



Training Module

for
Medical Practitioners



सत्यमेव जयते

Central TB Division
Directorate General of Health Services
Ministry of Health and Family Welfare
Nirman Bhawan
New Delhi-110 108

Revised National Tuberculosis Control Programme (RNTCP)

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New Delhi-110 011
(December 2010)

This module was prepared by a team from the Central TB Division,
Indian Medical Association and WHO-India

About This Module

Healthcare services in India are provided by multiple and diverse providers in the government, private, non-governmental organisation (NGO) and corporate sectors. Each sector has strengths as well as weaknesses. Tuberculosis (TB) patients are managed by several healthcare providers under these different sectors and the responsibility of providing quality patient care to achieve TB control is therefore, with all these sectors. Effective control of TB will be possible if all these sectors come together and work towards a common goal. The Central TB Division (CTD) at the Ministry of Health and Family Welfare, Govt. of India has been interacting with all sectors of healthcare since the early days of the Revised National Tuberculosis Control Programme (RNTCP). There are commendable examples of collaboration among various health sectors, like private, NGOs, corporate and other government organisations such as ESI, Railways, etc. These collaborations have contributed significantly towards the implementation of World Health Organization (WHO) recommended Directly Observed Treatment, Short-course (DOTS) strategy by these different healthcare sectors.

There was demand from medical practitioners outside the public health sector, and also a felt need, for a concise module on RNTCP that would facilitate their effective involvement in the programme. This module, produced by CTD, is in response to the field realities and is the result of various interactions with, and feedback from, all concerned sectors, including the Indian Medical Association (IMA). It tries to provide medical practitioners with updated information on RNTCP that will equip them to adopt and practice the diagnostic and treatment policies of RNTCP. It is expected to facilitate development of effective and sustainable partnerships among the public, private, NGO and corporate sectors to ensure delivery of quality services under RNTCP.

At the end of this modular training, the participants will be able to:

- Get a glimpse of the global and Indian TB scenario
- Understand the principles of RNTCP
- Correctly identify patients suspected of having TB

- Ensure quality sputum microscopy for TB suspects
- Categorise TB patients correctly as per RNTCP policies
- Understand the rationale of treatment (regimens, doses, side effects)
- Understand the mechanism of DOTS
- Understand the recording and reporting mechanisms
- Understand 'Referral for Treatment' and 'Transfer of Patients' protocols
- Provide monthly reports
- Understand the management of drugs and other supplies in RNTCP
- Understand monitoring and supervision in RNTCP.

The training module includes a package of standardised printed material, standardized power point slides, case studies, exercises and pre-test questions.

Facilitators' Guide

Prior to Training

- Pre-test questionnaire to be circulated to the participants during registration
- Request DTO to get copies of local RNTCP key staff contact details which includes the names and telephone numbers of the DTO, DTC, MOTC, STS, STLS, TBHVs, DMC list and TU list
- Ensure that all the background material are available prior to trainings
- Ensure availability of sufficient copies of 'Training Module for Medical Practitioners'
- Standardized training slides
- A CD contains- training slides, CME slides including scientific basis of DOTS, RNTCP Technical and Operational Guidelines
- Standardized IEC/PPM kit (diagnostic algorithm, RNTCP at a glance, desk reference etc.
- Ensure that a communication of the trainings has gone well in advance to all trainees and all key district RNTCP staff and IMA leaders

During the Training

- At the time of registration, distribute the pre-test questionnaire
- Introduction/ice breaking session by local IMA leader and DTO- 10 minutes. Project slides under 'slides for Chapters 1 and 2' of the medical practitioners training presentation that has been provided in the accompanying CD
- Read Chapter 3 and Chapter 4 involving all trainees in a group. Each trainee, by turn, is asked to come to the front and lead the reading for a few minutes
- At the time of reading Chapter 3 and Chapter 4, familiarize the trainees on laboratory form and treatment card

Facilitators' Guide

- At the end of Chapter 3, ensure that all trainees do Exercise 1, Part B individually. At the end of Chapter 4, get Exercises 2A and 2B done in the plenary (with the whole group)
- While covering Chapter 4, demonstrate adult and pediatric patient wise boxes, allowing each trainee to examine the box, the pouches and the strips
- Project 'Slides for Chapters 2,3 and 4' of the medical practitioners training presentation to recapitulate key learning from Chapters 2, 3 and 4
- Project 'Slides for Additional Information on MDR-TB and PPM schemes'
- Project 'Slides on International Standards of TB Care'
- Project 'Slides on Rational use of Anti-TB drugs including Fluoroquinolones'
- Post-test questionnaire to be given to the trainees.

Agenda for the training

Chapter	Duration
Pre-test questionnaire	During registration
Introduction	10 minutes
Slides on chapter 1	15 minutes
Chapters 2 and 3 including exercise and slides	90 minutes
Tea break	15 minutes
Case studies (5)	60 minutes
Slides for Chapters 6 & 7, MDR-TB, XDR, PPM, ISTC	30 minutes
Post-test questionnaire	15 minutes
Distribution of certificates and souvenirs	5 minutes

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1 Introduction

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. Pulmonary tuberculosis is the most common form of TB (more than 85% of all TB cases), while extra pulmonary tuberculosis can affect almost any organ in the body. Transmission occurs by the airborne spread of infectious droplets and droplet nuclei containing the tubercle bacilli. The source of infection is a person with sputum smear-positive pulmonary TB. Transmission often occurs indoors, where droplets and droplet nuclei can stay in the air for a long time.

Global and Indian Scenario

In 2007, there were globally an estimated 9.4 million new cases of TB, of which ~4 million were sputum smear-positive, and ~78% were in 22 high burden countries. One fifth of the global TB incidence is in India, with 1.9 million new cases occurring every year and 0.87 million of these being infectious smear-positive cases. In India, an estimated 2.76 lakh deaths occur from TB every year.

TB is a serious public health problem causing immense morbidity, mortality and distress to individuals, families and communities. TB kills more adults in India than any other infectious disease. The disease incidence peaks in people belonging to the most economically productive age group of 15-60 years. The link between TB and HIV is quite significant with WHO estimating that 6-7% of TB patients are also coinfecting with HIV.

EVERY DAY IN INDIA,

“more than 900 people die of TB (~2 deaths every 3 minutes)”

Magnitude of TB - Global and Indian scenario

	Incidence of disease	Prevalence of disease	Mortality	HIV prevalence among incident cases
Global	9.4 million (139/lakh/year)	11.1 million (165/lakh/year)	1.32 million (19.6/lakh/year)	15%
India	1.98 million (168/lakh/year)	2.18 million (185/lakh/year)	2.76 lakhs (23/lakh/year)	6.7%

National Tuberculosis Programme (NTP)

During the 1950s and 1960s, significant research on TB was undertaken in India, and in 1962 the National TB Control Programme (NTP) was launched. Three decades later in 1992, a review of the NTP found that the desired results had not been achieved. There was over-dependence on X-rays for diagnosis. Incomplete treatment was the norm rather than the exception. The 1992 review revealed that only 30% of existing TB cases were being diagnosed, and of these only 30% were completing treatment.

Revised National TB Control Programme (RNTCP)

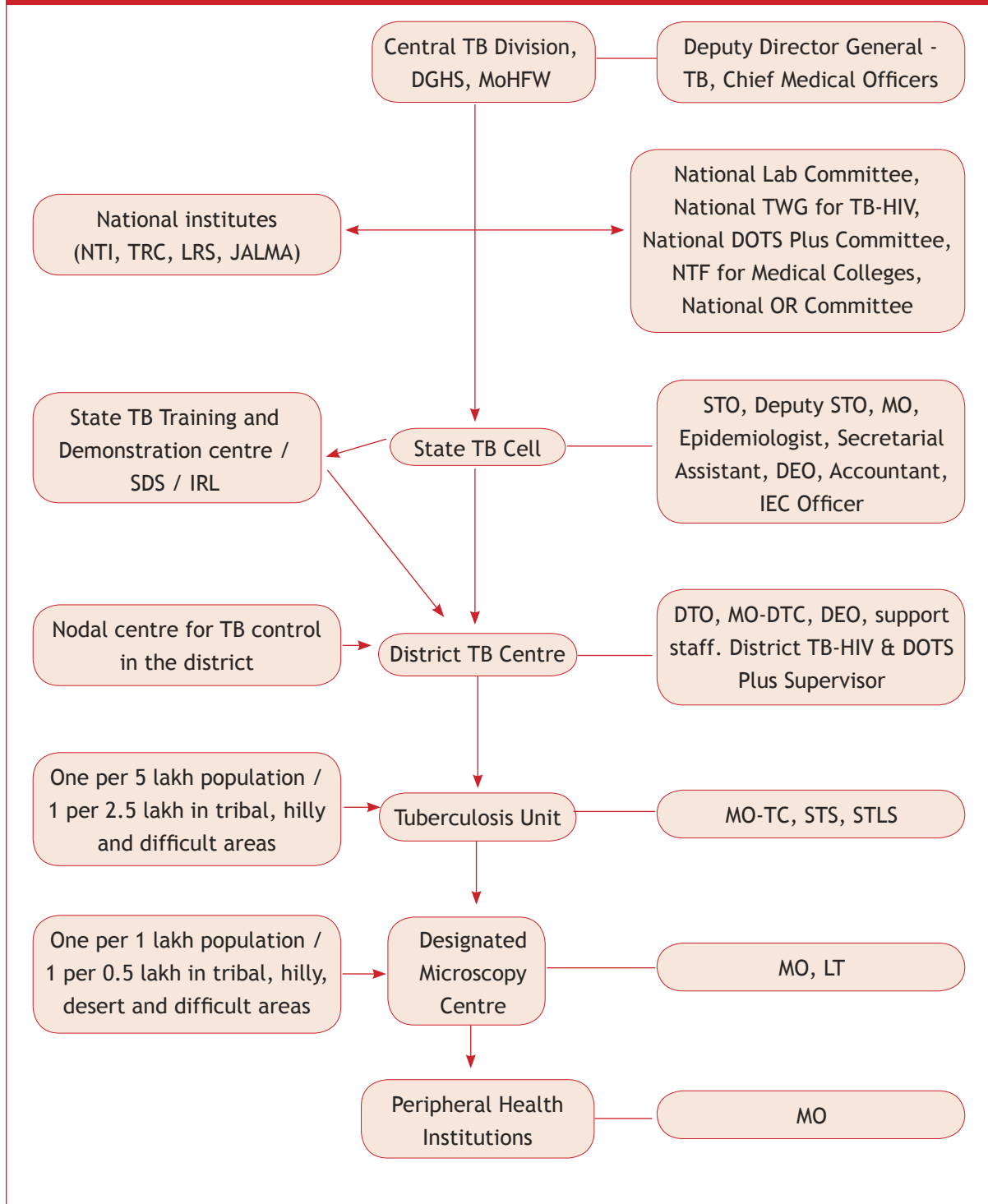
On the recommendations of an expert committee, a revised strategy to control TB was pilot tested in 1993-97. The Revised National TB Control Programme (RNTCP), based on the internationally recommended Directly Observed Treatment Short-course (DOTS) strategy, was launched in 1997 and expanded across the country in a phased manner. Full nationwide coverage was achieved in March 2006.

Since the inception of RNTCP and up to March 2009, more than 10 million patients have been initiated on treatment and about 1.8 million additional lives have been saved when compared to the earlier programme. Each month, more than 100,000 patients are initiated on treatment.

Structure of the RNTCP

The RNTCP is led by the Central TB Division (CTD) in the Ministry of Health and Family Welfare, Govt. of India in Delhi.

Organizational structure of RNTCP



Universal Access to TB Care

All TB patients in the community need to have access to early, good quality diagnosis and treatment services in a manner that is affordable and convenient to the patient in time, place and person. All affected communities must have full access to TB prevention, care and treatment; including women, children, elders, migrants, homeless people, alcohol and other drug users, prison inmates, people living with HIV and other clinical risk factors, and those with other life-threatening diseases. PPM is a critical path for achieving universal access.

Public Private Mix (PPM)

India has one of the largest private health care sectors in the world. This sector is often the first point of contact for a significant number of TB suspects and patients.

Other sectors like non-governmental organisations (NGO), corporate sector, etc. also cater to a considerable percentage of TB patients. Because of their flexibility and easy accessibility, these service providers have gained credibility and are popular among patients. The strengths of these sectors can be utilised to supplement the government's efforts to control TB. Standard quality of care and free drugs can be provided through effective public-private collaboration under RNTCP.

Experiences from pilot projects in the country and elsewhere show that partnerships between government, private, corporate and NGO health care sectors can increase TB case detection rates and improve patient adherence. Such partnerships reduce diagnostic delays and cost to the patients, who get quality RNTCP services from the provider of their choice. RNTCP has made a concerted effort to develop partnerships with all health care sectors. Guidelines for collaboration with NGOs (2001) and private practitioners (2002) were developed in consultation with experts from related sectors and are widely disseminated.

These guidelines have been revised in 2008. There are different schemes for participation of private practitioners (PPs) and NGOs in RNTCP. Information and documents on these revised schemes are available with DTOs and at the RNTCP website www.tbcindia.org.

To health providers participating in the programme, the RNTCP provides:

- Technical training
- Laboratory consumables
- Registers and forms

- Health education materials, and
- Free drugs in patient-wise boxes

There are different roles which the partners of RNTCP can take up. These include:

- Referral for diagnosis (sputum collection and transportation centres)
- Diagnosis
- Referral for treatment
- Treatment initiation
- Provision of Directly observed treatment (DOT)
- Health education and related activities
- Management and supervision of diagnostic and treatment activities at the sub-district level

A health provider can get involved in a single activity or in multiple activities depending on the provider's capacity, interest and the requirements of the programme.

All partners have to ensure that each patient with a history of cough for more than two weeks undergoes sputum smear examination for TB and patients diagnosed to have TB receive treatment as per RNTCP guidelines. It is also essential that all patients put on DOTS, receive treatment under direct observation.

Multidrug-resistant Tuberculosis (MDR-TB)

MDR-TB is defined as tuberculosis disease where the bacilli is resistant to isoniazid (H) and rifampicin (R), with or without resistance to other drugs. Irregular consumption and frequent interruption in taking treatment for TB is the most common cause of acquiring multidrug resistance. In India, MDR-TB amongst new cases are estimated at 2- 3% and amongst re-treatment cases at 14-17%. **Extensively Drug Resistant TB (XDR-TB)** is a subset of MDR-TB where the bacilli, in addition to being resistant to R and H, are also resistant to fluoroquinolones and any one of the second-line injectable drugs (namely Kanamycin, Capreomycin or Amikacin). Although XDR-TB has been reported in India, its magnitude remains undetermined as yet due to the lack of laboratories being capable of conducting quality assured second line drug susceptibility testing.

In India, a great concern is the potential threat of drug resistant TB (DR-TB) with the existing unregulated availability and injudicious use of first and second line anti-TB drugs in the country.

RNTCP and DOTS-Plus Services for MDR-TB

RNTCP reaffirms that the prevention of MDR-TB is a priority task which can be achieved only through the implementation of a good quality DOTS programme. Available information suggests that prevalence of MDR-TB is relatively low in India. However, this translates into a large absolute number of cases, estimated at over 99,000 in 2008. The country is slowly gearing up to manage tens of thousands of MDR-TB patients annually by 2012-13.

RNTCP reached a landmark achievement with the launching of RNTCP DOTS-Plus services for the management of MDR-TB patients in the states of Gujarat and Maharashtra in 2007. Specific guidelines have been formulated for the implementation of DOTS-Plus activities in a phased manner across the country. RNTCP aims to establish a network of accredited, quality assured culture and drug susceptibility testing laboratories across the country by 2012-13.

Pediatric TB

Children in the first five years of their life are likely to suffer from serious and fatal forms of TB, more so, if not vaccinated with BCG. Globally, it is estimated that about 1.1 million new cases are reported and 1,30,000 deaths occur annually due to TB among children. Reliable data on incidence and prevalence of the disease is not available due to difficulties in diagnosis of pediatric TB under field conditions. However, limited data available reveals that prevalence of TB among children in the age group 0-14 years is estimated to be 0.3% of radiological cases and 0.15% of bacteriological cases.

HIV Co-infection among TB Patients

In India, it is estimated that 2.31 million individuals are living with HIV infection, which equates to approximately 0.34% of the adult population of the country. Based on available country data of 2007, it is estimated that 4.9% of new adult TB patients in India are HIV positive. Hence, the TB epidemic in India continues to be predominantly driven by the pool of HIV negative TB infected individuals.

Tuberculosis is the most common opportunistic infection amongst HIV-infected individuals. It is a major cause of mortality among patients with HIV and poses a risk throughout the course of HIV disease, even after successful initiation of antiretroviral therapy (ART). In India, 55-60% of AIDS cases reported had TB, and TB is one of the leading causes of death in People living with HIV/AIDS (PLHA).

Goals, Components and Objectives of RNTCP

The goal of RNTCP is to decrease mortality and morbidity due to TB and cut transmission of infection until TB ceases to be a major public health problem. It aims to control TB by detecting and curing sputum smear-positive patients thereby interrupting the chain of transmission. The objectives of RNTCP are to achieve and maintain a cure rate of at least 85% among new sputum smear-positive cases and to achieve and maintain detection of at least 70% of such cases in the population. The only effective means to achieve the goal of RNTCP is the application of DOTS strategy.

Internationally WHO recommends the Stop TB Strategy for TB control which includes the DOTS strategy. The components of the Stop TB Strategy are given below.

Components of DOTS

DOTS is a systematic strategy having 5 components

- Political and administrative commitment
- Good quality diagnosis, primarily by sputum smear microscopy
- Uninterrupted supply of good quality drugs
- Directly observed treatment (DOT)
- Systematic monitoring and accountability

Points to Remember

- TB continues to be the leading killer disease for Indian adults amongst all infectious diseases
- One fifth of the world's TB incident cases are in India
- More than 80% of TB patients have pulmonary TB
- In developing countries, more than 75% of TB patients are in the economically productive age group of 15-45 years
- The DTO has the overall responsibility of implementing the programme at the district level
- Involvement of all sectors of health care is necessary for the control of TB in India

2 Diagnosis of Tuberculosis

Identification of Tuberculosis Suspects

The most common symptom of pulmonary TB is persistent cough, usually with expectoration. Persistent cough may be accompanied by other symptoms such as weight loss, tiredness, fever with evening rise, night sweats, chest pain, shortness of breath, anorexia and haemoptysis.

Pulmonary TB Suspects

Pulmonary smear-positive tuberculosis patients expel tubercle bacilli into the air while coughing/sneezing. Contacts of undiagnosed/untreated pulmonary smear-positive patients become infected when they inhale these tubercle bacilli.

A pulmonary TB suspect is defined as:

- An individual having cough of 2 weeks or more
- Contacts of smear-positive TB patients having cough of any duration
- Suspected/confirmed extra-pulmonary TB having cough of any duration
- HIV positive patient having cough of any duration

Persons having cough of 2 weeks or more, with or without other symptoms, are referred to as pulmonary TB suspect. They should have 2 sputum samples examined for AFB.

A patient with extra-pulmonary TB may have general symptoms like weight loss, fever with evening rise and night sweats. Other symptoms depend on the organ affected.

Examples of these symptoms are, swelling of a lymph node in TB lymphadenitis, pain and swelling of a joint in TB arthritis, neck stiffness and disorientation in a case of TB meningitis. Patients with EP TB who also have cough of any duration, should have sputum samples examined. If the smear result is positive, the patient is classified as pulmonary TB and his/her treatment regimen will be that of a case of smear-positive pulmonary TB.

In a health facility, at least 2% of new adult out-patients are estimated to be TB suspects. However, it can vary greatly in secondary and tertiary level health care settings. In a DMC, on an average, 5-15% of TB suspects are expected to have sputum smear-positive pulmonary TB.

