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Global Burden of TB

About one third of the world's population is infected by Mycobacterium tuberculosis. In 2016, 10.4 million fell ill with TB worldwide; 1.7 million deaths occurred due to the disease and 95% of deaths occurred in low- and middle-income countries. Tb is the leading killer of HIV-positive people; in 2016 40% of HIV deaths were due to TB.

Ending the TB epidemic by 2030 is among the health targets of the sustainable development goals.

TB in Mauritius

Mauritius is not a high burden country concerning Tuberculosis. The incidence of 10 per 100,000 people has been maintained over the past ten years. The notified cases in the last couple of years vary from 100-130 cases per year. In 2017 the total number of notified TB cases was 119. The number of TB/HIV co-infection cases for 2017 was 21.

The male to female ratio is 2:1. The largest number of cases is found in the 35-45 years age group. TB in children and adolescents is a rare event. The mortality from TB is less than 0.4 per 100,000 population.

Cases of Multidrug resistance TB is low (1-2 new cases per year).

The National Tuberculosis Control Centre

Because of the public health implications of prompt diagnosis and effective treatment of tuberculosis, most low-incidence countries designate a government public health agency as legal authority for controlling tuberculosis. In Mauritius, the National Tuberculosis Control Centre is based at the Chest Clinic Port Louis.

National Tuberculosis Control Programme (NTCP)

The National Tuberculosis Control Program (NTCP) of Mauritius exists since 1960. The NTCP is the only one programme for the control of TB in Mauritius. Overall objectives of the NTCP:

- To maintain the case detection rate of more than 85% of smear positive cases and to further improve it.
- To cure more than 90% of new smear positive cases with short course chemotherapy.
- To reduce mortality and morbidity attributed to TB.
- To prevent development of drug resistance.
The Structure of NTCP

The surveillance of tuberculosis in Mauritius is carried out from its specialized central unit, the Chest Clinic, where the national programme is based. Chest Clinic plays an important role in the implementation, coordination, facilitation and evaluation of tuberculosis services for the whole island. Chest Clinic has attached to it, its reference laboratory services along with its home visiting team and medical records department for reporting and monitoring TB patients. It also has Poudre d' Or Chest Hospital attached to its services for treating sputum smear positive TB patients. All cases of Tuberculosis with sputum smear positive are admitted at Poudre D'Or Hospital.

The core activities at Chest Clinic are:

- Improved case detection rate.
- Contact tracing.
- Reinforce integrated care to TB patients and better monitoring for improved treatment outcomes and prevent drug resistance.
- Strengthening collaboration between TB and HIV/AIDS programmes to ensure better management of TB/HIV co-infected patients.
- Raise public awareness about the disease TB.
- Liaise with WHO regional office and SADC region to exchange information and participate in making and adopting new policies regarding TB.

NTCP strategy for TB control

Only effective means to achieve the goal of NTCP is the application of DOTS Strategy.

The five components of DOTS (Directly Observed Treatment Supervised) have fully been implemented since 1990 to sustain TB control activities in Mauritius.

- The government is committed in the "Fight against TB" activities.
- Sputum smear microscopy to detect the infectious cases among the patients attending health care units is a priority.
- Standardized short course anti TB treatment is available for all diagnosed TB cases with direct observation of treatment at least for all sputum smear-positive cases during the intensive phase.
- A regular, uninterrupted supply of all anti-TB drugs, including second line TB drugs is currently available.
• A standardized recording and reporting system which allows assessment of treatment results and overall programme performance has been adopted.

Treatment with standardized short course chemotherapy is given under direct supervision (DOTS) at least in the initial intensive phase of treatment to all sputum smear-positive TB patients, to ensure high conversion rates.

Identifying the infectious patient is the most important aspect of tuberculosis control. We have a reference laboratory attached to the Chest Clinic for this purpose. The diagnosis of TB is established by documenting acid-fast bacilli in sputum by direct examination, by a PCR test (Gene Xpert) and then by culture. All smear positive and culture positive patients have drug susceptibility testing.

PROTOCOL FOR TB MANAGEMENT

1. Treatment of tuberculosis is focused on both curing the individual patient and minimizing the transmission of Mycobacterium tuberculosis to other persons, thus, successful treatment of tuberculosis has benefits both for the individual patient and the community in which the patient resides.

2. For any patient suspected of having pulmonary tuberculosis on the basis of signs and symptoms and radiologically, sputum sample for acid-fast bacilli (AFB) have to be sent, and the patient referred to a Chest Physician at Chest Clinic.

3. In case of high suspicion of TB and/or sputum smear is positive, the Chest Physician shall admit the patient at Poudre d’Or Hospital and treatment for pulmonary TB started.

4. All pulmonary TB patients having positive sputum for TB has to be seen by the chest physician at the Chest Clinic and for admission the patient shall be admitted at the Poudre D’Or Hospital or, in case having comorbidities which cannot be managed at Poudre D’Or Hospital in a Regional Hospital.

5. Extra pulmonary Tuberculosis (TB) having a negative sputum for TB may be treated in the private sector.
   ➢ The private clinic shall inform the CDCU and the programme manager for TB for any patient having extra pulmonary TB admitted in a private clinic.
   ➢ The programme manager for National Tuberculosis control programme and/or the Regional Public Health Superintendent (RPHS) CDCU shall visit any patient with extra pulmonary TB admitted in a private clinic.

6. The programme manager for TB and CDCU shall keep a register of all patients having TB.

7. All in-patients undergo sputum examination on three consecutive mornings. The first sputum sample is used for direct microscopy, Gene Xpert and culture for *M tuberculosis*.

8. Blood investigations include FBC, ESR, U&E, LTF, SGOT, SGPT, S. uric acid, and
ELISA for HIV.

9. If the 3 sputum samples are negative for AFB on microscopy, then 2 consecutive mornings' gastric juice samples are sent for smear for AFB.

