RNTCP laboratory network: Overview

Introduction:

The Revised National TB Control Programme (RNTCP), based on the internationally recommended Directly Observed Treatment Short-course (DOTS) strategy, was launched in 1997 and expanded across the country in a phased manner with support from World Bank and other development partners. Full nation-wide coverage was achieved, covering over a billion populations (1114 million) in March 2006. In terms of treatment of patients, RNTCP has been recognized as the largest and the fastest expanding TB control programme in the world.

The cornerstone strategy in case detection of TB is quality assured diagnosis. RNTCP has quality assured laboratory network for bacteriological examination of sputum in a three tier system consisting of Designated Microscopy Centre (DMC), Intermediate Reference laboratory (IRL), and National Reference laboratory (NRL). One of its National Reference laboratories (National Institute for Research in Tuberculosis – formerly TRC), Chennai is also one of the WHO designated supra-national reference laboratory (SNRL) for the South East Asia Region since 1997 and another the National Institute of TB and Respiratory Diseases (NITRD) New Delhi has been designated as a centre of excellence for TB mycobacteriology by WHO in the recent past. The National Expert Committee on Diagnostics and Treatment and the Coordination Committee of the National Reference laboratories are two advisory committee for providing the guidance to policy level changes pertaining to diagnosis of tuberculosis.

Structure and functions of RNTCP Laboratory network

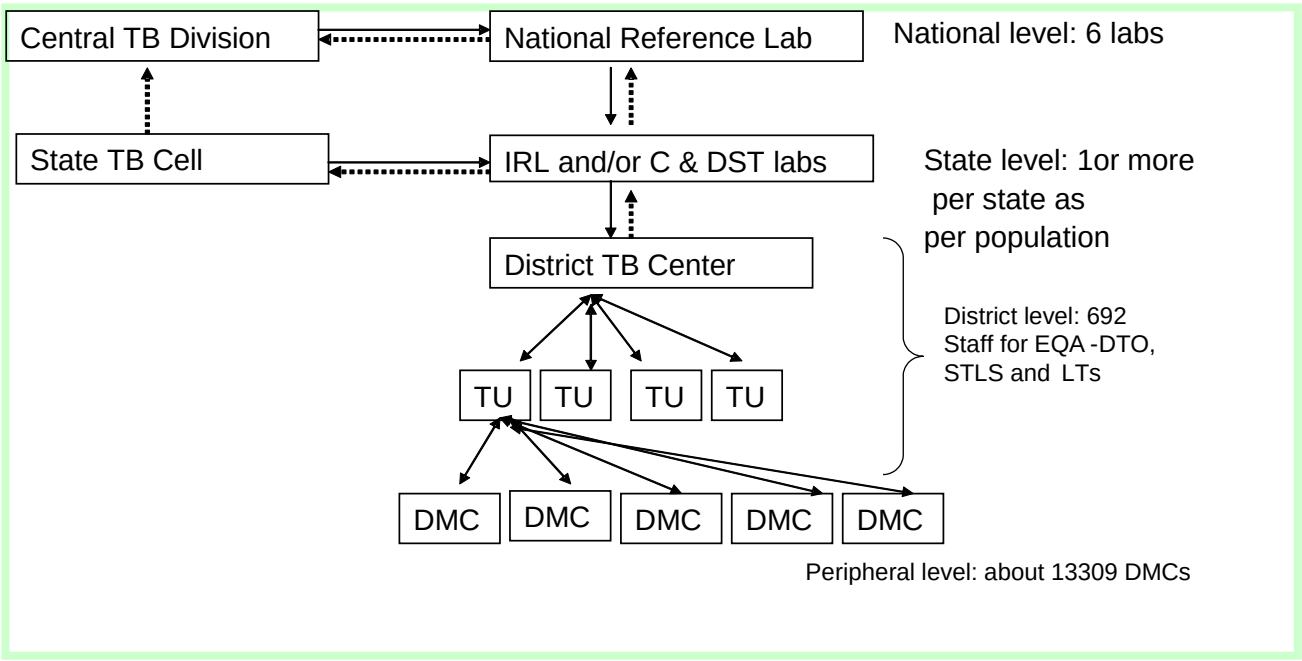
The RNTCP laboratory network is composed of National Reference Laboratories (NRLs), state level Intermediate reference laboratories (IRLs) and Culture & Drug Susceptibility Testing (C & DST) laboratories and peripheral level laboratories as designated microscopy centres (DMCs).