Referral for Sputum Examination

Pulmonary TB suspect (PTB suspects) at designated microscopy centers (DMC) are subjected for two sputum examinations, with one of them being a morning sputum specimen. PTB suspects attending health facilities other than DMC, are either referred to the nearest DMC for sputum examination or their sputum specimens are collected and transported to the DMC as per guidelines. Results of sputum tests should be reported within a day. In case the patient is not able to travel to the DMC, then both the morning and the spot specimens could be collected at the nearest health facility or sputum collection centre and transported to the DMC.

Designated Microscopy Centre

Generally, a PHI covering a population of 1 lakh and having a new adult OPD attendance of at least 100 per day is selected as a DMC. In difficult areas, more laboratories are required. Hence, in such areas, a PHI may be allowed to function as a DMC even if it covers a population of 50,000 and has a new adult OPD attendance of 60-100 per day. In addition, DMCs can be established in private or NGO or other public sector undertakings (other than Health Ministry) which fulfills the criteria.

The DMCs should satisfy the following criteria:

1. A qualified and RNTCP trained laboratory technician should be present
2. A functional Binocular Microscope should be present in the laboratory
3. Physical infrastructure in laboratory should meet RNTCP guidelines
4. Daily new adult OPD of at least 60-100 and/or workload of at least 3-5 sputum smears per day for the laboratory technician in the laboratory.
5. The laboratory should be under functional RNCTP Quality Assurance Programme.

RNCTP laboratory form for sputum examination has to be filled by the Medical Officer/ Health worker of the health facility appropriately and sent along with the patient for sputum examination.

Given below are the details of the tasks to be performed.

Tasks Performed before Sputum Collection

Before collecting the sputum specimen, the health worker should briefly explain to the patient the reasons for sputum collection. The **laboratory form for sputum examination** should be filled up completely, generally by the MO. This form is sent to the DMC along with the sputum specimens. Only one form needs to be filled for two sputum specimens collected from a patient. The form accompanies the patient's sputum specimens when they are transported from the peripheral health facility to the DMC for examination.

REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME							
Laboratory Form for Sputum Examination							
Name of referring health facility: _____						Date: _____	
Name of patient: _____				Age: _____		Sex: M <input type="checkbox"/> F <input type="checkbox"/>	
Complete address: _____							
Contact phone number/mobile: _____							
Type of suspect/disease:		<input type="checkbox"/> Pulmonary		Site: _____			
		<input type="checkbox"/> Extra-pulmonary					
Reason for examination:							
<input type="checkbox"/> Diagnosis							
<input type="checkbox"/> Repeat Examination for Diagnosis							
<input type="checkbox"/> Follow-up examinations							
<ul style="list-style-type: none"> • For new and previously treated cases - Month of follow-up • For MDR-TB cases - Month of follow-up 							
Treatment Regimens (tick ✓ appropriate box):							
<input type="checkbox"/> New cases <input type="checkbox"/> Previously treated <input type="checkbox"/> MDR-TB							
Patient's TB No. _____				(Name and signature of referring person/official)			
If sputum samples are being transported:							
Specimen Identification No.: _____				Date of sputum collection: _____			
Specimen collector's name and signature: _____							
RESULTS (To be completed in the laboratory of DMC)							
Name of DMC: _____							
Lab. Serial No.: _____							
Date of examination	Specimen	Visual appearance M,B,S)*	Results (Neg or Pos)	Positive (grading)			
	A			3+	2+	1+	Scanty**
	B						
* M = Mucopurulent, B = Blood stained, S = Saliva							
** Write actual count of AFB seen in 100 oil immersion fields							
Date: _____				Signature of Lab. Technician _____			

**REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME
LABORATORY REGISTER**

Lab. Serial No.	Date	Name in Full	Age	Sex M/F	Complete address (for new patients) and phone no.	Name of referring health facility	Reasons for Examination*			Results		Signature	Remarks
							Diagnosis	Follow-up		a	b		
								TB No.	Regimen NT/PT				
499	30/3	Sita Dixit		F	211, Pocket 3, Mayur Vihar	Modern TB Clinic	RE			Neg	Neg	Joshi	
500	30/3	Krishna Kanth	54	F	40 Sector II, Jamnagar	Jamnagar Health Centre	✓			Neg		Joshi	
501	30/3	Aswani Rai	39	F	225, Block 4, Babu Nagar	Jamnagar Health Centre	✓			Scanty		Joshi	
502	30/3	Abdul Hazan	44	M	Gali No.7, JJ Ram Rani Coloni	Aligarh Dispensary		20	PT	2+	2+	Joshi	MDR-TB suspect
503	01/4	Rama	38		422, Sector III, Rohini	Modern TB Clinic		102		Neg	Neg	Joshi	
504	01/4	Alex chopra	45	M	M.G. Road	ART Centre KRH	✓			1+	1+	Joshi	Referred out
504		Renu Sharma	37	F		Jamnagar Health Centre		✓		1+	2+	Joshi	
505	02/4	Kumar Bhatia	58	M	BB22/Block 4, Nehru Place	Jamnagar Health Centre	✓			Neg			
506	02/4	Deepak Dhawan	28	M		ICTC KRH	✓			1+	2+	Joshi	
507	02/4	Preeti Chandra	26	F	62, Lane No. 820, Kailash Colony		RE			Neg	Neg	Joshi	

* If sputum is examined for diagnosis, put a tick (✓) mark in the space under "Diagnosis" if sputum is examined for repeat diagnosis, put 'RE' in the space under Diagnosis

* If sputum is for follow-up of patients on treatment, write the patient's TB No. in the space under "Follow-up", treatment regimen as NT (new cases) or PT (previously treated cases) and month of follow-up.

- Points to be mentioned in the remarks column: date of starting treatment, treatment regimen, TB No. Referral details, MDR-TB suspect identified and remarks on unblinded rechecking of slides during OSE visits by the STLS, etc.

Note: Facilitator to discuss the laboratory register with participants.

One specimen positive out of the two is enough to declare a patient as smear-positive TB. Smear-positive TB is further classified as a new or re-treatment case based on their previous treatment history, and an appropriate therapy is prescribed.

Patients in whom both specimens are smear-negative should be prescribed symptomatic treatment and broad-spectrum antibiotics such as Co-trimoxazole for 10-14 days.

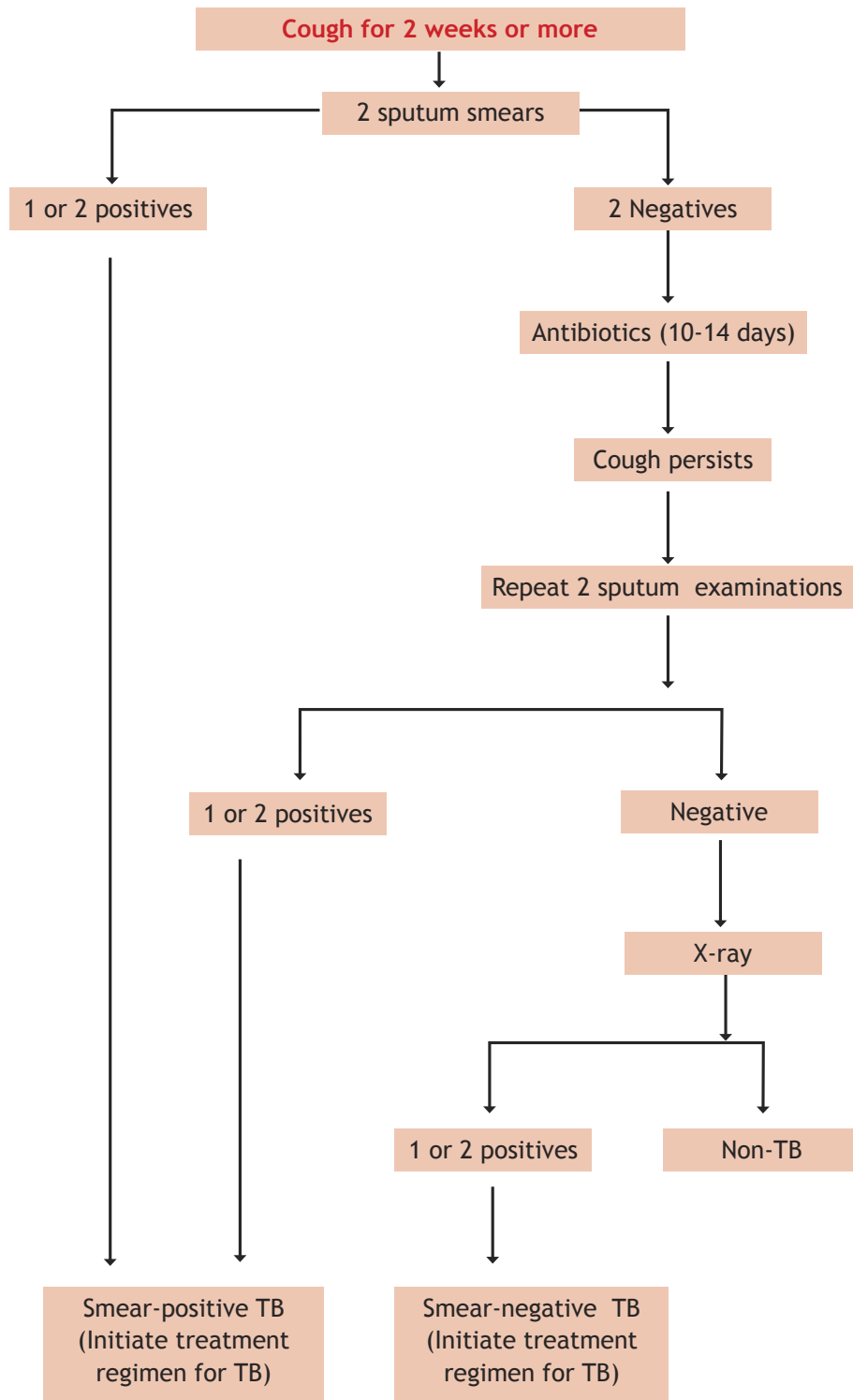
Antibiotics such as fluoroquinolones (ciprofloxacin, ofloxacin, levofloxacin etc.), rifampicin or streptomycin, which are active against tuberculosis, should never be used.

Most patients are likely to improve with antibiotics if they are not suffering from TB. If the symptoms persist after a course of broad spectrum antibiotics, repeat sputum smear examination (2 samples) must be done for such patients. If one or more smears are positive, the patient is diagnosed as having smear-positive pulmonary TB. If none of the repeat sputum specimens is positive, a chest X-ray is taken. If the findings of the X-ray are consistent with active pulmonary TB, and the medical practitioner decides to treat the patient with anti-TB drugs, the patient will be diagnosed as having pulmonary smear- negative TB.

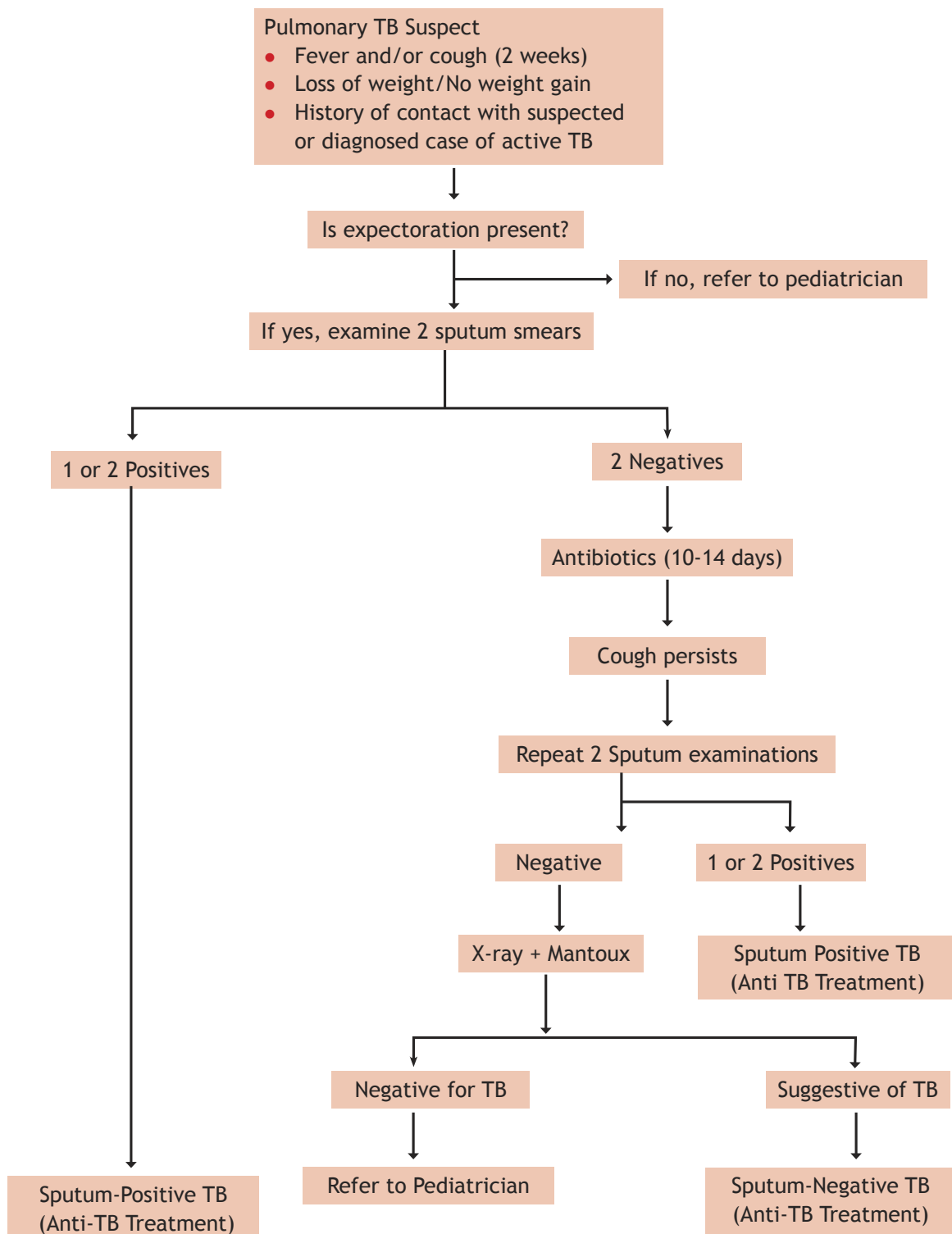
Patients with suspected EP TB should be referred to a competent medical practitioner for expert opinion. Diagnosis of such patients may be made using appropriate diagnostic procedures (such as FNAC/Biopsy) as well as clinical methods.

Diagnosis of TB by chest X-ray alone is unreliable because no radiological pattern is pathognomic of pulmonary TB. Unless the prescribed algorithm given below is followed, a large number of patients who do not have TB will be falsely diagnosed and treated.

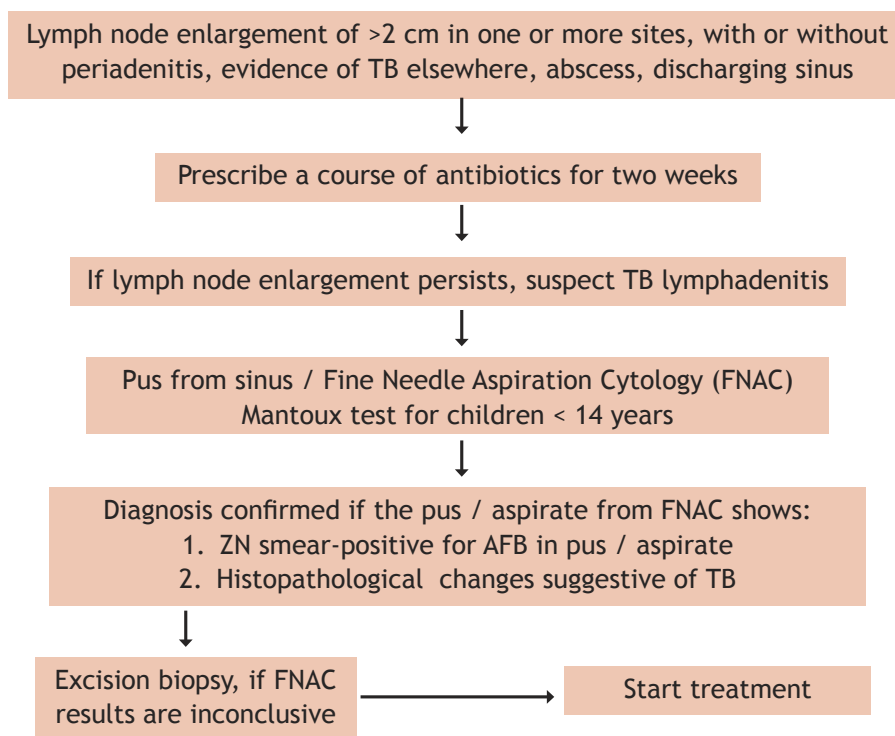
Diagnostic Algorithm for Pulmonary TB



Diagnostic algorithm for pediatric pulmonary tuberculosis



Diagnostic algorithm for TB lymphadenitis



Sputum smears are examined and interpreted as indicated in the table below

If the slide has:	No. of fields to be examined	Grading	Result
No AFB in 100 oil immersion fields	100	0	Neg
1-9 AFB per 100 oil immersion fields	100	Scanty*	Pos
10-99 AFB per 100 oil immersion fields	100	1+	Pos
1-10 AFB per oil immersion field	50	2+	Pos
More than 10 AFB per oil immersion field	20	3+	Pos

*Record actual number of bacilli seen in 100 fields - e.g. "Scanty 4"

Smear-positive results including those of scanty positives are always recorded in red ink in the tuberculosis laboratory register.

When the referring Medical Practitioner receives the results of sputum examination, and it is decided to put the patient on chemotherapy, health education must be imparted to the patient. The patient is told about TB, how it spreads, precautions to be taken to prevent the spread, importance of directly observed treatment and its duration, and the need for prompt evaluation of children under six years or contacts with cough of any duration living in the household. The patient should also be informed that his address would be verified by a competent person prior to the start of treatment.

Tools for diagnosis of Pulmonary TB in adults:

- Sputum smear microscopy
- Chest X-ray
- Sputum culture and DST for diagnosis of Drug Resistant TB
- Newer rapid diagnostic tools for detection of MDR TB
- Newer tools under evaluation for diagnosis of MDR/XDR TB

Sputum Microscopy

Sputum smear microscopy is the most widely used and acceptable testing tool for diagnosing smear-positive pulmonary TB. Ziehl-Neelsen staining technique is used in RNTCP. Sputum microscopy has the following advantages:

- Simple, inexpensive, requires minimum training
- High specificity
- High reliability with low inter-reader variation
- Can be used for diagnosis, monitoring and defining cure
- Results are available quickly
- Feasible at peripheral health institutions
- Correlates with infectivity in pulmonary TB cases

Therefore, this is the key diagnostic tool used for case detection in RNTCP.

X-ray

Chest X-ray as a diagnostic tool is more sensitive but less specific with higher inter and intra reader variation. However, it should be used judiciously. It should always be preceded by a repeat sputum smear examination, following treatment with antibiotics (refer to diagnostic algorithm). It is also useful for diagnosing extra pulmonary TB like pleural effusion, pericardial effusion, mediastinal adenopathy and miliary TB. The following are the limitations of chest X-ray as a diagnostic tool:

- High inter and intra-reader variation
- No shadow is characteristic of TB
- 10-15% culture-positive cases remain undiagnosed (under reading)
- 40% patients diagnosed as having TB by X-ray alone may not have active TB disease (over reading).

Sputum smear microscopy is the primary tool for diagnosing TB as it is more specific and has less inter and intra-reader variability than X-ray.

Diagnosis of Drug Resistant-TB

Culture of Mycobacterium tuberculosis bacilli is a very sensitive and specific tool. It is the gold standard for evaluating other tools of diagnosis. It is mainly used for the diagnosis of drug resistant TB as it is expensive (liquid culture systems) and time consuming (solid culture). Drug susceptibility testing using the proportion susceptibility method is the accepted gold standard.