10. **Anti-tubercular Treatment**
    Only the Ministry of Health and Quality of Life will procure Anti Tuberculosis drugs.

    Patient following treatment in the private for extra pulmonary TB will be supplied with Anti TB Drugs at the Chest Clinic provided they produce the following:
    
    1. A prescription from the treating doctor and
    2. A complete medical report from the treating doctor addressed to the programme manager National TB control programme handed over to the charge nurse on same day.
    3. After receiving the report the charge nurse will direct the patient to the pharmacy.
    
    The pharmacy of Chest Clinic shall maintain a register for all patients who are being treated with anti TB drugs.

    **Prophylaxis Anti TB treatment are offered to all HIV patients.**
    
    Drugs are prescribed in prison, are dispensed in prison itself.

    All the other HIV patients will receive the Anti TB drugs from the Chest Clinic or any of the Regional Health Hospitals, Souillac Hospital, Mahebourg Hospital and Dr Yves Cantin Community Hospital, provided that they produce a prescription from the medical officers working in the Aids Unit.

    All the pharmacy of the above mentioned hospitals shall send a monthly return to the pharmacy of the Chest Clinic.

    The pharmacy at the Chest Clinic shall maintain a register for all HIV patients on prophylactic Anti TB drugs and send a monthly return to the programme manager and CDCU.

    The Head of Aids Unit shall provide to the programme manager and CDCU a monthly return of all HIV patients on prophylactic Anti TB drugs.

    Treatment for TB is as per WHO DOTS protocol, consisting of an intensive phase for two months with 4 drugs (HRZE) followed by continuation phase for 4 months with 2 drugs (HR). The treatment is tailor-made according to patient's tolerance and response to the drugs.

    The decision to initiate combination chemotherapy for tuberculosis is based on clinical, radiographic, laboratory, patient, and public health factors. In addition, clinical judgment and the index of suspicion for tuberculosis are critical in making a decision to initiate treatment. For example, inpatients (children and adults) who, based on these considerations, have a high likelihood of having tuberculosis or are seriously ill with a disorder suspicious for tuberculosis, empiric treatment with a 4-drug regimen is initiated promptly even before the results of acid-fast bacilli (AFB) smear microscopy, molecular tests, and mycobacterial culture are known.
Factors to be considered in deciding to initiate treatment empirically for active tuberculosis (TB) (prior to microbiologic confirmation)

<table>
<thead>
<tr>
<th></th>
<th>Factors favouring Treatment Initiation</th>
<th>Factors favouring Delay or No treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENT</strong></td>
<td>• Risk for progression/dissemination (eg HIV)</td>
<td>• Elevated concern for adverse treatment events (eg. Severe liver disease, pregnancy)</td>
</tr>
<tr>
<td></td>
<td>• Age &lt; 2 years</td>
<td>• No TB exposure risk</td>
</tr>
<tr>
<td></td>
<td>• TB exposure risk (eg. Contact, High risk group - IVDA, Congregate setting, Prison)</td>
<td></td>
</tr>
<tr>
<td><strong>LABORATORY/ RADIOGRAPHIC</strong></td>
<td>• Radiographic imaging consistent with TB</td>
<td>• Radiographic imaging not consistent with TB</td>
</tr>
<tr>
<td></td>
<td>• Evidence of Mtb infection (Positive Mantoux)</td>
<td>• AFB smear positive, Gene Xpert negative</td>
</tr>
<tr>
<td></td>
<td>• Pathological findings consistent with TB</td>
<td>• AFB smear negative, Gene Xpert negative</td>
</tr>
<tr>
<td></td>
<td>• AFB smear Positive, Gene Xpert test Positive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• AFB smear Negative, Gene Xpert test Positive</td>
<td></td>
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<tr>
<td><strong>CLINICAL STATUS</strong></td>
<td>• Life-threatening disease</td>
<td>• Clinically stable</td>
</tr>
<tr>
<td></td>
<td>• Symptoms typical of TB</td>
<td>• Symptoms not typical of TB</td>
</tr>
<tr>
<td></td>
<td>• Alternative diagnosis less likely</td>
<td>• Alternative diagnosis</td>
</tr>
<tr>
<td><strong>PUBLIC HEALTH</strong></td>
<td>• Concern for loss to follow-up</td>
<td>• Low transmission risk</td>
</tr>
<tr>
<td></td>
<td>• High transmission risk (eg. Congregate setting, Correction centres)</td>
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</tr>
</tbody>
</table>

Once a decision is taken to start anti-TB treatment, the patient is educated about tuberculosis, its treatment, including possible adverse effects, expected outcomes of treatment, specifically the ability to cure the patient of the disease, about the duration of treatment, putting emphasis on drug compliance to avoid emergence of drug resistance; and discussing infectiousness and infection control measures, in simple language.

**DOTS:** Treatment is given under direct supervision by a Nursing Officer every morning on empty stomach. Pyridoxine tablet is given to all patients on regimen containing Isoniazid.

11. Patients are closely monitored for any side effects associated with anti-TB drugs.
12. Patient has to remain isolated in Poudre D'Or hospital until there is sputum conversion, that is, until he is no longer infective.
13. **Laboratory Services at Sir Edgar Laurent Laboratory - Chest Clinic, Port Louis**:  
The objective of the reference laboratory attached to the chest Clinic is to identify the infectious patient and confirm the diagnosis of Tuberculosis.

All specimens are sent (from private and public) to the TB laboratory for testing.

The laboratory technician should also insist that the request form should mention the following:

- name of patient;
- address of patient;
- contact number of patient and
- name and contact number of doctor who is requesting the test.

Diagnosis of Tuberculosis (TB) is established by documenting acid-fast bacilli in sputum by direct examination and then by culture.

