Ministry of Health

Guidelines for Tuberculosis Control in Brunei Darussalam

March 2013
GUIDELINES FOR TUBERCULOSIS CONTROL IN BRUNEI DARUSSALAM

MINISTRY OF HEALTH MARCH 2013
Foreword by Director General of Health Services

The initial “Guidelines for National Tuberculosis Programme and Manual of Technical Guidelines for National Tuberculosis Programme” were first published in the year 2000. Developments in tuberculosis control in Brunei Darussalam from the past decade however, have made the review of the existing guidelines necessary.

These guidelines are based on information available at the time of their preparation and in consultation with local experts in the field of infectious and respiratory diseases, paediatrics, general practice, public health, diagnostic, nursing, and other healthcare areas.

Identification of high risk groups, addressing issues such as delays in diagnosis and minimising the risk of emerging multidrug-resistant tuberculosis remain the mainstay of the publication. The main target group for this publication are healthcare workers at all levels particularly those that are involved in the management and control of tuberculosis.

I hope that the new guidelines will be instrumental in heightening awareness as well as assisting the country in its goal of eliminating TB in Brunei Darussalam.

The Department of Health Services wishes to congratulate the Guidelines Review Committee on the development of these reviewed guidelines as well as thank the supporting departments and units for their time and contribution to the review process.

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Contents

List of Abbreviations i
Background ii

1. National Tuberculosis Programme
   1.1 Vision, Mission, Goal, Objectives, Strategy and Targets 1
   1.2 National TB Committee 2
   1.3 Role of TB control service delivery centres 2
      1.3.1 National Tuberculosis Coordinating Centre (NTCC) 2
      1.3.2 Infectious Diseases Act (IDA, CAP. 204) 2
      1.3.3 DOTS Centres 3
      1.3.4 Division of Respiratory Medicine (DORM) 3
      1.3.5 National Isolation Centre (Tutong) 3
      1.3.6 National TB Reference Laboratory (NTRL), Department of Laboratory Services 4
      1.3.7 Occupational Health Division (OHD) 4
      1.3.8 Health Centres and MCH Clinics 4
      1.3.9 Community or village level 4
   1.4 Role of health workers 5
      1.4.1 Programme Manager 5
      1.4.2 Health NTP Coordinator 5
      1.4.3 Hospital NTP Coordinator 5
      1.4.4 Head NTCC 5
      1.4.5 Senior Medical Officer of Health/Medical Officer of Health 6
      1.4.6 Medical Officer (TB clinics /DOTS centre) 6
      1.4.7 Respiratory Physicians in Hospitals 6
      1.4.8 Scientific Officers (NTRL) 6
      1.4.9 Infection Control Nurses 6
      1.4.10 TB health workers and community health nurses in health centres and clinics 6
   1.5 Role of collaborating agencies 7
      1.5.1 Ministry of Education, Head of schools 7
      1.5.2 Labour Department and Immigration Department 7
      1.5.3 Royal Brunei Police Forces 7
      1.5.4 Medical Reception Services (MRS Clinics) 7

2. Case definitions, classifications, Policies and procedures
   2.1 Case definitions and classification 8
      2.1.1 Tuberculosis suspect 8
      2.1.2 Tuberculosis contact 8
      2.1.3 Case of tuberculosis 8
      2.1.4 Definite case of tuberculosis 8
   2.2 Types of patients and treatment outcomes 11
2.3 National Tuberculosis Programme Policies and Procedures

2.3.1 Notification, Isolation, Treatment and follow up of Tuberculosis index case 13
2.3.2 Isolation of infectious cases 15
2.3.2 (a) Working Protocol of TB isolation ward, National Isolation Centre 16
2.3.3 Transfer and Referral of TB patients 17
2.3.3 (a) Transfer from DORM to NTCC 17
2.3.3 (b) Transfer from DORM to National Isolation Centre 17
2.3.3 (c) Transfer from NTCC to DOTS clinics 18
2.3.3 (d) Transfer from NTCC to National Isolation Centre 18
2.3.3 (e) Transfer from Belait to National Isolation Centre 18
2.3.3 (f) Transfer from Health Centres to National Isolation Centre 19
2.3.3 (g) Transfer from Temburong to National Isolation Centre 20
2.3.4 Case finding (Identification and diagnosis of TB cases) 20
2.3.5 Laboratory Services- National TB Reference Laboratory Services 23
2.3.5 (a) Specimen Processing and Reporting 24
2.3.5 (b) Microscopy 24
2.3.5 (c) Culture 24
2.3.5 (d) Antibiotic Susceptibility Testing (AST) 24
2.3.5 (e) Nuclei Acid Amplification Testing (NAAT) 25
2.3.5 (f) Notification of positive results by NTRL 25
2.3.6 Adherence to Treatment; Directly Observed Treatment (DOTS) 26
2.3.7 Registration 27
2.3.7 (a) Initiation of treatment 27
2.3.7 (b) Monitoring compliance and response to treatment 28
2.3.7 (c) Management of adverse reactions to drugs 28
2.3.8 Recording and Reporting 28
2.3.8 (a) NTP records and reports forms 28
2.3.9 Logistics 29
2.3.10 Absentee/Defaulter tracing 29

2.4 Supervision & Evaluation 29
2.4.1 Supervision 29
2.4.2 Evaluation 30

2.5 BCG Immunization 30

3. Community Tuberculosis control

3.1 Contact Investigation
3.1.1 Structuring a contact investigation programme 31
3.1.2 Source- Case Investigation 33
3.1.3 Contact investigations in special circumstances 36
3.1.3 (a) Hospitals and other healthcare facilities 36
3.1.3 (b) Schools/higher Education Institutions 36
3.1.3 (c) Prisons and detention centres 37
3.1.3 (d) Contact tracing and prevention of TB among Travellers 37
3.1.3 (e) Contact Investigation at Work 37
3.1.4 Evaluation, Treatment and follow up Contact Investigation 38
3.1.5 Notification to overseas health authorities 40
3.2 Screening of TB 40
3.2.1 Mantoux test/ Tuberculin Skin Test (TST) 41
3.2.1 (a) Procedure for placing the Mantoux (TST) 41
3.2.1 (b) Interpretation of the Mantoux skin test 42
3.2.1 (c) Two-Step Tuberculin Skin Testing 43
3.2.2 Interferon-Gamma Release Assays (IGRAs) - Blood Tests for TB Infection 43
3.2.2 (a) Advantages of IGRAs 44
3.2.2 (b) Disadvantages and limitations of IGRAs 44
3.2.2 (c) Steps in administering an IGRA test 44
3.2.2 (d) Interpretation of IGRA test results 44
3.2.2 (e) Recommendations on when to use IGRA tests 45
3.3 Latent TB Infection 46
3.3.1 Diagnosis of Latent TB Infection or TB Disease 46
3.3.2 Treating Latent TB Infection 46
3.3.3 Treatment Options for Latent Tuberculosis Infection 47
3.3.3 (a) Choosing the Most Effective Regimen 47
3.3.3 (b) Adverse Drug Reactions 49
3.3.3 (c) Monitoring During Treatment 49
3.3.4 Special considerations for treatment of LTBI 49
3.4 Management of TB In Workplace 50
3.4.1 Implementation of TB Programme at Workplace 50
3.4.1 (a) Detecting TB at workplace 50
3.4.1 (b) Ensure a safe workplace environment 51
3.4.1 (c) Education and Training 51
3.4.2 Coordination with NTP 51
3.4.3 Ensuring sustainability of TB control activities 51
3.5 TB Screening in Foreign Workers 52
3.6 TB Screening for Health Care Workers 54
3.7 Biosafety for Health Care Workers 54
3.7.1 Infection control in Tuberculosis 55
3.7.2 Environmental factors that increase the risk for probability of transmission of M. tuberculosis 56
3.7.3 Risk for Health-Care–Associated Transmission of M. tuberculosis 56
3.7.3 (a) Administrative Controls 56
3.7.3 (b) Environmental Controls 57
3.7.3 (c) Respiratory-Protection Controls 57
3.7.3 (d) Personal Protection Equipment (respiratory protection) 57

4. Therapeutic Guideline 59

4.1 Flow Chart for New Case of Pulmonary TB 59
4.2 Standard treatment schedule for new TB patients
4.3 Recommended Doses of first line Anti-Tuberculosis drugs for adults
4.4 Standard regimens for previously treated TB patients- Defaulted / Relapsing
4.5 Management of treatment interruption
4.6 Management of TB in patients who develop hepatitis with alternate treatment regimens and change in duration of therapy as a consequence
4.7 Algorithm for the diagnosis of tuberculosis in Smear-negative patients
4.8 Algorithm of approach to Diagnosis of Extra Pulmonary Tuberculosis
4.9 Step-by-step diagnostic approach in patients with Extra-pulmonary Tuberculosis
4.10 Tests for all suspected Extra-pulmonary Tuberculosis
  4.10.1 TB lymphadenitis
  4.10.2 Pleural TB
  4.10.3 Pleural fluid analysis
  4.10.4 Skeletal TB
  4.10.5 CNS TB
  4.10.6 Abdominal TB
  4.10.7 Genitourinary TB
  4.10.8 Pericardial TB
  4.10.9 Disseminated TB
4.11 Co-management of HIV and active TB disease
4.12 TB treatment in people living with HIV
4.13 Management of Extra Pulmonary TB
  4.13.1 Meningeal TB
  4.13.2 Peripheral lymph node TB
  4.13.3 Bone and joint TB
  4.13.4 Pericardial TB
  4.13.5 Disseminated (including miliary) TB
4.14 Treatment regimens in special situations
  4.14.1 Pregnancy
  4.14.2 Breastfeeding
  4.14.3 Liver disorders
  4.14.4 Renal failure and severe renal insufficiency
  4.14.5 Unmanageable drug related adverse events with renal failure or hepatitis
4.15 Assessing treatment response in new and previously treated pulmonary TB patients, and acting on the results
4.16 Definitions of Treatment outcomes
4.17 Symptom based approach to managing side effects of Anti-TB drugs
4.18 Management of tuberculosis in children
  4.18 (a) Approach to diagnose TB in children
  4.18 (b) Recommended treatment regimens for children in each TB diagnostic category
  4.18 (c) Adverse events
5. **Guide for computing Indicators for Programme Evaluation**

5.1 Indicators for monitoring in Case Finding
5.2 Indicators for monitoring in Case Holding

References

Annexes

ANNEX I: TB SYMPTOMATICS MASTER LIST
ANNEX II: TUBERCULOSIS TREATMENT CARD
ANNEX III: TUBERCULOSIS REGISTER
ANNEX IV: QUARTERLY REPORT ON TUBERCULOSIS CASE FINDING
ANNEX V: TUBERCULOSIS REFERRAL / TRANSFER FORM
ANNEX VI: HOME VISIT FORM
ANNEX VII: MANTOUX TEST FORM
ANNEX VIII: CONTACT SCREENING FORM
ANNEX IX: PAMPHLET FOR SPUTUM COLLECTION PROCEDURE
ANNEX X: REVIEW COMMITTEE OF NATIONAL TB CONTROL PROGRAMME
List of Abbreviations

AFB Acid Fast Bacilli
ATT Anti-Tuberculosis Treatment
BAL Broncho-alveolar Lavage
BAL CP Broncho-alveolar Lavage Culture positive
BCG Bacille Calmette-Guérin vaccine
CPT Co-trimoxazole Preventive Therapy
DCD Disease Control Division
DEHS Director of Environmental Health Services
DGHS Director General of Health Services
DGMS Director General of Medical Services
DHS Director of Health Services
DORM Division of Respiratory Medicine
DOTS Directly Observed Treatment Short Course
DTCU District Tuberculosis Coordinating Unit
EPTB Extra Pulmonary Tuberculosis
HCW Health Care Worker
ICU Intensive Care Unit
IDA, CAP. 204 Infectious Diseases Act, Chapter 204
IGRA Interferon-Gamma Release Assay
IHR International Health Regulation
LTBI Latent TB Infection
MCH clinic Maternal and Child Health Clinic
MDR TB Multi Drug Resistant TB
MO Medical Officer
MOH Medical Officer of Health
NTCC National Tuberculosis Coordinating Centre
NTP National Tuberculosis Programme
NTRL National TB Reference Laboratory
OHD Occupational Health Division
PIHM hospital Pengiran Isteri Hajjah Mariam, Temburong Hospital
PMMPMHAMB hospital Pengiran Muda Mahkota Pengiran Muda Haji Al-Muhtadee Billah, Tutong Hospital
PTB Pulmonary Tuberculosis
RIPAS hospital Raja Isteri Pengiran Anak Saleha Hospital
SMO Senior Medical Officer
SMOH Senior Medical Officer of Health
SNCP Smear negative Culture Positive
SPCN Smear Positive Culture Negative
SPCP Smear Positive Culture Positive
SSBH Suri Seri Begawan Hospital, Kuala Belait
TAI Treatment after interruption
TB Tuberculosis
TB/HIV TB-HIV co infection
TST Tuberculin Skin Test
XDR TB Extensively Drug Resistant TB
Background

Brunei Darussalam has come a long way in the fight against tuberculosis. TB rates fell from more than 500 cases per 100 000 populations in 1960s to below 100 cases per 100,000 populations in the 1980s due to economic development, improved public health, better diagnostic facilities and treatment. In October 1995, awareness on TB stagnation and increasing trends were highlighted to The Ministry of Health. From 1-4 October 1997, SEAMIC/IMFJ technical meeting on TB was held in Brunei Darussalam to create further awareness of the problem among doctors and nurses. On 20th July 1999, WHO consultant on TB visited Brunei Darussalam to study the existing situation and advised on the implementation of NTP (National Tuberculosis Control Programme). On 29th March 2000 NTP was launched along with the first edition of National TB Guidelines and the NTP-Committee was established in the same year. The National Tuberculosis Coordinating Centre (NTCC) in Kiarong became functional from December 2000.

The first edition of The National TB Guidelines was launched in the year 2000 in the form of two booklets; Manual of Technical Guidelines for NTP and Guidelines for NTP. These Guidelines adhered to WHO recommendations and guidance. The formation of the NTP, along with an increased awareness of TB control services with an increase in identification and treatment of cases resulted in a reduction of TB incidence to 91.96 per 100,000 populations in the year 2000. The annual TB incidence rate continued to gradually decrease to 44.04 per 100,000 populations in 2005 and has remained at 60.81 per 100,000 populations until 2012.

In view of the emergence of multi & extensively drug-resistant tuberculosis in the last decade, the NTP has updated its TB control strategy along with developing improved diagnostic facilities. In April 2011, the Deputy Permanent Secretary (Professional & Technical), Ministry of Health, appointed a committee to look into reviewing the NTP. Along with the updated recommendations, the National TB Guidelines were reviewed by the committee in a series of meetings. The second edition of “Guidelines for Tuberculosis Control” was eventually endorsed 2013 in line with the current targets, objectives, recommendations and practices of the World Health Organization (WHO) as well as other internationally recognized organizations.
1.1 Vision, Mission, Goal, Objectives, Strategy and Targets

**Vision**

A Tuberculosis-free nation

**Mission**

To promote the early detection and treatment of all TB cases in the community and protect the community from the risk of TB transmission

**Goal**

1. To reduce the incidence of TB in Brunei Darussalam by 2015;
2. To continue reducing the prevalence and deaths due to TB by 50% in 2015 compared to the year 2000;
3. Eliminate TB by 2050

**Objectives**

1. Achieve universal access to quality diagnosis and patient-centred treatment
2. Protect vulnerable populations from TB, TB/HIV, MDR-TB and XDR-TB
3. Expand and strengthen TB/HIV collaborative activities
4. Intensify case-finding amongst identified high-risk population

**Targets**

1. To achieve a cure rate of over 85% annually
2. Proportion of notified TB cases among children under 14 years of age to less than 2% of all cases annually
3. To reduce annual HIV prevalence amongst TB patients to less than 2% by:
   - Co-trimoxazole Prevention Therapy (CPT) coverage among TB-HIV co-infected patients (100%)
   - People living with HIV shall receive periodic TB screening (at least 3 times a year)
   - People living with HIV shall receive Isoniazid Preventative Therapy (as indicated) (100%)

**Strategy**

The Global Plan to Stop TB (the Stop TB Strategy) was launched through the “Stop TB Partnership” in 2001. This strategic plan serves as a roadmap for reaching the goals of ensuring access to treatment and cure, protection of vulnerable populations from TB, and a reduction in the social and economic tolls of TB on families, communities, and nations. Components of the Stop TB Strategy are:

1. Pursue high-quality DOTS expansion and enhancement
2. Address TB-HIV, MDR-TB, and the needs of poor and vulnerable populations
3. Contribute to health system strengthening based on primary health care
4. Engage all care providers
5. Empower people with TB, and communities through partnership
6. Enable and promote research
1.2 National Tuberculosis Committee

The National Tuberculosis Committee is responsible for Policy and Planning issue related to TB as follows:

- defining the national strategy, including diagnosis and treatment policies,
- preparing and updating the National Tuberculosis Programme guidelines;
- planning, implementing and evaluating the NTP activities, including the preparation of budget and action plans;
- coordinating with the relevant administrative departments in ensuring that the allocation of adequate financial, human and material resources for the NTP is given high priority;
- coordinating with the laboratory to ensure that adequate sputum smear microscopy and culture services are in place;
- ensuring the regular and uninterrupted supply of anti-TB drugs, laboratory reagents and other materials;
- supervising the DOTS centre and ensuring adequate training of its health workers; and
- consolidating and evaluating monthly / quarterly / annual reports on notified cases and outcomes of treatment.

1.3 Role of TB Control Service Delivery Centres

1.3.1 National Tuberculosis Coordinating Centre (NTCC)

The centre is responsible for programme implementation, monitoring, coordinating and evaluation of TB prevention and control activities at all levels. This centre is managed by the Programme Manager with the help of Hospital and Health NTP Coordinators, DOTS Coordinators and TB Health Workers.

1.3.2 Infectious Diseases Act (IDA, CAP. 204)

Tuberculosis is a notifiable disease in Brunei Darussalam under the Infectious Diseases Act (IDA, Chapter 204). An infectious TB patient should be isolated for such period of time as may be necessary for the protection of the public in accordance with IDA Part III, Section 15 subsections (1) to (5).

“15. (1) The Director-General may order any person who is, or is suspected to be, a case or carrier or contact of an infectious disease to be detained and isolated in a hospital or other place for such period of time and subject to such conditions, as the Director-General may determine.

(2) Notwithstanding subsection (1), the Minister may, with the approval of His Majesty the Sultan and Yang Di-Pertuan, order the removal forthwith from Brunei Darussalam of any person referred to in subsection (1) who is not a citizen of Brunei Darussalam.

(3) The Director-General may order any person who is, or is suspected or continues to be suspected to be, a case or carrier or contact of an infectious disease, or who has recently recovered from or been treated for such disease, to remain and to be isolated and (if necessary) be treated, in his own dwelling place —

(a) for such period of time as may be necessary for the protection of the public; and
(b) subject to such conditions as the Director-General may consider necessary for this purpose.

(4) If any person against whom an order under subsections (1) or (3) is made —
(a) fails to proceed to the place in which he is to be isolated within the time specified in the order;
(b) without the permission of the Director-General, leaves or attempts to leave the place in which he is being isolated; or
(c) fails to comply with any condition to which the person is subjected to, that person is guilty of an offence.

(5) Any person in respect of whom an order under subsection (2) has been made who fails to comply with that order is guilty of an offence.”

1.3.3 DOTS Centres

DOTS Centres are located mainly in hospitals and health centres / clinics and also function as a Tuberculosis referral and reporting unit. Responsibilities of DOTS Centres are as follows:
- Ensuring the diagnosis of pulmonary TB is based on sputum smear microscopy and culture;
- Ensuring daily / three times a week, directly observed treatment (DOTS);
- Keeping the TB register up to date and providing monthly / quarterly reports on the notified cases and outcome of treatment to the NTP;
- Supervising, training and motivating the health workers of the DOTS Centre as well as those operating at village level; and
- Contact tracing of sputum smear positive pulmonary TB cases

1.3.4 Division of Respiratory Medicine (DORM) and Chest Clinics

TB cases should be referred to the Division of Respiratory Medicine (DORM) in RIPAS Hospital and the Chest Clinics of the respective hospitals for the initiation of TB treatment. TB treatment of patients admitted in hospital wards will also be initiated and supervised by the Respiratory Physicians. When a TB patient is discharged from a ward, the Respiratory Physician will refer the patient to NTCC or TB isolation ward (Tutong) to continue treatment.

1.3.5 National Isolation Centre (Tutong)

The Roles of the TB isolation ward are:
1. To isolate cases of sputum positive Tuberculosis, preventing active dissemination of the mycobacteria
2. To monitor adverse drug reactions during the course of treatment
3. To make sure that all TB cases are treated and monitored at one dedicated place for isolation
4. To implement infection control policy and barrier nursing to reduce the risk of infection to other patients and health care workers
5. To coordinate with NTCC in case notification and contact tracing
1.3.6 National TB Reference Laboratory (NTRL), Department of Laboratory Services

The National TB Reference Laboratory (NTRL) provides laboratory diagnosis for tuberculosis, other non-TB mycobacterial infections and Leprosy from clinical specimens for all hospitals and health clinics in Brunei Darussalam.

NTRL also collaborates with healthcare providers and NTCC for the effective surveillance, prevention and control of TB in Brunei Darussalam.

NTRL, in line with the departmental ISO 15189 quality management; performs the following services.

- Detection of acid-fast bacilli by microscopy using both Auramine O and Kinyoun staining
- Bacteriological culture of clinical specimens for mycobacteria using MGIT 960 system (liquid media) & Lowenstein-Jensen (solid media).
- Phenotypic and molecular identification of Mycobacterium tuberculosis complex (MTBC)
- Molecular identification of MTBC to species level
- Molecular identification of Mycobacteria other than Tuberculosis (MOTT) to ~30 species
- Performance of first-line drug susceptibility testing for Mycobacterium tuberculosis (BD MGIT 960 System)
- Performance of IQA (staining & media only)
- Performance of external quality assurance (RCPA on smear & culture only)

1.3.7 Occupational Health Division (OHD)

TB is one of the diseases that is screened under the occupational health screening programme amongst others. OHD also plays an important role in screening TB amongst foreign workers and liaise closely with DORM, NTCC and the Immigration Department for TB cases amongst the workers.

1.3.8 Health Centres and MCH Clinics

Staff at the Health Centres and MCH clinics have the following responsibilities:

- Identification and initial evaluation of suspected TB patients;
- Referring suspected TB patients for further investigations to the Hospital Chest Clinics / DORM;
- Patients with suspected TB and who are unwell will be referred to the medical officer on call for isolation and investigation;
- Referring smear positive patients for sputum and x-ray follow up towards the end of the treatment as required;
- Ensuring compliance of daily DOTS for TB patients and tracing of absentees;
- Ensure the recording of the intake of treatment in the patients’ treatment card;
- Provide basic TB information and health education to the patients’ family and community;
- Ensuring that the TB register is up to date by reporting TB cases and treatment outcomes to NTCC.

1.3.9 Community Leaders

Community leaders play an important role in prevention and control of TB disease which include;

- educating the community about TB and/or HIV while at meetings, or community gatherings;
- supporting TB programmes at National level, health facilities, and in the community levels;
- supporting the identification and referral of people with suspected TB.
Village heads (Ketua Kampong) are one of the key stakeholders in TB control programmes. They play an important role in approaching people who may be suspected of having TB symptoms (such as cough and expectoration for more than 2 weeks) in their village and also assisting in ensuring the compliance of DOTS as a treatment partner. They also play a supporting role during absentee/defaulter tracing activities.

1.4 Role of Health Care Workers

1.4.1 Programme Manager
- Responsible for development of TB prevention, control policy and decision making in programme management;
- Liaise with National Committee and other related sectors for TB control activities;
- Provide the periodical reports and information of the programme to the Ministry of Health and other related International Organisations;
- Ensuring availability and optimisation of budget;
- Ensuring implementation of TB control programmes in all schedules;
- Balancing the interests of internal and external stakeholders to align with the National TB Prevention and Control Program;
- Monitor the implementation, planning and timely evaluation of the programme.

1.4.2 Health NTP Coordinator
- Supporting the Programme Manager by coordinating all programme-related activities;
- Monitor the implementation of the NTP at all levels.
- Monitor and evaluate the implementation of the NTP at all levels and in all health facilities by assessing the following;
  - Analyse information from the report submitted
  - Cure rate achievement
  - Defaulter retrieval activities
  - Case investigation of seriously ill TB cases from ICU
- Prepare and submit quarterly and annually report to the Programme Manager;
- Act as a trainer in conducting in-service and refreshing training courses;
- Periodical evaluation of the programme.