Diagnostic Tools for MDR-TB / XDR TB

Drug resistant TB (MDR/XDR and other types) is a laboratory based diagnosis either phenotypically i.e., growing the bacteria (culture) and demonstrating the ability of bacteria to grow in the presence of the anti-TB drugs (drug sensitivity testing - DST) or genotypically by demonstrating the presence of resistance genes using molecular methods.

The conventional and newer rapid tools used for diagnosis are

- Solid culture medium - Egg-based Lowenstein Jensen or Agar-based 7H11/10 medium
- Liquid culture medium - Commercial automated MGIT 960.

Newer Rapid Diagnostic Tools include

Non-commercial solid culture methods - Nitrate Reductase Assay using the property of M.Tb to reduce nitrate to nitrite as means of detection of drug resistance.

Non-commercial liquid culture methods include - Microscopic observation of drug susceptibility assay (MODS) using 7H9 medium in microtitre wells and observing growth using an inverted microscope for both culture and DST.

Liquid culture system - Mycobacteria growth indicator tube system (MGIT) available in automated (MGIT-960) and MGIT manual systems. This can detect growth of mycobacteria as early as 4 days from inoculation and DST will be available in 21-28 days.

Molecular Assays - PCR based technologies using various modifications are used for detecting the presence of putative resistance genes (**rpoB for rifampicin, katG and inhA for INH etc**). The most widely evaluated and used assays are Line Probe Assays (LPA) which are based on in-situ hybridization on nitrocellulose strips of specific genetic targets for resistance genes. These are now available for RIF and INH resistance (MDR-TB) and will be

shortly available for XDR-TB (resistance to aminoglycosides, polypeptides, fluoroquinolones and ethambutol).

Newer tools under evaluation include, **Cepheid GeneXpert** - a completely closed automated system using real-time PCR which has a sensitivity of 70-90% even for smear negative cases and can also detect the presence of rifampicin resistance.

TB in HIV Positive Patients

Pulmonary TB (PTB) is most common form of TB disease. HIV positive and HIV negative patients with active pulmonary TB generally manifest similar clinical features, namely cough, fever, night sweats, haemoptysis and weight loss. The presentation may sometimes vary with the degree of immune suppression. In patients with mild immune suppression, the clinical picture often resembles usual adult post-primary pulmonary TB i.e., the sputum smear is frequently positive for acid-fast bacilli (AFB), and the chest X-ray (CXR) typically may show unilateral or bilateral upper lobe infiltrates, cavitations, pulmonary fibrotic changes, and/or volume loss.

In severely immune suppressed patients, the overall risk of TB is even higher, but it is more difficult to distinguish TB from other serious chest diseases. In persons with advanced HIV infection, disseminated and extrapulmonary TB (EPTB) are more common than in early HIV infection and may be as common as pulmonary TB. The most common forms of EPTB seen are lymphadenitis, pleural effusion, pericarditis, miliary disease and meningitis. In PTB, the features of the disease are frequently atypical, resembling those of primary TB as historically seen in children. Smear-negative TB is as common as smear-positive TB. The chest X-ray pattern in advanced HIV infection may show any pattern. Hilar lymphadenopathy is frequently observed and interstitial infiltrates tend to be common, especially in the lower zones; features such as cavitation or fibrosis are less common. Infiltrates may be unilateral or bilateral, and are seen more often in the lower lobes than in the upper lobes

Features of PTB	Stage of HIV Infection	
	Early	Late
Clinical Picture	Often resembles post-primary TB	Often resembles primary TB
Sputum Smear Result	Often positive	Often negative
Chest X-Ray Appearance	Often cavities	Often infiltrates with no cavities

The advent of HIV has made the diagnosis of TB more difficult, and false diagnosis of TB probably occurs frequently among patients affected by other HIV-related illnesses. These false-positive diagnosis in most cases, however account for a very small proportion of all forms of TB notified and thus do not negate the huge increase observed in TB notifications in HIV-endemic areas.

Intensified TB Case Finding at ICTCs, ART and Community Care Centres (CCCs)

Intensified TB case finding should be established in ICTCs, ART Centres & CCCs. Intensified case finding means screening for symptoms and signs of TB in places where HIV-infected people are concentrated, followed by diagnosis and prompt treatment; which increases chances of survival, improves quality of life and reduces transmission of TB.

All ICTC clients should be screened by the ICTC counselors for the presence of symptoms of TB disease (at pre, post and follow-up counseling). All clients who have symptoms or signs of TB disease, irrespective of their HIV status, should be referred to the nearest facility providing RNTCP diagnostic and treatment services.

Quality Assurance

An effective quality assurance (QA) system for sputum smear microscopy is an integral part of RNTCP. QA is a total system consisting of internal quality control (IQC), assessment of performance using external quality assessment (EQA) methods and continuous quality improvement (QI) of laboratory services.

3 components of EQA are:

- Onsite Evaluation (OSE)
- Random Blinded Re-checking (RBRC)
- Panel Testing

Points to Remember

- The most common symptom of pulmonary TB is a persistent cough for two weeks or more
- Patients suspected to have pulmonary TB should have two sputum smears examined
- Sputum samples should be examined as soon as possible and not later than 2 DAYS after it is collected
- The role of chest X-rays in the diagnosis of pulmonary TB is only supportive
- About 2-3% of new adult outpatients in a general clinic will be TB suspects and should be sent for sputum examination
- About 10% of TB suspects are expected to have sputum smear-positive pulmonary TB

Exercise 1

PART A: Write your opinion on the following case studies and complete the laboratory forms if the patient needs sputum examination:

1. Meena Patel, a 25 year old resident of 225, Bapu Nagar of your city complains that she feels tired for the last few days. On further questioning, she reveals that she has had a cough for 4 weeks. She does not have any other symptoms. She has never taken anti-TB drugs.
2. Lakshmi Kumari, 41 years and resident of 18, M.G. Road of your city, has had a cough for two months with fever, night sweats and occasional coughing up of blood. She had taken treatment for TB two years back for about 5 months and discontinued treatment on her own.
3. Ashok Patel, a 30 year old man who lives with his parents, is having cough for the past 8 days. His father is under treatment for sputum smear-positive pulmonary TB for the past 1 month. Ashok does not have any other complaint.
4. Paravathi Sinha, an 18 years old resident of 12, Bapu Nagar of your city presented with non-tender swelling of the lymph nodes in neck region which appeared 3 months ago. These nodes are slowly growing in size. She does not have cough.
5. Lallan Prasad, a 30 year old resident of 19, Sidharth Apartment city presented with complaints of fever for 1 month. He also complained of having cough for 1 month and loss of weight.

PART B: Complete the bottom section of the laboratory form. Start with the laboratory serial number. Specimens have been examined on 10th January 2008. Sign your own name.

Patient Number of AFB (visual appearance)

Meena Patel - A

30 AFB are seen in 100 oil immersion fields (muco-purulent)

140 AFB are seen in 50 oil immersion fields (muco-purulent)

400 AFB are seen in 50 oil immersion fields (muco-purulent)

Lakshmi Kumari -B

200 AFB are seen in 50 oil immersion fields (muco-purulent)

400 AFB are seen in 50 oil immersion fields (muco-purulent)

Ashok Patel - C

0 AFB are seen in 100 oil immersion fields (muco-purulent)

0 AFB are seen in 50 oil immersion fields (saliva)

Lallan Prasad - E

0 AFB are seen in 100 oil immersion fields (mucopurulent)

0 AFB are seen in 50 oil immersion fields (mucopurulent)

PART C: Complete the first page of the Laboratory Register using the laboratory forms you have prepared with information in Part 'A' and Part 'B'.

(NB: Training facilitators may distribute photocopies of laboratory register page)

3 Administering Treatment

Diagnosis of TB in itself has little purpose unless it is followed by effective treatment.

The goal of anti-TB treatment is to ensure cure, while preventing the emergence of drug resistance. A patient with TB should be put on treatment within one week of diagnosis.

The following is required before starting treatment:

- History of patient, including history of any previous treatment for TB
- Sputum smear examination results from an approved DMC
- Chest X-ray report if the case warrants radiographic examination
- Other supporting investigation reports, if any

The disease classification, type of case, sputum result, severity of illness and history of previous treatment are the factors that determine the regimen used for treating a TB patient.

RNTCP uses short course chemotherapy given intermittently - thrice weekly under Direct Observation for both pulmonary and extra pulmonary tuberculosis patients.

Scientific Basis of Treatment of TB

The strategies adopted in the treatment of TB are based on both scientific and operational research.

The following four components are discussed in brief.

1. Domiciliary treatment
2. Short course chemotherapy
3. Intermittent regimen
4. Direct observation of treatment

Domiciliary Treatment

Domiciliary chemotherapy has been proved to be as effective as sanatoria treatment. Studies in India have shown that smear-positive TB patients treated on a domiciliary basis have achieved high cure rates as good as those when treated at sanatorium, besides having other social benefits of being at home.

Short Course Chemotherapy

Short course chemotherapy regimens have made it possible to treat and cure TB patients in as short a period as six to eight months. Reduction in the duration of treatment regimens was possible because of the introduction of Rifampicin and Pyrazinamide. Treatment regimens of six months duration either given daily, or on intermittent basis have been found to be equally effective and achieve high cure rates, prevent emergence of drug resistance and minimize relapses. The shorter duration has contributed to improvement in the treatment adherence. Intermittent short course chemotherapy regimens of 6-8 months are recommended internationally for all forms of extra-pulmonary TB.

Basis of chemotherapy

(a) Bacteriological basis

i. Existence of naturally occurring drug resistant mutants

In an untreated smear-positive pulmonary tuberculosis patient, there are naturally occurring drug resistant mutants to different drugs at different frequencies. The larger the bacterial population, higher is the probability that resistant mutant strains are present. The number of bacilli are lower in smear-negative and extra pulmonary lesions. The number of viable bacilli commonly found inside the cavities sized about 2 centimeters in diameter on an average, is likely to be in excess of 100 million (10⁸). As a thumb rule, the frequency of occurrence of drug resistant mutants would be roughly ~ 1 in 10⁶ to isoniazid (H), ~ 1 in 10⁶ to streptomycin (S) and ~ 1 in 10⁸ to rifampicin (R). Based on these frequencies, the chances of naturally occurring organisms that is resistant to both H and R would be roughly ~ 1 in 10¹⁴, which is virtually negligible.

There would be appreciable numbers of mutants, resistant to any single drug before the start of the treatment, that are capable of multiplying and will not be affected by a single drug, e.g. isoniazid. This accounts for frequent failures observed with monotherapy of patients

harbouring large number of bacilli. Thus, if two or more drugs are given concurrently, in the initial Intensive Phase when the bacterial load is high, the chances of survival and selection of drug resistant organism to any drug would be very small as mutants resistant to one drug are as a rule susceptible to other and vice versa. This is the basis for the use of multi-drug therapy in the treatment of tuberculosis.

Role of intensive phase

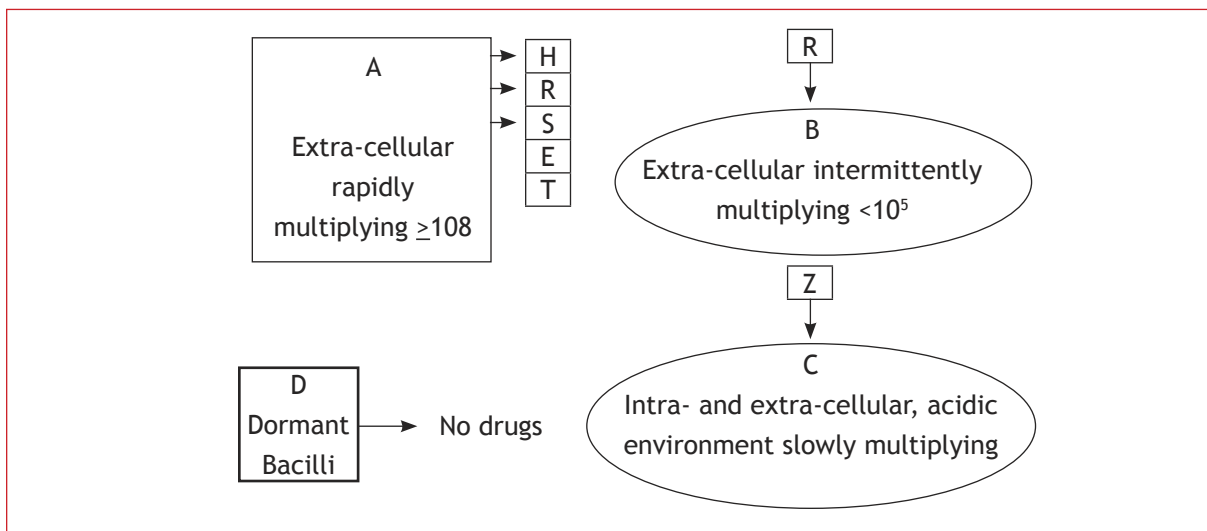
The objective of combining four drugs in the intensive phase (IP) is to achieve rapid killing of actively multiplying bacillary population. This phase will eliminate naturally occurring drug resistant mutants and prevent the further emergence of drug resistant mutants. An optimal minimum duration of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

Role of continuation phase

Continuation phase (CP) with fewer drugs for a comparatively longer time will ensure elimination of persisters which are responsible for relapses. The optimum duration of continuation phase is four months in new cases.

ii. Existence of sub-bacillary population

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



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

Anti-TB drugs have the following three actions:

- a. Early bactericidal activity
- b. Sterilizing activity
- c. Ability to prevent emergence of drug resistance

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

Rifampicin (R): Rifampicin is a potent bactericidal and sterilizing drug acting on semi-dormant bacilli which multiply intermittently, thereby causing relapse.

Pyrazinamide (Z): Pyrazinamide is a bactericidal and sterilizing drug effective in eliminating the semi-dormant bacilli multiplying slowly in an acidic environment.

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

Streptomycin (S): Streptomycin is a bactericidal drug known to reduce septicaemia and toxicity.

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

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

Pharmacological basis of treatment

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

Intermittent Treatment

Intermittent regimens should only be used in a programme of directly observed treatment (DOT). The formulation of intermittent regimens in the treatment of TB is based on the principle of existence of lag period. “In vitro experiments demonstrated that, after a culture of *M. tuberculosis* is exposed to certain drugs for some time, it takes several days before new growth occurs”. Thus, there is no need to maintain blood levels of drugs for 24 hours in the treatment of tuberculosis. The ability of the drugs to continue to exert its antimicrobial activity even after their withdrawal is called lag period. This renders the intermittent regimen possible. Intermittent dosing increases the efficacy of treatment by allowing organisms to re-enter the active metabolic phase in which the bactericidal drugs are more effective.

Advantages of intermittent regimen are:

- As effective as daily treatment
- Facilitates DOT
- Reduction in total quantity of drugs consumed
- Fewer adverse reactions

Directly Observed Treatment (DOT)

Studies in India and many other countries have consistently shown that at least one third of patients do not consume medicines regularly. DOT is a supportive mechanism that ensures the best possible results in treatment of TB. Here, a DOT Provider helps the patient in taking the treatment, thereby ensuring adherence. Many patients who do not receive directly observed treatment stop taking drugs once they feel better. It is neither possible to predict who these patients will be nor to prevent non-adherence through health education. Studies have shown that there will be poor treatment outcome and high death rates in the absence of DOT, even when regular supply of drugs is ensured. Hence, by providing DOT, RNTCP ensures that patients receive the right drugs, in the right doses, at the right intervals and for the right duration.

Definitions: The Revised National Tuberculosis Control Programme

Case definitions	Type of cases	Treatment outcomes
<p>Pulmonary Tuberculosis, Smear-Positive TB in a patient with atleast one smear-positive for AFB out of the two initial sputum smear examination by direct microscopy</p> <p>Pulmonary Tuberculosis, Smear Negative A patient with symptoms suggestive of TB with two smear examination negative for AFB, with evidence of pulmonary TB by microbiological methods (culture positive or by other approved molecular methods) or Chest X-ray is classified as having smear negative pulmonary tuberculosis</p> <p>Extra Pulmonary Tuberculosis* Tuberculosis in any organ other than lungs (eg. pleura, lymph nodes, intestine, genitor-urinary tract, joint and bones, meninges of the brain etc).</p> <p>The diagnosis should be based on strong clinical evidence with the following investigations</p> <ul style="list-style-type: none"> • Smear/Culture from extrapulmonary sites • Histopathological examination or • Radiological examination or • Biochemical and cytological examination including FNAC 	<p>New A TB patient who has never had treatment for TB or has taken anti-TB drugs for less than one month</p> <p>Relapse A TB patient who was declared cured or treatment completed by a physician and who reports back to the health facility and is now found to be sputum smear-positive</p> <p>Transferred in: A TB patient who has been received for treatment in a Tuberculosis Unit, after starting treatment in another TB unit where s/he has been registered.</p> <p>Treatment after default: A patient, who has received treatment for TB for a month or more from any source and returns for treatment after having defaulted i.e., not taken anti-TB drugs consecutively for two months or more and found to be smear-positive</p> <p>Treatment failure Any TB patient who is smear-positive at 5 months or more after initiation of treatment.</p> <p>Chronic A patient who remains smear-positive after completing regimen for previously treated but not initiated on MDR-TB treatment</p> <p>Others A patient who does not fit into the any of the types mentioned above. The reasons for labeling a patient under this type must be specified in the Treatment card and TB Register#</p>	<p>Cured Initially sputum smear-positive patient who has completed treatment and had negative sputum smears on two occasions, one of which was at the end of the treatment</p> <p>Treatment completed Initially sputum smear-positive patient who has completed treatment with negative smears at end of the intensive phase/two months in the continuation phase, but none at the end of the treatment is declared as treatment completed. Or Initially sputum smear negative patient who has received full course of treatment and has not become smear-positive at the end of the treatment or</p> <p>Extra pulmonary TB patient who has received full course of treatment and has not become smear-positive during or at the end of treatment</p> <p>Died Patient who died during the course of treatment regardless of any cause</p> <p>Failure Any TB patient who is smear-positive at five months or more after initiation of the treatment and not put on MDR-TB treatment</p> <p>Defaulted A Patient after treatment initiation has interrupted treatment consecutively for >2 months</p> <p>Transferred out A patient who has been transferred to another TU and whose treatment outcome is still not available.</p> <p>Switched over to MDR-TB Treatment A patient who has been diagnosed as having MDR-TB by an RNTCP accredited laboratory, prior to being declared as “Failure”, and is placed on the RNTCP MDR-TB treatment regimen</p>

* Pleurisy is classified as extra pulmonary tuberculosis,

* A patient diagnosed with both smear-positive pulmonary and extra pulmonary TB should be classified as pulmonary TB

Others can come both under new and previously treated.

Treatment Regimens

For the purpose of treatment regimen to be used, TB patients are classified into two groups, namely, “New” or “Previously Treated”, based on the history of previous treatment.

Regimen for New cases: This regimen is prescribed to all new pulmonary (smear-positive and negative), extra pulmonary and ‘others’ TB patients.

The regimen is $2H_3R_3Z_3E_3 / 4H_3R_3$.

Treatment is given in two phases. For “New” patients, the intensive phase consists of isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) given under direct observation thrice a week on alternate days and lasts for 2 months (8 weeks, 24 doses). This is followed by the continuation phase, which consists of 4 months (18 weeks; 54 doses) of isoniazid and rifampicin given thrice a week on alternate days with at least the first dose of every week being directly observed. If the sputum smear is positive after 2 months of treatment, the intensive phase of four drugs (H, R, Z and E) are continued for another one month (12 doses) and sputum examined after the completion of the extension of intensive phase. Irrespective of the sputum results after this extension of the intensive phase, the 4 months (18 weeks) of the continuation phase is started. If the sputum smear is positive after 5 or more months of treatment, the patient is declared as a “Failure” and is placed on the “Previously Treated” treatment regimen afresh, and sputa sent for culture and drug susceptibility testing (C&DST) to an accredited RNTCP C&DST laboratory.