For all smear positive cases, once confirmed, the result has to be sent immediately to:

1) Programme manager for National Tuberculosis Control Programme;
2) Chief Microbiologist;
3) Regional Public Health Superintendent, CDCU and
4) The treating doctor

For all the positive cases, the Laboratory technician should also inform about the following for the different tests carried out (AFB Stain, GeneXpert, Culture):

- date when specimen was received;
- date test has been done;
- date when result is being sent and
- culture report with date.

The laboratory should have a register of all positive cases.

14. **Investigations, Discharge and Follow-up** :

a. When there is sputum conversion, the patient is discharged and reviewed at Chest Clinic with a repeat sputum examination and a Chest X-ray.

b. Patient will, thereafter be reviewed regularly (monthly) until he completes his treatment successfully and is declared cured of TB.

A. Sputum examination:

- **At Month-1 (M1)**:
  
  Two sputum samples are sent for smear microscopy at the end of the 1st month.

  If both smears are negative, the patient is discharged on 4 drugs (HRZE) to complete the intensive phase, and reviewed at Chest Clinic Port Louis in 4 weeks (M2) with a repeat sputum microscopy for AFB and a Chest X-ray.
If one or both of the smears is still positive, then intensive phase is continued and the sputum microscopy for AFB repeated every two weeks until sputum conversion.

- **At Week 6:**
  
  If there is sputum conversion, the patient is discharged and the intensive phase is continued for two more weeks; the patient is reviewed at Chest Clinic Port Louis with a sputum smear for AFB and a Chest X-ray in two weeks (M2) to complete the intensive phase. If sputum is negative, the continuation phase is started.

- If the sputum smear is still positive for AFB, the intensive phase is continued and the sputum status checked after another two weeks (M2).

- **At Month-2 (M2):**
  
  If there is sputum conversion, the patient is discharged and continuation phase started, and the patient reviewed in 1 month (M3) with a repeat sputum smear for AFB and a Chest X-ray.

  If sputum smear is still positive, the intensive phase is continued for one more month (M3) before repeating sputum status for AFB.

- **At Month-3 (M3):**
  
  For patients who had sputum conversion before or at M2, sputum is checked for microscopy for AFB and cultured for MTB and for drug sensitivity test.

  For patients who were still positive at M2:

  If sputum smear is negative, continuation phase is started with HR for 5 months

  If sputum smear is still positive, then correlate with culture and sensitivity report.

  If the TB bacilli are susceptible to all anti-TB drugs, intensive phase is continued for one more month and sputum status checked again.

  If the TB bacilli are resistant to Isoniazid and Rifampicin, then the patient is put on 2nd line treatment.

- **B. Chest X-ray:**
  
  A. Chest x-ray is repeated at Month-1, 2 and at the end of the treatment.

- **C. Blood investigations:**
  
  Liver function tests are done on a weekly basis as long as the patient is in hospital and repeated as and when required thereafter.
15. **Home visit**

We have a very active home visiting service carried out by trained nursing staff. Patients receiving outpatient treatment are regularly visited to ensure that they are taking their drugs. The help of close relatives is also enlisted in the supervision of treatment.

16. **Contact screening**

**Definition of contacts**

These are people who share the same air for prolonged periods of time (8 continuous hours during the period of infectiousness) with people who have been diagnosed as having active pulmonary tuberculosis (sputum smear positive for AFB) and are coughing up the *M tuberculosis* into the air. These people are therefore at increased risk of getting infected, acquiring TB infection, developing active disease and spreading it to the community.

The **aims of contact tracing** in the context of a single index patient of drug susceptible TB are:

a) To identify contacts with active TB disease and initiate treatment early

b) To identify those at high risk of developing active tuberculosis/severe outcomes, i.e. young children and immune compromised persons, to prevent the development of TB by providing IPT.

c) To provide individual/ family education on infection control and counselling.

d) To identify the source case if not known.

**Assessment of contacts**

1) The first Step is to allocate contacts into groups with higher and lower risk of infection.

   a. 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 in work, leisure or other settings are not always "casual" contacts.

   b. Work sites should be visited: if there is overcrowding and poor ventilation these contacts may be considered "close".

• Start with higher-risk contacts. If there is no evidence of recent transmission of infection in this group, do not extend the investigation.

• 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.

- Periodically review the findings to determine whether to stop or extend the investigation.

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.

2) Contact tracing is done by a Nursing Officer from Chest Clinic. Information about close contacts should be obtained by the Nurse from the patient and a list of all appropriate contacts compiled within 3 days from the time of obtaining a positive sputum report for the index case.

3) The home visiting Nurse shall call within 3 to 7 days of obtaining a positive sputum report all potential contacts to attend Chest Clinic for assessment and TB chemoprophylaxis. Assessment comprises of a risk assessment for each contact and:
   a. **Symptom screen**: Contact is screened for TB symptoms (cough, sweating at night, fever and loss of weight), and if any of the symptoms are present, the person is immediately referred to a Chest Physician for further evaluation.
   b. **Investigations**: If contact is asymptomatic -
      i. **Mantoux test**:
         • Mantoux Normal: No further investigation. Contact advised TB chemoprophylaxis with Isoniazid for 6 months or with Isoniazid + Rifampicin for 4 months, with regards to close contacts.
         • Positive: Advised Chest X-ray.
      11. **Chest X-ray**:
         • Normal: Advise TB chemoprophylaxis
         • Abnormal, suggestive of TB: Advise Sputum smear for AFB and review on early appointment with Chest Physician

4) If contact does not report to Chest Clinic within 7 days, Nurse will visit contact at his/her residence/site of work to explain about the importance of the screening exercise and counsel. Mantoux test is carried out and an appointment at Chest Clinic is scheduled for Mantoux reading and for further assessment/chemoprophylaxis.
CHAPTER 1: HOW TB INFECTION DEVELOPS?