1.4.3 Hospital NTP Coordinator
- Participate in programme planning, policy decisions and budgetary requirement preparation;
- Provide technical assistance during training;
- Act as a coordinator and liaison officer between NTP and medical facilities;
- Act as trainer in conducting on-the job training in NTP of newly designated or recruited personnel.

1.4.4 Head NTCC
- Monitor the logistics, budget, human resources and other administrative issues;
- Monitors the activities of the NTCC and District Tuberculosis Coordinating Units (DTCU)
• Supervise all health workers in ensuring proper implementation of NTP guidelines and policies;
• Assist in the training of all categories of health workers involved in NTP.

1.4.5 Senior Medical Officer of Health/Medical Officer of Health for Districts
• Monitoring and Supervising the TB control programme in Districts on behalf of Programme Manager.

1.4.6 Medical Officer (TB Clinics /DOTS Centre)
• Continuation of TB treatment for TB cases as initiated by chest clinics or NTCC;
• Referral of TB cases to other health facilities if indicated;
• Ensures that all TB cases receive adequate clinical assessment and appropriate decision on regimen and management of adverse reactions to the drugs;

1.4.7 Respiratory Physicians in Hospitals
• Timely notification of newly diagnosed TB cases to DCD and NTCC;
• Ensures the implementation of infection control procedures in the wards and ICUs where TB cases are admitted;
• Referral of TB cases to NTCC and/or National Isolation Centre (Tutong) as indicated;
• Coordinate all NTP activities in the hospital as a Clinical Coordinator.

1.4.8 Scientific Officers (NTRL)
• Microscopic and culture diagnosis of pulmonary and extra-pulmonary tuberculosis;
• Molecular detection and identification of Mycobacterium tuberculosis complex;
• Performing first line drug susceptibility testing on all TB isolates;
• Timely notification of positive cases, including any resistant TB isolate to Isoniazid and/or Rifampicin or any MDRTB or XDRTB, to relevant health agencies in NTP
• Assist in the detection of Latent TB infection (LTBI).

1.4.9 Infection Control Nurses
• Ensuring the implementation of transmission base precaution is applied at all times in the ward/ facility;
• Annual updating of baseline Mantoux for previous exposures as part of monitoring personnel health;
• Conducting staff education and training in principles, policies and procedures of infection control with regards to TB. This includes personnel with support responsibilities as well as clinical staff;
• Responsible in ensuring that all personnel are aware of, and work within guidelines, policies and procedures to ensure that safe working practices are maintained for patients and staff.

1.4.10 TB Health Workers and Community Health Nurses in Health Centres and Clinics
• Assist the medical officer in supervising evaluation and continuation of treatment;
• Assist in case holding by adapting DOTS and retrieving absentees;
• Assist in supervision to ensure proper implementation of DOTS;
• Assist maintenance, analysis and submission of quarterly report on new cases / relapses and quarterly cohort analysis;
• Assist in ensuring adequate TB drugs and other supplies;
• Maintain records such as Treatment Card and list of TB symptomatics;
• Provide continuous health education to all TB patients placed under treatment, encourage community participation in NTP;
• Refer patients with adverse reactions to anti-TB drugs to the medical officer for further evaluation and management;
• Monitor sputum follow-up of all TB cases during the course of treatment.

1.5 Role of Collaborating Agencies
1.5.1. Ministry of Education, Head of schools
The Ministry of Education plays an important part in supporting early case detection and contact tracing in schools to prevent transmission of TB in the school environment.

1.5.2. Labour Department and Immigration Department
Co-operation of the above two government agencies are important in dealing with foreign workers who are infected with tuberculosis, particularly in the issuance of work permits and repatriation process.

1.5.3. Royal Brunei Police Forces
Assistance from the Royal Brunei Police Force may be obtained to enforce isolation of noncompliant patients.

1.5.4. Medical Reception Services (MRS Clinics)
MRS clinics from military camps work closely with NTCC in the diagnosis, contact tracing and continuation of treatment in soldiers with TB.
2.1 Case definitions and classification, Types of patients and Treatment outcomes

2.1.1 Tuberculosis Suspect:
Any person who presents with symptoms or signs suggestive of TB.
The most common symptom of pulmonary TB is productive cough for more than 2 weeks,
which may be accompanied by other respiratory symptoms (shortness of breath, chest
pains, haemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever,
night sweats, and fatigue).

2.1.2 Tuberculosis Contact:
Household contacts are defined as those who share a bedroom, kitchen, bathroom or
sitting room with the index case.
Close contacts: these can include a spouse/partner, close relative, frequent visitors to the
home of the index case, in addition to household contacts
Social contacts: those who have frequent gatherings with the index case (e.g. places of
worship, office, schools, sports activities)
Contact cases on aircraft: those who have sat on a flight which was longer than 8 hours.
The flight should have taken place not more than 3 months previously (refer to 3.1.3 (d))

2.1.3 Case of Tuberculosis: A definite case of TB (as defined below) or one in which a health
worker (clinician or other medical practitioner) has diagnosed TB and has decided to treat
the patient with a full course of TB treatment.
Note- Any person given treatment for TB should be recorded as a case. Incomplete “trial”
TB treatment should not be given as a method for diagnosis.

2.1.4 Definite Case of Tuberculosis: A patient with Mycobacterium tuberculosis complex
identified from a clinical specimen, either by culture or by a newer method such as
molecular line probe assay. A pulmonary case with one or more initial sputum smear
examinations positive for acid-fast bacilli (AFB) is also considered to be a “definite” case.
Cases of TB are also classified according to the following:
 a) anatomical site of disease;
 b) bacteriological results (including drug resistance);
 c) history of previous treatment;
 d) HIV status of the patient.

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

Extra-pulmonary tuberculosis (EPTB) refers to a case of TB (defined above) involving
organs with no involvement of the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary
tract, skin, joints and bones, meninges. Diagnosis should be based on at least one specimen
with confirmed M. tuberculosis or histological or strong clinical evidence consistent with
active EPTB, followed by a decision by a clinician to treat with a full course of tuberculosis
chemotherapy. The case definition of an EPTB case with several sites affected depends on
the site representing the most severe form of disease. Unless a case of EPTB is confirmed
by culture as caused by M. tuberculosis, it cannot meet the “definite case” definition
above.
b) Bacteriological results
A case of pulmonary TB is considered to be **smear-positive** if one or more sputum smear specimens at the start of treatment are positive for AFB.

**Smear-negative** PTB cases should either:

(I) have sputum that is smear-negative but culture-positive for M. tuberculosis:

➢ A case of pulmonary TB is considered to be smear-negative if at least two sputum specimens at the start of treatment are negative for AFB.

OR

(II) meets the following diagnostic criteria:

➢ decision by a clinician to treat with a full course of anti-TB therapy; and

➢ radiographic abnormalities consistent with active pulmonary TB and, with either,

   - a laboratory or strong clinical evidence of HIV infection or:

   - if HIV-negative, no improvement in response to a course of broad-spectrum antibiotics (excluding anti-TB drugs and fluoroquinolones and aminoglycosides).

c) History of previous treatment: patient registration group

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

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

<table>
<thead>
<tr>
<th>Registration group (any site of disease)</th>
<th>Bacteriology</th>
<th>Outcome of most recent prior treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New</strong></td>
<td>+ or –</td>
<td>–</td>
</tr>
<tr>
<td><strong>Previously treated</strong></td>
<td>Relapse</td>
<td>+</td>
</tr>
<tr>
<td>Treatment completed</td>
<td></td>
<td>Cured</td>
</tr>
<tr>
<td><strong>Failure</strong></td>
<td>+</td>
<td>Treatment failed</td>
</tr>
<tr>
<td><strong>Default</strong></td>
<td>+</td>
<td>Defaulted</td>
</tr>
<tr>
<td><strong>Transfer in: A patient who has been transferred from another TB register to continue treatment</strong></td>
<td>+ or –</td>
<td>Still on treatment</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>+ or –</td>
<td>All cases that do not fit the above definitions, such as patients • for whom it is not known whether they have been previously treated; • who were previously treated but with unknown outcome of that previous treatment and/or • who have returned to treatment with smear-negative PTB or bacteriologically negative EPTB</td>
</tr>
</tbody>
</table>
### Types of Patients

**New**

A patient who has never been treated for TB or who has taken anti-TB drugs for less than four weeks.

**Relapse**

A patient previously treated for TB who has been declared cured or treatment completed, and is diagnosed with bacteriologically positive (smear or culture) tuberculosis.

**Treatment failure**

A previously sputum smear-positive patients who, while on treatment, remained or became smear-positive again five months or later after commencing treatment. It is also a patient who was initially smear-negative before starting treatment and became smear-positive after the second month of treatment.

**Treatment after interruption (TAI) or (default)**

A patient who has taken at least four weeks of treatment but has subsequently interrupted treatment for two months or more, and returns to health facility with smear-spectrum positive.

**Transfer In**

A patient who has been transferred into the reporting unit from another reporting unit.

**Other**

Cases that do not fit any or the above definitions.
TREATMENT OUTCOMES

Cured

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

Treatment Completed

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

Treatment Failure

A patient whose sputum smear or culture is positive at 5 months or later during treatment. Also included in this definition are patients found to harbour a multidrug-resistant (MDR) strain at any point of time during the treatment, whether they are smear-negative or -positive.

Died

A patient who dies for any reason during the course of treatment.

Treatment interrupted (default)

A patient whose treatment was interrupted for 2 consecutive months or more.

Transfer out

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

Treatment success

A sum of cured and completed treatment.
2.3 National Tuberculosis Programme Policies and Procedures

2.3.1 Figure (1) Notification, Isolation, Treatment and follow up of Tuberculosis Index Case

- **Notification**
  - District Health Office
  - DCD
  - NTCC

- **Case Verification**
  - Sputum negative PTB/EPTB
    - Start initial course of treatment at DORM/Hospital Chest Clinic
    - Discharge from DORM/Hospital Chest Clinic
    - Refer to NTCC/District DOTS centres

  - Sputum positive or culture positive PTB/Laryngeal TB
    - Isolation at National Isolation Centre (Tutong)*
    - Sputum conversion after initial treatment
    - Discharge from Isolation

    - Initiate contact tracing

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**Note:**
*Patient may be admitted to Ward 16 in RIPAS Hospital if indicated*
2.3.2 Isolation of Infectious Cases

All patients diagnosed with smear positive PTB, should be referred to the National Isolation Centre (Tutong). The patient should be treated in the isolation ward until the smear becomes negative. After smear conversion, the patient can be discharged and referred to NTCC/District DOTS clinics for continuation of treatment. If the patient is non-Bruneian, the Occupational Health Division will be informed for them to liaise with the Immigration Department.

Note: If smear negative PTB or EPTB patient who is asymptomatic and is on anti-tuberculosis treatment for more than 2 weeks and is discharged for follow up at District Tuberculosis Coordinating Unit (DTCU) or NTCC should not be referred to isolation ward when the culture report [which usually takes 6 weeks’ time] becomes available and is reported as culture positive. Such patient does not need isolation and should be followed up by DTCU or NTCC.
2.3.2 (a) Working Protocol of TB isolation ward, National Isolation Centre

Figure (3) Referral, Isolation and Treatment in Tutong Hospital

- **Infectious Type of TB** (SPCP/BAL SP)
  - Before transfer
    - Inform to Isolation ward
    - Counsel patient
    - Arrangement for transport
    - Referral form, CXR, investigations
    - N95 & Surgical mask during transport
    - To be accompanied by nurse
  - Transfer
    - Admission in Isolation Ward
    - Notify to DCD/NTCC
    - Strict respiratory precaution for staff and visitors
    - Start/Continue ATT
  - After 2 weeks of ATT
    - Reassess sputum examination for SPCP & BAL SP PTB
      - 3 smears negative
        - Discharge from Isolation Ward
        - TB card
        - Case summary/referral

District DOTS centres (Belait, Tutong)  NTCC (Brunei Muara, Temburong)

SPCP-Smear positive Culture positive, BAL SP- Broncho-alveolar Lavage Smear positive
- SPCP cases after 2 weeks anti TB drugs, no further cough, unable to give sputum recheck may be discharged without repeat sputum if decided by treating physician.
- SPCP cases with multi organ failure/seriously ill/CNS involvement/serious TB treatment complications will be admitted in RIPAS hospital.
2.3.3 Transfer and Referral of TB Patients

TB patients under treatment should be transferred to the relevant Health Units according to the nature of disease and convenience to follow DOTS for better compliance. During transfer of patients to isolation ward (Tutong), the Health Centre/Clinic is responsible to ensure that the patient is admitted to isolation ward in the arranged time.

2.3.3 (a) Transfer from DORM/Respiratory Physician to NTCC/DTCU

For non-infectious TB patient diagnosed at DORM or by Respiratory Physician,

1. Treatment will be commenced by DORM or Respiratory Physician.
2. Continuation of treatment and follow up should be referred to NTCC/DTCU.
3. Staff nurse on duty from DORM will inform Head NTCC/DTCU about the transfer of the patient and make arrangement to send patient’s charts, case notes and chest X-ray in advance.
4. The patient will be supplied with treatment drugs for one week, and advised to continue with treatment in NTCC/DTCU and report to the TB clinic of NTCC/DTCU within the arranged time.
5. The staff nurse from DORM should cross check with NTCC/DTCU that the patient has reported to the centre and is continuing treatment in NTCC/DTCU.

2.3.3 (b) Transfer from DORM to National Isolation Centre (Tutong)

Figure (4) Transfer of Tuberculosis patient from DORM (RIPAS hospital) to National Isolation Centre (Tutong)
2.3.3 (c) Transfer from NTCC/DTCU to Health Centres
For convenience of patients’ location, those with non-infectious TB may continue DOTS in other health centres,

1. TB health worker from the NTCC/DTCU should inform the staff-in-charge at the health centre about the transfer of the patient, and send the patient’s case notes and chest X-ray in advance.
2. The patient should be given one week supply of treatment drugs, explained for continuation of treatment in the health centre, and advised to report to the clinic within the arranged time with self-transport
3. The TB health worker should follow up with the health centre to confirm the arrival and continuation of treatment in the clinic.

2.3.3 (d) Transfer from NTCC/DTCU to National Isolation Centre (Tutong)
Clinically stable patients with smear or culture positive who are diagnosed in NTCC/DTCU shall be referred to National Isolation Centre for isolation. NTCC/DTCU should make proper arrangement with the Isolation Ward prior to referral and advise patient to use surgical mask before admission and be admitted within arranged time with self-transport.

2.3.3 (e) Transfer from Belait to National Isolation Centre (Tutong)
Figure (5): Transfer of Tuberculosis patient from Belait to National Isolation Centre (Tutong)
2.33 (f) Transfer of smear-positive PTB patients from Health Centres to Isolation Ward for treatment

Figure(6) Transfer of Tuberculosis patient from Health Centres to National Isolation Centre (Tutong)/ Isolation Ward

1. **Pulmonary smear positive cases**
   - Health Centres
     - Clinically stable
       - Attending MO to inform MO in the Isolation Ward, National Isolation Centre for admission
       - Prepare the referral letter, chest x-ray reports, and sputum reports
       - Arrange transport
       - Transfer by MOH transport to National Isolation Centre for admission and initiation of treatment
     - Attending Nurse to inform the nurse in-charge of the Isolation Ward, National Isolation Centre regarding the admission
     - i. Escorting staff to wear N95 mask
        ii. Place surgical mask on patient if stable
     - Clinically unstable
       - Attending MO to contact Medical on-call MO at nearest hospital for possible admission to isolation ward
       - Transfer by ambulance to Hospital
       - Admit to isolation ward for initiation of treatment
2.3.3 (g) Transfer from Temburong to National Isolation Centre (Tutong)

Figure (7) Transfer of Tuberculosis patient from Temburong to National Isolation Centre (Tutong)

2.3.4 Case finding (Identification and diagnosis of TB cases)

► Rationale

Under the NTP, the first component directly linked to service delivery is case finding. It begins with the identification of TB suspects by the use of a set of signs and symptoms of TB.

Case finding focuses on sputum smear examination for ages 10 years and above because:
(a) Detection of infectious cases through microscopy and curing them has the greatest impact on the control of tuberculosis and;
(b) Majority of infectious cases are in this age group;
(c) Sputum collection is difficult in young children.

► Objective

The general objective of case finding is the early identification and diagnosis of TB cases.
Definition of terms

- **Passive case finding** - finding a case of tuberculosis among the TB symptomatics who present themselves at the health facility.
- **Active case finding** - purposeful effort by a health worker to find cases of TB from among TB symptomatics in the community who do not seek consultations (related to TB) in a health facility.
- **Tubercle bacillus** - term used for *Mycobacterium tuberculosis*, the bacterium that causes TB and which is “acid-fast” with special staining techniques.
- **Sputum microscopy for diagnosis** - refers to the sputum examination done for TB symptomatics to establish a case of tuberculosis.
- **Sputum microscopy for follow up** - performed to monitor the sputum smear status of a patient after he is initiated to treatment and, consists of only, two specimens - spot and morning.
- **Sputum specimen** - material from the respiratory tract brought out by coughing and used for bacteriological examination.

Guideline

- Smear microscopy and culture shall be the laboratory diagnostic tool performed in the National TB Laboratory.
- All symptomatics identified shall undergo smear examination prior to the initiation of treatment, regardless of the availability of x-ray results or whether suspected of having extra pulmonary tuberculosis. The only contra-indication for sputum collection is massive haemoptysis.
- Pulmonary TB symptomatics with smear negative results shall undergo other diagnostic tests of TB, such as x-ray, culture, etc.
- Diagnosis of tuberculosis shall not be made based on the results of x-ray or skin test alone.
- Passive case finding shall be implemented in all health facilities.

Procedures

- Identification and follow up of TB symptomatics:
  - Screen for suspected TB cases;
  - Register in the master list of TB Symptomatics at the clinic;
  - Conduct sputum smear examination for diagnosis as soon as possible;
  - Refer patients with a high index of suspicion who are sputum negative to DORM/ District Chest Clinics for further investigations;
  - Explain the purpose of the sputum examination. Demonstrate sputum collection by referring to the pamphlet in Annex VI;
  - Label collection container with patient’s name, identification number, type of specimen and date of collection:
    - **First specimen**: early morning specimen (at the time of consultation or as soon as TB suspect is identified);
    - **Second specimen**: early morning specimen (very first sputum produced in the morning) collected by the patient himself as per instruction of the health workers, and,
    - **Third specimen**: early morning specimen of the following day.
Page | 22

- The lid of the collection container shall be closed and tightened to prevent leakage. Seal the container in the zip locked section of the biohazard bag and place the request form in the pouch section.
- The specimen shall be transported to reception area of the Department of Laboratory Services, RIPAS Hospital or District Hospital. These specimens will be brought to NTRL for processing.

All samples being tested for TB by all government and private clinics and hospitals should be sent to NTRL.
2.3.5 Laboratory Services - National TB Reference Laboratory Services:

Figure (8) Laboratory diagnosis of TB

- **Microscopy**: Screening Auramine (Fluorescence) Stain, Confirmatory Kinyoun Stain
- **Culture**: Liquid BD MGIT 960 System, Solid Lowenstein-Jensen Slants

**Fluorochrome/AFB Seen?**
- **No**: Report as negative, Notify DCD, NTCC & Requesting Doctor
- **Yes**: Microscopy, AFB
  - **No**: Report as contaminants
  - **Yes**: MTBC Molecular or Antigen Detection
    - **No [MOTT]**: Molecular Identification
    - **Yes**: Molecular Identification & Full Profile AST
      - Results in END
2.3.5 (a) Specimen Processing and Reporting
- Only specimens which conform to the standards shall be processed for TB investigations
- Specimens such as saliva, volume of sputum less than 1mL and specimen found leaking from container shall not be processed
- Specimen shall be processed for both microscopy and culture unless requested otherwise
- NTRL processes samples received from private hospitals/clinics.

2.3.5 (b) Microscopy
- NTRL shall adopt a three specimen case finding strategy for the diagnosis of pulmonary TB
- Smears are stained and screened in Auramine O using fluorescence microscopy
- Auramine O slides of any new positive smear shall be re-stained using Kinyoun stain
- Quantification and reporting are performed as below:

Table (2) Reporting format used for microscopy

<table>
<thead>
<tr>
<th>AFB seen</th>
<th>Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No acid fast bacilli seen</td>
</tr>
<tr>
<td>1-9 / 100 fields</td>
<td>Fluorochrome bacilli seen in very small numbers. (1-9 / 100 fields)</td>
</tr>
<tr>
<td>10-99/ 100 fields</td>
<td>Fluorochrome bacilli seen in small numbers. (10-99 / 100 fields)</td>
</tr>
<tr>
<td>1-10/ field</td>
<td>Fluorochrome bacilli seen in moderate numbers. (1-10 / field)</td>
</tr>
<tr>
<td>&gt; 10/ field</td>
<td>Fluorochrome bacilli seen in large numbers. (&gt; 10 / field)</td>
</tr>
</tbody>
</table>

2.3.5 (c) Culture
- Examination by mycobacterial culture provides the ‘gold standard’ in the diagnosis of tuberculosis
- All cultures shall be performed using liquid modified Middlebrook 7H9 broth incubated in the BD MGIT 960 system
- Cultures positive for AFB detected by the system shall be further identified and speciated using Nuclei Acid Amplification Assays only

2.3.5 (d) Antibiotic Susceptibility Testing (AST)
- AST shall be performed using only 1st line drug by BD MGIT 960 system on Mycobacterium tuberculosis only
- The drugs available for testing are:
  - Streptomycin (1.0 µg/mL and 4.0 µg/mL)
  - Isoniazid (0.1 µg/mL and 0.4 µg/mL)
  - Ethambutol (5.0 µg/mL and 7.5 µg/mL)
  - Rifampicin (1.0 µg/mL)
  - Pyrazinamide (100 µg/mL)
- Molecular genetic detection of resistance genes to Rifampicin and/or Isoniazid from processed or pulmonary smear-positive specimens are also performed. The identification of Rifampicin resistance is enabled by the detection of rpoB gene and for Isoniazid resistance is by detection of katG and inhA gene only.
2.3.5 (e) Nuclei Acid Amplification Testing (NAAT)

- Request for molecular detection for Mycobacterium tuberculosis complex shall only be performed on the processed specimen only
- Molecular identification of isolates shall be performed as a confirmatory assay

Table (3) Turn-around Time

<table>
<thead>
<tr>
<th>NO</th>
<th>TYPES OF SERVICES</th>
<th>TURN AROUND TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Smear microscopy</td>
<td>2 Working Days</td>
</tr>
<tr>
<td>2</td>
<td>Culture</td>
<td>8 Weeks</td>
</tr>
<tr>
<td>3</td>
<td>Anti-mycobacterial Susceptibility Testing (using BD MGIT 960 System)</td>
<td>10 days</td>
</tr>
<tr>
<td>4</td>
<td>Interferon Gamma Release Assays (IGRA) IGRA Test (Performed Overseas)</td>
<td>10 days</td>
</tr>
<tr>
<td>5</td>
<td>Nucleic Acid Amplification Assay (Molecular) to detect the present of Mycobacterium tuberculosis complex DNA</td>
<td>1 week</td>
</tr>
<tr>
<td>6</td>
<td>Molecular detection of resistance genes to Isoniazid &amp; Rifampicin from smear positive clinical specimens</td>
<td>1 week</td>
</tr>
<tr>
<td>7</td>
<td>Notification of new smear positive case</td>
<td>24 hours</td>
</tr>
</tbody>
</table>

2.3.5 (f) Notification of Positive Results by NTRL

- Any new smear positive cases shall be notified within 24 hours to the NTCC, DCD and requesting doctor by fax & phone.
- Notification for molecular detection of both resistance genes to Isoniazid and Rifampicin indicating MDR-TB shall also be made to the Head Division of DORM and Head of Microbiology, Infection Control Unit.
- Head of NTRL shall monthly notify collectively by memo to the following:
  1. Director General of Health Services, Chairperson of National TB Programme
  2. Director of Health Services
  3. Director of Environment Health Services
  4. Director of Department of Laboratory Services
  5. Head, Microbiology Laboratory Services
  6. Head, Infection Control Unit (RIPAS)
  7. Hospital, National TB Programme Coordinator (Chest Physician)
  8. Health, National TB Programme Coordinator (Epidemiologist)
  9. Senior TB Health Visitor (NTCC Kiarong)
10. TB Health Visitor (Kuala Belait)
11. TB Health Visitor (Tutong)
12. Laboratory Officer, Suri Seri Begawan Hospital Laboratory

- Notification, Recording and Reporting
  - After the confirmation of diagnosis, the diagnosing doctor should notify to DCD & District Health Office within 48 hours. If the patient is diagnosed from a private clinic/hospital, the patient should be referred to Government Health Facilities (DORM/chest clinics).
  - DCD/District Health Office has to liaise with NTCC/District DOTS clinic for contact tracing if indicated; or inform to the Occupational Health Unit if the patient is non-Bruneian.
  - Follow-up on and enter diagnostic results in appropriate NTP records as soon as it is available.

