well as mass awareness.
- Awareness generation among clinicians through professional bodies. This would include organisation of continued medical education (CME) and workshops
- Advocacy with other departments to be carried out by NPTCCD
- Use Primary Healthcare Workers at MOH Divisions and other field level government officers (and NGOs volunteers in some areas) for community awareness and referral for sputum microscopy.

Involvement of NGOs and community workers in DOT provision (as already explained in chapter 8) will also serve two fold purpose – improved access by TB patients at convenient location and timings as well as spreading awareness among community members.

22. Medical Certificates for Leave

- Rules and regulations governing the issue of medical certificates to patients are embodied in the following government circulars:
 - General Circular 1006 / 20.06.79
 - General Circular 1086 / 07.05.80
 - General Circular 1481 / 21.10.86
- Public servants bounded by Public Service Commission rules and government funds are issued medical certificates in form 'medical 170' (major staff) and in form 'medical 331' (minor staff) free of charge.
- Private individuals, corporation and board employees and private sector employees are issued medical certificates in form 'H 307' on payment. The fee charged for the issue of private medical certificates will be according to the prevailing hospital charges circular issued by the government.
- The quantum of leave to be recommended for public servants and private sector, in each medical certificate is as follows:
 - 1st instance - Not exceeding one month
 - 2nd instance - Not exceeding one month
 - 3rd instance - two weeks
 - 4th instance - two weeks
- After a period of leave for three months, the patient concerned should be examined by a medical board. The medical board will decide whether the patient is fit for work or whether he needs further leave from work.
- For TB patients who may need more than three months leave, a medical board may be recommended in the first medical itself, so that the employer can take necessary steps to arrange for a medical board without delay.
- The medical officer who treated the patient cannot sit on the medical board for that particular patient (vide General Circular No 2951).
- Past absence from duty can be covered retrospectively up to five days from the day of issuing the medical certificate, and in the case of indoor patients, the period of stay in the hospital can be covered.
- Special TB leave granted to TB patients is governed by Establishment Code chapter (XII and XXIII) and as amended by Public Administration circulars 30/89 of 03.05. 89 and 32/93 of 24.12. 93.

- A TB patient who is in public service is entitled to four months of full pay special leave in the first instance.
 - In the event of a relapse, he is entitled again to four months of fully paid leave only after a period of 04 years.
 - This special TB leave of four months can be recommended only by a medical board as mentioned.
- TB patients who want to get their EPF money back before retirement age should be advised to apply for a medical board.
 - Any patient referred regardless of his employment status (private or public sector) should be screened for TB free of charge at any government health institution. The report in such a case should state only “no evidence of TB’ or ‘evidence of TB’ and issued free of charge.
 - Any individual referred by a private practitioner for any specific investigation other than the sputum for AFB should be charged the fee as mentioned in the prevailing hospital charges circular.

22.1 Medical certificates for financial assistance

- A TB patient with low income is entitled to seek financial assistance if he wishes to.
- Financial assistance is provided by the Social Services Department and the DTCO/MO of the chest clinic or chest hospital has to issue a medical certificate on Form SS/TB/M1.
- The necessary investigations as to whether the patient’s economic status deserves such assistance and the amount to be given depending on the number of dependents will be the responsibility of the Social Services Department.
- The assistance will be given only during the period of anti-tuberculosis treatment.

22.2 Conditions of eligibility for financial assistance

- The applicant should be examined and certified to be suffering from tuberculosis by a Medical Officer of a Chest Clinic or Chest Hospital.
- The applicant should accept and continue to follow regular treatment prescribed by the Medical officer

22.3 Administrative procedure for the TB Assistance scheme

The following steps should be followed regarding TB assistance for TB patients (in-patients and outpatients) of chest clinics and chest hospitals.