1.1 What is Tuberculosis?

Tuberculosis is an infectious disease caused by the bacterium Mycobacterium tuberculosis which usually enters the body by inhalation through the lungs.

They spread from the initial location in the lungs to other parts of the body via the blood stream, the lymphatic system, via the airways or by direct extension to other organs.

- Pulmonary tuberculosis is the infectious and most common form of the disease, occurring in over 90% of cases.

- Extra-pulmonary tuberculosis is a result of the spread of tuberculosis to other organs via blood, lymphatic or local extension; mostly pleura, lymph nodes, spine, joints, genito-urinary tract, nervous system or abdomen. Tuberculosis may affect any part of the body.

1.2 How does tuberculosis develop?

Tuberculosis develops in the human body in two stages. The first stage occurs when an individual breathes in TB bacilli and becomes infected (tuberculosis infection) but the immune system contains the infection. The second stage is when the infected individual develops the disease (tuberculosis).

1.3 How the tuberculosis disease spreads?

The infectiousness of a case of tuberculosis is determined by the concentration of micro-organisms within the lungs and their spread into the air surrounding the patient who has tuberculosis. When a TB patient with active pulmonary TB coughs or spits, he or she will produce small droplets in the air that contain TB bacilli. Anyone who inhales this infected air droplets can then be infected and may later develop TB disease.

The most infectious cases are those with a positive smear by microscopy (smear-positive cases). Those in whom micro-organisms cannot be seen directly under the microscope (smear-negative cases) are very much less infectious. Extra-pulmonary cases are almost never infectious, unless they have pulmonary tuberculosis as well.
1.4 How does the disease appear?

Among those who become infected, most will never become ill with tuberculosis unless their immunity or body defense system is seriously compromised with Malnutrition, Stress, HIV, Cancer and Diabetes.

The micro-organisms remain dormant within the body and their presence is indicated only by a significant size of induration in reaction to a tuberculin skin test, Mantoux.

BCG immunization gives up to 80% protection against the progression of TB infection to disease in children. Its protective role in adult is controversial. However, the main benefit of BCG is the protection against the development of the serious forms of TB (TB meningitis, military TB) in children.
Chapter 2: DIAGNOSING TUBERCULOSIS

2.1 How is Tuberculosis diagnosed?

The most common symptoms of pulmonary tuberculosis are:

a) Persistent cough for 2 weeks or more.

b) Sputum production which may be blood-stained

c) Shortness of breath and chest pain

d) Loss of appetite and loss of weight

e) A general feeling of illness (malaise)

f) Tiredness and loss of motivation

g) Night sweats and low-grade fever.

A patient presenting with these symptoms who is or was in contact with a person with infectious tuberculosis is more likely to be suffering from tuberculosis.

Symptoms of extra-pulmonary tuberculosis depend on the organ involved. Chest pain from tuberculous pleurisy, enlarged lymph nodes and sharp angular deformity of the spine are the most frequent signs of extra-pulmonary tuberculosis.

2.2 How is the diagnosis of Tuberculosis confirmed?

2.2.a Bacteriology

- Sputum

The examination consists of microscopic examination of a specimen which has been spread on a slide and stained by the Ziehl-Neelsen method. If TB micro-organisms, which are acid-fast bacilli, are detected by this method then the patient is said to have smear positive tuberculosis.

Three morning sputum specimens should be taken from a TB suspect.
Sputum results.

The laboratory must record the number of bacilli seen in each smear as follows:

<table>
<thead>
<tr>
<th>No AFB</th>
<th>per 100 oil immersion fields</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-9 AFB</td>
<td>per 100 oil immersions fields</td>
<td>exact no.</td>
</tr>
<tr>
<td>10-99 AFB</td>
<td>per 100 oil immersions fields</td>
<td>1+</td>
</tr>
<tr>
<td>1-10 AFB</td>
<td>per 1 oil immersion field</td>
<td>2++</td>
</tr>
<tr>
<td>&gt;10 AFB</td>
<td>per 1 oil immersion field</td>
<td>3+++</td>
</tr>
</tbody>
</table>

2.2. b When to do a sputum examination?

Three morning sputum samples are taken on three consecutive days for microscopic examination in a new patient or one or two morning samples during the course of treatment of pulmonary TB.

a) New Patient

When pulmonary TB is first suspected, 3 morning specimens on 3 consecutive days are sent for sputum microscopy and sputum culture; susceptibility testing is done in all sputum positive patients.

b) Monitoring Progress in Adult Pulmonary TB

During TB treatment, all pulmonary TB patients are monitored by sputum smear microscopy.

2.3 Monitoring the progress of Pulmonary TB

Sputum microscopy after 1 month of treatment

- At 1 month, send two sputum samples for smear microscopy for all new patients.
- If both smears are negative, patient is discharged and intensive phase is continued for 1 more month.
- If one or both of the smears is positive, it is repeated after 1 month.

Sputum investigations at 2 months of treatment

- Send two sputum samples for smear microscopy at 2 months.
- If both smears at 2 months are negative, then continuation phase of treatment should be given for 4 months so that a total of 6 months of treatment is given.
• If one or both of the smears is still positive, then intensive phase is continued for one more month. Sputum smear is repeated at three month; if negative, continuation phase is started. If sputum smear is still positive, then correlate with culture and sensitivity report.

• If the TB bacilli are susceptible to all anti-TB drugs, intensive phase is continued for one more month and sputum status checked again.

• If the TB bacilli are resistant to Isoniazid and Rifampicin, then the patient is put on 2nd line treatment.

Sputum investigations at 6 months of treatment

• Send 1 sputum sample for smear microscopy at 6 months.
• If smear is negative, treatment is stopped and patient is declared cured.
• If smear is positive, patient is re-admitted for further investigations.

2.4 Chest X-rays

All patients presenting with cough for more than 2 weeks are subjected to a CXR.