2.3.6 Adherence to Treatment
The public health priority of a National Tuberculosis Programme is to cure smear positive cases, while avoiding drug resistance. Ensuring adherence to treatment is necessary to achieve this priority and also to ensure the cure of patients with any form of TB. Patient compliance is the key factor to treatment success. Promoting adherence by directly observing treatment is much more effective than expending resources in defaulter tracing.

2.3.6 Directly Observed Treatment (DOTS)
2.3.6(a) What is directly observed treatment (DOTS)?
Directly observed treatment is the mainstay of the DOTS strategy, i.e. the WHO recommended policy package for TB control. Direct observation of treatment means that a supervisor observes the patient swallowing the tablets. This ensures that the patient takes the right drug, in the right doses, at the right intervals. Supervisors may observe patients’ treatment in in-patient as well as in out-patient settings. The supervisor may be a health worker or a trained or supervised community member. The NTP trains and monitors the community supervisors who directly observes treatment and nominates them as “treatment partners”. However it is important to ensure that confidentiality is maintained and that direct observation of treatment is acceptable to the patient.

Supervisor Vs Treatment Partner
NTP Supervisors are usually health care workers (TB Health Worker or DOTS in charge nurse from a health centre) who will supply the medicines, supervise treatment compliance and treatment outcome throughout the course of treatment. If the patient is not able to attend the health care facility themselves for any valid reason, the NTP may assign a community supervisor who may be nominated as a treatment partner who can supervise the patient on behalf of the NTP supervisor.

2.3.6(b) What type of TB patients shall undergo supervised treatment?
All TB patients, especially smear positive cases, shall undergo supervised treatment.

2.3.6(c) Who can serve as treatment partner of a TB patient during DOTS?
Any of the following persons may provide the necessary supervision of treatment of a TB patient:
  - Health care worker of the hospital/ health centre / clinic such as a nurse, TB health worker;
– A member of the community such as the Ketua Kampong (Village Head)/ government official or even a former TB patient;
– A member of the patient’s family (last option).

2.3.6(d) Where should DOTS be done?
Patients may be observed swallowing tablets in the following settings:
• by a nurse/health care worker in a health care facility;
• in a home/workplace of treatment partner.

2.3.6(e) How long is the treatment supervised?
Direct observation of treatment should be done on all active TB cases throughout the whole treatment regimen.

2.3.6(f) How is treatment compliance ensured through DOTS?
– Explain to the patient the importance of treatment compliance
– Supply medicine to the patient daily. Every morning, the patient shall report to the health care facility and swallows his medicine in front of the supervisor. If the patient cannot come to health care facility, he shall swallow the medicine in front of his treatment partner. After taking the medicine, the supervisor/treatment partner shall sign the treatment card.
– On Friday, Sundays and public holidays when the health care facility is closed, treatment may be taken at home under supervision of a treatment partner.
– During the maintenance phase, patient may take his drugs at home supervised by a treatment partner. Drugs may be distributed by the health care worker weekly to the patient. However, the supervisor should spot check the TB patient once a week.
– The supervisor or treatment partner should regularly motivate the TB patient by emphasizing key messages such as:
  • TB can be cured if treatment is taken regularly for the prescribed duration;
  • Patient should be advised to report any adverse reactions.
– Should the patient fail to report on the day he is expected, efforts should be made to contact him immediately.
– To monitor the response to treatment, sputum examination should be done on a specified date.
– At the end of the TB treatment, the patient shall be given a certificate to show that he is cured or that his treatment has been completed.

2.3.7 Registration
2.3.7(a) Initiation of Treatment
– Inform the patient that he has TB and motivate him to undergo treatment.
– Refer him to a responsible medical officer for pre-treatment evaluation and initiation of treatment.
– Open a treatment card and register him in the NTP TB register. If requested by the patient, he may be referred to another health care facility where he may have treatment supervised.
2.3.7 (b) Monitoring Compliance and Response to Treatment
Monitor sputum/smear status of all patients under treatment in your facility, including initially smear-negative patients, according to a recommended schedule. Sputum microscopy for follow-up requires two specimens - spot and morning.
Interrupted treatment (default): Any patient with interrupted treatment should be traced and continue with treatment immediately.
Outcome of treatment: At the time of the completion of treatment, the patient should be categorized by the treatment outcome according to the case definitions of treatment outcomes.

2.3.7 (c) Management of Adverse Reactions to Drugs
- Closely monitor the occurrence of minor reactions to drugs, especially during the intensive phase, and modify treatment regimen.
- Refer a patient with persistent minor reactions of more than 3 days to a medical officer.
- Follow-up closely on the medical officer’s evaluation and symptomatic treatment of minor reactions
- Discontinue anti-tuberculosis treatment and refer any patient with major adverse reactions to a medical officer as soon as suspected, for evaluation and management.

Adverse Reactions to specific drugs (Refer to 4.17: Table (13) Symptom-based approach to managing side-effects of anti-TB drugs, Page 81)

2.3.8 Recording and Reporting

Regular updating and periodic reporting are important tasks in the monitoring and evaluation of National TB Control Programme.
Objectives: To provide updated information and feedback to the Programme Manager and Policy Makers for programme evaluation and planning on TB control.
Guidelines: Recording and reporting shall include all cases of tuberculosis, classified according to internationally accepted case definitions; records and reports should allow the calculation of the main indicators for programme evaluation.

2.3.8 (a) NTP records and reports forms
2.3.8 (a-1) TB Symptomatic master list
This is maintained by the health facilities to keep track of accomplishment in the screening and confirmation of diagnosis of TB symptomatics. The list should be updated and kept in the clinics and reported to NTCC on a quarterly basis. (See forms in Annex I)

2.3.8 (a-2) Tuberculosis Treatment Card
All TB patients admitted to treatment should have a tuberculosis treatment card. This card should be filled-up completely with all the information regarding TB patient. It records the dates of drug collection which is designed on a daily basis during the intensive phase and weekly during the maintenance phase. A patient’s card is kept at the health unit where he is receiving treatment. (See forms in Annex II)

2.3.8 (a-3) NTP TB Register
This form is maintained by the nurse assigned at the health centre/clinic and district DOTS centre. It records information on the type and classification of TB cases, treatment regimen, monitoring of sputum follow-up and outcome of treatment in a catchment area. (See forms in Annex III)
2.3.8(a-4) NTP Identification Card
Once a patient is diagnosed as a TB case, he will be issued with an NTP identification card. This form is completed by the health worker. The card records the important information about patient’s diagnosis, drug regimen and follow up appointments. The card is kept in the clinic/DOTS centre. (See forms in Annex IV)

2.3.8(a-5) NTP Referral / Transfer From
This form is completed by a health worker when a patient is transferred or is referred to another health unit for the purpose of further diagnosis and/or treatment. When the patient reports to the unit, the bottom part is completed by the referred unit and sent back to the referring unit. (See forms in Annex V)

2.3.8(a-6) Quarterly Report on Tuberculosis case finding
This report form is completed by the NTP coordinators. It summarises NTP case finding on new smear positive cases, relapses and new smear negative cases. The information may be used to evaluate case finding on new smear positive & relapses and to monitor disease trend. It also provides information on treatment outcome of the patient who has completed treatment. (See forms in Annex VI)

2.3.9 Logistics
Adequate and uninterrupted supply of anti-TB drugs and other logistics should be available to all DOTS centres. Drug stock should be monitored and reported quarterly. Proper storage and management of drug supply system should be implemented. Drugs must be stored in a secured, clean and cool place. Practice the first expiring, first out (FEFO) rule. The use of drugs for every patient should be recorded and attached to the patient’s treatment chart.

2.3.10 Absentee/Defaulter tracing
1. The TB health worker should trace and follow-up any patient who missed an appointment or supervised treatment.
2. The TB health worker should make a phone call to remind the patient to comply with the treatment. If the patient cannot be reached by phone, the TB health worker should visit the patient’s house or workplace and arrange for the patient to continue treatment.
3. If the patient does not present themselves for treatment within one week, the TB health worker should visit the patient’s house and documents the reason(s) for being absent.
4. If the patient does not present themselves for treatment one week after the visit, the Head of NTCC shall seek advice from the NTP Committee.

2.4 SUPERVISION & EVALUATION
2.4.1 Supervision
Supervision is an important process in ensuring that technical policies and procedures of the programme are correctly carried out by the implementers. It is an opportunity for supervisors to:
(1) Praise and re-in force correct performance;
(2) Help health workers to identify gaps in performance and correct inadequacies or weaknesses;
(3) Update records and reports and;
(4) Give feedback and solicit ideas on how to improve the programme implementation.
The Health NTP Coordinator and a TB Health Visitor from NTCC shall visit District DOTS centres as well as its peripheral centres on a quarterly basis. The Senior Medical Officer of Health and TB Health
Workers are the NTP supervisors at the district level. Regular supervisory visits to the health facility will create a good working relationship between the Coordinator and the Health Workers.

2.4.1 (a) Procedures
- Identify the areas to visit. Those with problems should be visited more frequently.
- Use the following guide during the supervisory visits:
  a) Compare and verify NTP TB Register with NTP Treatment Cards
  b) Review NTP Treatment Cards:
     • Type / Classification of patient
     • Regimen of treatment
     • Sputum follow-up examination results
     • Drugs collection, Treatment compliance
  c) Review NTP TB Register
     • Review follow-up examination results
     • Treatment outcome
  d) Observe health workers
  e) Talk with health workers and patients
  f) Observe adequacy of logistics and other NTP supplies.
- After gathering information, the supervisor should give feedback to the health worker according to the findings. An appropriate action plan to solve any potential problems should be provided.

2.4.2 Evaluation
Since the aim of the programme is to reduce transmission by ensuring that TB patients are cured, the most important tool for programme evaluation is the cohort analysis. Evaluation of NTP should be implemented annually in order to get information on annual case detection and treatment outcomes.

During the first month of each quarter, the NTP Coordinator should prepare a “Quarterly Report on Tuberculosis case finding” by compiling the case detection, case holding and situation of logistics in NTP quarterly basis.

The timing of the visits to DOTS centres and clinics where TB cases are treated, is during the first or second week of every quarter, by the team including NTP coordinator, Senior/TB Health Visitor and TB Health workers assigned to that area.

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Month</th>
<th>Start</th>
<th>End</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>January</td>
<td>1 January</td>
<td>31 March</td>
</tr>
<tr>
<td>2nd</td>
<td>April</td>
<td>1 April</td>
<td>30 June</td>
</tr>
<tr>
<td>3rd</td>
<td>July</td>
<td>1 July</td>
<td>30 September</td>
</tr>
<tr>
<td>4th</td>
<td>October</td>
<td>1 October</td>
<td>31 December</td>
</tr>
</tbody>
</table>

The quarterly reports should be submitted to NTP within the first week of every quarter by DOTS centres and clinics. The annual report from the DOTS centres should be submitted in the first quarter of each year. All quarterly / annual reports from the implementing health facilities should be evaluated and analysed by the NTP coordinator. Feedback of the results and recommended measures should be instituted to ensure an effective implementation of tuberculosis control.

2.5 BCG Immunization
BCG is included in the Expanded Programme on Immunization (EPI) for children due to Brunei Darussalam’s status as an intermediate burden country for TB.
3. Community TB Control

3.1 Contact Investigation

3.1.1 Structuring a Contact Investigation Programme

3.1.1 (a) Assessing the risk of infection
A contact of a case of AFB smear-positive TB is much more likely to become infected with M. tuberculosis than the contact of an AFB smear-negative (culture positive or culture negative) case of TB. For contact investigations, pleural disease is grouped with pulmonary disease as sputum cultures can yield M. tuberculosis even when no lung abnormalities are apparent on a radiograph. Approximately 20%–30% of all contacts will have LTBI, and 1% will have TB disease. Of those contacts that will ultimately have the TB disease, approximately half would have acquired the disease in the first year after exposure. For this reason, contact investigations constitute a crucial prevention strategy. The NTP’s policy, therefore, is to perform contact evaluation of the TB index case. Contact investigations of persons with AFB smear-positive and/or culture positive sputum and cavitatory TB are assigned the highest priority.

Contact investigation should be initiated if the TB index case has:
1) Sputum smear positive Pulmonary / Laryngeal TB
2) Definite evidence of extensive parenchyma involvement with TB, but smear negative or smear and or culture not obtained prior to the treatment (to be verified on a case by case basis)
3) Sputum smear negative PTB but culture positive (SNCP)
4) Miliary TB with lesions in the lungs

When sputum samples have not been collected, either because of an oversight or as a result of the patient’s inability to expectorate, results from other types of respiratory specimens (e.g., gastric aspirates or bronchoalveolar lavage) may be interpreted in the same way as the recommendation for sputum examination.

Contact evaluation is not indicated for culture negative and solely extra-pulmonary TB cases.

The contact investigation and evaluation should be completed during 2 weeks of diagnosis of the index case.

Duration and proximity of contact
Risk of infection is greatest for contacts closest to the source case for the longest time.

It may take many hours or days to transmit an infectious dose, but casual exposures may lead to transmission if the case is sufficiently infectious and environmental air conditions are favourable or if the contact is at high risk of infection.

Environmental air factors
Droplet nuclei are transported from the source through the air; the greater the concentration in air, the greater the risk to contacts. The degree of ventilation or filtration in the environment is important.

3.1.1(b) Classifying Contacts

The first step is to allocate contacts into groups with higher and lower risk of infection.
Members of the immediate household and others who have shared accommodation with the index case are close contacts and are usually the top priority. However, contacts at work, leisure or other settings are not always ‘casual’ contacts.

Work sites should be visited. If there is overcrowding and poor ventilation these contacts may be considered ‘close contacts’. Contact tracing is often unnecessarily extensive in schools is screening the whole classroom and teachers may not be required.

3.1.1 (c) Establishing limits for contact investigations

The ‘stone in the pond’ concept or ‘concentric circle’ concept is used to limit contact investigations. By initially evaluating the higher-risk contacts for evidence of TB infection and/or disease, the infectiousness of the index case can be inferred. To limit the extent of contact investigation follow these guidelines.

1. Start with higher-risk contacts. If there is no evidence of recent transmission of infection in this group, do not extend the investigation.
2. If investigations suggest recent infection in the higher-risk group, extend to progressively lower-risk contacts until the levels of infection detected approximate the likely levels of infection in the local community.
3. Periodically review the findings to determine whether to stop or extend the investigation.

![Figure (9) Concentric circle approach to contact tracing](image_url)

- Close contacts (high priority)
- Other-than-close contacts (medium priority)
- Other-than-close contacts (low priority)

*Source: Reprinted from Etkind and Veen (2006), courtesy of Marcel Dekker Inc.*
3.1.1 (d) Determining the period of infectiousness

Contact investigation should extend back to the date of onset of cough in the index case or for three months if the date of onset of cough is unknown or there is no history of cough. The period of inquiry for contact exposure may also need to be extended if the source case is highly infectious.

3.1.2 Source-Case Investigation

If a child has tuberculosis, a source-case investigation should be done to find the index case that infected the child. TB disease in children aged <5 years typically indicates that the infection is recent. Source case investigations can be considered for children aged <5 years. Young children usually do not transmit TB to others, and their contacts are unlikely to be infected by exposure to them. A source-case investigation moves in the opposite direction of contact investigation, but the same overall principles used in contact investigation still apply. Seeking a source-case follows the same overall procedures as a standard contact investigation. Parents or guardians usually are the best informants. Such persons are termed associates. Attention focuses on ill associates who have symptoms of TB disease. A source-case investigation should begin with the closest associates (e.g., household members).

Child: 14 years or below
**Guidelines for Tuberculosis Control in Brunei Darussalam 2013**

**Figure (11) Contact tracing of Tuberculosis index case**

- **Index case**
  - Sputum smear/culture positive PTB/Laryngeal
  - Childhood TB (<5 yr)
  - Initiate contact tracing
  - Identification of close contacts
  - Source case investigation
  - Mantoux test at NTCC/District DOTS centres
  
  **Mantoux test**
  - Negative
    - Repeat Mantoux test after 8-10 weeks
    - Negative
      - Stop investigation and advise to seek medical attention for suspected symptoms
      - Discharge from treatment on completion
    - Positive
      - Undergo other investigations to detect active TB disease (Sputum, CXR, etc.)
        - Evidence of active TB
          - No
            - IGRA test
              - Negative
                - LTBI
              - Positive
                - LTBI
            - Yes
              - Case verification
                - Notification
          - Follow the flow chart Figure (1)
        - Yes
          - Case verification
            - Notification

  - Positive
    - Undergo other investigations to detect active TB disease (Sputum, CXR, etc.)
      - Evidence of active TB
        - No
          - IGRA test
            - Negative
              - LTBI
            - Positive
              - LTBI
        - Yes
          - Case verification
            - Notification

β Cut off points for Mantoux test reading in Page ....

* IGRA test should be used for review of Mantoux test if there is a high clinical suspicion

--- Optional pathway
Figure (12) Contact Tracing after exposure to MDR-TB cases

Patient with cough >2 weeks - send 3 sputum samples for AFB

Lab discovers sputum positive for AFB-MDR TB

Inform DORM as soon as possible

(is in-ward patient)

Inform Hospital Infection Control as soon as possible

Inform DCD

Isolate patient preferably in a negative pressure room

Establish whether infection control measures had been taken

Trace HCW contacts and that appropriate measures had been taken

Inform Occupational Health (OHD)

Infection control files a report with recommendations

Ensure environmental & individual bio-hazard techniques were followed

NTCC/DTCU traces community contacts

OHD makes a report on case with recommendations for improvement if any

DCD carries out appropriate investigations and refers appropriate patients for medical treatment

Report reviewed by Infection control committee and reports filed after discussion and review with recommendations for improvement if any
3.1.3 Contact Investigations in Special Circumstances

3.1.3 (a) Hospitals and other healthcare facilities
If a case of pulmonary disease has been in a hospital or other healthcare facility before diagnosis of TB and isolation, staff and patients may need assessment. Good communication between the public health, infection control and occupational health services is needed to clarify roles and responsibilities.

A risk assessment should be undertaken which takes into account:

- The degree of infectivity of the index case
- The length of time before the infectious person was isolated
- Whether other patients are unusually susceptible to infection
- The proximity of contact.

Contact tracing and testing should only be carried out for patients for whom the risk is regarded as significant.

In general, patients should be regarded as at risk of infection if they have spent more than eight hours in the same bay or room as an inpatient with smear-positive TB who had a cough.

Such patients should be given ‘inform and advise’ information. If patients were exposed to a patient with sputum smear-positive TB for long enough to be equivalent to a household contact, or an exposed patient is known to be particularly vulnerable to infection, they should be managed as close contacts.

Exposed patients may have been discharged by the time the contact investigations have begun. Infection Control should assist in identifying these patients for public health to follow up.

Health care workers may be less likely to comply with screening recommendations than non-health professionals, thus management support may be needed. If a healthcare worker, who has a documented Mantoux or IGRA test result within the past 12 months, is exposed to infectious TB, only one test is necessary to detect conversion. This test should be done eight weeks after the date of last exposure.

The Public Health Medical Officer overseeing the investigations must maintain an overview of both patients and staff. Data on the outcome of contact investigation in hospitals should be supplied to the Public Health Medical Officer, who should also provide feedback to Hospital Infection Control and Occupational Health Staff about the outcome of contact investigations, so that all parties have the same picture of the infectivity of the source-case.

3.1.3 (b) Schools/higher Education Institutions
In the case of a student / teacher with smear positive TB, case investigation should include obtaining the name list of:

- Students sharing any classes with a student with the index case
- Students in the classes of a teacher with the index case in the previous 3 months

If they are found to be close contact with an infectious TB patient, initiate contact tracing according to the guidelines for contact tracing.

Contact tracing of children and staff involved in extra-curricular activities and non-teaching staff should depend on:

- The degree of infectivity of the index case
- The duration and proximity of contact
- Whether contacts are unusually susceptible to infection.
Environmental inspection of the classrooms in schools / Higher Education Institutions should be implemented in cooperation with Environmental Health Division and Occupational Health Division to ensure the safe environment of schools / Higher Education Institutions.

3.1.3 (c) Prisons and Detention Centres
- All prison staff should be aware of the signs and symptoms of active TB.
- The Medical Officer in-charge of the prison should promote awareness among prisoners and prison staff.
- Screen all prisoners for TB by:
  - Filling in a health questionnaire on each entry to the prison
  - If there are signs and symptoms of active TB, a chest X-ray and microscopy on three consecutive sputum samples should be done.
- Should provide DOTS for all prisoners receiving treatment for active or latent TB;
- When a prisoner is transferred between prisons, ensure the continuity of care;
- Ensure plans are in place for continuing treatment (including referral to NTCC) after an early discharge, and;
- Provide pre- and on-employment screening for health care workers, prison staff and others who have regular contact with prisoners.

3.1.3 (d) Contact Tracing and Prevention of TB Among Travellers

In case of aircraft passenger later found to have TB;
Contact tracing is not usually needed unless;
- the flight was within the past 3 months and
- the flight lasted for more than 8 hours and
- the index case is sputum smear-positive and
  either
  - the index case coughed frequently during the flight or
  - the index case has MDR TB.

If contact tracing is recommended, ‘Inform and advice’ information should be provided to the airline, request from the airline the list of passengers who sat 3 rows behind and in front of the index case.

In case of aircraft crew member with TB (Sputum positive PTB);
Contact tracing is not usually needed for passengers but there is a need to assess the other members of staff as normal for workplace contacts.

For short term visitors (<3 months) or transit passengers found with active TB infection, they should follow the same guideline as other patients with active TB infection, and liaise with their corresponding Embassy for their stay in Brunei Darussalam. After being discharged, NTCC/DCD should notify the corresponding countries through NTP focal points and/or IHR focal points for continuation of treatment.

3.1.3 (e) Contact Investigation at work
NTCC shall send a memorandum to the employer for inspection of workplace for cases who are working. NTCC team should conduct a thorough contact investigation to the close contacts from the work environment as indicated.
3.1.4 Evaluation, Treatment and follow up Contact Investigation

3.1.4 (a) Symptomatic contacts of an infectious TB case
- For symptomatic contacts (both children and adults), routine investigations for active TB infection should be done. If there is evidence of active TB infection, anti TB treatment should be initiated according to the classification.
- If Mantoux test is positive with no evidence of active TB infection, Latent TB infection (LTBI) treatment should be initiated.

3.1.4 (b) Asymptomatic contacts of an infectious TB case
- For asymptomatic contacts, Mantoux test is indicated as first line investigation. If Mantoux test is found positive, routine investigations for active TB infection are indicated. If Mantoux test is positive without evidence of active TB infection, IGRA test may be considered for children who have had BCG vaccination.
- The following persons should have chemoprophylaxis initiated if they are found to have a negative Mantoux test and have been in contact with an infectious case within the past 3 months:
  - asymptomatic children <5 yrs and
  - persons of any age with HIV infection.
- Treatment should be continued in these persons if a repeat Mantoux test done 3 months after the last exposure, is positive.
- If the test remains negative, treatment should be discontinued unless there is continuing exposure to infection source-case.

3.1.4 (c) Monitoring of people not being treated
People who are at a higher risk of developing the TB disease, who have declined treatment or for whom the decision has been made not to treat for LTBI, should be monitored with CXRs at 6, 12 and 24 months. This group includes:
- children aged under five who are close contacts of smear- or culture-positive cases
- HIV-positive contacts
- contacts of multi-drug-resistant (MDR-TB) source cases
- people with inactive fibrotic scars on CXR.
CXR monitoring of other people who are untreated for LTBI is not usually recommended.

3.1.4 (d) Contacts with TB symptoms who refuse follow-up
If a person has symptoms and/or signs of active TB disease, particularly persons with a high suspicion of pulmonary TB, but refusing to be investigated further, this person should be brought to the attention of the responsible Public Health Medical Officer. This situation may apply if contacts of active TB cases refuse to be investigated or followed up. The Medical Officer may write an order (a letter) under Infectious Disease Act (IDA, CAP 204), requiring such a person suspected to have TB disease to undergo compulsory investigations to determine whether or not they have active TB disease.
Figure (13) Evaluation, Treatment and follow up of Tuberculosis contacts aged <5 years

Evaluate with medical history, physical examination, chest X-ray and TST

Does contact have symptoms consistent with TB?