While treating TB meningitis in “New” patients, streptomycin is to be used in place of ethambutol during the intensive phase ($H_3R_3Z_3S_3$ instead of $H_3R_3Z_3E_3$). The continuation phase of treatment for patients with TBM or spinal TB is for 7 months. Hence, the total duration of treatment will be for 9 months. Steroids as adjunctive therapy may be useful in patients with TB pericarditis and meningeal TB, with an initial high dose tapered downwards gradually over 6 - 8 weeks.

Regimen for Previously Treated cases: This regimen is prescribed for TB patients who have had more than one month anti-tuberculosis treatment previously. These patients are at a higher risk of having drug resistance. Hence, 5 drugs are prescribed in the intensive phase, and the total duration of treatment is 8 months. **Relapses, Treatment After Default, Failures and Others** are treated with this regimen.

The regimen is 2S₃H₃R₃Z₃E₃ / 1H₃R₃Z₃E₃ / 5 H₃R₃E₃.

Treatment is given in two phases. For “Previously Treated” cases, the intensive phase consists of two months (24 doses, 8 weeks) of isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E) and streptomycin (S), followed by one month (12 doses, 4 weeks) of isoniazid, rifampicin, pyrazinamide and ethambutol, all given under direct observation thrice a week on alternate days. Patient is subjected for follow-up sputum examination at the end of three months. If the sputum smear is positive at the end of 3 months of treatment, the intensive phase drugs (H, R, Z and E) are extended for another one month (12 doses, 4 weeks). Irrespective of the sputum results at the end extended intensive phase, 5 months (22 weeks) of continuation phase is started. If the sputum remains positive at the end of the extended intensive phase, sputum is sent to an accredited RNTCP C&DST laboratory for culture and drug susceptibility testing. The continuation phase consists of 5 months (22 weeks; 66 doses) of isoniazid, rifampicin and ethambutol given thrice a week on alternate days, with at least the first dose of every week being directly observed.

The experience in India and elsewhere has shown that this treatment regimen, if taken regularly, is effective and cures most patients. Relapse cases generally have better outcomes than those who are ‘Failure’ or ‘Treatment After Default’ cases. But even these latter types of patients generally respond well to treatment, provided they take it regularly and complete the treatment.

It is very important to elicit history of previous treatment for tuberculosis. It helps in defining a case; to identify patients with increased risk of acquired drug resistance and to prescribe appropriate treatment

The table below indicates the treatment regimen, type of patients and regimen prescribed.

Treatment groups	Type of patient	Regimen ¹	
		Intensive Phase (IP)	Continuation Phase (CP)
New*	Sputum smear-positive Sputum smear-negative Extra-pulmonary Others	2H ₃ R ₃ Z ₃ E ₃	4H ₃ R ₃

Previously Treated**	Smear-positive relapse Smear-positive failure Smear-positive treatment after default Others ²	2H ₃ R ₃ Z ₃ E ₃ S ₃ / 1H ₃ R ₃ Z ₃ E ₃	5H ₃ R ₃ E ₃
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1. The number before the letters refers to the number of months of treatment. The subscript after the letters refers to the number of doses per week. The dosage strengths are as follows: Isoniazid (H) 600 mg, Rifampicin (R) 450 mg, Pyrazinamide (Z) 1500 mg, Ethambutol (E) 1200 mg, Streptomycin (S) 750 mg.

- Patients who weigh 60 kg or more receive additional rifampicin 150 mg.
- Patients who are more than 50 years old receive streptomycin 500 mg. Patients who weigh less than 30 kg, receive drugs as per Paediatric weight band boxes according to body weight.

2. In rare and exceptional cases, patients who are sputum smear-negative or who have extra-pulmonary disease can have recurrence or non-resonse. This diagnosis in all such cases should always be made by an MO and should be supported by culture or histological evidence of current, active TB. In these cases, the patient should be typed as 'Others' and given treatment regimen for previously treated.

* New includes former categories I and III.

** Previously treated is former category II.

Patient wise Drug Boxes

Drugs are supplied in patient-wise boxes (PWB) containing the full course of treatment, and packaged in blister packs. The PWB have a color code indicating the **two regimen - Red for "New", Blue for "Previously Treated"**. In each PWB, there are two pouches; one for intensive phase and one for continuous phase. In the intensive phase, each blister pack contains one day's medication. For the continuation phase, each blister pack contains one week's supply of medication. The drugs for extension of the intensive phase (prolongation pouches) are supplied separately.

The table below indicates the blisters and doses in the regimen:

Regimen for New cases treatment consists of total 78 doses and for previously treated cases consists of 102 doses.

Regimen for	IP*			CP	
	Blisters	Doses	Extended IP blister and doses	Blisters	Doses
New cases (Cat-I)	24	24	12	18	54
Previously treated cases (Cat-II)	36	36	12	22	66

* Prolongation of IP for one month (12 doses) is given to new cases and previously treated cases who remain positive at the end of Intensive Phase

Drug dosages for adults in the blister packs *

Drugs	Dose (thrice a week)	Number of tablets in blister pack
Isoniazid (H)	600mg	2 x 300 mg
Rifampicin (R)	450mg**	1 x 450 mg
Pyrazinamide (Z)	1500mg	2 x 750 mg
Ethambutol (E)	1200mg	2 x 600 mg
Streptomycin (S)	0.75g***	-

*Adult patients who weigh <30kgs receive drugs in PWBs from the respective weight band suggested for paediatric patients

** Patients who weigh ≥60 kg at the start of treatment are given an extra 150 mg of Rifampicin

*** Patients over 50 years of age are given 0.5 g of Streptomycin

Treatment of Pediatric TB

Pediatric cases are to be treated under RNTCP with the same thrice weekly short course chemotherapy regimens (“New” or “Previously Treated”) given under DOT as for adult patients. They are to be registered in the respective RNTCP TB Register. Pediatric patient-wise boxes are available with different dosages as two product codes to be used under four weight bands for children weighing 6 to 10 kgs, 11 to 17 kgs, 18 to 25 kgs and 26 to 30 kgs.

Wherever possible, before a child is started on the “Previously Treated” regimen, s/he should be examined by a Pediatrician or TB expert.

Pediatric PWB with Dosages

Drugs	Product code (PC) -13		Product code (PC) -14		PC-15	PC-16
	IP 24 blisters	CP 18 blisters	IP 24 blisters	CP 18 blisters	12 blisters	12 blisters
Isoniazid	75 mg	75 mg	150 mg	150 mg	Prolongation of IP for PC 13	Prolongation of IP for PC 14
Rifampicin	75 mg	75 mg	150 mg	150 mg		
Pyrazinamide	250 mg		500 mg			
Ethambutol	200 mg		400 mg			

Pediatric patient wise boxes for new cases according to weight band

Weight band	For New cases		Prolongation of IP
	IP	CP	
6-10 Kg	PC 13		PC 15
11-17 Kg	PC 14		PC 16
18-25 Kg	PC 13 + PC 14		PC 15 + PC 16
26-30 Kg*	PC 14 + PC 14		PC 16 + PC 16

* For children weighing >30 kgs, adult PWB are to be used

** For patients falling in b/w weight bands should be put on lower wt band

Pediatric patient wise boxes for previously treated cases according to weight band

Weight	For previously treated cases		Prolongation of IP
	IP	CP	
6-10 Kg	(PC 13+ PC 15) + (24 vials Inj. SM *)	(PC 13 + 54 Tab E 200 mg) + (PC 15 without Z)	PC 15
11-17 Kg	(PC 14 + PC 16) + (24 vials Inj. SM *)	(PC 14 + 54 E 400 mg) + (PC 16 without Z)	PC 16
18-25 Kg	(PC 13 + PC 14 + PC 15 + PC 16) + (24 vials Inj. SM *)	(PC 13 + PC 14 + 54 Tab E 600 mg) + (PC 15+ PC 16 without Z)	PC 15 + PC 16
26-30 kg	(PC 14 x 2)+ (PC 16 x 2) + (24 vials Inj. SM*)	(PC 14 x 2+ 54 Tab E 800 mg) + (2 x PC 16 without Z)	PC 16 x 2

* Injection streptomycin 15mg/Kg body weight

- DOTS is the recommended strategy for treatment in adults and children
- All pediatric TB patients should be registered under RNTCP

Non-DOTS (ND) treatment regimen under RNTCP

In rare and exceptional situations, non-DOTS treatment (with a self-administered non-rifampicin containing regimen) may be needed in a few TB cases. Examples include:

- Those with adverse reactions to rifampicin and/or pyrazinamide
- “New” patients who refuse DOTS despite all efforts

To facilitate registration of patients started on non-DOTS regimens, a Tuberculosis Treatment Card should be filled. A maximum of 1% of patients may get non-DOTS treatment in an RNTCP

area. The justification for initiating patient on non-DOTS treatment should be specified in the “Remarks” column of the treatment card and TB register.

This is a treatment regimen of 12-month duration, comprising 2 months of SHE and 10 months of HE (2SHE / 10HE).

Dosages administered per day in the regimen are:

Isoniazid	-	300 mg
Ethambutol	-	800 mg
Streptomycin	-	750 mg (500 mg for those >50 years of age).

Those who weigh less than 30 kgs receive dosages calculated as per body-weight.

Organization of DOT and Flow of Patients for Treatment

After receipt of the sputum results, the MO of the Peripheral Health Institution (PHI) takes the following measures:

- Establishment of diagnosis of tuberculosis and decision on type of patient and treatment regimen
- Motivation of patients :
 - Explanation about the disease and assured cure.
 - Modalities of treatment-dosage schedule, duration, follow-up, common side-effects and methods to prevent them
 - Importance of directly observed treatment (DOT)
 - Need for screening of children and symptomatic contacts
- Identification of suitable DOT Centre and DOT Provider - accessible and acceptable to the patient and accountable to health system
- Opening of Tuberculosis Treatment Card (in duplicate) and the TB Identity Card
- Arrangement for shifting patient-wise box to the DOT Centre along with the duplicate TB Treatment Card, TB Identity Card and sputum containers for collection of early morning samples for follow-up examinations.

For the purpose of identifying an ideal DOT provider and an appropriate DOT Centre, a **DOT Directory** should be maintained at PHI level. This directory should contain a locality-wise list of DOT Centres / DOT Providers in the area. It should be updated regularly. **DOT can be provided by anyone other than the member of patient’s family. It** is the responsibility of the

Government field staff (PHWs / MPWs) to organize and ensure DOT for the patient. They would also monitor and supervise the community DOT Providers in their respective sub centres.

If the patient is to be given DOT by a **Peripheral Health Worker (PHW) / Community DOT Provider**, a duplicate treatment card will be prepared and given to the PHW. The MO of the PHI will give the patient-wise box containing drugs for the entire duration of treatment to the PHW and records the same in the drug stock register maintained at the PHI.

The PHW visits the house of the patient as soon as possible for confirmation of the residential address and has a detailed dialogue with the patient and other members of the family. Patient should be started on treatment within a week. Emphasis is given to the points similar to the ones mentioned above for the MO-PHI. This opportunity should also be used for screening of contacts. The initial home visit should be recorded in the treatment card in the space provided. A convenient location for drug administration and a suitable DOT provider is decided mutually by the PHW and the patient.

Documentation for Referral for Treatment

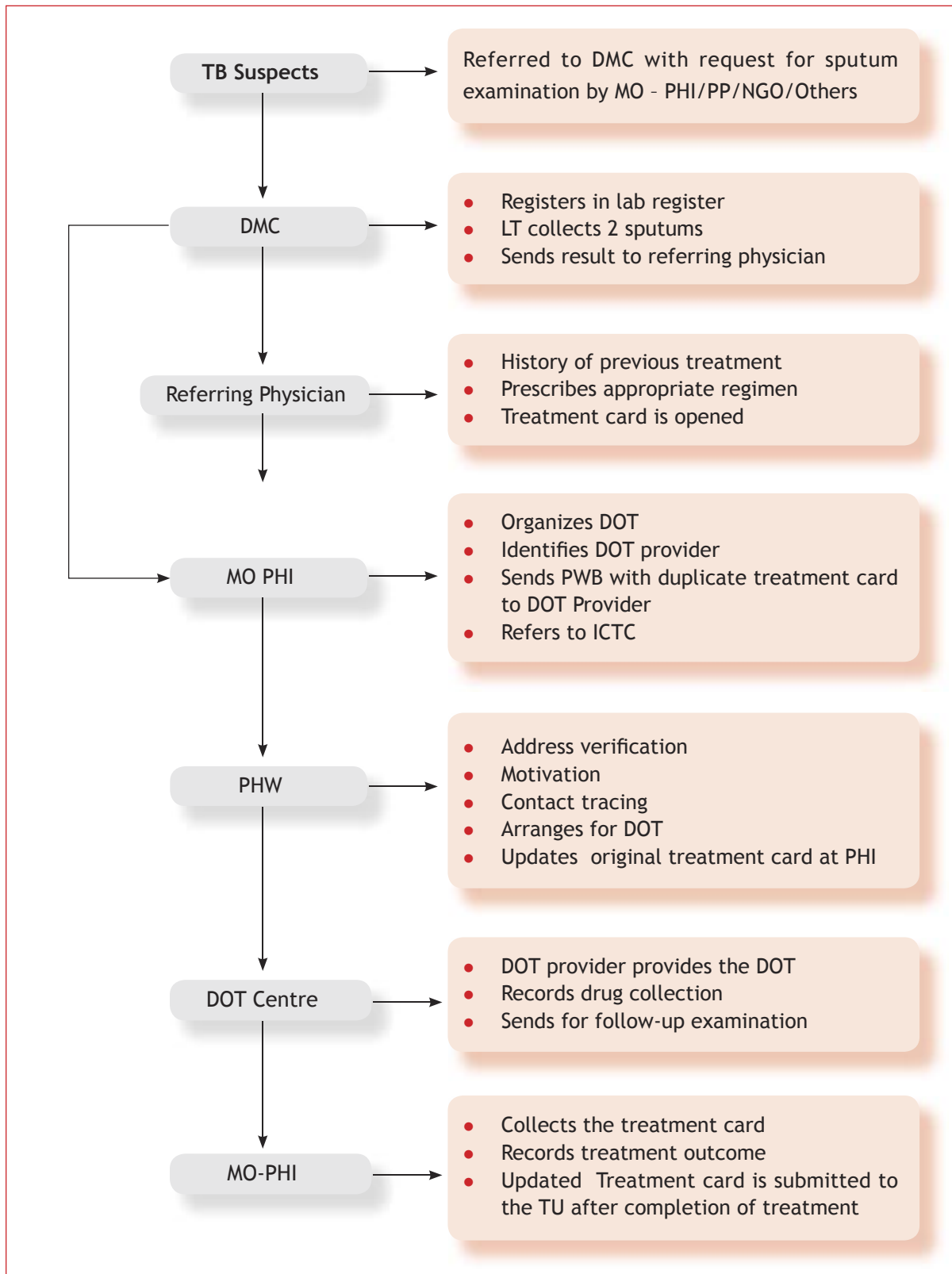
If the patient resides outside the jurisdiction of the referring institution, a copy of the 'Referral for Treatment' Form must be sent to the facility where the patient will begin treatment. A "Referral for Treatment" Register should be maintained in DMCs / DOT Centre of bigger hospitals, including that of medical colleges, that are referring large numbers of patients to other health facilities for treatment (after diagnosis). Information regarding referral of a patient should be noted in the "Referral for Treatment" Register as well as the "Remarks" column of the Tuberculosis Laboratory Register.

Peripheral health worker should visit patient's residence before the commencement of treatment. However this should not result in delay in treatment initiation.

Treatment Related Information

DOT and its necessity: It is important for the patient to take the drugs under observation. The real purpose of direct observation is to develop a human bond with the patient and not to mechanically watch the patient swallow the drugs. Patients, if given self administered

Flow of Patients for Treatment



treatment are likely to take it irregularly or discontinue the treatment upon relief of symptoms. **Early Disappearance of symptoms is not a sign of cure.** It is very important for the patient to know the **duration of treatment** and understand the necessity of taking all prescribed drugs regularly. It is dangerous to take only part of the prescribed drugs because in such cases the disease may become incurable.

A place mutually convenient to the patient and the provider can be chosen for provision of DOT. The necessity of direct observation of every dose of drugs taken during the intensive phase and the first dose of the weekly blister pack during the continuation phase should be emphasized to the patient. The patient is also explained about the importance of sputum smear conversion at the end of 2(3) months and at the completion of treatment. Patient should be made aware that **treatment services are provided free of cost.**

Role of rest, special diet and isolation: Patient and family members are made to understand that once the treatment is started, patient ceases to spread the infection and there is no need to isolate him in terms of accommodation, use of utensils and clothes. At the same time, health staff should be careful enough not to over emphasize on special diet and rest. They can be told to take the food they can afford and rest only if constrained by physical weakness. Patient should be impressed that it is the treatment alone which cures.

Cough hygiene and sputum disposal: Patient should be educated in exercising the cough hygiene - not resorting to indiscriminate coughing and spitting and covering the mouth while coughing or sneezing.

Provision of transfer facility during treatment: In case the patient wishes to shift or migrate to other TU / district / state after the initiation of the treatment, she/he should be informed that there is a provision of transfer facility for treatment. Any such event should be duly informed to the treating medical officer for completing the formalities for transfer and necessary arrangement for further treatment.

Referral for HIV counselling and testing: All the patients diagnosed as TB cases should be encouraged and referred to the nearest ICTC for HIV testing.

Co-morbid conditions; for example, diabetes, renal failure, patient on immunosuppressive drugs: History regarding the conditions mentioned above and any treatment for the same has to be elicited as these conditions and treatment for the same may adversely

interfere with the TB Treatment, Patients are to be referred to the respective speciality and managed appropriately depending upon the co-morbid conditions.

Adherence to follow-up schedules: The patients should be impressed upon the necessity of complying with periodic follow-up sputum examination schedule as advised. This will help in objective assessment of response to the treatment. Conversion to smear negativity is a fore-runner of successful treatment.

Sensitization on adverse reactions: In case patients experience any unusual symptoms after initiation/during treatment, they should be instructed to approach the medical officer and report the same. On their own, they should not take a decision either to stop or to continue the drugs.

Smoking: It should be impressed upon the patient that smoking of tobacco will adversely affect the treatment outcome. Patients should be protected from passive smoking. The environment of the patient has to be smoke free at home/office and at clinic. Smoking status of the TB patient should be checked at every interaction. The Medical Officer has to help the patient with simple tips to quit smoking. However, if this does not yield any positive result, he should be referred to the smoking cessation clinic.

Alcohol abuse: History of addiction to alcohol should be elicited. If found alcoholic, the patient should be advised to strictly refrain from alcohol as it would increase the chances of patient developing hepatitis (Jaundice), irregularity in drug intake and adverse treatment outcome. The patients should be encouraged to give up alcohol with the help of frequent motivation, family and social support.

Importance of screening symptomatic contacts and children below 6 years: Patients should be encouraged to bring symptomatic adult contacts and all children aged six years and below for screening at health facility. This will facilitate early detection of cases among them and appropriate treatment. Eligible children will be administered chemoprophylaxis.