- The Medical Officer of the Chest Clinic /Chest Hospital will issue a medical certificate on the prescribed form (SS/TB/M1) at the request of the patient for him to obtain the financial assistance. This form will be posted to the relevant divisional secretary, who will make suitable arrangements for the payment of TB assistance to the patient or his dependants.
- The divisional secretary will inform the patient / medical officer of the decision taken, after evaluation by the social service officer (S.S.O) in his office.
- The MO will issue a medical certificate on the prescribed form in the first instance for three months and thereafter a renewed medical certificate will be sent on the same form for every three months for renewal of the allowance.
- This will be issued only for the duration of anti-TB treatment.
- When the patient completes treatment, or defaults or dies, the medical officer should inform the Department of Social Services regarding the change.

22.4 Procedure for issue of medical certificates on form SS/TB/M1

- The Medical Officer should note in the BHT or patient's clinic file, the recommended period of TB assistance and should verify this period is correctly entered in the medical certificate before placing his signature.
- The relevant medical certificate number should be noted on the BHT or clinic file with the above entry before dispatch
- The medical officer should enter the relevant details in the counterfoil of the certificate issued.
- A register on the issue of medical certificates for financial assistance should be maintained. This should be maintained in serial order and the relevant date of posting the medical certificate should be entered in the register.
- All letters received from the Provincial Secretary regarding the payment /non-payment of TB assistance to TB patients should be kept filed in the relevant BHT/or clinic file.

The specimen signature of medical officers authorized to sign the medical certificates should be sent to the Provincial Secretary in advance.

ANNEXURE

Annexure

Formats of Recording and Reporting System

- a. District Tuberculosis Register (TB 03)
- b. Request for Sputum Examination (TB 05)
- c. Request for TB Culture and Drug Susceptibility Test (TB 06)
- d. Quarterly Report on Case Finding (TB 08)
- e. Quarterly Report on Sputum Conversion of Bacteriologically Confirmed Patients at the End of Intensive Phase (TB 09)
- f. Quarterly Report on the Results of Treatment of Patients Registered 12-15 Months Earlier (TB 10)
- g. Quarterly Report on Programme Management (District Level) (TB12)

a. District Tuberculosis Register (TB 03)

DISTRICT TUBERCULOSIS REGISTER

| Date Registered | District TB Number | Name in Full | Sex (M/F) | Age | Complete Address | DOT Centre/ DOT Provider | Referred by | Date treatment started | History of Previous Treatment | | | | | Transfer in ^a | | | | | | | | | | | |
|-----------------|--------------------|--------------|-----------|-----|------------------|--------------------------|-------------|------------------------|-------------------------------|---------|-------------------------|-----------------------------------|--------------------------|--------------------------|------------------------------------|--|--|--|--|--|--|--|--|--|--|
| | | | | | | | | | New | Relapse | Treatment after failure | Treatment after lost to follow-up | Other previously treated | | Previous treatment history unknown | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | |

a. Transferred-in patients have been transferred from another TB register to continue treatment. These patients are not included in the receiving unit's quarterly and annual reports of case registrations and treatment outcomes.

DISTRICT TUBERCULOSIS REGISTER

| Site of disease | Treatment Category | | HIV Testing done (Y / N) | Smear (S), Culture (C) or MTB/RIF (X) test results ^b | | | | Treatment outcome and date outcome reported ^d | | | | | Remarks | |
|-----------------|-----------------------------------------------|----------------------------------------------------|--------------------------|-----------------------------------------------------------------|---|--------------------------|------|----------------------------------------------------------|-------------------|------|-------------------|---------------|---------|---|
| | Initial regimen with first-line drugs (CAT I) | Retreatment regimen with first-line drugs (CAT II) | | At the time of diagnosis | | Month 2/3/4 ^c | | Cured | Treatment failure | Died | Lost to follow-up | Not evaluated | | |
| | | | | S | C | X | Date | | | | | | | S |
| PTB | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | |

b. Smear results: **0**: No AFB; **1-9**: Exact number of 1-9 AFB/ 100 HPF (scanty); **+**: 10-99 AFB/ 100 HPF; **++**: 1-10 AFB/ HPF; **+++**: >10 AFB/ HPF
 Culture results: **0**: No growth; **1-9**: <10 colonies (rept exact number; **+**: 10-100 colonies; **++**: >100 colonies; **+++**: innumerable or confluent growth
 Xpert MTB/RIF results: **T**: MTB detected, Rifampicin resistance not detected; **RR**: MTB detected, Rifampicin resistance detected; **TI**: MTB detected, Rifampicin resistance detected; **TT**: MTB detected, Rifampicin resistance detected
 Dates associated with the recorded examination results are **dates of sample collection**
 c. If more than one smear, culture or Xpert MTB/RIF test is done in a month, enter the most recent positive result.
 d. Insert the date when outcome was met in the respective column. If patient "transfers out" to another district make a note in the Remarks column. If no definitive outcome is obtained, record as *Not evaluated* or *Lost to follow-up* as appropriate.

b. Request for Sputum Examination (TB 05)

National Tuberculosis Programme

TB 05

**THE LABORATORY FORM
REQUEST FOR SPUTUM EXAMINATION**

Name of referring health institution:.....Ward no:..... Date:.....

Name of patient: Age:.....

Address in full:.....

.....Tel No.....

Sex M

F

Disease classification:

Pulmonary

Extra-pulmonary - Site:.....

District:.....

Reason for examination:

For diagnosis

For follow up – Month

OPD/BHT/CC/District TB No.:

Specimen Identification No.:.....
(For collection centres only)

Dates of sputum collection:,, Signature:

RESULTS

(To be completed in the Laboratory)

LAB. SERIAL NO:

a) Visual appearance of sputum:

| Specimen | Mucopurulent | Blood stained | Saliva |
|----------|--------------------------|--------------------------|--------------------------|
| 1 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 2 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 3 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

b) Microscopy:

| Date | Specimen | Results* | POSITIVE (grading) | | | |
|------|----------|----------|--------------------|----|----|--------|
| | | | 3+ | 2+ | 1+ | Scanty |
| | | | | | | |
| | | | | | | |
| | | | | | | |

*Write negative or positive.

Name of the CC/MC: Designation: Signature:

The completed form (with results) should be sent to the treatment unit to record the results on the treatment card
Mark positive in **RED**

Previous Cultures Done

| Lab Serial No. | ABST No. | MDR No. | Year | Result |
|----------------|----------|---------|------|--------|
| | | | | |
| | | | | |
| | | | | |

Other Relevant Clinical Details (e.g. HIV /Other Causes of Immune Suppression/X Ray/Mantoux)

.....

| |
|------------------------------------------------------------------------------------------------------|
| Signature of Medical Officer:..... Name: Designation: HO/ MO/DTCO/SHO/REG/SR/VP/VS/..... |
|------------------------------------------------------------------------------------------------------|

Please Refer to Lists Given to District Chest Clinic for the Following

- *Indications for Culture - List 1*
- *Indications for Xpert MTB/RIF - List 2*
- *Presumptive MDR Groups –List 3*

Laboratory Use Only

Lab Serial No:

| | | | | | |
|--------------|-------------|-------------|-------------|-----------------|----------|
| Smear | Positive 3+ | Positive 2+ | Positive 1+ | Positive scanty | Negative |
|--------------|-------------|-------------|-------------|-----------------|----------|

| | | | | |
|----------------|----------|----------|--------------|-------|
| Culture | Positive | Negative | Contaminated | Other |
|----------------|----------|----------|--------------|-------|

| | | | |
|-----------------------|-----|----------|-----------------|
| Identification | MTB | Atypical | Other (Specify) |
|-----------------------|-----|----------|-----------------|

Results of Sensitivity Test

| Result | Streptomycin | Isoniazid | Rifampicin | Ethambutol |
|-----------|--------------|-----------|------------|------------|
| Sensitive | | | | |
| Resistant | | | | |

.....
MLT /NTRL

Date :

.....
Consultant Microbiologist/NTRL

Date :

Contact No.: 011-2956702 or 011-2951428 or 011-2951751 or 011-2958271 Ext 409, 138 or 421