No

Is the chest X-ray abnormal?

No

BCG vaccinated? / TST unreliable

No

Is TST reaction >5mm?

No

>8 wks passed since last exposure?

No

Begin treatment for LTBI; repeat TST 8-10 wks post exposure

Is TST >5mm?

Yes

Household contact of people with active TB /Non-household contacts eg: workplace,school, airplane/ New entrants from high incidence countries

Yes

Fully evaluate for TB Disease

Yes

IGRA test +ve or TST +ve

Yes

Complete full treatment course for LTBI

No

Stop: no further evaluation or treatment required

Yes

Complete full treatment course for LTBI
3.1.5 Notification to Overseas Health Authorities

DCD should notify overseas NTP Focal Point and/or National IHR Focal Point regarding:
• TB cases diagnosed in Brunei who temporarily or permanently travel overseas
• Non-Bruneians diagnosed as having TB while in Brunei and returning to their home country
• Contact investigation among travellers.

3.2 Screening of TB

Routine screening of TB in asymptomatic cases is indicated for;
  • all foreign workers (Government & Private) who come to Brunei for the first time and at the time of their renewal of contract,
  • All Bruneians who undergo pre-employment medical examinations
  • Bruneians who are going abroad for studies, for work-related training courses, to work in overseas diplomatic missions
  • TB suspects / symptomatic on request by the attending doctor.

Regular screening to high risk groups such as immuno-compromised patients and health care workers who has had close contact with TB patients / specimens is also indicated on a yearly basis.

Health care workers indicated for regular TB screening are those working in any of the following;
  • NTRL
  • NTCC and DOTS Centres
  • DORM, Chest clinics, ICU, Isolation Wards
  • Flu clinics
  • Any other healthcare worker who is considered to be at high risk such as staff handling immune compromised patients (renal dialysis, cancer ward).

Periodic TB screening for HIV infected persons is also indicated at least 3 times a year.

The routine tools for screening of TB are;
  1. Symptomatic screening
  2. Mantoux test
  3. Chest X ray, and
  4. IGRA test if indicated.

Sputum tests are not indicated for screening of Mantoux test positive individuals who require medical fitness if they are asymptomatic and are not contacts of PTB patients and if they have a normal chest X-Ray. Sputum tests are time consuming and asymptomatic individuals are unlikely to produce sputum specimens.

The Mantoux test should not be repeated on a person who has written documentation of either a previous positive TST result or treatment of TB disease or Latent TB disease.
3.2.1 Mantoux Test/ Tuberculin Skin Test (TST)

The Mantoux or Tuberculin Skin Test (TST) is the recommended method of skin testing to determine whether a person could be infected with Mycobacterium tuberculosis. Multiple puncture tests (e.g., the Tine test) should not be used because they are harder to standardize and the results are less reliable. The TST is performed by injecting 0.1 ml of 5 tuberculin units of purified protein derivative (PPD) intradermally, using a 1 ml. tuberculin syringe and a fine-bore (27-gauge) hypodermic needle.

The preferred injection site is the front (ventral surface) of the forearm. Given the importance of the injection technique to obtaining an accurate result, instruction and training should be provided to those who will be required to place, read and interpret the TST.

As vaccination with a live virus vaccine can interfere with the Mantoux reaction, testing should be done either on the same day as vaccination with live virus vaccines or 4–6 weeks after the administration of the live-virus vaccine.

3.2.1 (a) Procedure for placing The Mantoux Test (TST)

- Explain the procedure to the person
- Wash and dry your hands
- Locate and clean the injection site
- Prepare the syringe
- Stretch the skin with the thumb
- Position the syringe at a 10–15 degree angle to the skin
- Insert the needle with the bevel facing upwards
- Push the needle in 2 to 3 mm and inject the PPD
- Remove the needle quickly. Discard it in a puncture-proof container
- Do not massage the injection site. Do not apply any dressing
- If properly done, a blanched wheal will appear in which the skin follicles can be clearly seen
- Mark the site and make a record of the date and time of the injection.
- The next step is to read the result of The Mantoux skin test by examining the patient’s arm for induration (palpable swelling). This is done 48 to 72 hours after giving the PPD injection.
- Using a ruler with millimeter measurements (preferably a transparent ruler), measure the largest transverse (horizontal) diameter of the indurated area at the site of the test on the person’s forearm. The area of erythema (redness) around the indurated area is not included in the measurement.
Table (4) Defining Positive Mantoux TST Reaction

<table>
<thead>
<tr>
<th>≥5 mm Induration</th>
<th>≥10mm Induration</th>
<th>≥15mm Induration</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-infected persons</td>
<td>HIV-infected persons</td>
<td>HIV-infected persons</td>
</tr>
<tr>
<td>Recent contacts of infectious TB cases</td>
<td>Recent contacts of infectious TB cases</td>
<td>Recent contacts of infectious TB cases</td>
</tr>
<tr>
<td>Persons with fibrotic changes on Chest X Ray consistent with prior TB</td>
<td>Persons with fibrotic changes on Chest X Ray consistent with prior TB</td>
<td>Persons with fibrotic changes on Chest X Ray consistent with prior TB</td>
</tr>
<tr>
<td>Organ transplant recipients</td>
<td>Organ transplant recipients</td>
<td>Organ transplant recipients</td>
</tr>
<tr>
<td>Persons who are immunosuppressed for other reasons, such as:</td>
<td>Persons who are immunosuppressed for other reasons, such as:</td>
<td>Persons who are immunosuppressed for other reasons, such as:</td>
</tr>
<tr>
<td>Taking the equivalent of ≥15 mg/day of prednisone for 1 month or more</td>
<td>Taking the equivalent of ≥15 mg/day of prednisone for 1 month or more</td>
<td>Taking the equivalent of ≥15 mg/day of prednisone for 1 month or more</td>
</tr>
<tr>
<td>Taking tumour necrosis factor alpha antagonists</td>
<td>Taking tumour necrosis factor alpha antagonists</td>
<td>Taking tumour necrosis factor alpha antagonists</td>
</tr>
<tr>
<td>≥10mm Induration</td>
<td>Recent immigrants (within last 5 years) from a high TB-prevalence country</td>
<td>Recent immigrants (within last 5 years) from a high TB-prevalence country</td>
</tr>
<tr>
<td>Injection drug users</td>
<td>Injection drug users</td>
<td>Injection drug users</td>
</tr>
<tr>
<td>Residents or employees of high-risk congregate settings</td>
<td>residents or employees of high-risk congregate settings</td>
<td>residents or employees of high-risk congregate settings</td>
</tr>
<tr>
<td>Mycobacteriology laboratory personnel</td>
<td>Mycobacteriology laboratory personnel</td>
<td>Mycobacteriology laboratory personnel</td>
</tr>
<tr>
<td>Children &lt;5 years of age, or children or adolescents exposed to adults at high risk</td>
<td>Children &lt;5 years of age, or children or adolescents exposed to adults at high risk</td>
<td>Children &lt;5 years of age, or children or adolescents exposed to adults at high risk</td>
</tr>
<tr>
<td>Persons with clinical conditions that increase the risk for TB infection progressing to disease</td>
<td>Persons with clinical conditions that increase the risk for TB infection progressing to disease</td>
<td>Persons with clinical conditions that increase the risk for TB infection progressing to disease</td>
</tr>
<tr>
<td>≥15mm Induration</td>
<td>Persons with no known risk factors for TB</td>
<td>Persons with no known risk factors for TB</td>
</tr>
</tbody>
</table>

3.2.1 (b) Interpretation of The Mantoux Skin Test

As there are many factors that can affect the result of the TST, it is important to ensure that the test has been placed and read correctly and a thorough history taken to help interpret the result.

- A positive reaction to the TST is taken to indicate that the person could be infected with TB
- A negative test result, in the absence of immune-compromising conditions (e.g. HIV infection and AIDS, post-measles syndrome, malnutrition, corticosteroid treatment and miliary tuberculosis) should be taken to indicate no previous contact with Mycobacterium tuberculosis.

False-Negative Mantoux TST Result

Some persons may not react to the TST even though they are infected with M. tuberculosis. The reasons for these false-negative reactions may include, but are not limited to, the following:

- Cutaneous anergy (anergy is the inability to react to skin tests because of a weakened immune system)
- Recent TB infection (up to 8–10 weeks following exposure)
- Very old TB infection (many years)
- Very young age (less than 6 months old)
- Recent live-virus vaccination (e.g., measles and smallpox)
- Overwhelming TB disease
- Some viral illnesses (e.g., measles and chickenpox)
- Incorrect method of TST administration
- Incorrect interpretation of reaction
False-Positive Mantoux TST Result
Some persons may react to the TST even though they are not infected with M. tuberculosis. The causes of these false-positive reactions may include, but are not limited to, the following:

- Infection with nontuberculosis mycobacteria
- Previous BCG vaccination
- Incorrect method of TST administration
- Incorrect interpretation of reaction
- Incorrect bottle of antigen used

Key Points:

- The TST should not be performed on a person who has written documentation of either a previous positive TST result or treatment of TB disease or Latent TB disease.
- Patients or family members should never measure TST results. This should only be done by a trained health care professional.
- Interpretation of TST results is the same for persons who had BCG vaccination.
- A TST that was not measured and recorded in mm of induration must be repeated.
- For routine TB screening, a two-step TST can be applied 3 weeks apart, if the first TST is negative.
- For contact tracing, The Mantoux Test should be applied 2 times, 8-10 weeks apart if the first Mantoux Test is negative.
- All positive Mantoux Tests, whether for health screening or contact tracing, from private hospitals/clinics should be referred to NTCC or District DOTS centres.

3.2.1 (c) Two-Step Tuberculin Skin Testing

In general, there is no risk associated with repeated tuberculin skin test placements and tuberculin testing is safe during pregnancy. If a person does not return within 48-72 hours for a tuberculin skin test reading, a second test can be placed as soon as possible. There is no contraindication to repeating the TST, unless a previous TST was associated with a severe reaction.

In some persons who are infected with M. tuberculosis, the ability to react to tuberculin may wane over time. When given TST years after infection, these persons may have a false-negative reaction. However, the TST may stimulate the immune system, causing a positive or boosted reaction to subsequent tests. Giving a second TST after an initial negative TST reaction is called two-step testing.

Two-step testing is useful for the initial skin testing of adults who are going to be retested periodically, such as health care workers or nursing home residents. This two-step approach can reduce the likelihood that a boosted reaction to a subsequent TST will be misinterpreted as a recent infection.
3.2.2 Interferon-Gamma Release Assays (IGRAs) - Blood Tests for TB Infection

TB blood tests measure how the immune system reacts to the bacteria that cause TB. An IGRA measures how strong a person’s immune system reacts to TB bacteria by testing the person’s blood in a laboratory.

➢ Interferon-Gamma Release Assays (IGRAs) are whole-blood tests that can aid in diagnosing Mycobacterium tuberculosis infection. They do not help differentiate latent tuberculosis infection (LTBI) from tuberculosis disease.
➢ IGRAs measure a person’s immune reactivity to *M. tuberculosis*. White blood cells from most persons that have been infected with *M. tuberculosis* will release interferon-gamma (IFN-g) when mixed with antigens (substances that can produce an immune response) derived from *M. tuberculosis*. To conduct the tests, fresh blood samples are mixed with antigens and controls.

3.2.2 (a) Advantages of IGRAs

- Requires a single patient visit to conduct the test.
- Results can be available within 24 hours.
- Does not boost responses measured by subsequent tests.
- Prior BCG (Bacille Calmette-Guérin) vaccination does not cause a false-positive IGRA test result.

3.2.2 (b) Disadvantages and limitations of IGRAs

- Blood samples must be processed within 8-30 hours after collection while white blood cells are still viable.
- Errors in collecting or transporting blood specimens or in running and interpreting the assay can decrease the accuracy of IGRAs.
- Limited data on the use of IGRAs to predict who will progress to TB disease in the future.
- Limited data on the use of IGRAs for:
  - Children younger than 5 years of age;
  - Persons recently exposed to *M. tuberculosis*;
• Immuno-compromised persons; and
• Serial testing.
• Tests may be expensive.

3.2.2 (c) Steps in administering an IGRA Test

Confirm arrangements for testing in a qualified laboratory, and arrange for delivery of the blood sample to the laboratory in the time the laboratory specifies to ensure testing of samples with viable blood cells.
• Draw a blood sample from the patient according to the test manufacturer’s instructions.
• Schedule a follow-up appointment for the patient to receive test results.
• Based on test results, provide follow-up evaluation and treatment as needed.

3.2.2 (d) Interpretation of IGRA Test Results

IGRA interpretations are based on the amount of IFN-g that is released or on the number of cells that release IFN-g. Both the standard qualitative test interpretation (positive, negative, or indeterminate) and the quantitative assay measurements (Nil, TB, and Mitogen concentrations or spot counts) should be reported.

As with the tuberculin skin tests (TSTs), IGRA tests should be used as an aid in diagnosing infection with M. tuberculosis. A positive test result suggests that M. tuberculosis infection is likely; a negative result suggests that infection is unlikely. An indeterminate result indicates an uncertain likelihood of M. tuberculosis infection. A borderline test result (T-Spot only) also indicates an uncertain likelihood of M. tuberculosis infection.

3.2.2 (e) Recommendations on when to use IGRA Tests

• IGRA tests can be used in place of (but not in addition to) TST in all situations in which TST is used as an aid in diagnosing M. tuberculosis infection, which includes contact investigations, testing during pregnancy, and screening of health care workers and others undergoing serial evaluation for M. tuberculosis infection.
• Populations in which IGRA tests are preferred for testing:
  o Persons who have received BCG (either as a vaccine or for cancer therapy); and
  o Persons from groups that historically have poor rates of return for TST reading.

Key Points:
• As with TST, IGRA tests generally should not be used for testing persons who have a low risk of infection and a low risk of disease due to M. tuberculosis.
• Each institution and TB control program should evaluate the availability and benefits of IGRA tests in prioritizing their use.
• Despite the indication of a preference, use of the alternative test (IGRA or TST) is acceptable medical and public health practice.
• TST is preferred over IGRA tests for testing children less than 5 years of age.
• IGRAs, unlike the TB skin tests, are not affected by prior BCG vaccination and are not expected to give a false-positive result in people who have received BCG.

• The person’s health care provider should choose which TB test to use. Factors in selecting which test to use include the reason for testing, test availability, and cost. Generally, it is not recommended to test a person with both TST and an IGRA.

• As with TST, live virus vaccines might affect IGRA test results. IGRA testing in the context of live virus vaccine administration should be done either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine and at least one month after smallpox vaccination.

3.3 Latent TB Infection

3.3.1 Diagnosis of Latent TB Infection or TB Disease

• If a person is found to be infected with TB bacteria, other tests are needed to see if the person has TB disease. A diagnosis of LTBI requires that TB disease be excluded by medical evaluation. This should include checking for signs and symptoms suggestive of TB disease, a chest radiograph, and, when indicated, examination of sputum or other clinical samples for the presence of M. tuberculosis.

• The presence of TB disease must be excluded before treatment for LTBI is initiated (i.e., waiting for culture results if specimens are obtained) because failure to do so may result in inadequate treatment and development of drug resistance.

• Decisions about a diagnosis of M. tuberculosis infection should also include epidemiological and historical information.

• If a person does not have TB disease, but has TB bacteria in the body, then latent TB infection is diagnosed. The decision by a physician about treatment for latent TB infection will be based on a person’s chances of developing TB disease.

3.3.2 Treating Latent TB Infection

In persons infected with Mycobacterium tuberculosis, the risk of progression to active TB disease varies according to the time since infection, age and other host factors. In healthy adults with TB infection but without risk factors, active TB disease will develop in about 10% (5% within 2 years of infection and 5% after 2 years). For young children, the risk for disease after infection is substantially higher and is inversely correlated with age (up to 40% risk in infants). In children and adults, conditions that compromise the immune system will also increase the risk of disease after infection. Treating TB infection, however, can significantly decrease the number of persons who might otherwise go on to develop active TB disease.

There are two types of situations in which treatment should be considered:

(a) **Primary Prophylaxis (window period prophylaxis):** the drug is given to an individual who is exposed to a known source of infection and who is considered to be very susceptible to becoming infected and at greater risk for progressing to active TB disease. This would include children <5 years of age and persons known to be significantly immunosuppressed. Treatment during the “window period” is recommended for contacts at high risk for rapid progression of infection to disease. Treatment may be discontinued if, after a period of eight weeks, the repeat Mantoux TST is negative and the contact remains asymptomatic and is immunocompetent. If the individual is unable to mount a delayed-type hypersensitivity reaction (e.g., an infant who is too young or individual with severe immunosuppression), consideration should be given to extending treatment for the full duration (9 months for INH).
(b) Treatment of Latent TB Infection (LTBI): Medical therapy is used to prevent progression to disease in people who have already been infected, as demonstrated by a positive Mantoux TST result or positive blood assay for *Mycobacterium tuberculosis*.

3.3.3 Treatment Options for Latent Tuberculosis Infection

Treatment of Latent Tuberculosis (TB) Infection (LTBI) is essential to in controlling and eliminating TB, as it substantially reduces the risk that TB infection will progress to TB disease. Certain groups are at very high risk of developing TB disease once infected. Once the diagnosis of LTBI has been made, health care providers must choose the most appropriate and effective treatment regimen, and make every effort to ensure those persons complete the entire course of treatment for LTBI. However, if exposed to and infected by a person with multi-drug-resistant TB (MDR TB) or extensively drug-resistant TB (XDR TB), preventive treatment may not be an option due to resistance.

<table>
<thead>
<tr>
<th>Groups Who Should be Given High Priority for Latent TB Infection Treatment</th>
<th>People who have a positive IGRA result or a TST reaction of 5 or more millimeters</th>
<th>People who have a positive IGRA result or a TST reaction of 10 or more millimeters</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-infected persons</td>
<td>Recent immigrants (&lt; 5 years) from high-prevalence countries</td>
<td></td>
</tr>
<tr>
<td>Recent contacts of a TB case</td>
<td>Injection drug users</td>
<td></td>
</tr>
<tr>
<td>Persons with fibrotic changes on chest radiograph consistent with old TB</td>
<td>Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities)</td>
<td></td>
</tr>
<tr>
<td>Organ transplant recipients</td>
<td>Mycobacteriology laboratory personnel</td>
<td></td>
</tr>
<tr>
<td>Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of &gt;15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists)</td>
<td>Children under 4 years of age, or children and adolescents exposed to adults in high-risk categories</td>
<td></td>
</tr>
</tbody>
</table>

3.3.3 (a) Choosing the Most Effective Regimen

Treatment of LTBI should be initiated after the possibility of TB disease has been excluded. Persons suspected of having TB disease should receive the recommended multi-drug regimen for treatment of disease until the diagnosis is confirmed or ruled out. Consultation with a TB expert is advised if the known source of TB infection has drug-resistant TB.
Table (6) Latent TB Infection Treatment Regimens

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Duration</th>
<th>Interval</th>
<th>Minimum doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>9 months</td>
<td>Daily</td>
<td>270</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly*</td>
<td>76</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>6 months</td>
<td>Daily</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly*</td>
<td>52</td>
</tr>
<tr>
<td>Isoniazid &amp; Rifapentine</td>
<td>3 months</td>
<td>Once weekly*</td>
<td>12</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>4 months</td>
<td>Daily</td>
<td>120</td>
</tr>
</tbody>
</table>

*Use Directly Observed Therapy (DOT)

**Note:** Due to the reports of severe liver injury and deaths, the CDC recommends that the combination of rifampicin (RIF) and pyrazinamide (PZA) should generally not be offered for the treatment of latent TB infection.

Although regimens are broadly applicable, there are modifications that should be considered under special circumstances (e.g., HIV infection, suspected drug resistance, pregnancy, or treatment of children). Table 6 lists the current recommended regimens.

**Isoniazid (INH)**

The standard treatment regimen for LTBI is nine months of daily INH. This regimen is very effective and is the preferred regimen for HIV-infected people taking antiretroviral therapy, and children aged 2-11 years of age. Although a 9-month regimen of isoniazid is the preferred treatment of LTBI for an individual patient, a 6-month regimen also provides substantial protection and has been demonstrated to be superior to placebo in both HIV-infected and HIV uninfected persons. From a societal perspective, treatment for 6 month rather than 9 month may provide a more cost-effective outcome. Thus, based on individual situations, health departments or other providers may prefer to concentrate efforts in ensuring the implementation of a 6-month rather than a 9-month course of isoniazid.

**Isoniazid (INH) and Rifapentine (RPT) Regimen**

The 12-dose regimen of INH and RPT does not replace other recommended LTBI treatment regimens; it is another effective regimen option for otherwise healthy patients aged ≥12 years who have predictive factor for greater likelihood of TB developing, which includes recent exposure to contagious TB, conversion from negative to positive on an indirect test for infection (i.e., interferon-γ release assay or tuberculin test), and radiographic findings of healed pulmonary TB.

This regimen is not recommended for:

- Children younger than 2 years old;
- People with HIV/AIDS who are taking certain antiretroviral treatment;
- People presumed to be infected with INH or RIF-resistant M. tuberculosis, and;
- Pregnant women or women expecting to become pregnant within the 12-week regimen.
3.3.3 (b) Adverse Drug Reactions

Patients on treatment for LTBI should be instructed to report any signs and symptoms of adverse drug reactions to their health care provider, including

- Unexplained anorexia, nausea or vomiting, dark urine*, or icterus;
- Persistent paresthesia of hands or feet;
- Persistent weakness, fatigue, fever, or abdominal tenderness;
- Easy bruising or bleeding.

*Advice patients taking RIF or RPT that they will notice a normal orange discoloration of body fluids, including urine and tears. Contact lenses may be permanently stained.

Obtain a list of patient’s current medications to avoid drug interactions. Some interactions to note:

- INH increases blood levels of phenytoin (Dilantin) and disulfiram (Antabuse);
- RIF and RPT decrease blood levels of many drugs including oral contraceptives, warfarin, sulfonureas, and methadone;
- RIF and RPT are contraindicated in HIV-infected individuals being treated with certain protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs).

3.3.3 (c) Monitoring During Treatment

Baseline and routine laboratory monitoring during treatment of LTBI are indicated only when there is a history of liver disease, HIV infection, pregnancy (or within 3 months post-delivery), or regular alcohol use. Baseline hepatic measurements of serum AST, ALT, and bilirubin are used in the situations mentioned above and to evaluate symptoms of hepatotoxicity. Laboratory testing should be performed to evaluate possible adverse reactions that occur during the treatment regimen.

Clinical monitoring, including a brief physical examination, should occur at monthly visits to assess adherence, rationale for treatment, and to identify signs or symptoms of adverse drug reactions.

3.3.4 Special Considerations for Treatment of LTBI

- In general, contacts who can provide written documentation of prior adequate treatment for LTBI do not need to be retreated. Retreatment may be indicated for persons at high risk of becoming reinfected and progressing to TB disease (e.g. young children and immunosuppressed persons)
- When isoniazid is chosen for treatment of LTBI in persons with HIV infection or those with radiographic evidence of prior TB, 9 months rather than 6 months is recommended.
- For pregnant, HIV-negative women, isoniazid given daily or twice weekly for 9 or 6 months is recommended. For women at risk for progression of LTBI to disease—especially those who are HIV-infected or who have likely been infected recently—initiation of therapy should not be delayed on the basis of pregnancy alone, even during the first trimester. For women whose risk for active TB is lower, some experts recommend waiting until after delivery to start treatment.
Breastfeeding is not contraindicated in women taking INH. Supplementation with 10-25 mg/d of pyridoxine (vitamin B6) is recommended for nursing women and for breast-fed infants. The amount of INH in breast milk is inadequate for treatment of infants with LTBI.

For contacts to an index patient with isoniazid-resistant, rifampicin-susceptible TB, rifampicin given daily for 4 months is recommended (6 months for children).

Active hepatitis and end-stage liver disease are relative contraindications to the use of isoniazid or pyrazinamide for treatment of LTBI.

Currently, there are no drug regimens that have been proven effective for treating LTBI resulting from exposure to a multi-drug-resistant TB (MDR-TB) source case; however, treatment may be indicated in certain high-risk situations. Consult an expert on MDR TB.

3.4 MANAGEMENT OF TB IN WORKPLACE

To control and manage TB in the workplace, every workplace should have a policy. It needs to be specifically devoted to TB and also, as an integrated response to issues affecting the health, well-being, and performance of an employee.