Treatment Card

Each patient who begins treatment for TB must have a tuberculosis treatment card. The information on the patient's treatment card should be accurate, reliable, relevant, up to date and legible as this would be the source of information for filling up of the TB register. This card

contains important information about the patient, including the following details:

General information	Data related to DOT	Treatment related information
<ul style="list-style-type: none"> • Name of the patient • Age and sex • Complete address and phone number of the patient • Occupation • Name, address and phone number of the contact person 	<ul style="list-style-type: none"> • TB unit with code • TB number with year • Name of the PHI • Name and designation of DOT provider • DOT centre • Initial home visit by whom (Name and Designation) with date 	<ul style="list-style-type: none"> • Disease classification and type • Details of sputum examination for diagnosis and follow-up • Details of X-ray and investigations for diagnosis of EPTB • History of previous anti-TB treatment • Treatment regimen • Drug intake in intensive and continuation phase • Retrieval actions for missed doses • Chemoprophylaxis for contacts aged ≤ 6 years • HIV related data • Treatment outcome with date • Remarks

The Tuberculosis Treatment Card is maintained at the health facility where the patient is initiated on treatment. For patients receiving treatment in a DOT centre other than the place of treatment initiation, a duplicate treatment card is prepared and maintained at the DOT centre by the DOT provider. The original treatment card at the PHI is to be updated at least once in a fortnight.

Administration and monitoring of treatment

Recording of drug administration and monitoring

There are two sections meant for recording the drug administration. One is for the intensive phase of treatment on the front of the card and the other, for the continuation phase on the reverse side.

Intensive phase

Month and year: Month and year of initiating the intensive phase is recorded.

Date of initiation of treatment: The date of initiation of treatment regimen prescribed is ticked (*J*) on the appropriate box under the date against the month. Subsequently, the dates on which the drugs were consumed under observation are also ticked. In this phase,

the patient comes three times a week on alternate days. Daily blisters are given either on Mondays, Wednesdays and Fridays or alternatively Tuesdays, Thursdays and Saturdays.

The date/day (for example 10th April) on which patient fails to attend for DOT is denoted by a circle (0) in the appropriate box. In case the patient attends to collect the drug the next day (for example on 11th April), the drugs missed are administered on that day and continues to take the drugs as per scheduled (for example on 12th April).

Month/year	1	2	3	4	5	6	7	8	9	10	11	12	13	14
April 10	✓		✓		✓	S		✓		0	✓	✓	S	

On the other hand, if the dose is entirely missed and the patient does not report to the health facility even on the next day, then the dose is given on the next scheduled day. It should be ensured that all doses in the intensive phase should be administered before the continuation phase is initiated. For example, if the patient was scheduled to come on 17th April but does not turn up on 17th or even on 18th but reports on 19th; the dose due on 17th is given on 19th and so on and so forth.

Month/year	15	16	17	18	19	20	21	22	23	24	25	26	27	28
April 10	✓		0		✓	S		✓		✓		✓	S	

Only under exceptional circumstances, unsupervised drug administration can be allowed for a limited number of doses. For instance, if a patient is being discharged from hospital after initiation of treatment, s/he will have to be provided with 3 doses of treatment so that her/his treatment does not get interrupted during her/his transfer to a nearby PHI. In such circumstances, the entry for unsupervised doses should be recorded by encircling the tick mark on the Tuberculosis Treatment Card and the reason for the same should be stated in the Remarks column of the treatment card.

Continuation phase

Drug administration in the continuation phase is recorded on the reverse side of the treatment card. Treatment regimen prescribed for the patient is ticked appropriately in the box provided. Number of tablets of the drugs prescribed in the regimen is also recorded in the boxes provided above the drugs.

During the continuation phase of treatment, patients collect the weekly blisters once a week on a designated day. First dose of the weekly blister is administered under direct

observation and the remaining doses in the weekly blister are given to the patient for self- administration. The month and the year in which the patient will be collecting drugs during the continuation phase are written under the Month and Year column in the table on the reverse of the Tuberculosis Treatment Card. An ‘X’ is recorded in the appropriate box (according to the dates of the month 1-31 as the case may be) to indicate the day the drugs were consumed under direct observation. A line is drawn through the remaining days of the week (after the X) to indicate that drugs for the remaining period of the week have been given (recorded as X-----) for self administration.

If the patient misses a weekly drug collection in the continuation phase completely, a circle is recorded on the day of the missed collection. On the day of the subsequent visit, the treatment is given and recorded, leaving the boxes blank as shown below:

Month/year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
June 10	S	X	—	—	—	—	—	S	0						S	X	—	

Monitoring of drug administration can be done by comparing the stock of drugs available in the patient-wise boxes with the dosages given and marked in the Tuberculosis Treatment Card. Any observed variation should be looked into and remedial measures taken.

NON-DOTS treatment (in intensive as well as continuation phases)

Date when drugs were collected by the patient is indicated by writing ‘C’ and drawing a horizontal line (C-----) to indicate the period for which drugs were supplied for self-administration. Usually drugs will be provided for a month.

Follow-up schedule for sputum examination

The most important method of monitoring the smear-positive PTB cases are by the follow-up sputum smear examinations which are carried out at the end of the intensive phase, the extended intensive phase (if applicable), two months into the continuation phase and at the end of treatment. These results determine the conversion rate from smear-positive to smear-negative at the end of intensive phase of treatment, and the cure rate at the end of the treatment. The follow-up sputum smear examination at the end of treatment is very important for evaluating the results of treatment outcome (to determine the cure rate).

Two sputum samples are to be collected, one as early morning and the other as spot sample.

The follow-up schedule for sputum collection and smear examination is provided in the table below.

Category	End of IP			Extended IP *			2 months into CP			End of treatment	
	Give sputum cup	Collect sputum #	Result by	Give sputum cup	Collect sputum #	Result by	Give sputum cup	Collect sputum #	Result by	Give sputum cup	Collect the sputum and Result by end of the treatment
New **	22	23	24	34	35	36	8	9	10	17	18
Previously Treated	34	35	36	46	47	48	8	9	10	21	22

* The Intensive Phase is extended by four weeks (12 doses) in initially smear-positive PTB patients who continue to be positive at the end of the 2 months of IP.

Early morning and spot specimens will be collected on this day.

** The numbers during the IP represent doses, whereas during the CP they represent weekly blister packs

Follow-up of sputum smear examinations of patients put on the RNTCP Non-DOTS regimen should be done at the end of 2, 6 and 12 months. It must be ensured that the patients undergo the follow-up sputum smear examination as scheduled and the last follow-up sputum examination is done before the completion of the last dose of treatment.

Chemoprophylaxis

Preventive chemotherapy with isoniazid (H) is administered to all the children aged 6 years and below who are in contact with smear-positive pulmonary TB case. The number of such children residing in the household should be enquired during the initial home visit. The parents are advised to bring their children to the Health Centre for screening for the evidence of TB. They are examined and investigated to rule out TB disease. If found to be suffering from the disease, they should be treated appropriately. Children found eligible for chemoprophylaxis after ruling out TB are to be administered preventive chemotherapy with INH 5mg/kg body weight daily for 6 months.

The number of children below 6 years of age, the number screened for TB and the number put on chemoprophylaxis should be mentioned on the reverse of the treatment card (see below).

Nos. of children below 6 Yrs	Nos. screened for TB	Nos. put on chemoprophylaxis

Determination of date of treatment outcome

Outcome	Date of determination	Illustrations
Cured or Treatment Completed	The last dose (Pyridoxine) of the 18 th blister in New and 22 nd blister in Previously Treated cases.	Patient administered last DOT in continuation phase on 16-06-2010. Last pyridoxine dose taken on 22-06-2010. then the outcome will be written as <i>Cured or treatment completed on 22-06-2010.</i>
Transferred out	Transferred out is the date in which the patient is supposed to have consumed the last dose of the drugs provided to him on transfer as recorded in the card. This is only an interim outcome. The actual outcome as reported from the unit where the patient was transferred will be updated in the card and in the TB register.	Generally drugs up to one week are given for self administration during transfer - maximum of three doses in the intensive or continuation phase. <i>Actual date on which transfer form was filled and sent is 20-06-2010; then the date of transferred out as a treatment outcome should be 27-06-2010. This is the date when the 3rd dose handed over during transfer is supposed to have been consumed.</i>
Defaulted	The scheduled date of administration of drug when patient interrupted treatment consecutively for ≥ 2 months.	Patient interrupted treatment on 16-9-2010. Record outcome as <i>'defaulted on 16-9-2010'</i> on or after 17-11-2010 within one month.
Failure	The date on which the sputum examination was found to be positive for AFB	If the smear result is positive on 18-05-2010, <i>Failure on 18-05-2010.</i>
Died	The actual date of death	Patient died on 11-08-2010, <i>Died on 11-08-2010.</i>
Switched to MDR-TB treatment	The date on which the patient is started on RNTCP MDR-TB treatment regimen.	Patient declared as MDR-TB on 01-01-2010 and put on MDR- TB treatment on 21-01-2010. the date for <i>Switched to MDR-TB treatment</i> would be 21-01-2010.

A patient will have only one outcome. The outcome which occurs first is considered and recorded in treatment card and subsequently in the TB register.

Remarks Column

The following information has to be recorded in the remarks column

- Adverse drug reactions, if any
- Reasons for unsupervised dose(s)
- Reason for discontinuation of drug collection (e.g., patient transferred to another district)
- Details of hospitalization if any during the treatment
- Information on dispatch of sputum for culture of sensitivity tests
- Any other relevant information about the patient such as smoking, diabetes mellitus, pregnancy status etc.,

HIV Related Data

This box is meant for recording information regarding the HIV status of the patient, and if positive, details of CPT and ART being administered.

Original TB Treatment Card

Information on HIV status, CPT delivery and ART referral and initiation of the TB patient are to be documented on the original TB treatment card and kept confidential within the health system. This should not be disclosed to the community DOT provider.

Additional Treatments					
HIV Status: Unknown	1.	<input type="checkbox"/> Positive	<input type="checkbox"/> Negative	(Date)	_____
CPT delivered on (date)	2.	(1)	(2)	(3)	(4) (5)
Pt referred to ART centre (date) :	_____				
Initiated on ART:	<input type="checkbox"/> No	<input type="checkbox"/> Yes	(date)	_____	

HIV Status

- i. HIV testing is a voluntary procedure and not mandatory. Patients not willing for HIV testing or sharing their HIV test result should not be forced to undergo testing or disclose their HIV status.
- ii. If HIV status of the patient is known, tick the appropriate box ('Pos' or 'Neg') and record the date of test along with PID Number if available. If the HIV status is not known, don't tick any box initially.
- iii. Patients already on HIV care should not be required to show proof of HIV test result.
- iv. If the HIV status is ascertained during the course of TB treatment, the latest information should be updated on the card.
- v. If HIV status of the patient remains unknown at the end of treatment, tick the appropriate box ('unknown'), at the time of declaring treatment outcome for the patient.

CPT (Cotrimoxazole Prophylactic Therapy) Delivery

- i. All known HIV-infected TB patients are to be provided access to CPT.
- ii. If CPT provided from the PHI, record dates of each monthly delivery in the space provided.
- iii. In case the TB patient is already on CPT before the initiation of TB treatment, record most recent date of CPT pickup.

Referral and initiation on ART

1. All known HIV-infected TB patients are to be referred for ART to the nearest ART Centre. For referred clients, record the date of referral.
2. If patient initiated on ART, tick the "yes" box, and the date of initiation of ART. ART Registration Number should be recorded on the treatment card.
3. In case the TB patient is already on ART before the initiation of TB treatment, tick yes, and record approximate date of initiation.

Adverse Reactions to Anti-TB Drugs

Adverse Drug Reactions (ADR) observed during treatment for tuberculosis are comparatively less in the intermittent chemotherapy than what is encountered in daily regimens. DOT providers should be aware of the commonly occurring adverse reactions so that they can identify it

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State: Karnataka City/District with code: Mysore TB Unit with code: _____ Patient TB No./Year: 4299
 Name: Raju Sex: M F Age: 52 Occupation: _____
 Complete Address & Telephone number: _____
 Name, Address & Phone No. of contact Person: Krishna Rao, sarpanch
 Name and designation of DOT provider & Phone. No : _____ PHI: _____
 Name of DOT Centre: _____ Signature of MO with date: _____ Date: _____
 Initial home visit by: _____ Ph.No.: _____
 H/O of Previous ATT with duration: _____

Disease Classification		Type of Patient				Month	Date	DMC	Lab. No.	Smear Result	Patient Weight
<input type="checkbox"/> Pulmonary	<input type="checkbox"/> New	<input type="checkbox"/> Relapse			Pretreatment	4/4	A	128	2+		
<input type="checkbox"/> Extra Pulmonary site	<input type="checkbox"/> Transfer in	<input type="checkbox"/> Treatment Failure			End of IP/Extended IP	29/5		246	1+		
_____	<input type="checkbox"/> TAD	<input type="checkbox"/> Others Specify)_____			2 Months X CP	26/7		210	NEG		
					End Treatment	30/9	S	506	NEG		

INTENSIVE PHASE - Prescribed regimen and dosages. Tick (✓) appropriate treatment regimen below:

Regimen for new cases

Regimen for Previously Treated

Month/year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
April 97						S	✓		✓		✓		S	✓		0	✓	✓	S	✓	✓	✓		✓	✓		S	✓		✓	
May 97	✓		S	✓			✓		0	✓	S		✓		✓		✓	S		✓	✓	✓		✓	S		0		✓		
June 97																															

promptly and refer the patient to the medical officer for further management. Any adverse reactions reported during treatment is recorded in the remarks column of the treatment card. Orange / red discoloration of the body fluids especially urine which is commonly encountered, is not an adverse reaction and patient should be made aware of this.

Symptom-based approach to evaluation of possible side effects of anti-TB drugs

Symptom	Drug (abbreviation)	Action to be taken by HW	Action to be taken by MO
Gastrointestinal (vomiting or epigastric discomfort)	Any oral medication	Reassure patient. Give drugs with less water and over a longer period of time (e.g. 20 minutes). Do not give drugs on an empty stomach. If the above fails, refer to MO.	Maintain hydration <ul style="list-style-type: none"> Consider treatment with anti-emetics (e.g. domperidone) and proton pump inhibitors (eg. Omeprazole)
Itching/Rashes	Isoniazid (and other drugs also)	Reassure patient If severe, stop all drugs and refer patient to MO	Itching without rash or a mild rash <ul style="list-style-type: none"> Continue treatment and give antihistamines Itching with moderate to severe rash <ul style="list-style-type: none"> Stop all drugs till symptoms subside Treat with antihistamines Patients with mucosal involvement, fever and hypotension will require treatment with corticosteroids When the reaction subsides reintroduce drugs one-by-one in this order 1. INH. 2. Rifa. 3. Pyra. 4. Etham Re-introduce each drug in a small dose and gradually increase over 3 days before introducing the next drug.
Tingling/ burning/ numbness in the hands and feet	Isoniazid	Refer to MO	<ul style="list-style-type: none"> Give pyridoxine 100 mg/day orally or parenterally until symptoms subside. Patients not responding to pyridoxine will require treatment with amitryptiline

Joint pains	Pyrazinamide	Reassure that it is a self limiting condition. Encourage patients to increase intake of liquids. If severe, refer patient to MO for evaluation	<ul style="list-style-type: none"> • Give NSAIDs like paracetamol, Aspirin or Ibuprofen and in severe cases Indomethacin for a week to 10 days • In severe cases, estimate serum uric acid levels • If uric acid levels are significantly raised, treat with NSAIDs and colchicine. Allopurinol is not effective. • In severe cases with normal or slightly elevated uric acid, consider reduction of the dose of Pyrazinamide.
Impaired vision	Ethambutol	STOP Ethambutol, refer patient for evaluation	<ul style="list-style-type: none"> • Refer to ophthalmologist for evaluation • Impaired vision usually returns to normal within a few weeks of stopping ethambutol.
Ringing in the ears, Loss of hearing, dizziness and loss of balance	Streptomycin	STOP Streptomycin, refer patient for evaluation	<ul style="list-style-type: none"> • Refer to otorhinolaryngologist for opinion • As hearing loss is usually not reversible, do not restart Streptomycin
Hepatitis: Anorexia nausea /Vomiting/ Jaundice	Isoniazid, Rifampicin or Pyrazinamide	STOP all anti TB drugs, Refer patient for evaluation	<ul style="list-style-type: none"> • Rule out other causes of hepatitis • Do not restart treatment till symptoms resolve and liver enzymes return to baseline levels • If liver enzymes cannot be performed, wait for 2 weeks after jaundice has disappeared to restart treatment • Restart treatment with one drug at a time starting with 1. INH 2. Pyra 3. Rifa • In patients with severe disease in whom treatment cannot be stopped, use a non hepatotoxic regimen consisting of Streptomycin and Ethambutol

In cases of jaundice, all anti-TB drugs should be stopped immediately and the patient referred for evaluation.

Management of Patients in Special Situations

Situation	Management
Hospitalization	Some of the indications for hospitalization:- Extremely ill patients. Patients with frequent haemoptysis, pneumothorax or massive pleural effusion leading to breathlessness Cases requiring surgical intervention.
Tuberculous meningitis	Patient should be referred to the hospital. Streptomycin is to replace ethambutol in IP. The continuation phase should be extended by 3 months in both new and previously treated cases. Steroids should be given initially and gradually tapered over 6-8 weeks.
Treatment of TB during pregnancy and postnatal period	Streptomycin is absolutely contraindicated during entire pregnancy. Breast feeding can be continued even when mother is on treatment for TB but mother should continue to practice cough hygiene. Child should be administered preventive chemoprophylaxis as per guidelines.
Treatment in patients with renal failure	Rifampicin, isoniazid and pyrazinamide can be safely given as they are excreted in entero-hepatic circulation. Dosage of streptomycin and ethambutol, should be adjusted according to the creatinine clearance.
Women on oral contraceptive pills	Rifampicin decreases the efficiency of oral contraceptives by increasing their metabolism. Increase in dosage of the oral contraceptive or switch over to alternate methods of contraception is advisable

Treatment of TB Disease in HIV-infected Patients

Early diagnosis and effective treatment of TB among HIV-infected patients are critical for controlling the disease, minimizing the adverse impact of TB on the course of HIV, and interrupting the transmission of TB in the community. Delays in the diagnosis of TB have been associated with worse outcomes. Hence, initiation of treatment is very important soon after the diagnosis of TB among HIV-infected persons. Treatment of TB is same as that in HIV-negative TB patients. Patients are to be treated with the RNTCP “New” or “Previously Treated” regimen according to the patient’s history of previous anti-TB treatment.

In addition to TB treatment under RNTCP, all HIV-infected TB patients must be provided access to care and support for HIV disease, including ART. ART reduces TB case fatality rates and the risk of recurrent TB. ICTC counsellors and treating physicians should counsel patients on the importance of ART and on the free availability of treatment with ART and evaluation.

HIV-infected TB patients should be promptly referred to the nearest ART centre by the treating physicians and ICTC counsellors. This visit to the ART centre, should preferably occur

at least two weeks after initiation of TB treatment, to ensure reduction in the potential of TB transmission from these patients prior to the visit to the centres being visited by large numbers of HIV-infected persons. TB patients referred to ART centres should be carefully educated on cough hygiene.

For details on ART eligibility, reference ART guidelines (available at www.nacoinia.org). NACO recommends that ART be given to:

- All patients with extrapulmonary TB (stage 4); and
- All those with pulmonary TB (stage 3) with CD4 count < 350 cells/mm³.

Cotrimaxazole preventative therapy (CPT): Cotrimaxazole preventative therapy has been shown to reduce mortality among HIV-infected TB patients, and is recommended by NACP for all HIV-infected patients. All HIV-infected TB patients should therefore be provided CPT. All the ART Centres should have minimum provisions of meeting the CPT requirements of atleast for a month for the benefit of those patients who are able to return to the ART centre on a monthly basis.

In states implementing RNTCP/NACP Intensified TB/HIV package, CPT should be made available for HIV-infected TB patients at all peripheral health institutions in the districts having a Medical Officer and an institutional DOT centre. The CPT should be procured, packed and supplied in monthly pouches at the state level. The local distribution is to be supervised by RNTCP staff in coordination with NACP. In this mechanism, CPT is delivered by the peripheral health institute staff, and not community DOT providers, to maintain confidentiality regarding HIV status within the health-care system.