QUARTERLY REPORT ON CASE FINDING

TB 08

d. Quarterly Report on Case Finding (TB 08)

District: Date of Completion of this Report: [] [] []

Name of DTCO: Signature:

Patients Registered During: Quarter [] Year []

| BLOCK 1: All TB Cases Registered During the Quarter | New | Retreatment Cases | | | | | TOTAL |
|---------------------------------------------------------------------|----------|-------------------|-------------------------|-----------------------------------|--------------------------|---------------------------------------|----------|
| | | Relapse | Treatment After Failure | Treatment After Loss to Follow-up | Other Previously Treated | Unknown Previous TB Treatment History | |
| Sputum smear positive | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Sputum negative and culture positive | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Sputum negative and WRD positive | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pulmonary, clinically diagnosed (Sputum smear negative) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Extrapulmonary, bacteriologically confirmed or clinically diagnosed | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TOTAL | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

BLOCK 3: Healthcare Workers and Foreign Nationals
 No of healthcare workers among diagnosed TB patients: []
 No of foreign nationals diagnosed with TB: []

BLOCK 4: TB/HIV Activities
 Patients with Positive HIV status at time of TB diagnosis (A): []
 Patients tested for HIV (B): []
 HIV positive among tested (C): []
HIV-positive TB patients -Total (A+C): 0
 HIV-positive TB patients on ART: []
 HIV-positive TB patients on CPT: []

BLOCK 2: Age and Sex Breakdown

| | Male | | | | | | | Female | | | | | | | | | | | | | |
|--------------------------------------|------|------|-------|-------|-------|-------|-------|--------|-----|-------|----|------|-------|-------|-------|-------|-------|-------|-----|-------|---|
| | <5 | 5-14 | 15-24 | 25-34 | 35-44 | 45-54 | 55-64 | 65-74 | >75 | Total | <5 | 5-14 | 15-24 | 25-34 | 35-44 | 45-54 | 55-64 | 65-74 | >75 | Total | |
| New | | | | | | | | | | | | | | | | | | | | | |
| Sputum smear positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and culture positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and WRD positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Pulmonary Clinically diagnosed | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Extrapulmonary | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Relapse | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum smear positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and culture positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and WRD positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Pulmonary Clinically diagnosed | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Extrapulmonary | | | | | | | | | | 0 | | | | | | | | | | | 0 |

QUARTERLY REPORT ON CASE FINDING

TB 08

| | Male | | | | | | | | | | Female | | | | | | | | | | |
|--------------------------------------|-------------------------|------|-------|-------|-------|-------|-------|-------|-----|-------|--------|------|-------|-------|-------|-------|-------|-------|-----|-------|---|
| | <5 | 5-14 | 15-24 | 25-34 | 35-44 | 45-54 | 55-64 | 65-74 | >75 | Total | <5 | 5-14 | 15-24 | 25-34 | 35-44 | 45-54 | 55-64 | 65-74 | >75 | Total | |
| | Treatment after Failure | | | | | | | | | | 0 | | | | | | | | | | |
| Sputum smear positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and culture positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and WRD positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Pulmonary Clinically diagnosed | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Extrapulmonary | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Treatment after Lost to Follow-up | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum smear positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and culture positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and WRD positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Pulmonary Clinically diagnosed | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Extrapulmonary | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Treatment after Lost to Follow-up | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum smear positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and culture positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and WRD positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Pulmonary Clinically diagnosed | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Extrapulmonary | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Treatment history | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Unknown Previous TB | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and culture positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Sputum negative and WRD positive | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Pulmonary Clinically diagnosed | | | | | | | | | | 0 | | | | | | | | | | | 0 |
| Extrapulmonary | | | | | | | | | | 0 | | | | | | | | | | | 0 |