The following principles form the basis of a workplace policy:

a. **Recognition of TB as a workplace issue.**
   Commitment by the organisation that TB is a workplace issue because it affects the health of the workers and productivity of enterprise

b. **Non-discrimination**
   It should protect the fundamental rights of the workers that no worker should face discrimination because of his TB status. Bruneian workers with TB are entitled to work so long as they are medically fit and appropriate work is available. Measures like flexible leave arrangements, rescheduling of working times and arrangements for return to work should be taken into account.

c. **Confidentiality**
   Confidentiality of his TB status should be strictly controlled. This should be between him and management.

d. **Healthy work environment**
   The work environment should be healthy and safe to prevent transmission of TB. Employers need to provide information and education on TB transmission, appropriate environmental measures and protective attires where relevant.

e. **Care and support**
   Management should provide access to health services. Collaboration between management and workforce is needed on these issues.

3.4.1 Implementation of TB Programme at Workplace

3.4.1 (a) Detecting TB at workplace

Patients with TB have the potential to infect others. As such, the most cost-effective approach to detect TB is to identify cases among workers who present at health facilities with symptoms of the disease. Prompt case finding is therefore a priority.

After identifying a case, it is important to maintain confidentiality at all times. Equally important is to inform the worker that TB is treatable and can be cured. Collaboration and support from
management is crucial and a committee with broad presentation e.g. health and safety committee should be responsible for successful implementation of the programme.

3.4.1 (b) Ensure a safe workplace environment

Environmental control of TB refers to implementing environment associated interventions to reduce air-borne transmission from unsuspected cases or from already diagnosed cases of TB to non-infected employees. The overall objective of cost-effective interventions at the workplace should be to control the spread of TB by minimising the concentration of airborne infective droplet nuclei through improved ventilation.

Environmental factors that enhance TB transmission are:
   a. Small enclosed spaces;
   b. Areas that lack sufficient ventilation to clean the air through dilution or removal of infectious droplet nuclei;
   c. Ventilation system circulating air.
To counteract this, requires systems that ensure a high flow of fresh air into the workplace environment by:
   a. Installing a directional air flow ventilation;
   b. Installing air dis-infection devices;
   c. Installing air filtration system within the existing air conditioning system;
   d. To open doors and windows to facilitate air circulation.

3.4.1 (c) Education and Training

It is recommended that some responsible workers e.g. health and safety committee members should be trained to recognise TB and to promote TB awareness.

The goals of TB awareness should be:
   • To raise awareness of TB and the fact that it can be cured;
   • To reduce the stigma associated with TB so that workers can take treatment early without fear of dismissal or other negative impacts;
   • To increase case findings via self-presentation followed by early and timely intervention.

These trained workers may be able to help by:
   - Determining the needs of the workplace;
   - Developing and monitoring the workplace TB prevention programme;
   - Passing health information to co-workers;
   - Assisting affected workers with their needs during treatment.

3.4.2 Coordination with NTP

It is essential to coordinate workplace TB control activities with the NTP, as most countries have NTPs that implement the DOTS strategy.

3.4.3 Ensuring sustainability of TB control activities

It is essential that employers make a commitment to sustaining TB control activities (in order to decrease the risk of generating drug-resistant TB) by:
   • building community capacity in collaboration with the NTP;
   • making plans for transfer of responsibility for TB control activities if the employer ceases operations;
   • making a commitment to continuing responsibility for TB control activities.
3.5 TB Screening in Foreign Workers

Figure (15) Screening for new foreign workers coming to work in Brunei
Figure (16) Screening for foreign workers at the time of renewal of contract in Brunei

Foreign Worker completes 2 year contract in Brunei

Employment re-entry visa & leaves the country

Employment Pass for 3 weeks Reminder slip A

Foreign Workers’ Health Screening Centre

1st visit within 1 week

X-ray form HIV Blood for MP

X-ray done at Private clinic (paid separately)

2nd visit after 2 weeks

Blood & X-ray report

X-ray film sent to Dept. of Radiology RIPAS Hospital

Normal

Notification to DCD & Malaria vigilance unit

FIT – Med. Certificate issued (Pink)

Employment Pass for 2 years

Abnormal

MP positive

X-ray abnormality

HIV positive

UNFIT

Notification & counselling by DCD

Liaise with Immigration

Treatment

Employer’s Appeal

PTB confirmed

UNFIT

Non PTB

Referred to DORM

NB: It is becoming crucial these days to consider whether or not it is necessary to introduce Mantoux test to domestic workers, as they have to look after the young children who are most vulnerable to infectious diseases including TB.
3.6 TB Screening for Health Care Workers

- Health Care Workers (HCW) are considered as high risk groups for contracting tuberculosis infection. Therefore, TB screening should be conducted during pre-placement, renewal and periodic examinations for all local and expatriate HCWs working in Brunei Darussalam.
- All expatriate health care workers found to have active TB during pre-employment screening may not be granted a work permit for Brunei Darussalam. Those who are currently working in Government service and later found to have active TB may be allowed to continue working in Brunei Darussalam. However expatriate health care workers working in the private sector may not be allowed to continue working in Brunei Darussalam if found to have active TB during periodic TB screening or renewal of contract.
- Mantoux Test shall be used as an initial screening test. An induration of ≥ 10 mm is considered as positive Mantoux Test.
- All HCWs with positive Mantoux Test results should be referred to NTCC for further investigations.

3.7 Biosafety for Health Care Workers

Health Care Workers are at the frontline when combating highly infectious diseases including TB. It is not uncommon for them to get infected due to close proximity to infected patients in the course of their day-to-day work.
3.7.1 Infection Control in Tuberculosis

General measures

- Patients with suspected/confirmed respiratory tuberculosis, regardless of sputum status, should not be admitted to an open ward containing immune-compromised patients, transplant or oncology patients until pronounced non-infectious by the physician in charge, preferably in consultation with a respiratory physician.
- The Infection Control Team should be informed. Staff and visitors who are non-immune should be warned of the risk.
- Infection control precautions in PTB should remain until sputum microscopy is negative for AFB.

Infection Control Precautions

- Isolation
  - Isolate in a single room with negative air flow ventilation in relation to the surrounding areas. Alternatively, a single room with good ventilation may be used.
  - The room should have its own washbasin and preferably with an attached toilet.
  - The door should be kept closed at all times. Self-closing doors are ideal.
  - Ensure adequate supply of handwash antiseptics and single use towels.
  - Ensure a clinical waste bag is kept inside the room.
  - A sputum mug containing 5% Phenol (Lysol) for sputum should be provided. This is ideally autoclaved before disposal. If facilities are not available for autoclaving they should be disposed by burning or deep burying after disinfection using 5% phenol or 1% hypochlorite for 30 minutes. For stainless steel sputum cups after disinfection, wash with general purpose detergent.
  - Visitors should be restricted, as far as possible.
  - Contact with staff should be kept to a reasonable minimum without compromising patient care.

- Protective Clothing
  - Gloves are not usually necessary, but should be worn for contact with respiratory secretions or contaminated articles.
  - Patients should ideally have a surgical mask on and healthcare staff should at least be wearing a N95 mask during patient contact.
    NB: Wearing a mask is not a substitute for good infection control

- Hand Hygiene
  - Hands must be washed after touching the patient or potentially contaminated articles and before taking care of another patient.
  - Wash hands thoroughly with an antiseptic and dry with a single use towel.

- Equipment
  - Ideally, disposable respiratory equipment and accessories should be used.
  - Where this is not possible, they should be thoroughly cleaned and disinfected or sterilized before re-use.
3.7.2 Environmental factors that increase the risk for probability of transmission of *M. tuberculosis*

The probability of the risk for transmission of *M. tuberculosis* is increased as a result of various environmental factors.

- Exposure to TB in small, enclosed spaces.
- Inadequate local or general ventilation that results in insufficient dilution or removal of infectious droplet nuclei.
- Recirculation of air containing infectious droplet nuclei.
- Inadequate cleaning and disinfection of medical equipment.
- Improper procedures for handling specimens.

3.7.3 Risk for Health-Care–Associated Transmission of *M. tuberculosis*

Transmission of *M. tuberculosis* is a risk in health care settings. The magnitude of the risk varies by setting, occupational group, and prevalence of TB in the community, patient population, and effectiveness of TB infection-control measures. Health-care associated transmission of *M. tuberculosis* has been linked to close contact with persons with TB disease during aerosol-generating or aerosol-producing procedures, including bronchoscopy, endotracheal intubation, suctioning, other respiratory procedures, open abscess irrigation, autopsy, sputum induction, and aerosol treatments that induce coughing.

Of the reported TB outbreaks in health care settings, multiple outbreaks involved transmission of MDR TB strains to both patients and HCWs. The majority of the patients and certain HCWs were HIV-infected, and progression to TB and MDR TB disease was rapid.

One of the most critical risks for health-care associated transmission of *M. tuberculosis* in health-care settings is from patients with unrecognized TB disease who are not promptly handled with appropriate airborne precautions or who are moved from an isolation room too soon (e.g., patients with unrecognized TB and MDR TB).

3.7.3 (a) Administrative Controls

- Assigning responsibility for TB infection control in the setting;
- Conducting a TB risk assessment of the setting;
- Developing and instituting a written TB infection-control plan to ensure prompt detection, airborne precautions, and treatment of persons suspected or confirmed for TB;
- Implementing effective work practices for the management of patients with suspected or confirmed TB disease;
- Ensuring proper cleaning and sterilization or disinfection of potentially contaminated equipment (usually endoscopes);
- Training and educating HCWs regarding TB, with specific focus on prevention, transmission, and symptoms;
• Screening and evaluating HCWs who are at risk for TB disease or who might be exposed to M. tuberculosis (i.e., TB screening program);
• Using appropriate signage advising respiratory hygiene and cough etiquette.

3.7.3 (b) Environmental Controls

The second level of the hierarchy is the use of environmental controls to prevent the spread and reduce the concentration of infectious droplet nuclei in ambient air.

a. Primary environmental controls consist of controlling the source of infection by using local exhaust ventilation (e.g. hoods, tents, or booths) and diluting and removing contaminated air by using general ventilation.

This can be further explained by means of Controlled Natural Ventilation (to ensure doors and windows are maintained in an open position that enhances ventilation) should be provided in waiting areas and examination rooms to maximise natural ventilation. Negative pressure ventilation should be used in health facilities with high risk of transmission e.g. Isolation wards, ICUs and TB laboratories. When producing sputum smear specimens for TB diagnosis, it should be carried out in the open air away from other people. When this is not possible, it should be done in an adequately ventilated booth and not in small rooms such as toilets or other enclosed areas.

b. Secondary environmental controls (Filtration) consist of controlling the airflow to prevent contamination of air in areas adjacent to the source (All rooms) and cleaning the air by using high efficiency particulate air (HEPA), filtration, or ultraviolet germidicial irradiation (UVGI).

This is usually conducted in small rooms with limited number of patients or in other small enclosed areas, room air cleaners with high efficiency particulate air (HEPA) filters may be a useful alternative to mechanical ventilation requiring structural changes.

3.7.3 (c) Respiratory-Protection Controls

The third level of the hierarchy is the use of respiratory protective equipment in situations that pose a high risk for exposure. Use of respiratory protection can further reduce risk for exposure of HCWs to infectious droplet nuclei that have been expelled into the air from a patient with infectious TB disease.

The following measures can be taken to reduce the risk for exposure:

• Implementing a respiratory-protection program;
• Training HCWs on respiratory protection, and;
• Training patients on respiratory hygiene and cough etiquette procedures

3.7.3 (d) Personal Protection Equipment (Respiratory Protection)

Personal respiratory protection involves training in the selection and use of respirators. If a respirator is needed, a USA certified N95 (or greater) or EU certified FF2 (or greater) respirator should be used. All staff should undergo training of proper fitting of face mask.
Respirators should be distinguished from face mask such as surgical mask made of cloth or paper. Use of face mask is not generally recommended for health care staff because they do not protect against TB transmission by aerosol.

However, the use of face mask in high risk settings for drug resistant TB is recommended for patients to reduce risk of droplet nuclei generation and spread. Respiratory protection may be used as an interim measure, while selected administrative and or environmental control measures are awaiting implementation.
4. Therapeutic Guideline

4.1 Figure (18) Flow Chart for New Case of Pulmonary TB

- History
- Sputum for AFB smear and culture
- Chest X Ray, Mantoux Test/IGRA
- Molecular probe

Sputum positive for TB

Start First line Anti TB according to weight

Isolate Patient

Sputum Negative smear

DOTS Clinic

Mantoux positive Sputum negative
CXR normal

*Latent

Sputum negative for TB

Suspicion

High

Low

Repeat Sputum/Bronchoscopy

Observe/investigate for another cause

Negative

Discharge

NOTE: If smear positive for AFB, treat as TB; however, if Culture available, shows MOTT, stop ATT and treat MOTT if appropriate

* Refer to Table (6) Page 48 for Latent TB Infection Treatment Regimens

4.2 Standard regimen for new TB patients

Drug sensitivity testing to be done for all new TB patients

<table>
<thead>
<tr>
<th>Intensive phase treatment</th>
<th>Continuation phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months of HRZE</td>
<td>4 months of HR</td>
</tr>
</tbody>
</table>

Guidelines for Tuberculosis Control in Brunei Darussalam 2013
Drugs for treatment of tuberculosis should only be prescribed by doctors from DORM, chest clinics, DOTS clinics or designated paediatricians.

4.3 Table (7) Recommended doses of first-line Anti-tuberculosis drugs for adults

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended dose</th>
<th>3 times per week</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Daily 3 times per week</td>
<td>Dose and range (mg/kg body weight)</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>5 (4–6)</td>
<td>300</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>10 (8–12)</td>
<td>600</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>25 (20–30)</td>
<td>–</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>15 (15–20)</td>
<td>–</td>
</tr>
<tr>
<td>Streptomycin*</td>
<td>15 (12–18)</td>
<td>15 (12–18)</td>
</tr>
</tbody>
</table>

* Patients aged over 60 years may not be able to tolerate more than 500–750 mg daily, so some guidelines recommend reduction of the dose to 10 mg/kg per day in patients in this age group. Patients weighing less than 50 kg may not tolerate doses above 500–750 mg daily (WHO Model Formulary 2008, www.who.int/selection_medicines/list/en/).

4.4 Figure (19) Standard regimens for previously treated TB patients- Defaulted / Relapsing

Previously treated TB patient with worsening cough constitutional symptoms and worsening chest X ray

Sputum for smear and culture with Drug susceptibility testing (DST)

Smear Positive

Resistant to

Any mono resistance or poly resistance

Susceptible organism
2HRZES / 1 HRZE / 5HRE for full course of treatment Ref. Culture report

MDR Tuberculosis

Inform DORM, discuss and immediately notify infectious diseases

Treatment started at DORM

Transfer if stable to National Isolation Centre (Tutong)
4.5 Management of Treatment Interruption

If a patient misses an arranged appointment to receive treatment, the NTP should ensure that the patient is contacted within a day after missing treatment during the initial phase, and within a week during the continuation phase. The patient can be traced using the locating information previously obtained. It is important to find out the cause of the patient’s absence so that appropriate action can be taken and treatment can continue.

The management of patients who have interrupted treatment takes into consideration several factors, each of which, if present, will necessitate further caution and probably additional treatment:

- The patient is found to be smear- or culture-positive upon returning from default;
- Interruption occurs in the intensive, rather than the continuation, phase;
- Interruption occurs early (rather than later) in the continuation phase;
- The interruption is of long duration;
- The patient is immune compromised (living with HIV or another condition);
- The patient had poor response to treatment before the interruption;
- Drug-resistant disease is known or suspected.

Culture and DST should be performed once patient returns.

Interruptions in therapy are common in the treatment of tuberculosis. When interruptions occur, the person responsible for supervision must decide whether to restart a complete course of treatment or simply to continue as intended originally. This decision depends in part on whether the interruption occurred during the initial or the continuation phase of therapy. In general, the earlier the break in therapy and the longer its duration, the more serious the effect and the greater the need to restart the treatment from the beginning. Continuous treatment is more important in the initial phase of therapy, when there is the highest bacillary population and the chance of developing drug resistance is greatest. During the continuation phase, the number of bacilli is much smaller and the goal of therapy is to kill the persisting organisms. The duration of the interruption and the bacteriological status of the patient before and after the interruption are also important considerations.

There is no evidence on which to base detailed recommendations for managing interruptions in treatment, and no recommendations will cover all of the situations that may arise. The following approach, modified from the New York City Bureau of Tuberculosis Control Clinical Policies and Protocols (22), is presented as an example.

1. If the interruption occurs during the initial phase of treatment and the lapse is 14 days or more in duration, treatment should be restarted from the beginning.
2. However, if the lapse is less than 14 days, the treatment regimen should be continued. In either instance the total number of doses targeted for the initial phase should be given.
3. If the interruption in treatment occurs during the continuation phase after the patient has received more than 80% of the planned total continuation phase doses given by DOT, further treatment may not be necessary if the patient’s sputum was AFB smear negative on initial presentation.
4. However, for patients who were smear positive initially, continued treatment to complete the planned total number of doses is warranted.
5. If the patient has received less than 80% of the planned total doses and the lapse is 3 months or more in duration, treatment should be restarted from the beginning.
6. If the lapse is less than 3 months in duration, treatment should be continued to complete a full course.
At the time the patient is returned to treatment, sputum cultures should be obtained and repeat drug susceptibility testing performed. If the cultures are still positive, the treatment regimen should be restarted. If sputum cultures are negative the patient could be treated as having culture-negative tuberculosis and given an additional 4 months of combination chemotherapy. Regardless of the timing and duration of the interruption, DOT should be used. If the patient was already being managed with DOT, additional measures will be necessary to ensure completion of therapy. Consultation with an expert is recommended to assist in managing treatment interruptions.

Table (8) TB Treatment Phases

<table>
<thead>
<tr>
<th>Phase</th>
<th>Purpose</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial phase</strong></td>
<td></td>
<td>Initial 2-month treatment regimen (Daily)</td>
</tr>
<tr>
<td></td>
<td>• Kills most of the tubercle bacilli during the first 8 weeks of treatment, but some bacilli can survive longer</td>
<td>• Includes four drugs in the treatment (usually INH, RIF, PZA, and EMB)</td>
</tr>
<tr>
<td></td>
<td>• Prevents the emergence of drug resistance</td>
<td>• Each of the drugs plays an important role for short-course regimens with high cure rates</td>
</tr>
<tr>
<td></td>
<td>• Determines the ultimate outcome of the regimen</td>
<td>• Multiple drugs are needed to prevent the development of drug-resistant TB disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>An addition of either 4 or 7 months of treatment (Daily/3 times weekly)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 4 months is used for majority of patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 7 months is recommended only for persons</td>
</tr>
<tr>
<td></td>
<td></td>
<td>➢ Who have drug-susceptible cavitary or extensive pulmonary TB disease and whose sputum culture obtained at the time of completion of 2 months of treatment is positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>➢ Whose initial phase of treatment did not include PZA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>➢ Who are treated with once-weekly INH and RPT and whose sputum culture at the time of completion of the initial phase is positive</td>
</tr>
<tr>
<td><strong>Continuation phase</strong></td>
<td>• Kills remaining tubercle bacilli (after initial phase)</td>
<td>Duration depends on</td>
</tr>
<tr>
<td></td>
<td>• If treatment is not continued long enough, the surviving bacilli may cause TB disease in the patient at a later time</td>
<td>• Drugs used</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Drug susceptibility test results of the isolate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Patient’s response to therapy</td>
</tr>
<tr>
<td><strong>Treatment completion</strong></td>
<td>Defines the number of doses ingested within a specified time frame</td>
<td>Most patients with previously untreated pulmonary TB disease can be treated with either</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 6-month regimen (preferred) containing INH, RIF, and initially PZA or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 9-month regimen containing INH and RIF</td>
</tr>
</tbody>
</table>
### Table (9) Follow-up After Treatment

<table>
<thead>
<tr>
<th>Patients</th>
<th>Type of Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have a satisfactory response to 6- or 9-month regimen with both INH and RIF</td>
<td>Routine follow-up after treatment is not necessary</td>
</tr>
<tr>
<td>Have organisms that were fully susceptible to drugs being used</td>
<td>Patients should promptly report any of the following symptoms:</td>
</tr>
<tr>
<td></td>
<td>• Prolonged cough</td>
</tr>
<tr>
<td></td>
<td>• Fever</td>
</tr>
<tr>
<td></td>
<td>• Weight loss</td>
</tr>
<tr>
<td>Have organisms resistant to INH and RIF</td>
<td>Patients should be monitored for 2 years post-treatment</td>
</tr>
<tr>
<td>Have organisms resistant to INH or RIF</td>
<td>Follow-up must be individualized</td>
</tr>
</tbody>
</table>

**Figure (20) Algorithm for Management of Initial Phase Treatment Interruption**

1. **Treatment is interrupted**
2. **Is it for <14 days?**
   - No: Start over from the beginning
   - Yes: **Can the initial phase treatment be completed within 3 months?**
     - No: Start over from the beginning
     - Yes: **Continue treatment to complete total doses required**

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Guidelines for Tuberculosis Control in Brunei Darussalam 2013
Treatment Interruption during Continuation Phase
If the interruption occurred during the continuation phase, the following guidelines apply (Figure 21) (Table 10). If the patient received:

- ≥80% of doses, and sputum was acid-fast bacilli (AFB) smear negative on initial testing – further therapy may not be necessary;
- ≥80% of doses, and sputum was AFB smear positive on initial testing – continue therapy;
- <80% of doses, and lapse is less than 3 months in duration – continue therapy until all doses are completed (full course); or
- <80% of doses, and lapse is greater than 3 months in duration – restart therapy from the beginning of initial phase.

Figure (21) Algorithm for Management of Continuation Phase Treatment Interruptions
Table (10) Treatment Interruptions

<table>
<thead>
<tr>
<th>When Interruption Occurs</th>
<th>Situation</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During initial phase</strong></td>
<td>Lapse is &lt;14 days in duration</td>
<td>Continue treatment to complete planned total number of doses (as long as all doses are completed within 3 months)</td>
</tr>
<tr>
<td></td>
<td>Lapse is ≥14 days in duration</td>
<td>Restart treatment from the beginning</td>
</tr>
<tr>
<td><strong>During continuation phase</strong></td>
<td>Received ≥80% of doses and sputum was AFB smear negative on initial testing</td>
<td>Further therapy may not be necessary</td>
</tr>
<tr>
<td></td>
<td>Received ≥80% of doses and sputum was AFB smear positive on initial testing</td>
<td>Continue therapy until all doses are completed</td>
</tr>
<tr>
<td></td>
<td>Received &lt;80% of doses and lapse is &lt;3 months in duration</td>
<td>Continue therapy until all doses are completed (full course)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If treatment cannot be completed within recommended timeframe for regimen, restart therapy from the beginning</td>
</tr>
<tr>
<td></td>
<td>Received &lt;80% of doses and lapse is ≥3 months in duration</td>
<td>Restart therapy from the beginning, new initial and continuation phase</td>
</tr>
</tbody>
</table>
4.6 Management of TB in patients who develop hepatitis with alternate treatment regimens and change in duration of therapy as a consequence

<table>
<thead>
<tr>
<th>AST and ALT level</th>
<th>Levels of Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST and ALT less than 5 times the upper limit of normal</td>
<td>Mild</td>
</tr>
<tr>
<td>AST and ALT 5-10 times the upper limit of normal</td>
<td>Moderate</td>
</tr>
<tr>
<td>AST and ALT more than 10 times the upper limit of normal</td>
<td>Severe</td>
</tr>
</tbody>
</table>

The management of hepatitis induced by TB treatment depends on:
— Whether the patient is in the intensive or continuation phase of TB treatment;
— The severity of the liver disease;
— The severity of the TB, and;
— The capacity of the health unit to manage the side-effects of TB treatment.

If it is thought that the liver disease is caused by the anti-TB drugs, all drugs should be stopped. If the patient is severely ill with TB and it is considered unsafe to stop TB treatment, a non-hepatotoxic regimen consisting of streptomycin, ethambutol and a fluoroquinolone should be started.
If TB treatment has been stopped, it is necessary to wait for liver function tests to revert to normal and clinical symptoms (nausea, abdominal pain) to resolve before reintroducing the anti-TB drugs. If the signs and symptoms do not resolve and the liver disease is severe, the non-hepatotoxic regimen consisting of streptomycin, ethambutol and a fluoroquinolone should be started (or continued) for a total of 18–24 months.

Once drug-induced hepatitis has resolved, the drugs are reintroduced one at a time. If symptoms recur or liver function tests become abnormal as the drugs are reintroduced, the last drug added should be stopped.