Many diseases mimic TB on chest x-ray and this may lead to incorrect diagnosis. X-rays may show lung fibrosis or destruction due to old TB and this may also lead to over diagnosing of pulmonary TB.

Radiology plays an important role in the diagnosis of pulmonary tuberculosis and must be interpreted in the light of their history and clinical findings. CXR helps to rule out or diagnose other diseases.

2.5 TB Culture

Conventional TB culture and sensitivity testing is a slow diagnostic technique. It still has its indications and being done on:

• All direct sputum sample positive for AFB to confirm the diagnosis and to confirm that infection is by typical organism, the Mycobacterium tuberculosis.

• For patients, who have two negative smears and initially have had a course of antibiotics but TB is still suspected.

2.6 Gene XPERT MTB/RIF

This technique has been introduced in 2012 and is very useful especially for suspected drug-resistant TB and the diagnosis of TB in HIV patients. It detects mutations in the rpoB region of M. Tuberculosis DNA, which are responsible for >95% of rifampicin-resistant strains. All patients identified by molecular methods are initiated on an appropriate WHO-recommended treatment regimen as soon as possible.
When rifampicin resistance is detected by Gene XPERT, a WHO-recommended regimen for MDR-TB with the addition of isoniazid is initiated (when susceptibility to isoniazid is not known). When DST results are available, the MDR-TB treatment regimen is tailor-made based on these results.

Gene XPERT MTB/RIF is not used for monitoring of treatment response since results can stay positive for *M. tuberculosis* by detection of DNA in dead organisms after viable bacteria have been eliminated, resulting in false-positive results.

### 2.7 Tuberculin Skin Test

The tuberculin test measures the body’s cell-mediated immune system response to an injection of tuberculin purified protein derivative (PPD).

**Mantoux test** is done by injecting 0.1mL of PPD intradermally, ensuring that the injection goes into and not under the skin. The reaction to the test at the site of injection is measured after 48-72 hours.

Measure the diameter (in millimeters) of the reaction at the widest point of the raised, thickened skin area for the Mantoux.

To help measure accurately, mark the edges of the induration at the widest point with a pen and measure the exact distance between the two points.

A result of up to 10 mm in a healthy person is considered normal.

**What does a positive skin tuberculin test mean?**

<table>
<thead>
<tr>
<th>Tuberculin Test (Mantoux Test)</th>
<th>Normal</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immuno-competent</td>
<td>1-10 mm</td>
<td>&gt;10 mm</td>
<td>0 mm</td>
</tr>
<tr>
<td>Immuno-compromised</td>
<td>1-5 mm</td>
<td>&gt;5 mm</td>
<td>0 mm</td>
</tr>
</tbody>
</table>

- A positive test indicates infection with TB, but not necessarily active TB disease.
- In a child under 5 years a strongly positive skin test (>15 mm) indicates recent (6 weeks or more) infection which is a risk factor for progression to disease.
- In the presence of other features like history of TB contact in the family, signs and symptoms of TB and X-ray changes, a positive tuberculin skin test is suggestive of active TB disease in children.
- A positive reaction occurs after previous BCG immunization and should remain positive for several years thereafter. This reaction is usually weaker than the reaction to natural infection with mycobacterium tuberculosis.
• A positive reaction is only one piece of evidence in favor of the diagnosis.

**What does a negative tuberculin skin test mean?**

• A negative tuberculin skin test does not exclude TB

• Some conditions can suppress the tuberculin skin test and give a false negative result includes: HIV infection, Malnutrition, Severe viral infections (measles, chickenpox), Cancer, Immunosuppressive drugs (steroids), Severe disseminated TB.
Chapter 3: CASE DEFINITIONS

3.1 Standard Case Definitions

**Presumptive TB case:** Patient who has symptoms or signs suggestive of tuberculosis.

**Bacteriologically confirmed TB case:** Patient whose biological specimen is positive by smear microscopy, culture or Xpert MTB/RIF.

**Clinically diagnosed TB case:** Patient who is started on full treatment for active TB but does not fulfill criteria for bacteriologically confirmed case. Such patients are reported as having sputum negative TB.

**a. New**

Patient who has never had treatment for TB, or have taken anti-TB drugs for less than 1 month.

**b. Cured**

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

**c. Previously treated patients have received 1 month or more of anti-TB drugs in the past. They are further classified by the outcome of their most recent course of treatment as follows:**

i. **Relapse patients** are previously treated for TB, were declared cured or treatment completed at the end of their most recent treatment episode and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by re-infection).

ii. **Treatment after failure patients** are previously treated for TB and whose treatment failed at the end of their most recent treatment episode.

iii. **Treatment after loss to follow-up patients** are previously treated for TB and were declared Lost to follow-up at the end of their most recent treatment episode. (These were previously known as Treatment after default patients).

iv. **Other previously treated patients** are previously treated for TB but with an unknown or undocumented outcome for their most recent treatment episode.

**Patients with unknown previous TB treatment history** do not fit into any of the categories listed above.
d. **Treatment Completed**

Patient who completes its treatment without proof of cure.

e. **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.

f. **Died**

Patient who dies for any reason during the course of TB treatment.

g. **Lost to follow-up**: Patient who did not start treatment or whose treatment was interrupted for 2 months or more.

h. **Not evaluated**: No treatment outcome assigned, including “transferred out” to another treatment unit and where the treatment outcome is unknown to the reporting unit.

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

### 3.2 Why standardize case definitions?

- To standardize patient registration case notification
- To evaluate the trend in the proportions of new smear-positive cases and smear-positive relapse and other retreatment cases
- To allocate cases to standardized treatment categories
- For cohort analysis which allows valid comparisons
- To be able to accurately measure progress

### 3.3 Why match treatment to standardized category?

- To allow priority to be given to infectious cases
- To avoid under-treatment of sputum smear-positive cases and therefore to prevent acquired resistance
- To increase cost-effective use of resources and to minimize side-effects for patients by avoiding unnecessary over-treatment
3.4 What Determines Case Definitions?