QUARTERLY REPORT ON CASE FINDING

TB 08

| Block 5: Type of Extra Pulmonary TB | | |
|-----------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|-------------|
| ICD-10 Code | Site | No of Cases |
| A15: Respiratory tuberculosis, bacteriologically and histologically confirmed | | |
| A15.4 | Tuberculosis of intrathoracic lymph nodes | |
| A15.6 | Tuberculous pleurisy | |
| A15.8 | Other respiratory tuberculosis (mediastinal, nasopharyngeal, nose, sinus [any nasal]) | |
| A15.9 | Respiratory tuberculosis unspecified | |
| A16: Respiratory tuberculosis, not confirmed bacteriologically or histologically | | |
| A16.3 | Tuberculosis of intrathoracic lymph nodes | |
| A16.5 | Tuberculous pleurisy | |
| A16.8 | Other respiratory tuberculosis (mediastinal, nasopharyngeal, nose, sinus [any nasal]) | |
| A16.9 | Respiratory tuberculosis unspecified | |
| A17: Tuberculosis of nervous system | | |
| A17.0 | Tuberculous meningitis | |
| A17.1 | Meningeal tuberculoma | |
| A17.8 | Other tuberculosis of nervous system | |
| A17.9 | Tuberculosis of nervous system, unspecified | |

Official Stamp:

| ICD-10 Code | Site | No of Cases |
|-----------------------------------------------|--------------------------------------------------------------|-------------|
| A18: Tuberculosis of other organs | | |
| Tuberculosis of bones and joints | | |
| A18.0 | Spinal TB (Includes Vertebral Column - M49.0*) | |
| | Tuberculosis of other bones and joints (Excluding spinal TB) | |
| A18.1 | Tuberculosis of genitourinary system | |
| A18.2 | Tuberculous peripheral lymphadenopathy (TB adenitis) | |
| A18.3 | Tuberculosis of intestines, peritoneum and mesenteric glands | |
| A18.4 | Tuberculosis of skin and subcutaneous tissue | |
| A18.5 | Tuberculosis of eye | |
| A18.6 | Tuberculosis of ear | |
| A18.7 | Tuberculosis of adrenal glands | |
| Tuberculosis of other specified organs | | |
| | Pericardium | |
| | | |
| A18.8 | | |
| | | |
| | | |
| | | |
| | | |
| Site not Specified | | |
| TOTAL | | 0 |

QUARTERLY REPORT ON SPUTUM CONVERSION OF BACTERIOLOGICALLY CONFIRMED PATIENTS AT THE END OF INTENSIVE PHASE

TB 09

e. Quarterly Report on Sputum Conversion of Bacteriologically Confirmed Patients at the End of Intensive Phase (TB 09)

District: Patients Registered During: Quarter: Year: Date of Completion of this Report:

Name of DTCO: Signature:

| | Total Registered | | Sputum at 2-Months | | | | Sputum at 3-Months ^a | | | | Sputum at 4-Months ^b | | | | Died | | Lost to Follow Up ^c | |
|---------------------------------------------------------|------------------|---|--------------------|----------|---------------|----------|---------------------------------|---------------|----------|----------|---------------------------------|----------|----------|---------------|------|---|--------------------------------|---|
| | M | F | Negative | Positive | Not Available | Negative | Positive | Not Available | Negative | Positive | Not Available | Negative | Positive | Not Available | M | F | M | F |
| Sputum smear positive | | | | | | | | | | | | | | | | | | |
| New pulmonary bacteriologically confirmed | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| Sputum negative and WRD positive | | | | | | | | | | | | | | | | | | |
| Relapse | | | | | | | | | | | | | | | | | | |
| Treatment after failure | | | | | | | | | | | | | | | | | | |
| Treatment after loss to follow up | | | | | | | | | | | | | | | | | | |
| Other previously treated | | | | | | | | | | | | | | | | | | |
| Unknown previous TB treatment history (All other cases) | | | | | | | | | | | | | | | | | | |

No. of patients changed to *Bacteriologically Confirmed* from *Clinically Diagnosed*

Official Stamp:

- a. To be done for new patients with positive smear at 2-months and sputum not available at 2-months and re-treatment patients
- b. To be done for retreatment patients with positive smear at 3-months
- c. If patient has interrupted treatment but the definition of lost to follow up is not fulfilled, then the patient should be included under N. A. (Not Available).