Some advise starting with rifampicin because it is less likely than isoniazid or pyrazinamide to cause hepatotoxicity and is the most effective agent. After 3–7 days, isoniazid may be reintroduced.

In patients who have experienced jaundice but tolerate the reintroduction of Rifampicin and Isoniazid, it is advisable to avoid pyrazinamide.

1. **Treatment without pyrazinamide**
   - If pyrazinamide is discontinued before the patient has completed the intensive phase, the total duration of isoniazid and rifampicin therapy may be extended to 9 months.

2. **Treatment without ethambutol**
   - In rare occasions when ethambutol use is contraindicated, the streptomycin may be considered. Streptomycin can also be used as a 5th Medication for defaulter with pansensitive Tuberculosis.

3. **Treatment without rifampicin**
   - If Rifampicin causes a reaction and cant be reintroduced, a suggested regimen without Rifampicin is 2 months of Isoniazid, Ethambutol and Streptomycin followed by 10 months of Isoniazid and Ethambutol.

4. **Treatment without isoniazid**
   - If isoniazid cannot be used, 6–9 months of Rifampicin, Pyrazinamide and Ethambutol can be considered.

5. **Treatment without isoniazid and rifampicin.**
   - If neither Isoniazid nor Rifampicin can be used, the non-hepatotoxic regimen consisting of Streptomycin, ethambutol and a fluoroquinolone should be continued for a total of 18–24 months.

6. **Hepatitis with jaundice occurring during the intensive phase of TB treatment with isoniazid, rifampicin, pyrazinamide and ethambutol.**
   - Once hepatitis has resolved, restart the same drugs EXCEPT replace Pyrazinamide with Streptomycin to complete the 2-month course of initial therapy, followed by Rifampicin and Isoniazid for the 6-month continuation phase.

7. **Hepatitis with jaundice occurring during the continuation phase**
   - Once hepatitis has resolved, restart Isoniazid and Rifampicin to complete the 4-month continuation phase of therapy.
4.7. **Figure (23)** Algorithm for the diagnosis of tuberculosis in Smear-negative patients

![Algorithm Diagram]

<table>
<thead>
<tr>
<th>Patient with cough for more than 2 weeks which may be accompanied by other respiratory symptoms (shortness of breath, chest pains, haemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• History</td>
</tr>
<tr>
<td>• Sputum for AFB smear and culture</td>
</tr>
<tr>
<td>• Chest X Ray. Mantoux Test/IGRA</td>
</tr>
<tr>
<td>• Molecular probe</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td><strong>Sputum Negative for TB</strong></td>
</tr>
<tr>
<td><strong>Low suspicion</strong></td>
</tr>
<tr>
<td><strong>Observe/investigate for another cause</strong></td>
</tr>
<tr>
<td><strong>High Suspicion</strong></td>
</tr>
<tr>
<td><strong>Repeat Sputum Negative</strong></td>
</tr>
<tr>
<td><strong>Diagnosis made- Treat appropriately</strong></td>
</tr>
<tr>
<td><strong>Repeat Sputum/ Bronchoscopy</strong></td>
</tr>
<tr>
<td><strong>Negative for AFB</strong></td>
</tr>
<tr>
<td><strong>Smear and Culture- negative/</strong></td>
</tr>
<tr>
<td><strong>IGRA- negative</strong></td>
</tr>
<tr>
<td><strong>Suspicion of TB very high and Physician decides to treat</strong></td>
</tr>
<tr>
<td><strong>Start first line Anti TB according to weight</strong></td>
</tr>
<tr>
<td><strong>Positive for AFB +/- or IGRA- positive or PCR - positive</strong></td>
</tr>
<tr>
<td><strong>Isolate Patient</strong></td>
</tr>
<tr>
<td><strong>DOTS Clinics</strong></td>
</tr>
</tbody>
</table>

---

**Table (11) Recommended Examinations for Baseline Monitoring**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommended Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>Measure aminotransferases (i.e. AST, ALT), bilirubin, alkaline phosphatase and serum creatinine and a platelet count. HIV status.</td>
</tr>
<tr>
<td>Patients at risk of Hepatitis B or C (injection drug user, born in Asia or Africa or HIV infected)</td>
<td>Conduct serological tests</td>
</tr>
<tr>
<td>Patients taking ethambutol</td>
<td>Test visual acuity and colour vision</td>
</tr>
<tr>
<td>HIV infected patients</td>
<td>Obtain CD4+ lymphocyte count</td>
</tr>
</tbody>
</table>
4.8 Figure (24) Algorithm of approach to Diagnosis of Extra Pulmonary Tuberculosis

4.8.1 Procedures

1. Intra Thoracic - Excisional biopsy-obtained with mediastinoscopy or thoracoscopy.
2. Pleural Effusion - Do a thoracentesis. Pleural fluid analysis is performed. Pleural biopsy is indicated when the patient has a lymphocyte-dominant exudative effusion send specimen for AFB culture and histology.
3. Cold abscesses, if present, may be aspirated for AFB smear and culture. CT-guided biopsy in vertebral TB may have positive microbiology or histology.
4. Synovial biopsy should be done to diagnose TB arthritis.
5. CSF is submitted for cell count with differential, glucose, protein, AFB smear and culture, Gram stain, and bacterial culture. AFB culture is the definitive standard for diagnosis but treatment must not wait until culture results are available.
6. Abdominal TB - ascitic fluid or a peritoneal/organ biopsy culture growth of M tuberculosis from ascitic fluid or a biopsy of the lesion.
7. Genito-urinary TB- culturing TB from morning urine samples (3 are recommended) or biopsy of the lesion.
8. Pericardial TB - requires aspiration of pericardial fluid or, usually, pericardial biopsy.

4.9 Step-by-step diagnostic approach in patients with Extra-pulmonary Tuberculosis

Many forms of extra pulmonary TB (EPTB) are paucibacillary, and the diagnosis of EPTB is therefore challenging. Acid-fast bacilli (AFB) smear of biological specimens is often negative. Tuberculin skin testing (TST) and interferon-gamma release assays (IGRA) are adjunctive diagnostic tools, at best.
Constitutional symptoms associated with EPTB, (such as fever, weakness, and weight loss) may be infrequent and non-specific. In addition, EPTB is less common than pulmonary tuberculosis (PTB) and may be less familiar to clinicians.

A high level of suspicion is important in evaluating a patient with presence of risk factors. A firm diagnosis of TB requires culturing of Mycobacterium tuberculosis and is important for drug-susceptibility testing. Appropriate specimens are obtained and tested microbiologically and histologically. Although culture remains the diagnostic standard, it can take up to 8 to 10 weeks using a solid media, and in 10% to 15% of patients the diagnosis of TB is based on clinical grounds. Delays in diagnosis and initiation of therapy are associated with increased mortality.

4.10 Tests for all Suspected EPTB

As the lungs may be involved in patients with EPTB, sputum for AFB smear and culture is indicated for all suspected patients. Culture-positive sputum becomes useful when the specimens from extra pulmonary sites are culture-negative, and it may also add further information on the infectiousness of the patient. Chest x-ray should be part of the basic work-up and may show evidence of active or old TB. Tuberculin skin test (TST) is also done in all patients with suspected EPTB, although the sensitivity may range from 30% to 90% depending on the site of disease. A positive TST is helpful for diagnosis, but a negative TST does not rule out active disease. If the suspicion of TB is high or the patient is very ill, consideration can be given to starting anti-tuberculous medicines as soon as diagnostic specimens are obtained.

Interferon-gamma release assay (IGRA) is an in vitro test, which the Centers for Disease Control and Prevention (CDC) recommends can be used in all circumstances in which the TST is currently used, including contact investigations, evaluation of recent immigrants, and sequential-testing surveillance programmes for infection control (e.g., those for healthcare workers).

Several molecular diagnostic methods (nucleic acid amplification tests) are available. They are based on amplification of mycobacterial nucleic acid. These methods enable the laboratory to provide the results to clinicians within a day, with higher specificity and sensitivity than AFB smear.

It is recommended that all patients with TB have an HIV test within 2 months of diagnosis.

HIV infection and its treatment may alter the treatment of TB; treatment of HIV may be crucial to the morbidity of HIV-infected TB patients.

4.10.1 TB Lymphadenitis

Patients most commonly present with enlarged lymph nodes in the cervical or supra-clavicular areas that may be unilateral or bilateral. If a patient with superficial lymphadenitis is suspected of having TB, the first diagnostic test is FNA, especially if the lymph node is fluctuant. If the diagnosis remains in question, then a surgical consultation is obtained for lymph node excision (not incisional biopsy, due to the risk of sinus tract formation).
If the patient has inaccessible lymphadenitis (e.g., mediastinal), biopsy is obtained with mediastinoscopy or thoracoscopy.

4.10.2 Pleural TB

Pleural TB usually presents with symptoms such as pleurisy, pleuritic chest pain, cough, and fever, and a chest x-ray showing a unilateral effusion. The effusion is commonly small to moderate in size; bilateral TB effusions are rare and associated with disseminated disease.

In addition to a chest x-ray, sputum cultures, and TSTs, a thoracentesis is done. Chest x-ray may show no obvious parenchymal disease in 50% of patients with pleural TB; sputum cultures are positive in 20% to 30% of those without definite parenchymal involvement. False-negative TSTs are also common.

4.10.3 Pleural fluid analysis is performed on the sample obtained from thoracentesis. Pleural fluid is sent for AFB smear and culture, cell count with differential, protein, LDH, glucose, and pH. AFB smear is rarely positive. Pleural fluid analysis usually shows an exudative effusion that is lymphocyte-predominant and often has low glucose level. The adenosine deaminase (ADA) level may be measured because it is often elevated in pleural TB (sensitivity and specificity approximately 90%).

Although results of pleural fluid analysis may be helpful, they will seldom confirm a diagnosis of pleural TB. Because a malignancy may also cause a lymphocyte-predominant exudative effusion, the diagnosis of pleural TB is based on microbiology, pathology (granulomas), and negative cytology. It is important to obtain a TB isolate for susceptibility testing. Therefore pleural biopsy is indicated when the patient has a lymphocyte-dominant exudative effusion, or even at the same time as thoracentesis if clinical suspicion for TB is very high. The combination of AFB culture and histology from pleural biopsy is the most sensitive to diagnose pleural TB. If results of biopsy are non-diagnostic, thoracoscopy or thoracotomy may be indicated.

4.10.4 Skeletal TB

About 70% to 90% of patients may have a positive TST. One half of cases will have abnormalities on chest x-ray consistent with TB.

Pain of the involved area is the most common complaint in skeletal TB; constitutional symptoms are usually absent. Diagnosis is based on tissue biopsy. Onset of pain is gradual (over weeks to months) and diagnosis is frequently delayed. Local swelling and limitation of movement may be present. Cold abscesses (non-tender) with sinus tracts may form.

If skeletal TB is suspected, MRI (especially in spinal involvement) or CT is obtained. Microbiological confirmation of TB is also essential. AFB smears are unlikely to be positive due to low bacillary loads. Cold abscesses, if present, may be aspirated for AFB smear and culture. CT-guided biopsy in vertebral TB will have positive microbiological or histological yields in 65% to 90% of patients.

Synovial biopsy should be done to diagnose TB arthritis. Biopsy may yield culture positive in 90% to 95% and can be performed if the diagnosis of TB arthritis remains in question. In joint involvement, evaluation of synovial fluid is usually not diagnostic; WBC counts in TB arthritis are usually 10,000 to 20,000/mL, but can be much higher. AFB smear is positive in <20% but culture may be positive in up to 80%.
4.10.5 CNS TB

CNS TB may present with meningitis or intracranial tuberculomas. Diagnosis of TB meningitis is dependent upon CSF examination, and its rapid diagnosis is essential for improved outcomes.

Signs and symptoms of meningeal TB include headache, neck stiffness, altered mental status, and cranial nerve abnormalities. Only 38% of children with TB meningitis have fever and 9% report photophobia. Seizures are common in children and the elderly.

In the presence of meningeal signs, the patient undergoes lumbar puncture and the CSF is submitted for cell count with differential, glucose, protein, AFB smear and culture, Gram stain, and bacterial culture. The usual results of analysis include a lymphocyte predominance, elevated protein, and reduced glucose. Although smears of spinal fluid are frequently negative, the diagnostic yield is dependent on the volume of CSF submitted and the quality of examination.

In order to maximise the sensitivity of TB diagnosis by spinal fluid analysis, some experts suggest increased CSF volume (at least 6 mL of spinal fluid for AFB) and repeated sampling (up to 3 lumber punctures on different days).

AFB culture is the definitive standard for diagnosis but treatment must not wait until culture results are available. Treatment is initiated presumptively based on clinical suspicion, risk factors, and CSF results.

Head CT or MRI may show oedema, hydrocephalus, basilar meningeal thickening, or tuberculomas. Tuberculomas present as a slowly growing focal lesion, or, rarely, with signs and symptoms consistent with increased intracranial pressure. CSF analysis is usually normal and diagnosis is based on CT or MRI findings.

Up to 50% of patients have chest x-ray abnormalities consistent with pulmonary TB.

4.10.6 Abdominal TB

TST may be positive in 70% and chest x-ray may show evidence of old TB. Abdominal TB includes TB peritonitis and TB of the GI tract. Definitive diagnosis is based on culture growth of M tuberculosis from ascitic fluid or a biopsy of the lesion. Patients may have disease for months before the diagnosis is made. Peritoneal disease is the more common presentation. The presenting symptoms include abdominal swelling, abdominal pain, fever, and change in bowel habits. In TB enteritis (TB of the GI tract), the ileocaecum is the most commonly involved area, followed by the ileum, caecum, and ascending colon. Chronic abdominal pain is the most common symptom in addition to changes in bowel habits and haem-positive stool. Patients may develop small bowel obstruction or a right lower quadrant mass.

CT scan of the abdomen, ascitic fluid analysis, and peritoneal biopsy are done initially.

CT scan may show ascites, bowel-wall thickening, or abdominal lymphadenopathy
Ascitic fluid analysis is non-specific and rarely AFB smear-positive. Although the sensitivity of culture from peritoneal fluid is high (92%), results require up to 8 weeks and delay in initiating treatment is associated with higher mortality.

Peritoneal biopsy (laparoscopy or laparotomy) is the most effective means for diagnosis. Direct inspection may reveal miliary nodules over the peritoneum and allow a presumptive diagnosis in 80% to 95%. Biopsy demonstrates caseating granulomas (up to 100%) and the presence of AFBs on examination in 67% of samples.

Colonoscopy and biopsy are carried out to diagnose TB enteritis. Colonoscopy will reveal ulcers, pseudo-polyps, or nodules. Definitive diagnosis is based on biopsy, which usually shows granulomas and culture positive for TB.

4.10.7 Genitourinary TB

Chest x-ray is abnormal in 40% to 75% of patients. TST is positive in up to 90% of patients.

Diagnosis relies on culturing TB from morning urine samples (3 are recommended) or biopsy of the lesion. The common symptoms are dysuria, haematuria, and urinary frequency. Symptoms may be absent in 20% to 30% of patients. Genital TB in men may present as a scrotal mass and in women may be asymptomatic or cause pelvic pain. Constitutional symptoms are rare. Extensive renal destruction may have occurred by the time GU TB is diagnosed.

Urinalysis is done initially. Results commonly show pyuria, haematuria, or proteinuria, although they may be normal. Urine culture for TB may be positive in 80% of patients; 3 samples for culture improve sensitivity. The classic finding of sterile pyuria is neither sensitive nor specific. Definitive diagnosis of genital TB is based on tissue biopsy.

4.10.8 Pericardial TB

Chest x-ray shows cardiomegaly (in 70% to 95% of cases) and pleural effusion (in about 50%). ECG is low voltage (in about 25%) and shows T-wave inversion (in about 90%). Echocardiography, CT, or MRI shows pericardial effusion and thickness across the pericardial space. Diagnosis of pericardial TB requires aspiration of pericardial fluid or, usually, pericardial biopsy. Pericardial fluid is exudative with increased leukocytes, predominantly lymphocytes. Haemorrhagic effusion is often seen. AFB smear of the fluid is commonly negative and cultures are positive in 50% to 60% of cases. Pericardial biopsy offers a higher diagnostic yield.

4.10.9 Disseminated TB

The diagnosis of disseminated TB concentrates on the organs most likely to be involved. The most commonly involved organs (in order) are lungs, liver, spleen, kidneys, and bone marrow. Patients with disseminated TB will typically have constitutional symptoms including fever (90%), anorexia (78%), and sweats (76%).

If disseminated TB is suspected, chest x-ray (if non-diagnostic, consider a chest CT), sputum for AFB smear and culture, blood culture for mycobacteria, and first-morning-void urine for AFB are obtained; lumbar puncture and biopsy of superficial lymph nodes are also done if applicable.
smear will be positive in one-third of patients with culture positive in about 60%. TST is positive in only 45% of patients with disseminated disease.

As delays in treatment are associated with increased mortality, a rapid diagnostic test (i.e., faster than culture results) is frequently needed. If sputum smears are negative and chest x-ray is abnormal, bronchoscopy with transbronchial biopsies are indicated. If results are non-diagnostic, bone marrow or liver biopsy is also done. Both have similar sensitivities, but bone marrow biopsy may be preferred because of its lower procedure risk. If thrombocytopenia or leukopenia is present, the sensitivity of bone marrow biopsy is increased.

4.11 Co-Management of HIV and Active TB Disease

All patients known or suspected to have TB should receive HIV testing and counseling. Irrespective of epidemic setting, WHO recommends HIV testing for patients of all ages who present with signs or symptoms that suggest tuberculosis, whether TB is suspected or already confirmed. TB is often the first clinical indication that a person has underlying HIV infection, and TB services can be an extremely important entry point to HIV prevention, care and treatment. In addition, the HIV status of TB patients makes a difference to their TB treatment. Detecting HIV infection in a TB patient is also critical for the TB patient’s household members: HIV-positive TB patients may have household members who are also living with HIV.

4.12 TB Treatment in People Living with HIV

Among treated TB patients, death rates are higher in HIV-positive than in HIV-negative patients. Case-fatality is higher in people living with HIV with smear-negative pulmonary and extrapulmonary TB, as these patients are generally more immuno-suppressed than those with smear-positive TB. Please refer the patient to either Division of Respiratory Medicine or the Division of Infectious Diseases for further evaluation and treatment.

4.13 Management of Extra Pulmonary TB

4.13.1 Meningeal TB

Patients with active meningeal TB should be offered a treatment regimen lasting for 12 months. The intensive phase comprises Isoniazid, Pyrazinamide, Rifampicin and a fourth drug (for example, Ethambutol) for the first 2 months. This is followed by Isoniazid and Rifampicin for the rest of the treatment period-i.e. 10 months.

A glucocorticoid at the dose equivalent to prednisolone 20–40 mg if the patient is on Rifampicin can be given. If not on Rifampicin the dose can be reduced to 10–20 mgs, with gradual withdrawal of the glucocorticoid starting within 2–3 weeks of initiation.

Clinicians prescribing treatment for active meningeal TB should consider as first choice a daily dosing schedule.
4.13.2 Peripheral Lymph Node TB

For patients with active peripheral lymph node tuberculosis, the first choice of treatment should be the standard recommended regimen (2 months intensive and 4 months continuation phase) using a daily dosing schedule.

Patients with active peripheral lymph node TB who have had an affected gland surgically removed should still be treated with the standard recommended regimen.

Drug treatment of peripheral lymph node TB should normally be stopped after 6 months, regardless of the appearance of new nodes, residual nodes or sinuses draining during treatment.

4.13.3 Bone and Joint TB

The standard recommended regimen should be planned and started in people with active spinal TB and active TB at other bone and joint sites. Clinicians prescribing treatment for active bone and joint tuberculosis should consider as first choice a daily dosing schedule.

A computed tomography (CT) or magnetic resonance (MR) scan should be performed on patients with active spinal TB who have neurological signs or symptoms. If there is direct spinal cord involvement (for example, a spinal cord tuberculoma), management should be as for meningeal TB.

Routine therapeutic surgery in Bone and joint TB.

- In patients with spinal TB, anterior spinal fusion should not be performed routinely.
- In patients with spinal TB, anterior spinal fusion should be considered if there is spinal instability or evidence of spinal cord compression.

4.13.4 Pericardial TB

For patients with active pericardial TB, the first choice of treatment should be the standard recommended regimen use a daily dosing schedule include combination tablets.

In addition to anti-TB treatment, patients with active pericardial TB should be offered a glucocorticoid equivalent to prednisolone of 1 mg/kg/day (maximum 40 mg/day) with gradual withdrawal of the glucocorticoid starting within 2–3 weeks of initiation.

4.13.5 Disseminated (including miliary) TB

For patients with disseminated (including miliary) TB, the first choice of treatment should be the standard recommended regimen- use a daily dosing schedule.

Treatment of disseminated (including miliary) TB should be started even if initial liver function tests are abnormal. If the patient’s liver function deteriorates significantly on drug treatment, advice on management options should be sought from DORM.

Patients with disseminated (including miliary) TB should be tested for central nervous system (CNS) involvement by brain scan (CT or MRI) and/or lumbar puncture for those with CNS signs or symptoms lumbar puncture for those without CNS signs and symptoms.
If evidence of CNS involvement is detected, treatment should be the same as for meningeal TB.

### 4.14 Treatment Regimens in Special Situations

The treatment of TB in pregnancy and breast-feeding, liver disorders, and renal failure is discussed below.

#### 4.14.1 Pregnancy

- Women of child-bearing age should be asked about current or planned pregnancy before starting TB treatment.
- A pregnant woman should be advised that successful treatment of TB with the standard regimen is important for successful outcome of pregnancy.
- Untreated tuberculosis presents a much greater risk to a pregnant woman and her foetus than does the treatment of the disease.
- With the exception of streptomycin, the first line anti-TB drugs are safe for use in pregnancy: streptomycin is ototoxic to the fetus and should not be used during pregnancy.
- Doses of anti-tuberculosis drugs given in pregnancy are similar to that in a non-pregnant patient.
- Rifampicin interacts with oral contraceptive pills, with a risk of decreased protective efficacy against pregnancy, a woman who usually takes the oral contraceptive pill may choose between an oral contraceptive pill containing a higher dose of oestrogen (50 mcg) or use another form of contraception after consultation with a doctor.

#### 4.14.2 Breast-Feeding

- A breast-feeding woman who has TB should receive a full course of TB treatment.
- Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to the baby.
- Tuberculosis treatment in lactating mothers is safe as the amount of drug ingested by nursing infant is minimal.
- Mother and baby should stay together and the baby should continue to breastfeed if the mother at the time of delivery is smear-negative.
- If the mother at the time of delivery is smear-positive, the newborn should be separated from the mother at least for a period of two weeks. Breastfeeding is best avoided during these two weeks and expressed milk should be given to the child.
- After active TB in the baby is ruled out, BCG should be given as scheduled and the baby should be given 6 months of isoniazid preventive therapy, followed by Mantoux test at the end of 6 months. In the event of absence of scar, BCG vaccination should be repeated.

Pyridoxine supplementation is recommended for all pregnant or breast-feeding women taking isoniazid.

#### 4.14.3 Liver Disorders

This section covers TB treatment in patients with pre-existing liver disease.

- Patients with the following conditions can receive the usual TB regimens provided that there is no clinical evidence of chronic liver disease:
  1. Hepatitis virus carriage.
  2. A past history of acute hepatitis.
However, hepatotoxic reactions to anti-TB drugs may be more common among these patients and should therefore be anticipated.

- In patients with unstable or advanced liver disease, liver function tests should be done at the start of treatment, if possible.
- If the serum alanine aminotransferase level is more than 3 times normal before the initiation of treatment, the following regimens should be considered.
- The more unstable or severe the liver disease is, the fewer hepatotoxic drugs should be used.

Possible regimens include:

- **Two hepatotoxic drugs: (rather than the three in the standard regimen):**
  - 9 months of isoniazid and rifampicin, plus ethambutol (until or unless isoniazid susceptibility is documented);
  - 2 months of isoniazid, rifampicin, streptomycin and ethambutol, followed by 6 months of isoniazid and rifampicin;
  - 6–9 months of rifampicin, pyrazinamide and ethambutol.

- **One hepatotoxic drug:**
  - 2 months of isoniazid, ethambutol and streptomycin, followed by 10 months of isoniazid and ethambutol.

- **No hepatotoxic drugs:**
  - 18–24 months of streptomycin, ethambutol and a fluoroquinolone.