- Site of TB disease
- Bacteriology (result of sputum smear)
- History of previous treatment of TB

Site of TB disease: Pulmonary or Extra Pulmonary

- Pulmonary TB refers to disease involving the lung parenchyma. Therefore tuberculosis intra-thoracic lymphadenopathy e.g mediastinal or hilar, tuberculosis pleural effusion without radiographic abnormalities in the lungs, constitute a case of extra-pulmonary TB.
- A patient with both pulmonary and extra-pulmonary TB constitutes a case of pulmonary TB.
- The case definition of an extra-pulmonary case with several sites affected depends on the site representing the most severe form of the disease.

Bacteriology (result of smear)

Smear-positive PTB case

- There are at least 2 sputum smears positive for AFBs or
- 1 sputum smear positive for AFBs and chest x-ray abnormalities consistent with active TB or culture positive TB or
- 1 sputum smear and clinically ill.

It is advisable that even if the first specimen is positive pre-treatment another specimen should be taken. This will reduce the chances of a false-positive result as administrative errors may occur.

Smear-negative PTB case

- At least 2 sputum smears are negative for AFBs.
- Chest x-ray abnormalities are consistent with active TB

Note

A patient with 2 negative smears and with a suspicious chest x-ray should be given a trial of broad-spectrum antibiotics for at least 7 days then re-assessed.

3.5 History of Previous Treatment: treatment after interruption, treatment failure and relapse.

It is important to define a case according to whether or not the patient has previously received anti-TB treatment to identify patients at increased risk of acquired drug resistance and the prescription of appropriate treatment.
Chapter 4: PRINCIPLES OF TREATMENT

The key to stop the spread of TB in a community is to start treating patients who are coughing up live TB bacilli as soon as possible. For treatment to be effective, it is crucial that correct doses of anti tubercular drugs are given for the correct period of time. All patients should be given fixed dose combination for total of six months.

4.1 The essential Anti-TB Drugs

There are three main properties of anti-TB drugs:

- Bactericidal,
- Sterilizing and,
- The ability to prevent resistance.

The anti-TB drugs possess these properties to different extents. Isonaizid and Rifampicin are the most powerful bactericidal drugs, active against all populations of TB bacilli. Pyrazinamide and streptomycin are also bactericidal against certain populations of TB bacilli. Pyrazinamide is active in an acid environment against TB bacilli inside macrophages. Streptomycin is active against rapidly multiplying extracellular bacilli. Ethambutol is a bacteriostatic drug.

4.2 Irregular Drug Intake

New Patient

Intensive phase

- Maximum 2 weeks in total may be accepted, but must be added on to the end of the intensive phase.
- If more than 2 weeks doses are missed, the patient should be started on a standardized TB re-treatment regimen.

Continuation phase

When more than two months of treatment, in total, is missed:

- If sputum is smear negative, complete the continuation phase;
- If sputum is smear positive begin retreatment.

Retreatment Patients

Retreatment patients are more likely to develop multi-drug resistance. They are hospitalized. Initial culture and susceptibility testing should be done on every retreatment patient. Total duration of treatment will be of 8-9 months.
4.3  Initiation of treatment

Fixed dose combination Anti Tubercular treatment is started as soon as possible after diagnosis of TB is made to stop the spread of the disease. Make sure that the correct dose is given to the patient.

4.4  Chemoprophylaxis

Active case-finding of index case is recommended for all family members especially children under the age of 5 years. Such children in close household contact with a smear positive case of pulmonary TB should be given Isoniazid chemoprophylaxis.

The correct regimen to give as prophylaxis to a healthy child under 5yr is 10mg of Isoniazid per kg for six months.

4.5  TB Preventive therapy

TB preventive therapy has been proven to prevent TB in HIV positive patients. TB disease can be prevented in 60% of such people by offering Isoniazid prophylaxis for 6 months. IPT is now given to HIV patients in Mauritius since 2014.

4.6  Treatment Protocol

<table>
<thead>
<tr>
<th>Category of treatment</th>
<th>Type of patient</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>New ss-positive</td>
<td>2(HRZE) + 4HR</td>
</tr>
<tr>
<td></td>
<td>Seriously ill* new ss-negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seriously ill new extrapulmonary</td>
<td></td>
</tr>
<tr>
<td>Category II</td>
<td>ss-positive Relapse</td>
<td>2S(HRZE) + 1HRZE + 5HR</td>
</tr>
<tr>
<td></td>
<td>ss-positive Failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ss-positive Treatment after Default</td>
<td></td>
</tr>
<tr>
<td>Category III</td>
<td>New ss-negative, not seriously ill</td>
<td>2(HRZE) + 4HR</td>
</tr>
<tr>
<td></td>
<td>New extra-pulmonary, not seriously ill</td>
<td></td>
</tr>
</tbody>
</table>

* Extensive pulmonary TB, TB meningitis, Milliary TB; ss: sputum smear
R=Rifampicin, H=Isoniazid, Z=Pyrazinamide, E=Ethambutol, S=Streptomycin
Doses= as per body wt: R=10mg/Kg body wt, H=5mg/Kg body wt, Z=25-35mg/Kg body wt, E=20-25mg/kg body wt, S= 15mg/kg body wt.