**QUARTERLY REPORT ON THE RESULTS OF TREATMENT OF
PATIENTS REGISTERED 12-15 MONTHS EARLIER**

TB 10

f. Quarterly Report on the Results of Treatment of Patients Registered 12-15 Months Earlier (TB 10)

District: Patients Registered During: Quarter: Year: Date of Completion of this Report:

Name of DTCO: Signature:

| | Number Registered | | Cured | | Treatment Completed | | Treatment Failure | | Died | | Lost to Follow Up | | Not Evaluated | | Total Evaluated (Total with Outcome) | | |
|-------------------------------------------------------------------|----------------------------------------------------|---|-------|---|---------------------|---|-------------------|---|------|---|-------------------|---|---------------|---|--------------------------------------|---|--|
| | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F | |
| New Cases | A. Sputum smear positive | | | | | | | | | | | | | | | | |
| | B. Sputum negative and bacteriologically confirmed | | | | | | | | | | | | | | | | |
| | C. Sputum positive and WRD positive | | | | | | | | | | | | | | | | |
| | D. Pulmonary clinically diagnosed | | | | | | | | | | | | | | | | |
| | E. EPTB | | | | | | | | | | | | | | | | |
| F. TOTAL NEW CASES (A + B + C + D + E) | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Retreatment Cases | G. Relapse | | | | | | | | | | | | | | | | |
| | H. Treatment after failure | | | | | | | | | | | | | | | | |
| | I. Treatment after lost to follow up | | | | | | | | | | | | | | | | |
| | J. Other previously treated | | | | | | | | | | | | | | | | |
| K. TOTAL RETREATMENT CASES (G + H + I + J) | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| L. Unknown Previous TB Treatment History (All Other Cases) | | | | | | | | | | | | | | | | | |
| M. GRAND TOTAL (F + K + L) | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |

No. of patients changed to Bacteriologically Confirmed from Clinically Diagnosed:

Official Stamp:

| TB/HIV Activities | | Outcome Not Evaluated | |
|---------------------------------|--|-----------------------|--|
| HIV positive TB patients | | Diagnosis Changed | |
| HIV-Positive TB patients on ART | | Still on Treatment | |
| HIV-positive TB patients on CPT | | Other | |

g. Quarterly Report on Programme Management (District Level) (TB12)

TB 12

National Programme for Tuberculosis Control and Chest Diseases

**QUARTERLY REPORT OF PROGRAMME MANAGEMENT
(DISTRICT LEVEL)**

| | | |
|-----------------------------------------------------------|-----------------------------------------------------------------------------|-----------------|
| Name of the District:..... Year:..... Quarter:..... | Name of DTCO:..... Signature:..... Date of completion of report:..... | Official Stamp: |
|-----------------------------------------------------------|-----------------------------------------------------------------------------|-----------------|

1. Basic information about the TB services in the district

Population of district No. of functioning Microscopy Centres (including DCC) No. of branch clinics

2. Facility and providers linked to national programme (Excluding Facilities directly under Chest Clinics)

| Facility/provider type | Total number of facilities involved in TB Diagnosis or Treatment* (a) | Facilities with laboratory services | | Facilities providing HIV services | |
|------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------|
| | | Total No. conducting sputum smear microscopy in the district (b) | Out of (b), No. involved in Lab. Quality Assurance (c) | Out of (a), No. providing HIV testing & counsel. to all TB patients (d) | Out of (a) No. providing ART to TB patients (e) |
| Govt health facility | | | | | |
| Public health facility outside Health Ministry | | | | | |
| Private facility/provider | | | | | |

*Includes facilities providing DOTs

3. Patient Referral by facility/providers/community

| No. of patients registered in the quarter | Referred By | | | | | |
|-------------------------------------------|-------------|-------|-----------|-----|-----|------------------|
| | Government | | Private | | NGO | Community Worker |
| | Hospitals | Other | Hospitals | GPs | | |
| | | | | | | |
| | | | | | | |