  1. Note that TB itself may involve the liver and cause abnormal liver function.
  2. In some cases of concurrent acute (i.e. viral) hepatitis not related to TB or TB treatment, it may be possible to defer TB treatment until the acute hepatitis has resolved.

Expert consultation is advisable in treating patients with advanced or unstable liver disease. Clinical monitoring (and liver function tests, if possible) of all patients with pre-existing liver disease should be performed during treatment.

### 4.14.4 Renal Failure and Severe Renal Insufficiency

- The recommended initial TB treatment regimen for patients with renal failure or severe renal insufficiency is 2 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.
- There is significant renal excretion of ethambutol and metabolites of pyrazinamide, and doses should therefore be adjusted.
- Three times per week administration of these two drugs at the following doses is recommended: pyrazinamide (25 mg/kg), and ethambutol (15 mg/kg).
- While receiving isoniazid, patients with severe renal insufficiency or failure should also be given 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 must be used, the dosage is 15 mg/kg, two or three times per week, to a maximum of 1 gram per dose, and serum levels of the drug should be monitored.
### Table (12) Dosing recommendations for adult patients with reduced renal function and for adult patients receiving hemodialysis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Change in frequency?</th>
<th>Recommended dose and frequency of patients with creatinine clearance &lt; 30 ml/min or patients receiving hemodialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>No change</td>
<td>300 mg once daily, or 900 mg three times per week</td>
</tr>
<tr>
<td>Rifampin</td>
<td>No change</td>
<td>600 mg once daily, or 600 mg three times per week</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Yes</td>
<td>25-35 mg/kg per dose three times per week (not daily)</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Yes</td>
<td>15-25 mg/kg per dose three times per week (not daily)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Yes</td>
<td>750-1,000 mg per dose three times per week (not daily)</td>
</tr>
<tr>
<td>Cycloserine</td>
<td>Yes</td>
<td>250 mg once daily, or 500 mg per dose three times per week*</td>
</tr>
<tr>
<td>Ethionamide</td>
<td>No change</td>
<td>250-500 mg/dose daily</td>
</tr>
<tr>
<td>p-Aminosalicylic acid</td>
<td>No change</td>
<td>4g/dose, twice daily</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Yes</td>
<td>12-15 mg/kg per dose two or three times per week (not daily)</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>Yes</td>
<td>12-15 mg/kg per dose two or three times per week (not daily)</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>Yes</td>
<td>12-15 mg/kg per dose two or three times per week (not daily)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Yes</td>
<td>12-15 mg/kg per dose two or three times per week (not daily)</td>
</tr>
</tbody>
</table>

Standard doses are given unless there is intolerance.

The medications should be given after hemodialysis on the day of hemodialysis.

Monitoring serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity.

Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing, using serum concentration monitoring.

* The appropriateness of 250 mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity

**4.14.5 NOTE:** Unmanageable drug related adverse events with renal failure or hepatitis should be referred to DORM or a respiratory physician for further action.
4.15 Assessing treatment response in new and previously treated pulmonary TB patients, and acting on the results

Sputum monitoring by smear microscopy in new pulmonary TB patients
Note: If a patient is found to harbour a multidrug-resistant strain of TB at any time during therapy, treatment is declared a failure and the patient is re-registered and should be referred to an MDR-TB treatment programme.

<table>
<thead>
<tr>
<th>Months of treatment</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<tr>
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</tr>
</tbody>
</table>

If smear-positive at month 2, obtain sputum again at month 3. If smear-positive at month 3, obtain culture and DST.

<table>
<thead>
<tr>
<th>Months of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>[========</td>
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</tbody>
</table>

Key:
[========] Intensive phase of treatment (HRZE)
[--------] Continuation phase (HR)
• Sputum smear examination
sm + Smear-positive
   a Omit if patient was smear-negative at the start of treatment and at 2 months.
b Smear- or culture-positivity at the fifth month or later (or detection of MDR-TB at any point) is defined as treatment failure and necessitates re-registration and change of treatment.

Sputum monitoring of pulmonary TB patients receiving the 8-month retreatment regimen with first-line drugs

<table>
<thead>
<tr>
<th>Months of treatment</th>
</tr>
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<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>[========</td>
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<tr>
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</tr>
</tbody>
</table>
Key:
[========] Intensive phase: 2 months of HRZES followed by 1 month of HRZE
[------------] Continuation phase with 5 months of HRE

- Sputum smear examination
  sm + Smear-positive

A Smear- or culture-positivity at the fifth month or later (or detection of MDR-TB at any point) is defined as treatment failure and necessitates reregistration and change of treatment.

**A positive sputum smear at the end of the intensive phase may indicate any of the following:**

- The initial phase of therapy was poorly supervised and patient adherence was poor;
- Poor quality of anti-TB drugs;
- Doses of anti-TB drugs are below the recommended range;
- Resolution is slow because the patient had extensive cavitation and a heavy initial bacillary load;
- There are co-morbid conditions that interfere either with adherence or with response;
- The patient may have drug-resistant M. tuberculosis that is not responding to first-line treatment;
- Non-viable bacteria remain visible by microscopy.

The programme should carefully review the quality of the patient’s support and supervision and intervene promptly if necessary. Patient treatment records should be reviewed with the responsible health care worker, and reasons for any interruptions should be explored and addressed.

It is unnecessary, unreliable and wasteful of resources to monitor the patient by chest radiography.

New pulmonary TB patients whose sputum smear microscopy was negative (or not done) at the start of treatment; it is important to recheck a sputum specimen at the end of the intensive phase in case of disease progression (due to non-adherence or drug resistance) or an error at the time of initial diagnosis (i.e. a true smear-positive patient was misdiagnosed as smear-negative). Pulmonary TB patients whose sputum smear microscopy was negative (or not done) before treatment and whose sputum smears are negative at 2 months need no further sputum monitoring. They should be monitored clinically; body weight is a useful progress indicator.

**Extra-Pulmonary TB**

For patients with extra-pulmonary TB, clinical monitoring is the usual way of assessing the response to treatment. As in pulmonary smear-negative disease, the weight of the patient is a useful indicator.

**4.16 Definitions of Treatment Outcomes**

(refer to Chapter 2.2- Types of patients and treatment outcomes, page 11)
### 4.17 Table (13) Symptom-based approach to managing side-effects of anti-TB drugs

<table>
<thead>
<tr>
<th>Major Side-effects</th>
<th>Drug(s) probably responsible</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin rash with or without itching</td>
<td>Streptomycin, isoniazid, rifampicin, pyrazinamide</td>
<td>Stop responsible drug(s) and refer to clinician urgently</td>
</tr>
<tr>
<td>Deafness (no wax on otoscopy)</td>
<td>Streptomycin</td>
<td>Stop streptomycin</td>
</tr>
<tr>
<td>Dizziness (vertigo and nystagmus)</td>
<td>Streptomycin</td>
<td>Stop streptomycin</td>
</tr>
<tr>
<td>Jaundice (other causes excluded), hepatitis</td>
<td>Isoniazid, pyrazinamide, rifampicin</td>
<td>Stop anti-TB drugs</td>
</tr>
<tr>
<td>Confusion (suspect drug-induced acute liver failure if there is jaundice)</td>
<td>Most anti-TB drugs</td>
<td>Stop anti-TB drugs</td>
</tr>
<tr>
<td>Visual impairment (other causes excluded)</td>
<td>Ethambutol</td>
<td>Stop Ethambutol</td>
</tr>
<tr>
<td>Shock, purpura, acute renal failure</td>
<td>Rifampicin</td>
<td>Stop rifampicin</td>
</tr>
<tr>
<td>Decreased urine output</td>
<td>Streptomycin</td>
<td>Stop streptomycin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor Side-effects</th>
<th>Drug(s) probably responsible</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia, nausea, abdominal pain</td>
<td>Pyrazinamide, rifampicin, isoniazid</td>
<td>Give drugs with small meals or just before bedtime, and advice patient to swallow pills slowly with small sips of water. If symptoms persist or worsen, or there is protracted vomiting or any sign of bleeding, consider the side-effect to be major and refer to clinician urgently.</td>
</tr>
<tr>
<td>Joint pains</td>
<td>Pyrazinamide</td>
<td>Aspirin or non-steroidal anti-inflammatory drug, or paracetamol</td>
</tr>
<tr>
<td>Burning, numbness or tingling sensation in the hands or feet</td>
<td>Isoniazid</td>
<td>Pyridoxine 50–75 mg daily</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>Isoniazid</td>
<td>Reassurance. Give drugs before bedtime</td>
</tr>
<tr>
<td>Orange/red urine</td>
<td>Rifampicin</td>
<td>Reassurance. Patients should be told when starting treatment that this may happen and is normal</td>
</tr>
<tr>
<td>Flu syndrome (fever, chills, malaise, headache, bone pain)</td>
<td>Intermittent dosing of rifampicin</td>
<td>Change from intermittent to daily rifampicin administration</td>
</tr>
</tbody>
</table>

Please refer to WHO document “Treatment of Tuberculosis guidelines” for detailed management of drug toxicity.
4.18 Management of Tuberculosis in Children

4.18 (a) Approach to Diagnose TB in Children

1. Careful history (including history of TB contact and symptoms consistent with TB)

   a. Contact

      • All children aged 0–4 years and children aged 5 years and above who are symptomatic, who have been in close contact with a smear-positive TB case, must be screened for TB.
      • When any child (aged less than 15 years) is diagnosed with TB, an effort should be made to detect the source case (usually an adult with sputum smear-positive pulmonary TB) and any other undiagnosed cases in the household.
      • If a child presents with infectious TB, child contacts must be sought and screened, as for any smear-positive source case. Children should be regarded as infectious if they have sputum smear-positive pulmonary TB or cavitary TB on CXR.

   b. Symptoms

      In most cases, children with symptomatic TB develop chronic symptoms. The commonest are:

      • Chronic cough : An unremitting cough that is not improving and has been present for more than 21 days;
      • Fever : Body temperature of >38 °C for 14 days, after common causes have been excluded;
      • Weight loss or failure to thrive.

      In addition to asking about weight loss or failure to thrive, it is necessary to look at the child’s growth chart.

2. Clinical examination (including growth assessment)

   There are no specific features on clinical examination that can confirm that the presenting illness is due to pulmonary TB. Some signs, although uncommon, are highly suggestive of extra-pulmonary TB. Other signs are common and should prompt an investigation into the possibility of childhood TB. Important physical signs are:

   a. physical signs highly suggestive of extra-pulmonary TB:

      • Gibbus, especially of recent onset (resulting from vertebral TB)
      • Non-painful enlarged cervical lymphadenopathy with fistula formation

   b. physical signs requiring investigation to exclude extra-pulmonary TB:

      • Meningitis not responding to antibiotic treatment, with a sub-acute onset or raised intracranial pressure
      • Pleural effusion
      • Pericardial effusion
      • Distended abdomen with ascites
- Non-painful enlarged lymph nodes without fistula formation
- Non-painful enlarged joint
- Signs of tuberculin hypersensitivity (e.g. phlyctenular conjunctivitis, erythema nodosum).

Documented weight loss or failure to gain weight, especially after being treated in a nutritional rehabilitation programme, is a good indicator of chronic disease in children, of which TB may be the cause.

**Common ways of obtaining samples for smear microscopy include the following.**

**a. Expectoration**

Sputum should always be obtained in adults and older children (10 years of age or older) who are pulmonary TB suspects. Among younger children, especially children under 5 years of age, sputum is difficult to obtain and most children are sputum smear-negative. As with adult TB suspects, three sputum specimens should be obtained: an on-the-spot specimen (at first evaluation), an early morning specimen and a second on-the-spot specimen (at a follow-up visit).

**b. Gastric Aspiration**

Gastric aspiration using a nasogastric feeding tube can be performed in young children who are unable or unwilling to expectorate sputum. Gastric aspirates should be sent for smear microscopy and mycobacterial culture. A gastric aspirate should be obtained on each of three consecutive mornings. Performing the gastric aspiration properly usually requires two people. Children with a low platelet count or bleeding tendency should not undergo the procedure.

The following equipment is needed:

- Gloves
- Nasogastric tube (usually 10 French or larger)
- 5, 10, 20 or 30 ml syringe, with appropriate connector for the nasogastric tube
- Litmus paper
- Specimen container
- Pen (to label specimens)
- Laboratory requisition forms
- Sterile water or normal saline (0.9% NaCl)
- Sodium bicarbonate solution (8%)
- Alcohol / chlorhexidine.

**Procedure**

The procedure can be carried out as an inpatient first thing in the morning when the child wakes up, at the child’s bedside or in a procedure room on the ward (if one is available), or as an outpatient (provided that the facility is properly equipped). The child should have fasted for at least 4 hours (infants for 3 hours) before the procedure.

1. Find an assistant to help.
2. Prepare all equipment before starting the procedure.
3. Position the child on his or her back or side. The assistant should help to hold the child.
4. Measure the distance between the nose and stomach, to estimate distance that will be required to insert the tube into the stomach.
5. Attach a syringe to the nasogastric tube.
6. Gently insert the nasogastric tube through the nose and advance it into the stomach.
7. Withdraw (aspirate) gastric contents (2–5 ml) using the syringe attached to the nasogastric tube.
8. To check that the position of the tube is correct, test the gastric contents with litmus paper: blue litmus turns red (in response to the acidic stomach contents). (This can also be checked by pushing some air (e.g. 3–5 ml) from the syringe into the stomach and listening with a stethoscope over the stomach).
9. If no fluid is aspirated, insert 5–10 ml sterile water or normal saline and attempt to aspirate again.
   • If still unsuccessful, attempt this again (even if the nasogastric tube is in an incorrect position and water or normal saline is inserted into the airways, the risk of adverse events is still very small).
   • Do not repeat more than three times.
10. Withdraw the gastric contents (ideally at least 5–10 ml).
11. Transfer gastric fluid from the syringe into a sterile container (sputum collection cup).
12. Add an equal volume of sodium bicarbonate solution to the specimen (in order to neutralize the acidic gastric contents and so prevent destruction of tubercle bacilli).

After the Procedure

1. Wipe the specimen container with alcohol / chlorhexidine to prevent cross-infection and label the container.
2. Fill out the laboratory requisition forms.
3. Transport the specimen (in a cool box) to the laboratory for processing as soon as possible (within 4 hours).
4. If it is likely to take more than 4 hours for the specimens to be transported, place them in the refrigerator (4–8 °C) and store until transported.
5. Give the child his or her usual food.

c. Sputum Induction

Several recent studies have found that sputum induction is safe and effective in children of all ages and the bacterial yields are as good as or better than for gastric aspirates. Sputum induction is an aerosol-generating procedure. Where possible, therefore, this procedure should be performed in an isolation room that has adequate infection control precautions (negative pressure, ultraviolet light (turned on when room is not in use) and extractor fan.

General Approach

Examine children before the procedure to ensure they are well enough to undergo the procedure.

Children with the following characteristics should not undergo sputum induction:
• Inadequate fasting: if a child has not been fasting for at least 3 hours, postpone the procedure until the appropriate time;
• Severe respiratory distress (including rapid breathing, wheezing, hypoxia);
• Intubated;
• Bleeding: low platelet count, bleeding tendency, severe nosebleeds (symptomatic or platelet count <50/ml blood);
• Reduced level of consciousness;
• History of significant asthma (diagnosed and treated by a clinician).

Procedure

1. Administer a bronchodilator (e.g. salbutamol) to reduce the risk of wheezing.
2. Administer nebulized hypertonic saline (3% NaCl) for 15 minutes or until 5 cm³ of solution have been fully administered.
3. Give chest physiotherapy is necessary; this is useful to mobilize secretions.
4. For older children not able to expectorate, follow procedures as described in “a. Expectoration” p.83, to collect expectorated sputum.
5. For children unable to expectorate (e.g. young children), carry out either: (i) suction of the nasal passages to remove nasal secretions; or (ii) nasopharyngeal aspiration to collect a suitable specimen. Any equipment that will be reused will need to be disinfected and sterilized before use for a subsequent patient.

Table (14) Common forms of extra-pulmonary TB in children and practical approach to their diagnosis

<table>
<thead>
<tr>
<th>Site</th>
<th>Practical approach to diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral lymph nodes (especially cervical)</td>
<td>Lymph node biopsy or fine needle aspiration</td>
</tr>
<tr>
<td>Miliary TB (e.g. disseminated)</td>
<td>Chest X-ray and lumbar puncture (to test for meningitis)</td>
</tr>
<tr>
<td>TB meningitis</td>
<td>Lumbar puncture (and computerized tomography where available)</td>
</tr>
<tr>
<td>Pleural effusion (older children and adolescents)</td>
<td>Chest X-ray, pleural tap for biochemical analysis (protein and glucose concentrations), cell count and culture</td>
</tr>
<tr>
<td>Abdominal TB (e.g. peritoneal)</td>
<td>Abdominal ultrasound and ascitic tap</td>
</tr>
<tr>
<td>Osteoarticular</td>
<td>X-ray, joint tap or synovial biopsy</td>
</tr>
<tr>
<td>Pericardial TB</td>
<td>Ultrasound and pericardial tap</td>
</tr>
</tbody>
</table>
4.18 (b) Recommended treatment regimens for children in each TB diagnostic category

Dosages of anti-tuberculosis medicines for the treatment of tuberculosis in children:

Isoniazid (H) – 10 mg/kg (range 10–15 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 (30–40 mg/kg)
Ethambutol (E) – 20 mg/kg (15–25 mg/kg)

Children with suspected or confirmed pulmonary tuberculosis or tuberculous peripheral lymphadenitis who are HIV-negative can be treated with a three drug regimen: (HRZ) for 2 months followed by a two-drug (HR) regimen for 4 months.

During the continuation phase of treatment, thrice-weekly regimens can be considered for children known to be HIV-uninfected living in settings with well-established directly-observed therapy (DOT).

In addition to anti-TB treatment, patients with active pericardial TB should be offered prednisolone 1 mg/kg/day (maximum 40 mg/day) with gradual withdrawal starting within 2–3 weeks of initiation.

Children with suspected or confirmed tuberculosis meningitis should be treated with a four-drug regimen: HRZE for 2 months, followed by a two-drug regimen (HR) for 10 months; the total duration of treatment being 12 months. The dosages are the same as those described for pulmonary tuberculosis. Also give prednisolone 1–2 mg/kg, maximum 40 mg, with gradual withdrawal of the starting within 2–3 weeks of initiation.

Children with suspected or confirmed osteoarticular tuberculosis should be treated with a four-drug regimen: (HRZE) for 2 months followed by a two-drug regimen (HR) for 10 months; the total duration of treatment being 12 months.

Children with proven or suspected pulmonary tuberculosis or tuberculous meningitis caused by multiple drug-resistant bacilli can be treated with a fluoroquinolone in the context of a well-functioning MDR-TB control programme and within an appropriate MDR-TB regimen. The decision to treat should be taken by a clinician experienced in managing paediatric tuberculosis.

Infants (aged 0–3 months) with suspected or confirmed pulmonary tuberculosis or tuberculous peripheral lymphadenitis should be promptly treated with the standard three drug regimen: (HRZ) for 2 months followed by a two-drug (HR) regimen for 4 months.

Isoniazid Prevention Therapy in Children contact with an infectious TB patient

Neonates who have been in close contact with people with sputum-smear-positive TB should be started on isoniazid for 3 months followed by a Mantoux Test. If the Mantoux Test is positive the baby should be assessed for active TB; if negative for active TB, isoniazid should be continued for a total of 6 months. If the Mantoux Test is negative, it should be repeated together with an interferon-gamma test. If both are negative then isoniazid should be stopped and a BCG vaccination performed.
BCG-vaccinated children older than 4 weeks but younger than 2 years, in close contact with people with sputum-smear-positive respiratory TB, should have a Mantoux test. If this is positive (15 mm or greater), the child should be assessed for active TB. If active TB is excluded, then treatment for latent TB infection (either 3 months of rifampicin and isoniazid or 6 months of isoniazid) should be given.

If the result of the test is less than 15 mm, it should be repeated after 6 weeks together with an interferon-gamma test. If the repeat Mantoux Test is also less than 15 mm, and the interferon-gamma test is also negative, no further action is needed.

If the repeat Mantoux Test becomes more strongly positive (15 mm or greater and an increase of 5 mm or more over the previous test), or the interferon-gamma test is positive the child should be assessed for active TB. If active TB is excluded, treatment for latent TB infection, a regimen of either 3 months of rifampicin and isoniazid or 6 months of isoniazid should be given.

Table (15) Recommended treatment regimens for children in each TB diagnostic category

<table>
<thead>
<tr>
<th>TB cases</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected or confirmed pulmonary tuberculosis or tuberculous peripheral lymphadenitis</td>
<td>2HRZ 4HR</td>
</tr>
<tr>
<td>Infants (aged 0–3 months) with suspected or confirmed pulmonary tuberculosis or tuberculous peripheral lymphadenitis</td>
<td>2HRZ 4HR</td>
</tr>
<tr>
<td>TB meningitis</td>
<td>2HRZE 10HR</td>
</tr>
<tr>
<td>Suspected or confirmed osteoarticular tuberculosis</td>
<td>2HRZE 10HR</td>
</tr>
<tr>
<td>Chronic and MDR-TB</td>
<td>Specially designed standardized or individualized regimens</td>
</tr>
</tbody>
</table>

4.18 (c) Adverse Events

Adverse events caused by anti-TB drugs are much less common in children than in adults.

The most important adverse event is the development of hepatotoxicity, which can be caused by isoniazid, rifampicin or pyrazinamide. Serum liver enzyme levels should not be monitored routinely, as asymptomatic mild elevation of serum liver enzymes (less than five times the normal values) is not an indication to stop treatment. However, the occurrence of liver tenderness, hepatomegaly or jaundice should lead to investigation of serum liver enzyme levels and the immediate stopping of all potentially hepatotoxic drugs. Patients should be screened for other causes of hepatitis, and no attempt should be made to reintroduce these drugs until liver functions have normalized. If treatment for TB needs to be continued for severe forms of TB, non-hepatotoxic anti-TB drugs should be introduced (e.g. ethambutol, an aminoglycoside and a fluoroquinolone).