At the top of laboratory network hierarchy are six designated NRLs namely National Institute for Research in Tuberculosis (NIRT), Chennai; National Tuberculosis Institute (NTI) Bangalore; National Institute of TB & Respiratory Diseases (NIRTD) New Delhi, National Japanese Leprosy Mission for Asia (JALMA) now renamed Central JALMA Institute of Leprosy other Mycobacterial diseases, Agra, Regional Medical Research Centre (RMRC), Bhubaneswar and

Bhopal Memorial Hospital and Research Centre, (BMHRC) Bhopal. NIRT, Chennai in addition to being one of the NRLs is also one of the WHO designated supranational reference laboratory for the South-east Asia Region. There are twenty seven Intermediate Reference Laboratories (IRLs), at the State level (at least one per a major state, with a plan for one additional IRL for large states having more than 100 million population) in addition to C & DST laboratories in medical colleges and other private sector. At the peripheral level Designated Microscopy Centers (DMCs) is located at District TB centre and sub-district TB units.

The laboratory network and diagnostic services are guided by the National Expert Committee on Diagnosis and Management of Tuberculosis the apex committee which provide the technical advice to the programme for the laboratory policy. National Reference Laboratory Coordination Committee reviews the progress and facilitates newer initiatives.

The laboratory network under RNTCP is shown in **Figure 1** below.



National Reference Laboratory (NRL): NRL conducts annual On-site evaluation/supervisory visits to laboratories for assessing quality of microscopy, Culture and DST, and for improvement of overall laboratory quality .NRLs also assist CTD, in developing laboratory guidelines, SOPs, conduct trainings to state level Intermediate reference laboratories and other technical issues., . All States are distributed amongst the NRLs for this purpose. The programme has provided HR support by way of three microbiologists and four senior laboratory technicians to each NRL for these activities under the head of NRL strengthening. The functions of the NRLs include conduct of Culture and DST trainings to the IRLs, develop SOPs for the technical procedures, equipment maintenance, infection control, and recording and reporting. It is also responsible for offering second line DST for MDR TB

treatment failures. NIRT the SRL of the Region is responsible for the external Quality Assurance of the other 5 NRLs. NIRT is in turn quality assured through the SRL coordinating laboratory at Antwerp, Belgium. In addition, NRLs are also responsible for the conduct of research for the programme and evaluation of newer tools for diagnosis of TB.

Intermediate Reference Laboratory (IRL): There is at least one IRL per state, situated in the STDC campus or an identified location in a state government hospital. The IRL was initially set up to function as a Culture and Drug Susceptibility Testing (C & DST) facility for the conduct of state wise TB Drug Resistance Surveillance and to execute smear EQAP for the State. At present its functions have been expanded to provide culture and DST for the category IV services in the State and its capacity has been built with support from central level by additional training, Human Resource and technical assistance from national and international agencies. The IRL conducts on-site evaluation visits to districts for sputum microscopy at least once a year. The IRL undertakes panel testing of STLS at each DTC. The IRL ensures the proficiency of staff performing RNTCP smear microscopy activities by providing training to laboratory technicians and STLS.

Culture and DST Laboratories(C & DST): In additional to IRLs, The programme also involves the microbiology department of Medical colleges for providing diagnostic services for drug resistance Tuberculosis, Extra-pulmonary Tuberculosis (EP-TB) and research. The RNTCP provides additional human resources, equipments and training to C & DST laboratories.