4. OPD and Case finding activities

| | | In DCC | In Decentralized Units | Total |
|---|-----------------------------------------------------------------|--------|------------------------|-------|
| A | No. of adult out patients (>15 yrs.) | | | |
| B | No. of chest symptomatics referred for TB diagnosis | | | |
| C | No. of chest symptomatics examined with sputum smear microscopy | | | |
| D | Of C, number found sputum smear positive | | | |
| E | Of D, number put on treatment in the district | | | |
| F | Of D, number referred out of the district for treatment | | | |

5. Quality assessment of sputum microscopy

- No. of microscopy centres where slides were taken for random blinded rechecking by DCC
- No. of microscopy centres with any error in random blinded rechecking
- No. of sputum slides sent for rechecking from the DCC to the National Reference laboratory

| |
|--|
| |
| |
| |

6. Supervisory activities in the district (Completed indicates that a report is available on the supervision)

| Done By | Type of facility | Total No. in district | Month 1 | | Month 2 | | Month 3 | | MOH and Private Hospital Visits |
|-------------------------------------|-------------------------|-----------------------|------------|--------------|------------|--------------|------------|--------------|-------------------------------------|
| | | | No Planned | No Completed | No Planned | No Completed | No Planned | No Completed | |
| DTCO/MO | Chest Clinic Laboratory | | | | | | | | No. Of MOH Areas |
| | Drug Stores | | | | | | | | No of visits to MOH Offices |
| | DOTS Centers | | | | | | | | No of MOH Conferences Attended |
| Pharmacist Dispenser MLT PHLT | Microscopy Centres | | | | | | | | |
| | Decentralized Units | | | | | | | | |
| | Decentralized Units | | | | | | | | No of Private Hospitals in the Area |
| PHI | Home Visits | | | | | | | | |
| | DOTS Centers | | | | | | | | No of visits to Private hospitals |
| | Decentralized Units | | | | | | | | |

9) DOT Provision and Contact Screening

| Activity | New | | | | | | Retreatment | | | | Total |
|-----------------------------------|---------------------------|-----------|--------------------------------|------|---------|-----|-------------|-------|---------|-------|-------|
| | Pulmonary Bact. Confirmed | | Pulmonary Clinically Diagnosed | EPTB | Relapse | TAF | TALF | Other | Unknown | | |
| | Smear + | Culture + | | | | | | | | WRD + | |
| Total No of Registered Cases | | | | | | | | | | | |
| By Government Institution | | | | | | | | | | | |
| By Private Institution | | | | | | | | | | | |
| By Public Health Worker | | | | | | | | | | | |
| By Community Provider | | | | | | | | | | | |
| No of Patients screened | | | | | | | | | | | |
| No of Contacts identified | All | | | | | | | | | | |
| | <15 Yrs. | | | | | | | | | | |
| No of Contacts Screened | All | | | | | | | | | | |
| | <15 Yrs. | | | | | | | | | | |
| No of TB positive contacts | | | | | | | | | | | |
| No of Patients where Culture done | | | | | | | | | | | |
| No of Patients where DST done | | | | | | | | | | | |
| No of Patients where WRD done | | | | | | | | | | | |

10) INAH Prophylaxis

| | No Identified | | | No Started on INAH Prophylaxis | | | No INAH Prophylaxis Completed (From patients registered within 6-9 months before) | | |
|----------|---------------|-----------|----------|--------------------------------|-----------|----------|-----------------------------------------------------------------------------------|-----------|----------|
| | <5 Yrs. | 5-14 Yrs. | >14 Yrs. | <5 Yrs. | 5-14 Yrs. | >14 Yrs. | <5 Yrs. | 5-14 Yrs. | >14 Yrs. |
| Contacts | | | | | | | | | |
| HIV + | | | | | | | | | |
| Other | | | | | | | | | |
| Total | | | | | | | | | |