Isoniazid may cause symptomatic pyridoxine deficiency, particularly in severely malnourished children and HIV-infected children on highly active ART. Supplemental pyridoxine (5–10 mg/day) is recommended in: (i) malnourished children, (ii) HIV-infected children, (iii) breastfeeding infants and (iv) pregnant adolescents.
5. Guide in Computing Programme Indicators

5.1 Indicators for monitoring in Case Finding

1. Incidence rate per 100,000 pop = \( \frac{\text{No. of new cases registered in the year}}{\text{Total population of the year registered}} \times 100,000 \) pop

2. Prevalence rate per 100,000 pop = \( \frac{\text{No. of new cases + old cases from last year on 1st Jan}}{\text{Total population of the year registered}} \times 100,000 \) pop

3. Rate of new smear positive cases per 100,000 pop = \( \frac{\text{No. of new smear positive cases registered}}{\text{Total population of the year registered}} \times 100,000 \) pop

4. Case detection rate (%) = \( \frac{\text{Annual new smear positive pulmonary TB cases}}{\text{Estimated annual new smear positive pulmonary TB cases}} \times 100 \)

5.2 Indicators for monitoring in Case Holding

1. Sputum conversion rate at the end of 2 months (%) = \( \frac{\text{No. of new smear positive cases converted to smear negative}}{\text{Total number of new smear positive cases given treatment}} \times 100 \)

2. Treatment Outcomes

   a) Cure rate (%) = \( \frac{\text{No. who are cured}}{\text{Total no. of new sputum smear positive PTB cases (Local Bruneians only)}} \times 100 \)

   b) Treatment Completion rate (%) = \( \frac{\text{No. who completed treatment}}{\text{Total no. of New PTB cases (Local Bruneians only)}} \times 100 \)

   c) Treatment Success rate (%) = \( \frac{\text{No. of cured + No. of treatment completed cases}}{\text{Total no. of New PTB cases (Local Bruneians only)}} \times 100 \)

   d) Treatment failure (%) = \( \frac{\text{No. new cases smear positive cases, still positive at 5th month}}{\text{Total no. of new smear positive cases registered}} \times 100 \)

   e) Death rate per 100,000 pop = \( \frac{\text{No. of deaths (during the course of treatment) in a year}}{\text{Total population of the year registered}} \times 100,000 \) pop:
References

2. Laws of Brunei. 2010. Chapter 204, Infectious Diseases, S 34/03; Control of Infectious Diseases, Part III; 15 subsections (1) to (5).
5. World Health Organization. 1988; Laboratory Services in Tuberculosis Control.
8. Pan American Health Organization. 2010; Caribbean Guidelines for the Prevention, Treatment, Care, and Control of Tuberculosis and TB/HIV: 11-12.
9. Ministry of Health, New Zealand; Guidelines for Tuberculosis Control in New Zealand 2010; Published in September 2010:115-132.
20. RAPID ADVICE: Treatment of Tuberculosis in children Key recommendations, © World Health Organization 2010
22. Tuberculosis: Clinical Diagnosis and Management of Tuberculosis, and Measures for its Prevention and Control www.nice.org.uk/guidance/CG117
# ANNEXES

## ANNEX I: TB SYMPTOMATICS MASTER LIST

*National Tuberculosis Control Programme, Brunei Darussalam*

<table>
<thead>
<tr>
<th>DATE</th>
<th>MRN No.</th>
<th>IC</th>
<th>NAME</th>
<th>AGE</th>
<th>GENDER</th>
<th>ADDRESS &amp; CONTACT NUMBER</th>
<th>MANTOUX</th>
<th>SPUTUM FINDING</th>
<th>X-RAY FINDING</th>
<th>DIAGNOSIS</th>
</tr>
</thead>
<tbody>
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<td>Result</td>
<td>Date</td>
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</tbody>
</table>

Guidelines for Tuberculosis Control in Brunei Darussalam 2013
## ANNEX II: TUBERCULOSIS TREATMENT CARD

**NAME:** __________________________  **CONTACT PERSON:** __________________________

**ADDRESS:** __________________________

________________________________________ PHONE __________________________

**ISLAND:** __________________________  **VILLAGE:** __________________________

**SEX:** _______  **YEAR OF BIRTH:** ____________  **AGE:** ____________

**INTENSIVE PHASE:** Date started ____________  Treatment regimes and number of tables

### Adults

<table>
<thead>
<tr>
<th></th>
<th>R (300mg)</th>
<th>H (300mg)</th>
<th>Z (400mg)</th>
<th>E (400mg)</th>
<th>S (1gm)</th>
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<tbody>
<tr>
<td>□</td>
<td>Cat I (2RHZE)</td>
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<tr>
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<td>Cat II (2RHZES / 1RHZE)</td>
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<tr>
<td>□</td>
<td>Cat III (2RHZ)</td>
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</tbody>
</table>

### Children

<table>
<thead>
<tr>
<th></th>
<th>R (300mg)</th>
<th>H (300mg)</th>
<th>Z (400mg)</th>
<th>S (1gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>□</td>
<td>Cat I (2RHZS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□</td>
<td>Cat III (2RHZ)</td>
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</tbody>
</table>

- **R** = Rifampicin;  **H** = Isoniazid;  **Z** = Pyrazinamide;  **E** = Ethambutol;  **S** = Streptomycin

### SPUTUM EXAMINATION RESULTS

<table>
<thead>
<tr>
<th>Month</th>
<th>Date</th>
<th>Result</th>
<th>Weight</th>
<th>Date next appointment</th>
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</thead>
<tbody>
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<td>0</td>
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</tbody>
</table>

### DISEASE CLASSIFICATION

- Pulmonary smear positive
- Pulmonary smear Negative
- Extra Pulmonary: Site ____________

### TYPE OF PATIENT

- NEW
- TRANSFER IN
- RELAPSE
- TREATMENT FAILURE
- TREATMENT AFTER INTERRUPTION
- OTHER  (Specify) ________________

### SPUTUM EXAMINATION

<table>
<thead>
<tr>
<th>Month</th>
<th>Date</th>
<th>Result</th>
<th>Weight</th>
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<tbody>
<tr>
<td>0</td>
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<td>8</td>
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</tbody>
</table>

* Enter in the box the number of tablets.

** Enter X on day when medications were swallowed under direct observation. Draw a horizontal line through the days to indicate the number of days' supply given for self-administration.
### CONTINUATION PHASE: Regimens and number of tablets

**Adults**

<table>
<thead>
<tr>
<th></th>
<th>R (300mg)</th>
<th>H (300mg)</th>
<th>E (400mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat I and Cat III (4RH)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Cat II (5RHE)</td>
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</tr>
</tbody>
</table>

**Children**

<table>
<thead>
<tr>
<th></th>
<th>R (100mg)</th>
<th>H (100mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat I and Cat III (4RH)</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

**REMARKS:**

Enter X on the day when medication were swallowed under direct observation. Draw a horizontal line through the days to indicate the number of days’ supply given for self-administration.

The number before the letter is the duration in months of the administration of the drugs; 2 RHZES / 1RHZE means 2 months with 5 drugs and 1 month with 4 drugs without S.

Treatment outcomes: Cured ☐ Treatment completed ☐ Treatment failure ☐ Died ☐ Treatment interrupted ☐ Transferred out ☐
## ANNEX III: TUBERCULOSIS REGISTER

<table>
<thead>
<tr>
<th>Date Registered</th>
<th>TB Registration No.</th>
<th>Name</th>
<th>Sex (M/F)</th>
<th>Age</th>
<th>Address</th>
<th>Name of treatment centre</th>
<th>Treatment start date</th>
<th>Regimen**</th>
<th>Disease Classification</th>
<th>Type of Patient ***</th>
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<td>TAI (Default)</td>
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<td>Transfer In</td>
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<td>Other</td>
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</tbody>
</table>

* Usually the name of health facility where the patient is doing the continuation phase;  ** Write Cat. I or Cat. II or Cat. III;

*** New : Never previously treated for as much as 4 weeks  
Relapse : Previously treated and declared cured, returns smear positive  
Failure : Positive smear 5 or more months after starting treatment, put on retreatment  
TAI (Treatment after interruption) : Returns smear positive after interruption of 2 months or more  
Transfer In : Registered and starts treatment in another DOTS Centre  
Other : Patients that do not fit any of the previous definitions.
### TUBERCULOSIS REGISTER (Continued)

<table>
<thead>
<tr>
<th>Results of sputum smear examination and date, according to the duration of treatment</th>
<th>Treatment outcomes **** and date ***** (according to the smear result at the completion)</th>
<th>Name of the treatment partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td></td>
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<tr>
<td>Result Date</td>
<td>End 2&lt;sup&gt;nd&lt;/sup&gt; month Result Date</td>
<td>End 3&lt;sup&gt;rd&lt;/sup&gt; month Result Date</td>
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</table>

**** Cured: Negative smear at the last month of treatment and on one previous occasion  
Died: Died for any reason during treatment  
Treatment completed: No proof of cure as determined by smear examination  
Treatment Interrupted (Defaulted): Failed to collect medications for 2 months or more  
Treatment failure: Positive smear at 5 months or later during treatment  
Transfer out: Sent to another reporting unit for continuation of treatment

***** Write the date in the correspondent box
### ANNEX IV: QUARTERLY REPORT ON TUBERCULOSIS CASE FINDING

**Name of DOTS centre/clinic:** TB Health Worker /Nurse in charge of DOTS clinic

**Report for**_ Quarter of the year: **Signature** **Date**

**Quarters:**
- 1st quarter – 1 Jan to 31 Mar
- 2nd quarter – 1 April to 30 June
- 3rd quarter – 1 July to 30 September
- 4th quarter – 1 Oct to 31 Dec

No. of suspects examined during this quarter ____________

<table>
<thead>
<tr>
<th>All cases (PTB, EPTB &amp; Others) registered in this quarter (in)</th>
<th>No. of Pulmonary sputum smear positive</th>
<th>No. of Pulmonary sputum smear negative</th>
<th>No. of New Extra Pulmonary</th>
<th>Other*</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>New cases</td>
<td>Relapses</td>
<td>Treatment after failure</td>
<td>Treatment after default</td>
<td>&lt; 5 yrs</td>
<td>5-14 yrs</td>
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* Other: cases that do not fit into the other categories (transferred in are excluded)

*Detail information of cases (in) should be filled in the attached table in page 2.*

| New Smear Positive cases registered in this quarter (in) |
|---|---|---|---|---|---|---|---|---|---|---|
| 0-14 yr | 15-24 yr | 25-34 yr | 35-44 yr | 45-54 yr | 55-64 yr | 65 yr + | TOTAL |
| M | F | M | F | M | F | M | F | M | F | M | F | M | F | TOTAL |

| Tuberculosis Treatment outcomes of cases in this quarter (out) |
|---|---|---|---|---|---|---|---|---|
| Type of case | Cured | Treatment completed | Failure | Died | Defaulted | Transfer out/Deport | TOTAL |
| New Smear positive | | | | | | | |
| Relapse/retreatment (Smear positive) | | | | | | | |
| Smear negative, EPTB & others # | | | | | | | |

* # transferred in are excluded

*Detail information of cases (out) should be filled in the attached table in page 3*
### QUARTERLY REPORT ON TUBERCULOSIS CASE FINDING (Continued)

Details of the cases registered in this quarter (in) Refer to all cases & new smear positive cases tables from page 1

<table>
<thead>
<tr>
<th>Code No.</th>
<th>Name</th>
<th>IC no.</th>
<th>Age</th>
<th>Gender</th>
<th>Address</th>
<th>Nationality</th>
<th>smear positive PTB/ smear negative PTB/ EPTB/others</th>
<th>Date of treatment started</th>
<th>Remark</th>
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</table>
QUARTERLY REPORT ON TUBERCULOSIS CASE FINDING (Continued)

Details of the cases out in this quarter Refer to tuberculosis treatment outcomes table from page 1

<table>
<thead>
<tr>
<th>Code No.</th>
<th>Name</th>
<th>IC No.</th>
<th>Age</th>
<th>Gender</th>
<th>Address</th>
<th>Nationality</th>
<th>Cured/Completed/Trout/Died</th>
<th>Date of treatment started &amp; stopped</th>
<th>Remark</th>
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</tbody>
</table>

Drug stock for this quarter

<table>
<thead>
<tr>
<th>No.</th>
<th>Item (per tablets in each bottle)</th>
<th>Balance from last Quarter</th>
<th>Received</th>
<th>Used</th>
<th>Balance at the end of this quarter</th>
<th>Requirement for next quarter</th>
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<tbody>
<tr>
<td>1</td>
<td>Isoniazid tablet 100 mg (tab)</td>
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<td>Rifampicin capsule 150 mg (cap)</td>
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<td>Ethambutol HCl tablet 400 mg (tab)</td>
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<td>8</td>
<td>Streptomycin injection 1 g (vial)</td>
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<td>Pyridoxine tablet mg (tab)</td>
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<tr>
<td>10</td>
<td>Tuberculin PPD 23 SS1 2T.U./0.1 ml 1.5 ml/vial app for 7 persons</td>
<td></td>
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</table>
ANNEX V: TUBERCULOSIS REFERRAL / TRANSFER FORM

National Tuberculosis Control Programme, Brunei Darussalam

Name of the referring / transferring unit: ________________________________
Name of the unit to which the patient is referred: ________________________________
Name of the patient: ___________________________ Age _______ Sex: _______
Address where the patient is residing: __________________________________________
TB No: __________
Date treatment: Started: ______________ Treatment regimen: __________________________
Drugs patient received: __________________________________________
Sputum examination results: __________________________________________
Reason for referral / transfer: __________________________________________
Remark: __________________________________________
Name and Signature: __________________________________________
Designation: __________________________ Date __________________________

For the use by the health unit where the patient has been referred / transferred.
Name of the patient: ________________________________
TB No.: ____________ Age: _______ Sex: ____________
Date: Referred / transferred: __________________________
The above patient reported at this health unit on the date: __________________________
Name and signature of the receiving officer: __________________________
Name of the health unit: __________________________ Date: ____________
(Send this part back to the referring unit as soon as the patient has reported and registered)

For use by the health unit where the patient treatment ended.
Date treatment ended: __________________________
Treatment Outcome: Cured [ ] Completed [ ] Died [ ] Transfer out [ ]
Treatment failure [ ] Treatment Interrupted (Defaulter) [ ]
(Send treatment outcome to the DOTS Centre where the patient was originally registered)
## ANNEX VI: HOME VISIT FORM

**PUSAT KOORDINASI TIBI KEBANGSAAN, KIARONG**  
*(Lawatan Ke Rumah Pesakit)*

### SECTION A

<table>
<thead>
<tr>
<th>No. Pendaftaran TB:</th>
<th>Nama Pesakit:</th>
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<tbody>
<tr>
<td>Alamat:</td>
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<tr>
<td>No. Tel.:</td>
<td>Perkerjaan:</td>
</tr>
<tr>
<td>No. Kad Pintar:</td>
<td>Kerakyatan:</td>
</tr>
<tr>
<td>Umur:</td>
<td>Bangsa:</td>
</tr>
<tr>
<td>Orang yang senanang dihubungi:</td>
<td></td>
</tr>
<tr>
<td>Hubungan:</td>
<td>No. Tel:</td>
</tr>
<tr>
<td>Tarih dimasukan hospital:</td>
<td>Tarih dikeluarkan hospital:</td>
</tr>
<tr>
<td>Tarih mula rawatan TB:</td>
<td>Pusat DOTS pesakit:</td>
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### SECTION B

<table>
<thead>
<tr>
<th>Rawatan diterima</th>
<th>Dose</th>
<th>Tarih perjumpaan Dr</th>
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</thead>
<tbody>
<tr>
<td>Cap. Rifampicin</td>
<td>Mg</td>
<td>Setiap hari / 3x seminggu</td>
</tr>
<tr>
<td>Tab. Isoniazid</td>
<td>Mg</td>
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</tr>
<tr>
<td>Tab. Ethambutol</td>
<td>Mg</td>
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</tr>
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<td>Tab. Pyrazinamide</td>
<td>Mg</td>
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<td>Tab. Pyridoxine</td>
<td>Mg</td>
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<tr>
<td>Inj. Streptomycin</td>
<td>Gm</td>
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### SECTION C

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<tr>
<th>Nama &amp; tandatangan pengurus pesakit:</th>
<th>Kawasan: Zone</th>
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<th>B</th>
<th>C</th>
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Guidelines for Tuberculosis Control in Brunei Darussalam 2013
SECTION D

(Laporan Ketua Bahagian)

Sebelum Lawatan :-

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<tr>
<th></th>
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<td>Office / School Visit</td>
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<td>Family Contact</td>
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<td>Office / School Contact</td>
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<tr>
<td>TB Allowance</td>
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</tr>
<tr>
<td>Letter to Office / School</td>
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<tr>
<td>Letter to Occupational Health</td>
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</table>

Diserahkan Kepada : (Nama & Jawatan)

Selepas Lawatan :-

Tandatangan

Diserahkan Kepada : (Nama & Jawatan)

Tandatangan

---

LAJORAN LAWATAN KERUMAH PESAKIT

SECTION E

Keadaan rumah pesakit :

Keadaan pesakit :

Pendapatan pesakit:

Ahli keluarga terdekat pesakit :

Penerangan penjagaan kesihatan:

<table>
<thead>
<tr>
<th>Tarikh / Jam</th>
<th>Rumusan Laporan Lawatan</th>
<th>Lain-lain Hal</th>
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</table>
ANNEX VII: MANTOUX TEST FORM  
NATIONAL TUBERCULOSIS CO-ORDINATING CENTRE, KIARONG  
Mantoux Skin Test

| Name |  
| I/C No | Contact Tel No. |  
| Occupation | Send by (Department) |  
| Sex | Request by Dr |  
| Age |  
| Family History of TB | Yes | No | Previous Mantoux Test if any (Date) |  

Mantoux test will be done during office hours ONLY.

Venue :- National Tuberculosis Co-ordinating Centre  
2nd Floor, Spg. 253-47  
Kg. Kiarong, BSB  
Negara Brunei Darussalam  
Tel :- 2430409

♦ Note :- Mantoux reading should be done after 48 – 72 hours ONLY.  
Mantoux test not done if reading falls on public Holidays.

* For NTCC use

| Name: - |  
| I/C No: - | Sex: - | Age: - |  
| Occupation: - | Department: - |  
| Send by (OPD): - | Request by Dr: - |  
| 1st Mantoux test done on: - | Mantoux reading on: - |  
| 2nd Mantoux test done on: - | Mantoux reading on: - |  
| Result of 1st mantoux test: - ( ) mm |  
| Result of 2nd mantoux test: - ( ) mm |  

Note:-  
I. < 10 mm, Need to repeat mantoux after 1 - 3 weeks  
II. > 10 mm, Need further investigation and will be review in NTCC kiarong

Guidelines for Tuberculosis Control in Brunei Darussalam 2013
### ANNEX VIII: CONTACT SCREENING FORM

**PUSAT KOORDINASI TIBI KEBANGSAAN KIARONG**  
Spg 253-47 Kg Kiarong, Tingkat II  
Negara Brunei Darussalam  
Tel: 2430409

#### SCREENING OF CLOSE CONTACT FOR TB INFECTION

<table>
<thead>
<tr>
<th>INDEX CASE No.</th>
<th>Microscopy</th>
<th>PULMONARY TUBERCULOSIS</th>
<th>Culture</th>
<th>EXTRA PULMONARY TUBERCULOSIS</th>
<th>X-Ray</th>
<th>Biopsy</th>
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Name:  
Age in years:  
Sex: Male ( ) Female ( )  
Nationality: BR ( ) NBR ( )  
Date of Diagnosis: / /  
Clinically referred:  
Date of treatment: / /  
Referred for BCG Vaccination:  

#### COLLEGE CONTACTS

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<tr>
<th>No.</th>
<th>NAME</th>
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<th>I/C NO.</th>
<th>RELATION</th>
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*** Please record actual measurement in millimeters  
RELATION TO INDEX CASE:  
Date of Mantoux Test Done: / /  
Date of Reading: / /  
Address:  
Tel No:  

---

Guidelines for Tuberculosis Control in Brunei Darussalam 2013
ANNEX IX: PAMPHLET FOR SPUTUM COLLECTION PROCEDURE

PERATURAN PENGAMBIAN KAHAK BAGI PESAKIT
1. Pengambilan kahak akan dilakukan dalam masa 3 hari berturut-turut.
2. Pesakit disarankan untuk mengambil kahak pada awal pagi, selepas bangun tidur.
3. Sebelum memulakan pengambilan, pastikan mulut bersih dari makanan.
4. Pastikan bekas atau botol ditulis dengan nama, nombor kod pengenal dan tarikh pengambilan kahak. Bekas yang tidak ada keterangan pesakit tidak akan diuji oleh pihak makmal.
5. Kahak sepatutnya kelihatan tebal dan boleh berwarna keluning atau kehijauan.
6. Jumlah minima yang diperlukan bagi membuat ujian makmal adalah 3ml.
7. Bekas yang berisi kahak hendaklah dimasukkan ke dalam beg plastik biohazard yang ditutup rapat bersama dengan borong ujian permohonan makmal.

RULES FOR COLLECTING PATIENT’S SPUTUM
1. Sputum is to be taken in 3 consecutive days.
2. Patient is recommended to take sputum early in the morning after getting up from bed.
3. Ensure that your mouth is clean from food before collection.
4. The sputum should look thick and could be yellowish or greenish in colour.
5. A minimum of 3ml of sample is required for laboratory testing.
6. Ensure that container is labelled with your name, identity card number and date of collection. Container without label will not be processed by the laboratory.

TATACARA PENGAMBIAN KAHAK BAGI UJIAN MAKMAL TB
SPUTUM COLLECTION PROCEDURE FOR TB LABORATORY TESTS

1. Berkurum-kurum dengan air untuk membersihkan mulut
   Rinse mouth with water

2. Tarik dan keluarkan nafas 3 kali, seterusnya batukkan dari dalam dada
   Breath in and out 3 times, then cough from within the chest

3. Dekatkan mulut ke bekas yang disediakan dan keluarkan kahak
   Put your mouth close to the container and give a sputum sample

4. Tutup bekas dengan betul dan rapat untuk mengelakkan dari kebocoran
   Close and tighten the lid of the container properly to prevent leakage

5. Masukkan bekas yang berisi kahak ke dalam beg plastic biohazard
   Put container containing sputum in the biohazard plastic bag

MAKMAL RUJUKAN TB KEBANGSAAN
JABATAN PERKHIDMATAN MAKMAL
Tel: 2221821 / 2221843 ext: 130 / 131 / 129
Fax: 2220869

KEMENTERIAN KESEHATAN
NEGARA BRUNEI DARUSSALAM
### ANNEX X: REVIEW COMMITTEE OF NATIONAL TB CONTROL PROGRAMME

<table>
<thead>
<tr>
<th>Role</th>
<th>Sr.</th>
<th>Designation</th>
<th>Name</th>
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</thead>
<tbody>
<tr>
<td>Advisors</td>
<td>1.</td>
<td>Director General of Medical Services</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.</td>
<td>Director General of Health Services</td>
<td></td>
</tr>
<tr>
<td></td>
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<td>Director of Health Services</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.</td>
<td>Director of Environmental Health Services</td>
<td></td>
</tr>
<tr>
<td>Co-Chairs</td>
<td>5.</td>
<td>Head of Disease Control Division</td>
<td>Dr Haji Ahmad Fakhri DP Haji Junaidi</td>
</tr>
<tr>
<td></td>
<td>6.</td>
<td>Head of Division of Respiratory Medicine</td>
<td>Dr Luke Mathew</td>
</tr>
<tr>
<td>Review Members</td>
<td>7.</td>
<td>Head of National TB Coordinating Centre</td>
<td>Hajah Rafizah Haji Abd Hamid</td>
</tr>
<tr>
<td></td>
<td>8.</td>
<td>SMO, Primary Health Care</td>
<td>Dr Hajar Salizawati bt. Mohd Zainal</td>
</tr>
<tr>
<td></td>
<td>9.</td>
<td>Head of General Paediatrics, RIPAS</td>
<td>Dr Pandare Sugathan</td>
</tr>
<tr>
<td></td>
<td>10.</td>
<td>Head of Occupational Health Division</td>
<td>Dr N B P Balalla</td>
</tr>
<tr>
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<td>11.</td>
<td>Chief Scientific Officer, National TB Reference</td>
<td>Michael Liew</td>
</tr>
<tr>
<td></td>
<td>12.</td>
<td>Head of TB Isolation Ward, Tutong</td>
<td>Dr Nasir Jeved</td>
</tr>
<tr>
<td></td>
<td>13.</td>
<td>Staff In charge, TB Ward, Tutong</td>
<td>Nursyazwani Abdullah</td>
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<tr>
<td></td>
<td>14.</td>
<td>Consultant Microbiologist/ Infection Control, RIPAS</td>
<td>Dr Terrence Rohan Chinniah</td>
</tr>
<tr>
<td></td>
<td>15.</td>
<td>Public Health Specialist</td>
<td>Dr Ong Sok King</td>
</tr>
<tr>
<td>Resource Persons</td>
<td>16.</td>
<td>SMO, Primary Health Care</td>
<td>Dr Bala Subramanian</td>
</tr>
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<td>17.</td>
<td>Respiratory Consultant, Division of Respiratory Medicine</td>
<td>Dr Hajar Khalizah bte Haji Jamil</td>
</tr>
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<td></td>
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<td>MO, Division of Respiratory Medicine</td>
<td>Dr Haji Osama Abouzied Abdel Hameed Aly</td>
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<td>19.</td>
<td>MO, Division of Respiratory Medicine</td>
<td>Dr Manoj Pethe</td>
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<td>MO, Division of Respiratory Medicine</td>
<td>Dr Panduru Venkata Kishore</td>
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<td>Consultant Physician (KB)</td>
<td>Dr Dilip Thottacherry</td>
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<td>SMO, Infectious Diseases, RIPAS</td>
<td>Dr Hajar Riamiza Natalie Haji Abd Momin</td>
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<td>SMOH, Belait District</td>
<td>Dr Maimunah Haji Mokim</td>
</tr>
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<td>SMOH, Tutong District</td>
<td>Dr Hajar Shodeena Haji Mohamad</td>
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<td>MOH, Temburong District</td>
<td>Dr Win Naing</td>
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<td>MO, Primary Health Care</td>
<td>Dr Mohd Ismail Hasim</td>
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<td>Scientific Officer, National TB Reference Laboratory</td>
<td>Nor Azian Haji Hafneh</td>
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<td>MO, Disease Control Division</td>
<td>Dr Kyaw Thu</td>
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<td>Dr Hlaing Myo Tun</td>
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<td>Dr Shailesh Hegde</td>
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<td>Dr Lena Matsalleh</td>
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<td>Act: Nursing Officer, Division of Respiratory Medicine</td>
<td>Sara Siliang</td>
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<td>33.</td>
<td>Act: Senior TB Health Visitor, National TB Coordinating Centre</td>
<td>Hardew Kaur</td>
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<td>34.</td>
<td>Staff Nurse, National TB Coordinating Centre</td>
<td>Hajah Mimy Haslina Haji Alias</td>
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