OR

Patient whose body wt is ≤50kg R450mg+H300mg+Z1250mg+E800 mg.
Patient whose body wt is ≥50Kg R600mg+H300mg+Z1500mg+E1000 mg.
1.1 Note
- Streptomycin should not be used in pregnancy
- Rifampicin reduces the efficacy of oral and injectable contraceptives. It is very important when introducing new patients to treatment to:
  - Ask about contraception, Explain the problem
- Ask patients about other drugs (including ARV) they may be taking and check that there is no cross reaction. Get expert advice if necessary.
Chapter 5: Drug Resistant (DR) TB

5.1 Categories of drug resistance
1) Mono-resistance: resistance to one antituberculosis drug.
2) Poly-resistance: resistance to more than one antituberculosis drug, other than both isoniazid and rifampicin.
3) Multidrug-resistance: resistance to at least isoniazid and rifampicin.
4) Extensive drug-resistance: resistance to any fluoroquinolone, and at least one of three injectable second-line drugs (capreomycin, kanamycin and amikacin), in addition to multidrug-resistance.

5.2 Pathways leading to active drug-resistant TB
1) Acquired (secondary) drug resistance which results from inadequate, incomplete or poor treatment quality of TB patients.
2) Primary drug resistance whereby a person infected with drug-resistant strain.

5.3 Factors contributing to the spread of drug-resistant TB
1) Poor socioeconomic background
2) Presence of immunocomprising conditions (HIV, undernutrition, smoking, drug abuse, alcohol abuse etc)
3) Poor compliance especially among IVDA’s, HIV patients, alcoholics, the homeless and destitute.
4) Large influx of migrant workers from countries with high prevalence of drug-resistant TB
5) Prescription of inadequate chemotherapy:
   - Adding one extra drug in the case of treatment failure, and often adding a further drug when the patient relapses after amounts to mono-therapy.
   - Successive mono-therapies help in selection of resistant bacilli.

5.4 Prevention, Diagnosis and Management of drug-resistant TB

5.4.a Prevention:
1. Early detection and high quality treatment of drug-susceptible TB.
2. Early detection and high quality treatment of drug-resistant TB.
3. Effective implementation of infection control measures.
4. Strengthening and regulation of the health system.

5. Addressing underlying risk factors and social determinants.

6. Ensuring patient adherence to treatment by providing DOTS (Direct Observed Treatment Supervised).

5.4.b When to suspect Drug-Resistant TB

- Retreatment patients who remain sputum smear-positive after three months’ of intensive therapy
- Treatment failure and interruption cases
- Close contacts of drug-resistant tuberculosis cases
- Exposure in institutions that have drug-resistant TB outbreaks or a high drug-resistant TB prevalence
- Residence in areas with high drug-resistant TB prevalence
- History of using anti-TB drugs of poor or unknown quality
- Co-morbid conditions associated with malabsorption or rapid-transit diarrhoea
- HIV in some settings

5.4.c Diagnosis of Drug-Resistant TB

Drug-resistant TB is diagnosed by culture and drug susceptibility testing as well as molecular techniques such as Xpert MTB/RIF. Xpert MTB/RIF is recommended for diagnostic testing for the presence of *M. tuberculosis* and detection of mutations associated with rifampicin resistance.

Microscopy for AFB cannot distinguish viable from non-viable organisms nor differentiate between drug-susceptible and drug-resistant *M. tuberculosis* bacteria, or between different species of mycobacteria. Its usefulness in drug-resistant TB treatment monitoring is therefore limited: samples showing AFB by smear microscopy but negative to culture suggest that bacilli are not viable (caution is nonetheless warranted for these patients to be considered as possibly infectious); while samples showing AFB by smear microscopy but negative by molecular tests are likely to harbour non-tuberculous mycobacteria (NTM).

Gene Xpert MTB/RIF should be used rather than conventional microscopy, culture and DST as the initial diagnostic test in adults and children suspected of having MDR-TB or HIV associated TB.

DR-TB is confirmed through laboratory tests that show that the infecting isolates of *Mycobacterium tuberculosis* grow in vitro in the presence of one or more antituberculosis drugs.
### Treatment regimens for the management of mono- and polyresistant TB

<table>
<thead>
<tr>
<th>PATTERN OF DRUG RESISTANCE</th>
<th>SUGGESTED REGIMEN</th>
<th>MINIMUM DURATION OF TREATMENT (MONTHS)</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>H (+ S)</td>
<td>R, Z and E (±FQ)</td>
<td>6–9</td>
<td>Use Xpert MTB/RIF at month 0, 2, and 3 and if rifampicin resistance is found switch to full MDR-TB treatment. Some experts add a FQ to the regimen.</td>
</tr>
<tr>
<td>H and E (± S)</td>
<td>R, Z, and FQ</td>
<td>9–12</td>
<td>Use Xpert MTB/RIF at month 0, 2, and 3 and if rifampicin resistance is found switch to full MDR-TB treatment and check DST to first- and second-line anti-TB drugs. Some experts recommend using a second-line injectable agent for the first three months.</td>
</tr>
<tr>
<td>H, E, Z, (±S)</td>
<td>R, FQ, plus ethionamide, plus a secondline injectable agent for the first 2–3 months. (±Z)</td>
<td>18</td>
<td>A longer course (6 months) of the second-line injectable may strengthen the regimen for patients with extensive disease. Continued.... Z should be added if resistance is uncertain. Use Xpert MTB/RIF at month 0, 2 and 3 and if rifampicin resistance is found switch to full MDR-TB treatment and check DST to second-line anti-TB drugs. If culture positive after month 2, repeat DST to first- and second-line anti-TB drugs.</td>
</tr>
<tr>
<td>R mono- or polydrug resistance</td>
<td>Full MDR-TB regimen plus H</td>
<td>20</td>
<td>Full MDR regimen: 8Km_{Lfx7-Eto7-Cs7-Z7}/12Lfx7-Eto7-Cs7-Z7</td>
</tr>
<tr>
<td>MDR</td>
<td>MDR-TB regimen</td>
<td>20</td>
<td>8Km_{Lfx7-Eto7-Cs7-Z7}/12Lfx7-Eto7-Cs7-Z7</td>
</tr>
</tbody>
</table>

*a The use of Xpert MTB/RIF at month 0, 2 and 3 is not intended for monitoring response to therapy as the test may be positive for *M. tuberculosis* for patients with a positive response and even after cure. Rather, it is intended only to detect rifampicin resistance amplification during therapy.