Treatment of TB in HIV positive patients on second line ART/ alternate First Line with Protease Inhibitors (PI) based regimen

The effectiveness of second-line antiretroviral therapy depends on the introduction of protease inhibitors (PIs) in the new regimen. However, there are significant drug interactions with the PIs and rifampicin. Consequently, the treatment options are limited for TB patients who require PI-based therapy or develop TB while on PIs. PIs should not be used with rifampicin-containing regimens due to hepatic enzyme inducing capacity of rifampicin, which risks rendering PI levels sub-therapeutic.

Another rifamycin, Rifabutin is a less potent inducer of CYP 3A4 liver enzyme as compared to rifampicin, while being equally safe and effective for treatment of TB. It can be administered in the presence of PI-containing ART regimen without compromising the efficacy of ART or Anti TB treatment. In the presence of the boosting drug like Ritonavir (PI), rifabutin metabolism is also altered, and less rifabutin is needed than would be without ritonavir.

Therefore, in patients taking lopinavir/ritonavir (LPV/r) based ART regimens, NACP and RNTCP have recommended the substitution of Rifabutin for rifampicin for the duration of TB treatment. The dosage of Rifabutin during the administration of second line ART regimen containing LPV/r shall be 150 mg Rifabutin, dosed thrice-weekly for all patients >30 kg weight.

Rifabutin will be supplied through the respective State TB Cell on an individual basis.

Tobacco Smoking and Tuberculosis

The diagnosis of TB disease is an opportune moment for imparting behaviour change in the patients' smoking habit, with patients more likely to accept the behaviour change needed for improving their health. Tobacco smoking may lead to delayed sputum conversion in sputum smear-positive PTB cases, lower treatment success rates and higher rates of relapse of TB disease and death.

Hence, the past and present history of tobacco smoking (cigarette / beedi / pipe / cigar / hukka) should be elicited from each TB case at the time of initiating treatment. Smoking cessation advice to current smokers should become an integral part of TB case management. Such interventions may help improve outcomes of anti-TB treatment and reduce transmission of infection in the short term, and improve the quality of life of TB cases by preventing chronic respiratory and other disease associated with smoking in the long term. Tobacco cessation advice has been demonstrated to be successful in TB cases even in the absence of costly Nicotine Replacement Therapy.

Patients who smoke should be motivated to make an informed decision to stop smoking. All cases should be informed personally about the harmful effects of smoking on health in general and the potential for poorer outcomes of anti-TB treatment with continued smoking. The potential benefits of stopping smoking to the health of the individual should be suitably communicated. The patient's past experience with cessation and relapse of smoking may be

discussed in an understanding atmosphere. Patients may be told that they can be successful even if they have not been able to quit smoking during earlier attempts. During the conversation, the patients are asked to identify situations and moods that trigger smoking (working/getting out of bed/having a cup of coffee/pleasant moments/while dealing with personal or professional problems/group smoking). They are encouraged to devise their own ways to respond to the circumstances that encourage smoking.

Patients should also be advised not to smoke in the presence of others, since increased frequency of coughing due to smoking increases the risk of TB infection among their household and other contacts. That smoking is prohibited in public places according to 'Prohibition of Smoking in Public Places Rules, 2008' may be clearly communicated to them.

5 As Approach to Tobacco Cessation

This is a form of counseling. Before saying anything to motivate the patient to quit tobacco use, the health professional needs to identify the tobacco user and find out the stage of readiness to change that the patient is in, by asking a few questions.

1. Ask the patient if he/she is a tobacco user.
2. Briefly advise against continuing tobacco use and link the current condition/ailment to continued tobacco use, where possible. E.g. "Quitting smoking/tobacco use would improve your health and will aid in early recovery".
3. Then assess readiness to quit by asking the patient whether he or she is ready to quit at this time. E.g. "How recently have you thought about quitting tobacco?"
If the patient appears ready to change (quit), next steps are:
4. Assist the tobacco user in making a quit plan.
5. Arrange for follow-up by setting the next contact.

5 Rs Approach for Non willing Tobacco Users

If the tobacco user is not yet thinking about quitting tobacco use (pre contemplation), the doctor will have to promote greater awareness of the relevance to the patient of the advice to quit, the risks of use and rewards (benefits) of quitting. Many tobacco users are largely unaware of the potential harm that tobacco use can do to them. If the patient is not ready to quit, the doctor must not push the patient. People usually need time to change (incremental nature of change).

If the patient is at least thinking about (contemplating) quitting, the doctor can find out the patients' roadblocks (barriers) to quitting and help the patient see ways to overcome these. This process may be enough to help the patient get ready to quit (without pushing).

At the next visit, this process should be repeated so that the information about relevance, risks of continuing and rewards of quitting can sink in a little more and some roadblocks removed.

As you can see, the doctor must try to make the tobacco user think about quitting. This is important because there are so many other forces acting that are difficult to control, physiological compulsions to use tobacco, learned habits, social pressures, accessibility etc. Engaging the mind of the tobacco user, bolstering it with new knowledge and a sense of caring by the person counseling can help motivate him/her to change. Follow-up is important to help keep the tobacco user on track until he or she is confident about remaining tobacco free.

Diabetes and Treatment of Tuberculosis

There is conflicting evidence on the role of diabetes, its control and response to TB treatment. Some studies suggest that there is no co-relation between the two, whereas others suggest that sputum conversion is delayed and treatment outcomes are poorer in diabetics who are poorly controlled during their treatment for TB.

However, in general, the treatment for TB in patients with diabetes is the same as for those who are non-diabetic. In a few cases, rifampicin may induce early phase hyperglycemia due to augmented intestinal absorption. Although relapse rates themselves are unchanged, in diabetics who relapse, the prognosis is poorer.

Principles of management of co-existent TB and diabetes comprise:

- 1) Proper care and hospitalization in patients with poor diabetic control;
- 2) Ideally insulin should be used to control blood sugar during anti-TB treatment. However oral hypoglycaemics can be used if the patient is well stabilized on them;
- 3) Drug interactions with rifampicin need to be kept in view and recognised if they occur;
- 4) Glycaemic equilibrium is essential with goals of maintaining fasting blood sugar <100 mg % and glycosylated HB <6%
- 5) Monitoring for adverse effects, particularly of hepatic and nervous systems should be done as it may lead to peripheral neuropathy; and
- 6) Use of potentially neuropathic agents in patients with peripheral neuropathy demands special consideration and administration of pyridoxine.

Multidrug Resistant TB and DOTS-Plus

Prevention of MDR-TB

The management of MDR-TB is very complex, and hence preventing its development by effective implementation of the DOTS strategy under RNTCP is crucial.

Selection of appropriate treatment regimen for patients by the medical officer, after eliciting history of previous treatment, is very important. The diagnosed patients should be explained why it is essential to reveal previous TB treatment and to take drugs under direct observation. Similarly, DOT Providers should be educated and convinced about the importance of Directly Observed Treatment (DOT). DOTS has been documented to not only prevent the emergence of multidrug resistant TB, but also to decrease its prevalence in the community.

Prevention of MDR-TB is given priority under RNTCP rather than its treatment

Management of MDR-TB

National guidelines and plans for scaling up the management of MDR-TB have been developed under RNTCP. In the interim, while RNTCP DOTS Plus services are being expanded across the country, all health care providers in the public and private sector managing MDR-TB cases, need to adhere to the national guidelines.

MDR-TB management has to be preferably undertaken only at selected health institutions with experience, expertise and availability of required diagnostic and treatment facilities.

Identification of MDR-TB Suspects

The following are the criteria to label a patient as MDR-TB suspect.

- A new smear-positive patient remaining smear-positive at the end of fifth month.
- A new smear-negative patient becoming smear-positive at the end of fifth month.
- A patient treated with regimen for previously treated remaining positive at fourth month
- Smear-positive contacts of an established/confirmed MDR-TB case

MDR-TB suspects may include additional groups as the program expands in future. Check the status with the local program manager.

Diagnosis of MDR-TB

For patients in whom drug resistance is suspected, diagnosis of MDR-TB should be done through culture and drug susceptibility testing from a quality-assured laboratory. On being diagnosed as an MDR-TB case, the patient will be referred to a designated state level DOTS-Plus site. These sites are specialized centres which are limited in number. At least one such center is expected to be in each state which has ready access to an RNTCP accredited culture and DST laboratory. The DOTS-Plus site will be supported by qualified staff available to manage patients using the second-line RNTCP MDR-TB regimen given under daily DOT and standardized follow-up protocols. There will be a mechanism to deliver ambulatory DOT after an initial short period of up to one week of in-patient care to stabilize the patient on second line drug regimen. Logistics and standardized information will be made available in such places.

RNTCP MDR-TB Treatment Regimen

The RNTCP is using a standardised treatment regimen (STR), comprising of 6 drugs (kanamycin [Km], levofloxacin (lvx), ethionamide [Eto], pyrazinamide [Z], ethambutol [E] and cycloserine [Cs]) during 6-9 months of an Intensive Phase, and 4 drugs (lvx, Eto, E and Cs) during the 18 months of the Continuation Phase. p-aminosalicylic acid (PAS) is included in the regimen as a substitute drug if any of the drugs (bactericidal—kanamycin/ethionamide) cannot be tolerated. Dosages of drugs are based upon three weight bands.

Drug	16-25 Kg	26-45 Kg	> 45 Kg
Km	500 mg	500 mg	750 mg
LVX	200 mg	500 mg	750 mg
Eto	375 mg	500 mg	750 mg
E	400 mg	800 mg	1000 mg
Z	500 mg	1250 mg	1500 mg
Cs	250 mg	500 mg	750 mg
PAS	5 g	10 g	12 g
Pyridoxine	50 mg	100 mg	100 mg

Dosage and Weight band Recommendations

All drugs should be given in a single daily dosage under DOT by a DOT Provider. All patients will receive drugs under direct observation on 6 days of the week. On the 7th day (Sunday), the oral drugs will be administered unsupervised and kanamycin will be omitted. If intolerance occurs to the drugs, ethionamide, cycloserine and PAS may be split into two dosages and the morning dose administered under DOT. The evening dose will then be subsequently self-administered. The empty blister packs of the self-administered doses will be checked the next morning during DOT. 100mg of pyridoxine is administered to all patients on the RNTCP MDR-TB treatment regimen. If a patient gains at least 5kgs of weight during treatment and crosses the weight-bands range, the DOTS-Plus site committee may consider moving the patient to the higher weight-band drug dosages. The new higher dosages are provided whenever the patient is due for the next 3-monthly supply of drugs in the normal course of treatment and not as soon as change of weight is noted.

Duration of Treatment

Intensive Phase (IP) should be given at least 6 months. It is extended up to seven/eight/nine months in patients who have a positive culture result taken in fourth/fifth/sixth month of treatment correspondingly. Continuation Phase (CP) is given for 18 months following the IP.

Follow-up Schedule

Smear examination should be conducted monthly during the IP and at least quarterly during the CP. Culture examination should be done at least at 4, 6, 12, 18 and 24 months of treatment.

Treatment Adherence and Support

Patients initiated on treatment and their family members should be intensively counselled prior to treatment initiation and during follow-up visits.

To reduce the risk of development of resistance to second-line anti-TB drugs and to promote optimal treatment outcomes, all efforts should be made to administer treatment under direct observation (DOT) over the entire course of treatment.

Health care facilities/practitioners managing MDR-TB patients should maintain a systematic record of treatment regimen, doses, duration, side-effects, result of the investigations and treatment outcome for all patients initiated on second line treatment.

- MDR TB is a laboratory diagnosis
- Cat IV - MDR TB treatment is daily supervised treatment and not intermittent
- DOTS plus treatment can be initiated only by plus site committee and not by DTO/individual doctor

Action for Patients Who Interrupt Treatment

One of the principles of RNTCP is that the responsibility of curing the patient lies with the programme and not with the patient. Providers may be too far from where the patients reside or may have inconvenient timings. Patients also tend to discontinue treatment when they improve symptomatically, thinking that they are cured of the disease. There can be other socio-economic causes for discontinuation of treatment. Proper counselling is essential to motivate patients to take the prescribed medications regularly and as per the treatment schedule. The treating practitioner should take the necessary steps to prevent and help retrieve patients who interrupt treatment. The concerned supervisory staff at the sub-district level (TU) should be informed immediately, if efforts by the DOT provider prove to be futile. If a patient interrupts treatment at any stage during the course of treatment, visits to his/her home should be made to bring them back under treatment. This should be done by the concerned DOT provider, or other health staff, no later than the day after the patient was due to come for treatment in the IP and within a week of the missed dose in the CP. Treatment of patients retrieved depends on the type of patient, duration of treatment taken, length of interruption and the patients' sputum status. Decision on further management may be taken as per the RNTCP protocol available at DTC.

Exercise 2

Part A: Categorise those patients in Exercise I who needed anti-TB treatment.

Part B: Meena Patel was started on treatment on 16th June. Her initial weight was 41kg. She missed the scheduled 12 dose and also the 15 and 16 doses in the Intensive Phase 7 dose was missed, but taken on the subsequent day. The 9 dose was taken unsupervised for which a home visit was made. However, the patient was found to be out of station. The as she was unable to come to DOT centre for personal reasons. She did not come in the 5th week of the Continuation Phase and completely missed the doses of that week. All follow-up sputum examinations were negative, i.e., at end of Intensive Phase - laboratory no. 209, dated 13/08/03 (weight 45 kg), at the end of 4th month - laboratory no 407, dated 18/10/03 (weight 47kg) and at the end of treatment - laboratory no. 630, dated 29/12/03 (weight 49kg).

4 Supervision and Monitoring

Formal supervision and monitoring will be carried out by RNTCP staff. As far as RNTCP is concerned, referring units, microscopy centres and DOT centres in the private, non-government or corporate sector are treated at par with the equivalent government health facilities.

Supervision: Supervisory staff such as the STS and STLS should visit all participating PHIs at least once a month. In addition, the MO-TC and the DTO would also visit all sites on a periodic basis. The purpose of these visits is to provide technical support, identify problems faced by the individual provider and to help solve them. This type of supportive supervision from RNTCP would help to improve the quality of the programme.

It is important that the medical practitioner supervises her/his own personnel who are involved in various aspects of the programme in order to ensure that they are carrying out their tasks correctly. Stores should be periodically supervised to ensure adequate supply, and to avoid expiry of, or damage to, drugs and other materials. Patients should also be interviewed to ascertain that they are being treated as per RNTCP guidelines and have understood the health education information given to them.

Monitoring: There are two important ways to monitor the progress of TB patients on treatment. These are:

1. To monitor the results of sputum smear examinations at regular intervals during treatment (as explained earlier in this book)
2. To monitor the consumption and collection of drugs by the patient to ensure that these are taken and collected as per protocol (also explained earlier).

The best way to monitor the progress of treatment of pulmonary smear-positive patients is to check for the smear conversion of their sputum. It is expected that at least 80% of new smear-positive patients will convert (become sputum smear-negative) by the end of two months of treatment. At the end of three months, more than 90% of such patients could be expected to have converted.

- TB continues to be the leading killer disease for Indian adults amongst all infectious diseases.
- Supervision and monitoring are usually the responsibility of the RNTCP staff.
- Interview your patients regularly.
- Monitoring of treatment is best done by regular follow-up sputum examination.

Appendices

Appendix 1

Infection Control in Hospital Settings

When individuals with Pulmonary TB cough or sneeze, they generate infectious particles. Cough induction, or bronchoscopy, also generate infectious, aerosolized particles. These infectious particles spread throughout a room or a building by air currents and can be inhaled by another individual which can lead to TB infection. In order to prevent nosocomial transmission of TB infection, it is important to address airborne infection control in health facilities. Airborne infection control activities can be grouped under three levels: Administrative, Environmental and Personal.

Administrative Controls

Objective: To reduce risk of exposure, infection, and disease through policy and practice.

- All patients should be screened as soon as possible for prompt identification of pulmonary TB suspects.
- Pulmonary TB suspects and cases should be placed in a well ventilated, separate waiting area such as a sheltered, open air space.
- The diagnosis and management of these persons should be speeded up so that they spend as little time as possible at the facility.
- Sputum collection should be undertaken in an open area.
- Patients who are immunocompromised, or at increased risk of getting TB (Eg. HIV positive, diabetes, etc.) should be segregated from pulmonary TB suspects and smear-positive patients including drug resistant TB patients.
- All health facilities should have an airborne infection control plan which should be part of the general infection control plan of the health facility.
- All staff should be trained on TB and the infection control plan of the health facility.

Environmental Controls

Objective: To reduce concentration of infectious bacilli in air in areas where contamination of air is likely.

- Maximise natural ventilation in areas of health facility which are frequented by TB suspects/patients, by simple measures such as opening of doors and windows, replacement of glass panes with wired mesh, etc. Ventilation is especially important in the patient waiting area, out/in-patient clinics/wards, laboratory, etc.
- If the health facility is air-conditioned, ensure that the air-conditioning equipment circulates adequate fresh air, and not just re-circulates the air existing inside the building.
- Consider supplementing natural ventilation by use of equipment for forced ventilation, eg. exhaust fans, etc.
- Instruct TB suspects/patients on respiratory hygiene/cough etiquette. Covering cough by palm, elbow, cloth, etc. reduces generation of airborne infectious particles.
- The laboratory technician should be trained in disposal of bio-medical waste at the DMC.
- Additional equipment such as UV lights are not required unless the health facility is providing in-patient care to drug-resistant TB cases. In such situations, careful planning will be required for maintenance of the equipment and protection of humans from over-exposure to UV lights.

Personal Measures

- The patient should be trained on cough hygiene. Patient should be encouraged to cover the cough or wear masks while receiving care in the hospital.
- Protective mask for health workers may be needed in rare situations in settings such as the bronchoscopy room.

Appendix 2

Solutions to Exercises

Exercise I

PART A

A. Meena Patel

Answer:

- a. Suspect pulmonary TB
- b. Refer to a DMC convenient to the patient for sputum microscopy with a properly completed laboratory form.

B. Lakshmi Kumari

Answer:

- a. Suspect pulmonary TB.
- b. Refer to a DMC convenient to the patient for sputum microscopy with a properly completed laboratory form.

C. Ashok Patel

Answer:

- a. Suspect pulmonary TB.
- b. Refer to a DMC convenient to the patient for sputum microscopy with a properly completed laboratory form (Symptomatic contacts of sputum smear-positive pulmonary TB patients should undergo sputum examination irrespective of the duration of symptoms).

D. Paravathi Sinha

Answer:

- a. Suspect lymph node TB.
- b. Refer the patient for lymph node biopsy/FNAC and for expert opinion.

E. Lallan Prasad

Answer:

- a. Suspect pulmonary TB.
- b. Refer to a DMC convenient to the patient for sputum microscopy with a properly completed laboratory form

PART B

(See completed laboratory forms)

PART C

(See the laboratory register)

Exercise II

Part A

Patient A:

New sputum smear-positive pulmonary TB - CAT I.

Patient B:

Re-treatment: Sputum smear-positive pulmonary TB; Treatment after Default - CAT II.

Patient C:

Patient treated with broad-spectrum antibiotic for 10-14 days and re-assessed.

Patient D:

Patient treated as EP, not seriously ill patient - CAT III.

Patient E:

Patient treated as pulmonary sputum smear-negative - CAT III.