District TB Centre (DTC): The district TB centre (DTC) is the nodal centre for all TB control activities of a district. At the DTC, all reports from the sub-districts are consolidated and sent to the next level. The DTO is responsible for all TB activities in the district including EQA activities-mainly Random Blinded Rechecking (RBRC) procedure. Maintenance of a regular supply of good quality laboratory consumables and reagents to all DMCs in the district is also the responsibility of the DTO.

Tuberculosis Unit (TU): The Tuberculosis unit is a sub-district supervisory unit, established for 500,000 population (250,000 in tribal and hilly areas). Programme has provided a Senior Tuberculosis Lab Supervisor, on contractual basis, to each TU for carrying out EQA activities-On-site evaluation visits to DMCs and Random blinded rechecking of routine DMC slides coordinated by the DTO at the DTC level. STLS prepares staining solutions for smear microscopy, checks the quality using internal QC slides and ensures adequate supplies to DMCs.

Designated Microscopy Centre (DMC): The most peripheral laboratory under the RNTCP network is the designated microscopy centre (DMC) which serves a population of around 100,000 (50,000 in tribal and hilly areas). RNTCP has provided financial assistance for upgrading existing health facilities,

supplied a binocular microscope for each DMC and ensured adequate supply of staining reagents and consumables at the DMCs. DMCs are manned by a trained laboratory technician (LT) of the state health system.

1. **RNTCP endorsed diagnostic technologies for TB & DR-TB**

Diagnosis of tuberculosis:

Site of disease

- **Pulmonary TB case :**

Patient with TB of the lungs (with or without involvement of any extra-pulmonary locations).

- **Extra-pulmonary TB case :**

Patient with TB of any organ other than the lungs, such as pleura, lymph notes, intestines, genito-urinary tract, skin, bones and joints, meninges of the brain, etc, diagnosed with microbiological, histological, radiological, or strong clinical evidence.

The following RNTCP endorsed technologies for diagnosis of tuberculosis (Pulmonary and Extra-Pulmonary).

1. **Smear Microscopy (for AFB):**

– Sputum smear stained with Zeil-Nelson Staining or
– Fluorescence stains and examined under direct or indirect microscopy with or without LED.

2. **Culture:**

– Solid (Lowenstein Jansen) media or Liquid media (Middle Brook) using manual, semi-automatic or automatic machines e.g. Bactec , MGIT etc.

3. **Rapid diagnostic molecular test:**

– Conventional PCR based Line Probe Assay for MTB complex or

– Real-time PCR based Nucleic Acid Amplification Test (NAAT) for MTB complex e.g. GeneXpert

[Sputum Smear Microscopy (for AFB): Sputum smear stained with Zeil-Nelson Staining or Fluorescence stains and examined under direct or indirect microscopy. Sputum Culture: Sputum culture on solid (Lowenstein Jansen) media or liquid media (Middle Brook) using manual, semi-automatic or automatic machines e.g. Bactec , MGIT etc. Rapid diagnostic molecular test: Line Probe Assay for MTB or Nucleic Acid Amplification Test (CB-NAAT).Note: Diagnosis of TB based on radiology (e.g. X-ray) will be termed as clinical TB.

- **Drug Resistance Tuberculosis**
    - **Multi Drug Resistance Tuberculosis (MDR-TB)/ Rifampicin Resistance:** Patient with a drug susceptibility test result from a RNTCP-certified

laboratory or WRD (WHO-endorsed Rapid Diagnostics) drug susceptibility test report showing resistance to rifampicin.

- **XDR TB case:** An MDR TB case whose recovered M. tuberculosis isolate is resistant to at least isoniazid, rifampicin, a fluoroquinolone (ofloxacin, levofloxacin, or moxifloxacin) and a second-line injectable antiTB drug (kanamycin, amikacin, or capreomycin) at a RNTCP-certified Culture & DST Laboratory.
- **Mono-Poly Drug Resistance Tuberculosis**

The RNTCP endorsed technologies for DR-TB is as bewlo:

- **MDR-TB:**
  - Rapid Molecular Test (LPA/ CB-NAAT)
  - Liquid Culture & DST
  - Solid Culture & DST
- **XDR-TB:**
  - Liquid Culture & DST
  - Solid Culture & DST