H=isoniazid; S=streptomycin; R=rifampicin; Z=pyrazinamide; E=ethambutol; FQ=fluoroquinolone; K=Kanamycin; Eto=Ethionamide; Q=Quinolones; Ofloxacin (Ofx); Levofloxacin (Lvx); Cs=Cycloserine.
5.5 Extensively Drug Resistant (XDR) Tuberculosis

XDR-TB, is a form of TB which is resistant to at least four of the core anti-TB drugs. XDR-TB involves resistance to the two most powerful anti-TB drugs, isoniazid and rifampicin, also known as multidrug-resistance (MDR-TB), in addition to resistance to any of the fluoroquinolones (such as ofloxacin or moxifloxacin) and to at least one of three injectable second-line drugs (amikacin, capreomycin or kanamycin). XDR-TB can develop when these second-line drugs are also misused or mismanaged and therefore also become ineffective. Because XDR-TB is resistant to first- and second-line drugs, treatment options are seriously limited. It is therefore vital that TB control is managed properly.
Chapter 6: Investigation and Treatment of Contacts of Persons with Infectious Tuberculosis

6.1 DEFINITIONS

1) Index case (index patient)
The initially identified case of new or recurrent TB in a person of any age in a specific household or other comparable setting in which others may have been exposed.

2) Contact
2a. Household contact
A person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the 3 months before commencement of the current treatment episode.

2b. Close contact
A person who is not in the household but shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods during the day with the index case during the 3 months before commencement of the current treatment episode.

3) Contact investigation
A systematic process intended to identify previously undiagnosed cases of TB among the contacts of an index case and also includes testing for LTBI to identify possible candidates for preventive treatment.

6.2 Recommendations for contact investigations

1) Contact investigation is conducted for household and close contacts when the index case has any of the following characteristics:
• sputum smear-positive pulmonary tuberculosis,
• sputum negative and Gene XPERT MTB/RIF positive.
• MDR-TB or XDR-TB (proven or suspected),

NB: Contact investigation is not usually conducted for an index case with only extrapulmonary TB.

6.3 Contact clinical evaluation

Clinical evaluation is undertaken for household and close contacts. If symptoms of TB are:

(a) not present,
  • Mantoux Test
  • C X-ray (if Mantoux is > 10mm)

(b) present (further evaluation is undertaken):
• detailed medical history
• physical examination
• tuberculin skin test
• C X-ray
• microbiological assessment of specimens from sites of suspected involvement,
• invasive diagnostic tests like BAL, pleural biopsy, lymph node biopsy etc
• Gene XPERT MTB/RIF wherever necessary
Algorithm for contact investigation and treatment

Clinical evaluation is undertaken for household and close contacts for all patients diagnosed with infectious tuberculosis.

Any symptoms of tuberculosis in contacts*

Yes

CXR

Normal

Mantoux Test

Positive ≥10mm

Treat for LTBI

Negative <10mm

Abnormal

Sputum and other investigations (BAL etc)

Positive ≥10mm

Treat for LTBI

Negative <10mm

Abnormal

CXR

Normal

Mantoux Test (Other than in PLHIV and children <5years)

Positive ≥10mm

Treat for LTBI

Negative <10mm

*Symptoms of TB include cough >2 weeks, hemoptysis, low-grade fever, night sweats, loss of appetite, weight loss, chest pain, shortness of breath, fatigue / malaise.
6.4 Treatment for LTBI:

(a) All household or close contacts of TB patients who are asymptomatic with a normal C X-ray, but with a Mantoux > 10 mm are given isoniazid 300 mg/day for 6 months.

(b) HIV-positive household or close contacts of people with TB and who, after an appropriate clinical evaluation, are found not to have active TB are given isoniazid 300 mg/day for at least 6 months.

(c) Children < 5 years who are household or close contacts of people with TB and who are found not to have active TB are treated for LTBI with isoniazid at a dose of 10 mg/kg for 6 months.
Chapter 7: Tuberculosis and HIV

Tuberculosis (TB) is a leading cause of HIV-related deaths worldwide. In some countries with high HIV prevalence, up to 80% of people with TB test positive for HIV. In 2012, there were an estimated 1.1 million new cases of tuberculosis globally among PLWHIV and an estimated 430 000 of them died despite the fact that TB is curable.

In Mauritius, the recent increase in the number of TB/HIV cases is a matter of concern. As TB is one of the commonest diseases that co-exist with HIV, we are intensifying our screening program for active TB in HIV patients and treat them effectively. All TB patients receive voluntary counseling and testing for HIV.

For many years, the efforts to tackle TB and HIV have been largely separate, despite the overlapping epidemiology. However, it is now increasingly recognized that only through combined and coordinated efforts for both TB and HIV can this dual epidemic be halted. The WHO recommends twelve collaborative TB/HIV actions and 'The Three Is': Isoniazid Preventive Treatment (IPT), intensified case finding (ICF) for active TB, and TB Infection Control (IC), are key public health strategies focused on decreasing the impact of TB on people living with HIV.

The HIV/AIDS and TB departments and their partners focus on joint efforts for TB/HIV advocacy, policy development and implementation in countries. WHO also develops and promotes tools and guidelines to support countries in improving TB/HIV collaboration.

HIV infection has multiple effects on the natural history of TB — for example, it increases the risks for reactivation of latent infection and for exogenous infection.

In 2017, Mauritius registered a total of 110 cases of Pulmonary TB where 13 had co-infection with HIV.

Undoubtedly there will be an increase in this trend as it has been worldwide and we need to remain very vigilant. This is why we advocate strengthened TB-HIV collaboration.