Part B

(See the completed treatment card)

Appendix 3

Zeihl Neelsen Staining

1. Select a new unscratched slide and label it with the laboratory serial number using a diamond marking pencil.
2. Make a smear from the yellow muco-purulent portion of the sputum sample using a broomstick. A good smear is spread evenly, is about 2 cm x 2 cm in size and is neither too thick nor too thin. The optimum thickness of the smear can be assessed by placing the smear on printed matter. The print should be just readable through the smear.
3. Allow the slide to dry in air for 15 to 30 minutes.
4. Fix the slide by passing it over a flame 3 to 5 times, for 3 to 4 seconds each time.
5. Pour 1% filtered carbol fuchsin to cover the entire slide.
6. Gently heat the slide with the carbol fuchsin on it, until vapours rise. Do not allow it to boil.
7. Leave carbol fuchsin on the slide for five minutes.
8. Gently rinse the slide with tap-water until all the free carbol fuchsin stain is washed away. At this point, the smear on the slide looks red in colour.
9. Pour 25% sulphuric acid onto the slide.
10. Let the slide stand for 2 to 4 minutes.
11. Rinse gently with tap-water, then tilt the slide to drain off the water.
12. A properly decolourised slide will appear light pink in colour. If the slide is still red, reapply sulphuric acid for 1 to 3 minutes and rinse gently with tap-water. Wipe the back of the slide clean with a swab dipped in sulphuric acid.
13. Pour 0.1% methylene blue onto the slide.
14. Leave the methylene blue on the slide for 30 seconds.
15. Rinse gently with tap-water.
16. Allow the slide to dry.
17. Examine the slide under the microscope using the x40 lens to select a suitable area and then examine this area under the x100 lens using a drop of immersion oil.
18. Record the results in the laboratory form and also in the laboratory register.
19. Store all positive and negative slides serially in the same slide box until instructed by the supervisor.
20. Disinfect all the contaminated material before discarding.

Appendix 4

References

1. Managing the Revised National Tuberculosis Control Programme in Your Area- A Training Course, Modules (1-9), Central TB Division
2. Technical and Operational Guidelines for Tuberculosis Control, Central TB Division
3. TB India 2009- RNTCP Status Report, Central TB Division.
4. Joint Tuberculosis Programme Review, India, September 2003, World Health Organization
5. Toman's Tuberculosis, Second Edition.
6. TB- A Clinical Manual for South-East Asia, World Health Organization, 1997
7. Key Concepts of RNTCP, Central TB Division
8. Treatment Guidelines for TB in HIV Infected, NACO and Central TB Division
9. Global Tuberculosis Control, Surveillance, Planning, Financing, WHO Report 2009

Appendix 5

Monthly PHI Report

REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME

Monthly Report on Programme Management, Logistics and Microscopy

Peripheral Health Institution Level

- Note: 1. All PHCs/CHCs/referral hospitals/major hospitals/specialty clinics/TB hospitals/ Medical colleges to submit their monthly reports in this format.
2. PHIs without DMCs have to fill only the relevant details on page 2.

Name of Peripheral Health Institution: _____

TU: _____

District: _____

Month: _____

Year: _____

Medications

Item (PWB)	Stock on first day of month (a)	Stock received during month (b)	Patients initiated on treatment (c)	Stock on last day of month (d)=(a+b)-c	Quantity Requested (e)= (c X 2) - d
Regimen for New patients (NT)					
Regimen for previously treated patients (PT)					

Adult Patient Wise Boxes

Prolongation Pouches and Inj SM

Item	Stock on first day of month (a)	Stock received during month (b)	Consumption during month (c)	Stock on last day of month (d) =(a+b)-c	Quantity Requested (e) =(cX2) -d
Prolongation pouches (Pouches each with 12 blister strips)					
Streptomycin 0.75 g (vials)					

RNTCP Loose Drugs

Item	Stock on first day of month (a)	Stock received during month (b)	Consumption during month (c)	Stock on last day of month (d) = (a+b)-c	Quantity Requested (e) = (cX2)-d
Tab INH 300 mg					
Tab INH 100 mg					
Cap Rifampicin 150 mg					
Tab Ethambutol 800 mg					

Supervisory activities

Supervisory Visit by	DTO/2 nd MO-DTC	MO-TC	DOTS Plus & TB-HIV Supervisor	STS	STLS
Number of visits in last 1 month					

IEC

Number of TB Patient Provider meetings held	
Number of Community meetings organized	

Referral Activities (To be filled in by all PHIs from OPD Register)

a. Number of new adult outpatient visits	
b. Out of (a), number of TB suspects referred for sputum examination	

Microscopy Activities (To be filled in by only PHIs which are a DMC from Laboratory Register)

c. Number of TB suspects whose sputum was examined for diagnosis	
d. Out of (c), number of sputum smear-positive patients diagnosed	
e. Number of TB suspects subjected to repeat sputum examination for diagnosis	
f. Out of (e), number of sputum smear-positive patients diagnosed	
g. Total number of sputum smear-positive patients diagnosed (d + f)	

Treatment Initiation (To be filled in by only PHIs which are a DMC from Laboratory Register and Referral for Treatment Register)

h.	Of the smear-positive patients diagnosed (g), number put on DOTS	
i.	Of the number of smear-positive patients diagnosed (g), number put on RNTCP Non-DOTS (ND1 and ND2)	
J	Of the smear-positive patients diagnosed (g), the number referred for treatment to other TUs within the district	
k.	Of the smear-positive patients diagnosed (g), the number referred for treatment outside the district	

MDR-TB case finding activity (To be filled in by only PHIs which are a DMC from Laboratory Register)

Number of MDR-TB suspects identified	
--------------------------------------	--

Laboratory Consumables

(To be filled in by only PHIs which are a DMC)

Item	Unit of Measurement	Stock on first day of month	Stock received during month	Consumption during month	Stock on last day of month	Quantity requested
Sputum containers*	Nos.					
Universal containers for C & DST	Nos					
Slides	Nos.					
Carbol Fuchsin (1% solution)	Litres					
Methylene Blue (0.1% solution)	Litres					
Sulphuric Acid (25% solution)	Litres					
Phenolic solution (for disinfection--40% pure solution)	Litres					
Immersion oil/Liquid Paraffin (Heavy)	mL					
Methylated Spirit	Litres					

* PHIs that are not a DMC, but have been supplied with sputum containers, should complete this row.

Equipment in place (To be filled in by only PHIs which are a DMC)

Item	Number in place	In working condition
Binocular microscopes		

Name of officer reporting (in capital letters) : _____

Signature: _____

Date: _____

Appendix 6

Summary: International Standards for Tuberculosis Cure

The purpose of the International Standards for Tuberculosis Care is to describe a widely accepted level of care that all practitioners, public and private, should seek to achieve in managing patients who have, or are suspected of having, tuberculosis. The standards are intended to facilitate the effective engagement of all care providers in delivering high quality care for patients of all ages, including those with sputum smear-positive and sputum smear-negative tuberculosis, extrapulmonary tuberculosis, tuberculosis caused by drug-resistant (Dr) *Mycobacterium tuberculosis* complex (*M. tuberculosis*) organisms, and tuberculosis combined with HIV infection and other co-morbidities.

The basic principles of care for persons with, or suspected of having, tuberculosis are the same worldwide: a diagnosis should be established promptly and accurately; standardized treatment regimens of proven efficacy should be used, together with appropriate treatment support and supervision; the response to treatment should be monitored; and the essential public health responsibilities must be carried out. Prompt, accurate diagnosis and effective treatment are not only essential for good patient care, they are the key elements in the public health response to tuberculosis and are the cornerstones of tuberculosis control. Thus, all providers who undertake evaluation and treatment of patients with tuberculosis must recognize that, not only are they delivering care to an individual, they are assuming an important public health function that entails a high level of responsibility to the community, as well as to the individual patient.

Although government program providers are not exempt from adherence to the standards in the *ISTC*, non-program providers are the main target audience. It should be emphasized, however, that national and local tuberculosis control programs may need to develop policies and procedures that enable non-program providers to adhere to the *ISTC*. Such accommodations may be necessary, for example, to facilitate treatment supervision and contact investigations, as described in the *ISTC*.

In addition to health care providers and government tuberculosis programs, both patients and communities are part of the intended audience. Patients are increasingly aware of and

expect that their care will measure up to a high standard. Having generally agreed upon standards will empower patients to evaluate the quality of care they are being provided. Good care for individuals with tuberculosis is also in the best interest of the community.

The standards in the *ISTC* are intended to be complementary to local and national tuberculosis control policies that are consistent with World Health Organization recommendations. They are not intended to replace local guidelines and were written to accommodate local differences in practice. They focus on the contribution that good clinical care of individual patients with or suspected of having tuberculosis makes to population-based tuberculosis control. A balanced approach emphasizing both individual patient care and public health principles of disease control is essential to reduce the suffering and economic losses from tuberculosis.

The *ISTC* should be viewed as a living document that will be revised as technology, resources, and circumstances change. As written, the standards in the *ISTC* are presented within a context of what is generally considered to be feasible now or in the near future.

The *ISTC* is also intended to serve as a companion to and support for the *Patients' Charter for Tuberculosis Care (PCTC)*. The PCTC specifies patients' rights and responsibilities and will serve as a set of standards from the point of view of the patient, defining what the patient should expect from the provider and what the provider should expect from the patient.

Standards for Diagnosis

- Standard 1.** All persons with otherwise unexplained productive cough lasting two-three weeks or more should be evaluated for tuberculosis.

- Standard 2.** All patients (adults, adolescents, and children who are capable of producing sputum) suspected of having pulmonary tuberculosis should have at least two sputum specimens submitted for microscopic examination in a quality-assured laboratory. When possible, at least one early morning specimen should be obtained.

- Standard 3.** For all patients (adults, adolescents, and children) suspected of having extrapulmonary tuberculosis, appropriate specimens from the suspected

sites of involvement should be obtained for microscopy, culture, and histopathological examination.

Standard 4. All persons with chest radiographic findings suggestive of tuberculosis should have sputum specimens submitted for microbiological examination.

Standard 5. The diagnosis of sputum smear-negative pulmonary tuberculosis should be based on the following criteria: at least two negative sputum smears (including at least one early morning specimen); chest radiographic findings consistent with tuberculosis; and lack of response to a trial of broad-spectrum antimicrobial agents. (Note: because the fluoroquinolones are active against *M. tuberculosis* complex and, thus, may cause transient improvement in persons with tuberculosis, they should be avoided.) For such patients, sputum cultures should be obtained. In persons who are seriously ill or have known or suspected HIV infection, the diagnostic evaluation should be expedited and if clinical evidence strongly suggests tuberculosis, a course of antituberculosis treatment should be initiated.

Standard 6. In all children suspected of having intrathoracic (i.e., pulmonary, pleural, and mediastinal or hilar lymph node) tuberculosis, bacteriological confirmation should be sought through examination of sputum (by expectoration, gastric washings, or induced sputum) for smear microscopy and culture. In the event of negative bacteriological results, a diagnosis of tuberculosis should be based on the presence of abnormalities consistent with tuberculosis on chest radiography, a history of exposure to an infectious case, evidence of tuberculosis infection (positive tuberculin skin test or interferon-gamma release assay), and clinical findings suggestive of tuberculosis. For children suspected of having extrapulmonary tuberculosis, appropriate specimens from the suspected sites of involvement should be obtained for microscopy and for culture and histopathological examination.

Standards for Treatment

Standard 7. Any practitioner treating a patient for tuberculosis is assuming an important public health responsibility to prevent ongoing transmission of the infection and the development of drug resistance. To fulfill this

responsibility the practitioner must not only prescribe an appropriate regimen, but also utilize local public health services and other agencies, when necessary, to assess the adherence of the patient and to address poor adherence when it occurs.

Standard 8. All patients (including those with HIV infection) who have not been treated previously should receive an internationally accepted first-line treatment regimen using drugs of known bioavailability. The initial phase should consist of two months of isoniazid (INH), rifampicin (rIF), pyrazinamide (PZA), and ethambutol (EMb). The continuation phase should consist of isoniazid and rifampicin given for four months. The doses of antituberculosis drugs used should conform to international recommendations. Fixed dose combinations (FDCs) of two (isoniazid and rifampicin), three (isoniazid, rifampicin, and pyrazinamide) and four (isoniazid, rifampicin, pyrazinamide, and ethambutol) drugs are highly recommended.

Standard 9. To assess and foster adherence, a patient-centered approach to administration of drug treatment, based on the patient's needs and mutual respect between the patient and the provider, should be developed for all patients. Supervision and support should be individualized and should draw on the full range of recommended interventions and available support services, including patient counseling and education. A central element of the patient-centered strategy is the use of measures to assess and promote adherence to the treatment regimen and to address poor adherence when it occurs. These measures should be tailored to the individual patient's circumstances and be mutually acceptable to the patient and the provider. Such measures may include direct observation of medication ingestion (Directly Observed Treatment or DOT) and identification and training of a treatment supporter (for tuberculosis and, if appropriate, for HIV) who is acceptable and accountable to the patient and to the health system. Appropriate incentives and enablers, including financial support, may also serve to enhance treatment adherence.

Standard 10. Response to therapy in patients with pulmonary tuberculosis should be monitored by follow-up sputum microscopy (two specimens) at the

time of completion of the initial phase of treatment (two months). If the sputum smear is positive at completion of the initial phase, sputum smears should be examined again at 3 months and, if positive, culture and drug susceptibility testing should be performed. In patients with extrapulmonary tuberculosis and in children, the response to treatment is best assessed clinically.

- Standard 11.** An assessment of the likelihood of drug resistance, based on history of prior treatment, exposure to a possible source case having drug-resistant organisms, and the community prevalence of drug resistance, should be obtained for all patients. Drug susceptibility testing should be performed at the start of therapy for all previously treated patients. Patients who remain sputum smear-positive at completion of 3 months of treatment and patients who have failed, defaulted from, or relapsed following one or more courses of treatment should always be assessed for drug resistance. For patients in whom drug resistance is considered to be likely, culture and testing for susceptibility/resistance to at least isoniazid and rifampicin should be performed promptly. Patient counseling and education should begin immediately to minimize the potential for transmission. Infection control measures appropriate to the setting should be applied.
- Standard 12.** Patients with or highly likely to have tuberculosis caused by drug-resistant (especially MDR/XDR) organisms should be treated with specialized regimens containing second-line antituberculosis drugs. The regimen chosen may be standardized or based on suspected or confirmed drug susceptibility patterns. At least four drugs to which the organisms are known or presumed to be susceptible, including an injectable agent, should be used and treatment should be given for at least 18-24 months beyond culture conversion. Patient-centered measures, including observation of treatment, are required to ensure adherence. Consultation with a provider experienced in treatment of patients with MDR/XDR tuberculosis should be obtained.
- Standard 13.** A written record of all medications given, bacteriologic response, and adverse reactions should be maintained for all patients.

Standards for Addressing HIV Infection and other Co-morbid Conditions

- Standard 14.** HIV testing and counseling should be recommended to all patients with, or suspected of having, tuberculosis. Testing is of special importance as part of routine management of all patients in areas with a high prevalence of HIV infection in the general population, in patients with symptoms and/or signs of HIV-related conditions, and in patients having a history suggestive of high risk of HIV exposure. Because of the close relationship of tuberculosis and HIV infection, in areas of high HIV prevalence integrated approaches to prevention and treatment of both infections are recommended.
- Standard 15.** All patients with tuberculosis and HIV infection should be evaluated to determine if antiretroviral therapy is indicated during the course of treatment for tuberculosis. Appropriate arrangements for access to antiretroviral drugs should be made for patients who meet indications for treatment. However, initiation of treatment for tuberculosis should not be delayed. Patients with tuberculosis and HIV infection should also receive cotrimoxazole as prophylaxis for other infections.
- Standard 16.** Persons with HIV infection who, after careful evaluation, do not have active tuberculosis should be treated for presumed latent tuberculosis infection with isoniazid for 6-9 months.
- Standard 17.** All providers should conduct a thorough assessment for co-morbid conditions that could affect tuberculosis treatment response or outcome. At the time the treatment plan is developed, the provider should identify additional services that would support an optimal outcome for each patient and incorporate these services into an individualized plan of care. This plan should include assessment of and referrals for treatment of other illnesses with particular attention to those known to affect treatment outcome, for instance care for diabetes mellitus, drug and alcohol treatment programs, tobacco smoking cessation programs, and other psychosocial support services, or to such services as antenatal or well baby care.

Standards for Public Health

- Standard 18.** All providers of care for patients with tuberculosis should ensure that persons who are in close contact with patients who have infectious tuberculosis are evaluated and managed in line with international recommendations. The determination of priorities for contact investigation is based on the likelihood that a contact: 1) has undiagnosed tuberculosis; 2) is at high risk of developing tuberculosis if infected; 3) is at risk of having severe tuberculosis if the disease develops; and 4) is at high risk of having been infected by the index case. The highest priority contacts for evaluation are:
- Persons with symptoms suggestive of tuberculosis
 - Children aged <5 years
 - Contacts with known or suspected immunocompromise, particularly HIV infection
 - Contacts of patients with MDR/XDR tuberculosis
- Other close contacts are a lower priority group.
- Standard 19.** Children <5 years of age and persons of any age with HIV infection who are close contacts of an infectious index patient and who, after careful evaluation, do not have active tuberculosis, should be treated for presumed latent tuberculosis infection with isoniazid.
- Standard 20.** Each healthcare facility caring for patients who have, or are suspected of having, infectious tuberculosis should develop and implement an appropriate tuberculosis infection control plan.
- Standard 21.** All providers must report both new and re-treatment tuberculosis cases and their treatment outcomes to local public health authorities, in conformance with applicable legal requirements and policies.

Appendix 7

Presentation Handouts

Medical Practitioners Training Presentations

Central TB Division
Directorate General of Health Services
Ministry of Health and Family Welfare
Nirman Bhawan
New Delhi 110 108

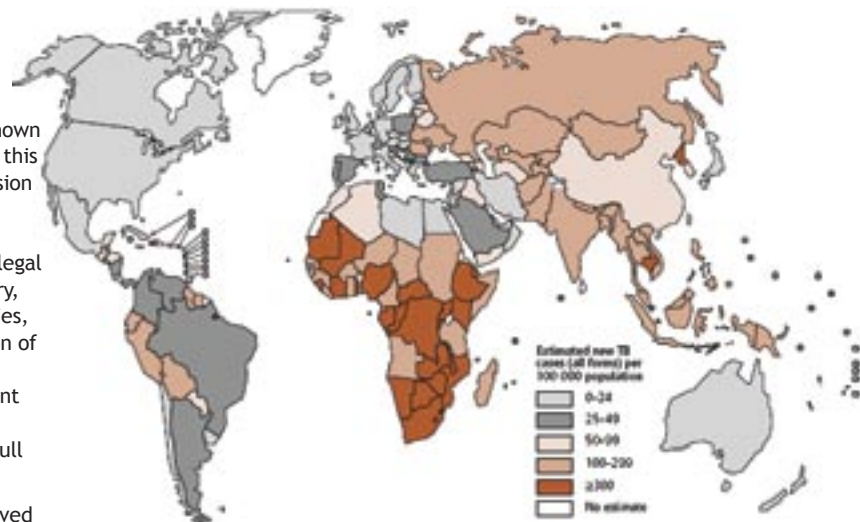


Slides for Chapter 1

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

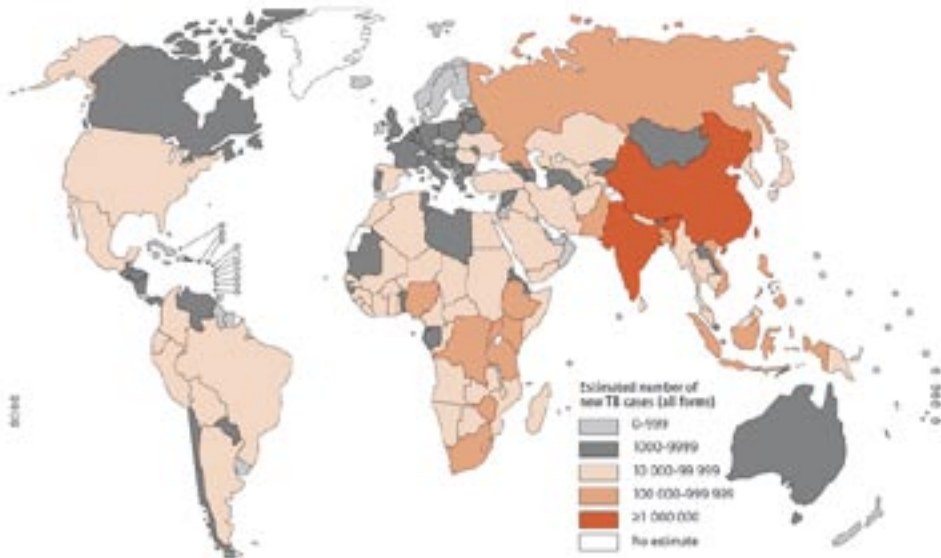
© WHO 2006. All rights reserved

Source: Global TB Report, 2009 World Health Organization



Estimated numbers of new cases, 2007

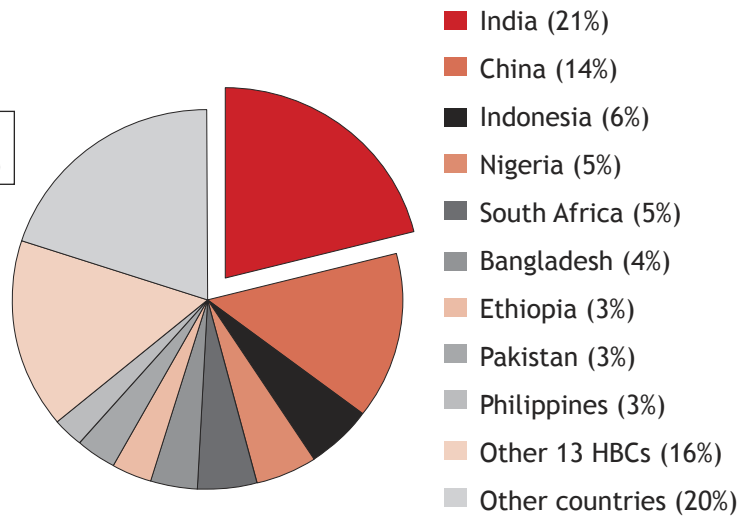
Estimated number of new TB cases, by country, 2007



India is the highest TB burden country accounting more than one fifth of the global incidence

Global annual incidence = 9.23 million
India annual incidence = 1.96 million

India is 17th among 22 High Burden Countries (in terms of TB incidence rate)



Source: WHO Geneva; WHO Report 2009: Global Tuberculosis Control; Surveillance, Planning and Financing

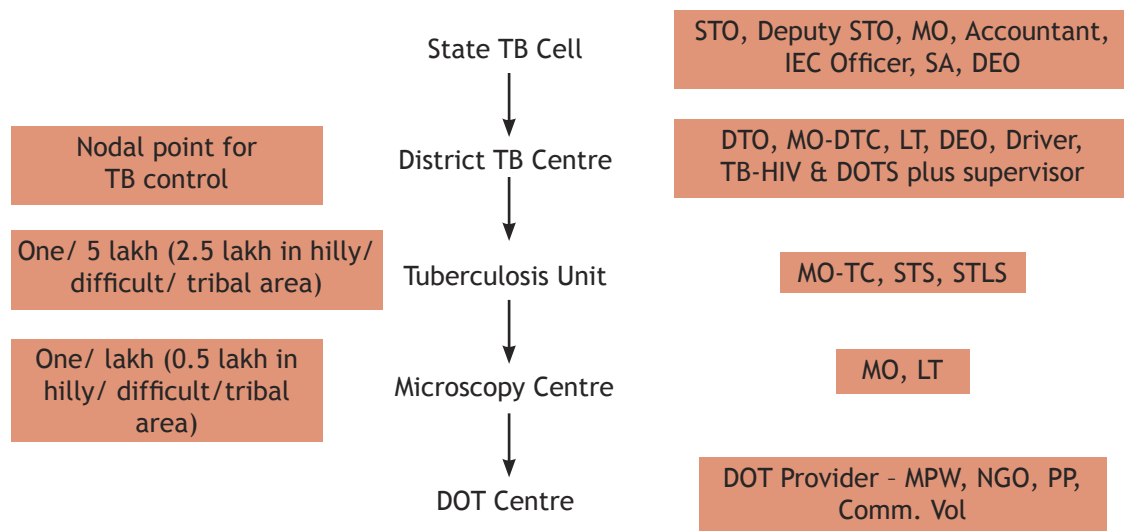
Problem of TB in India

- Prevalence of TB infection
 - 40% (~400m) infected with *M. tuberculosis* (with a 10% lifetime risk of TB disease in the absence of HIV)
- Incidence of TB disease: 1.9 million new TB cases annually (0.8 million new infectious cases)
- Prevalence of TB disease: 3.8 million bacteriologically positive (2000)
- Deaths: about 325,000 annual deaths due to TB (2006)
- TB/HIV: ~2.5 million people with HIV & ~1 million co-infected with TB-HIV
 - 10-15% annual risk (60% lifetime risk) of developing active TB disease in PLWHA
 - < 5% of TB patients estimated to be HIV positive
- MDR-TB in new TB cases ≤3%
- MDR-TB in Retreatment cases 13-17%
- Substantial socio-economic impact

Evolution of TB Control in India

- 1950s-60s Important TB research at TRC and NTI
- 1962 National TB Programme (NTP)
- 1992 Programme Review
 - Only 30% of patients diagnosed;
 - Of these, only 30% treated successfully
- 1993 RNTCP pilot began
- 1998 RNTCP scale-up
- 2001 450 million population covered
- 2004 >80% of country covered
- 2006 Entire country covered by RNTCP
- 2010 DOTS Plus Implementation in 11 States

Structure of RNTCP at State level



Slides for Chapters 2, 3 and 4

Goal, Components and Scientific Basic

RNTCP – Goal and Objectives

- Goal
 - The goal of TB Control Programme is to decrease mortality and morbidity due to TB and cut transmission of infection until TB ceases to be a major public health problem in India.
- Objectives:
 - To achieve and maintain a cure rate of at least 85% amongst new smear-positive cases
 - To achieve and maintain a case detection of at least 70% of the estimated new sputum positive TB patients

Directly Observed Treatment, Short-course (DOTS) – Components

- Political and administrative commitment



- Diagnosis by microscopy



- Adequate supply of SCC drugs



- Directly observed treatment



- Accountability

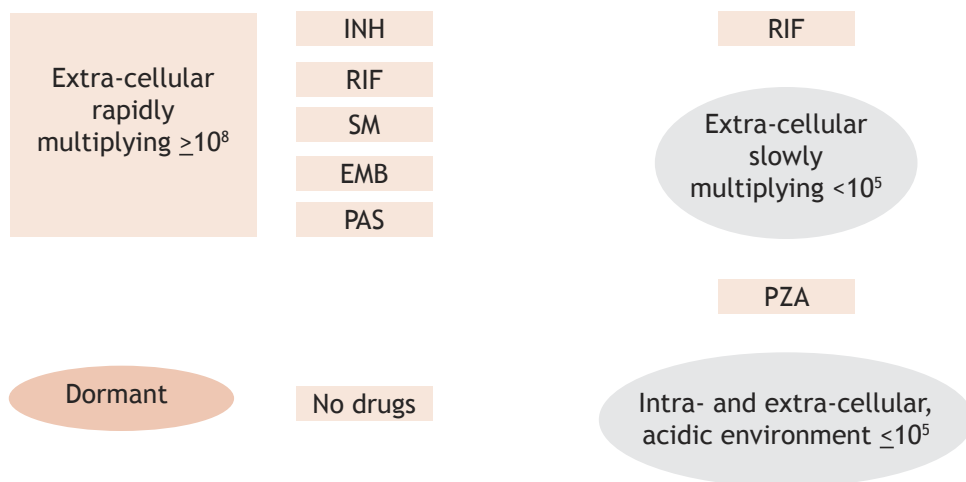


Note: Directly Observed Treatment (DOT) is only one of the five components of DOTS strategy

Diagnosis of tuberculosis

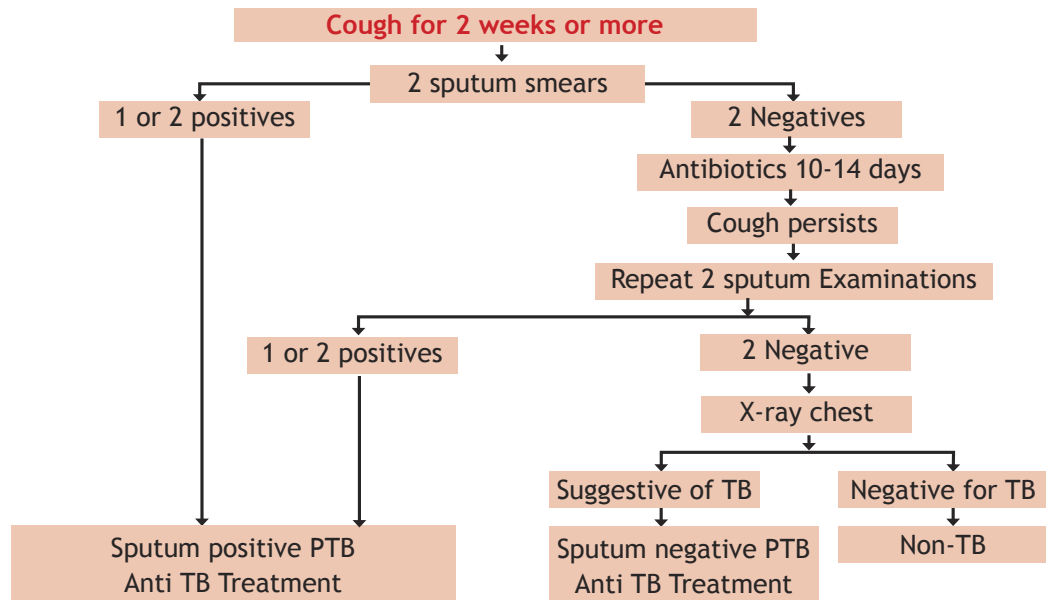
Tools	Merits	De-merits
Tuberculin test	Can identify infection Good epidemiological tool	Cannot differentiate infection & disease
X-ray	Sensitive	Not specific
Sputum Sm. Microscopy	Definitive diagnosis Easy to perform at the periphery Replicability Less costly	Sensitivity 60-80%
Culture for MTB	Highly sensitive & specific	Costly, not freely available Long waiting period

Drug action on TB bacillary population

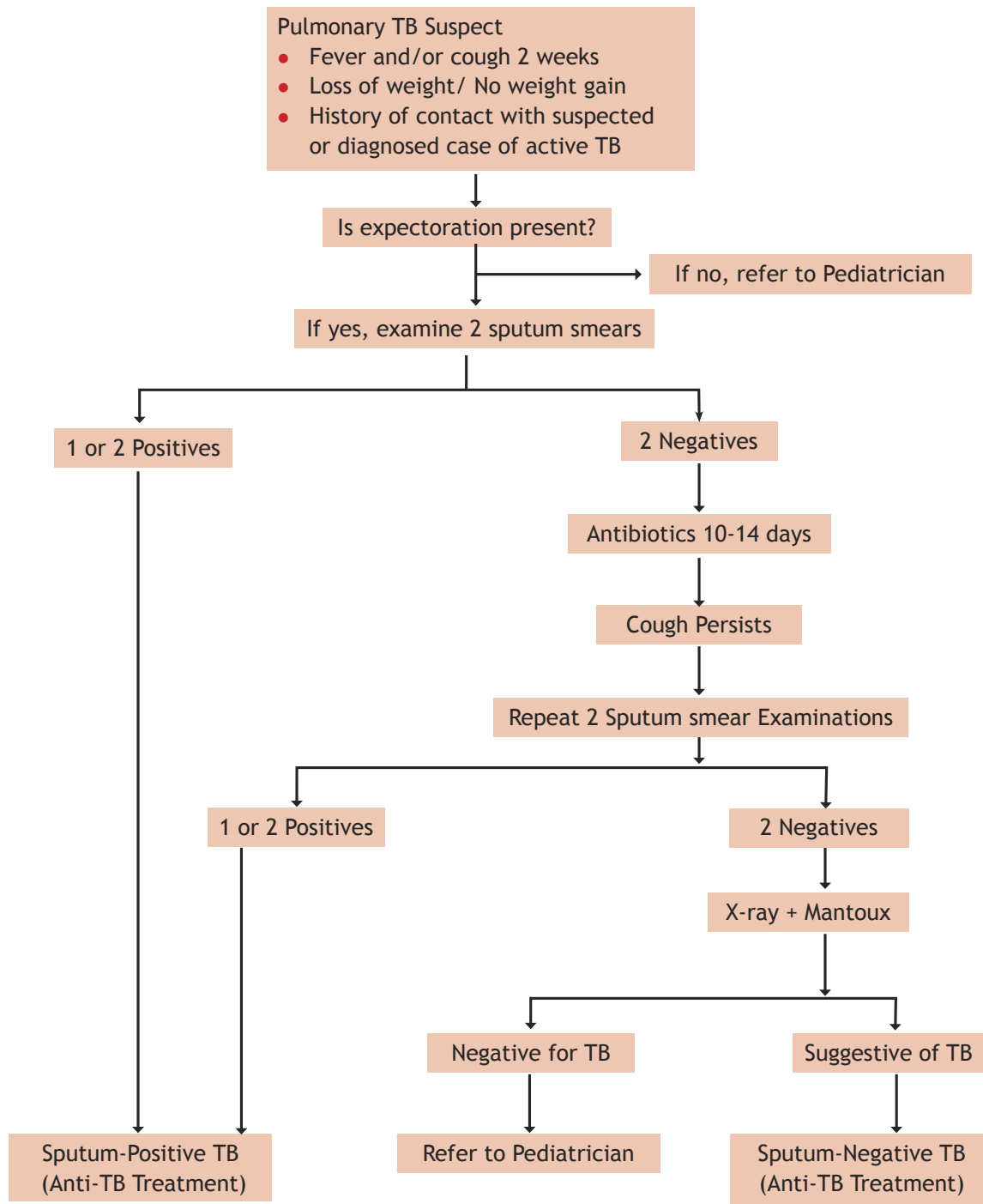


Diagnosis of Tuberculosis

Diagnostic Algorithm for Pulmonary TB



Diagnostic algorithm for pediatric pulmonary tuberculosis



Treatment Regimens

Treatment groups	Type of patient	Regimen ¹	
		Intensive Phase (IP)	Continuation Phase (CP)
New*	Sputum smear-positive Sputum smear-negative Extra-pulmonary Others	2H ₃ R ₃ Z ₃ E ₃	4H ₃ R ₃
Previously Treated**	Smear-positive relapse Smear-positive failure Smear-positive treatment after default Others ²	2H ₃ R ₃ Z ₃ E ₃ S ₃ / 1H ₃ R ₃ Z ₃ E ₃	5H ₃ R ₃ E ₃

Diagnosis of Tuberculosis

Sputum smears are examined and interpreted as indicated in the table below:

Examination finding	Result as recorded	Grading	No. of fields examined
> 10 AFB per oil immersion field	Positive	3+	20
1–10 AFB per oil immersion field	Positive	2+	50
10–99 AFB per 100 oil immersion fields	Positive	1+	100
1–9 AFB per 100 oil immersion fields	Positive	Scanty*	100
No AFB in 100 oil immersion fields	Negative	Negative	100

* Record exact number seen in 100 fields

Patient - Wise Box



Slides for Chapters 6 and 7

Reporting & Reporting Formats

- TUBERCULOSIS LAB REGISTER
Kept at DMC
- TUBERCULOSIS TREATMENT CARD
Kept at PHI & duplicate also with DOTS Provider
- TUBERCULOSIS REGISTER
Maintained by STS & kept at TU. Every patient has a unique TB Register No. given by STS
- LABORATORY FORM
To be used for Sputum Examination, one for two Sputum Examinations
- PATIENT IDENTITY CARD
Issued to all Patients

Logistic Management

- The Senior Treatment Supervisor (STS) and the Senior Tuberculosis Laboratory Supervisor (STLS) of the respective TUs should be appraised of any impending shortages of material (PWB and lab reagents) so as to prevent any disturbance in running the Programme.
- There is always Reserve Stock of Drugs Available at every PHI, TU & District
- The prompt supply of the drugs to the DOTS Centre as and when required is ensured under RNTCP (when patient is initiated on treatment).

Slides for additional information on MDR-TB & PPM schemes

Terminology

Multidrug-Resistant TB (MDR-TB):

Resistance to at least Isoniazid (INH) and Rifampin (RIF)

Extensively Drug-resistant TB (XDR-TB):

MDR-TB plus resistance to a fluoroquinolone and at least one of three injectables (Amikacin, Kanamycin, or Capreomycin)

Addressing Drug Resistant TB

- Prevention by implementing quality DOTS
- Drug resistant TB is a laboratory diagnosis
 - A network of quality assured culture and DST reference laboratories are being planned
- Treatment
 - With second line drugs using standardized regimen (24-27 months), supervised treatment, bacteriological & clinical follow-up and reporting of outcomes.
 - 200 times costly than 1st line drugs, more toxic and less effective

Standardised Treatment Regimen for the treatment of MDR-TB

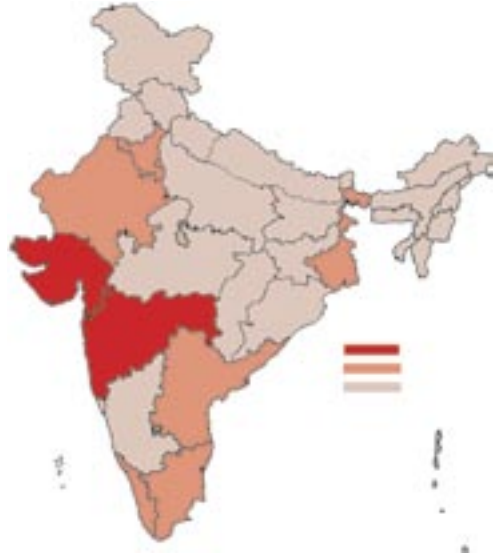
RNTCP CATEGORY IV REGIMEN:

Intensive phase	6 (9) Km Lvx Eto Cs Z E (daily)
Continuation phase	18 Lvx Eto Cs E (Daily)

Prefixed numbers indicate months

RNTCP DOTS Plus Plan

- Plan for phased expansion of reference laboratories for diagnosis of MDR-TB and DOTS-Plus site for treatment
- By 2012, entire country to be covered



Best way to Prevent MDR / XDR TB

Cure TB patients with the first line treatment using DOTS

FIRST HIT IS BEST HIT



USE DOTS

RNTCP PP Schemes

Scheme for treatment adherence

- All private practitioners can be involved as DOT Centres
- Eligibility criterion
 - PP has to undergo 6 hours of intensive training in Training Module for Medical Practitioners

Grant –in –aid

- **Rs 400/-** per patient successfully treated with all services i.e. treatment including initial home visit and default retrieval
- **Rs 250/-** per patient successfully treated, where initial home visit and default retrieval are the responsibility of:
 - An NGO, if it is working on the scheme for providing Directly Observed Therapy in the same area (for which the NGO will be reimbursed at the rate of **Rs 150/-** per patient cured/treatment completed)
- Category 4 patients: **Rs 1000** after completion of IP and **Rs 1500** after completion of CP.

Designated Microscopy & Treatment centre (a + b)

Eligibility

- NGO or Private labs with adequate civil works
- Collective OPD of > 60 /day or 3-5 samples per day
- Trained Medical Officer & Laboratory Technician
- Functional Binocular Microscope

Role of Private Practitioner

- To perform smear microscopy as per RNTCP guidelines
- Covered under EQA

Role of RNTCP (DTO/STO)

- Training of concerned staff and provision of lab consumables
- Ensure quality assurance, supervise and monitor

Annual grant-in-aid of Rs. 1,50,000

If the DMC wishes to start a Treatment centre then it may be allowed but only Honorarium will be paid. No further administrative costs will be given

Rs 25 per slide if only private lab (without any treatment centre is available)

Slides for International Standards

International Commitment:

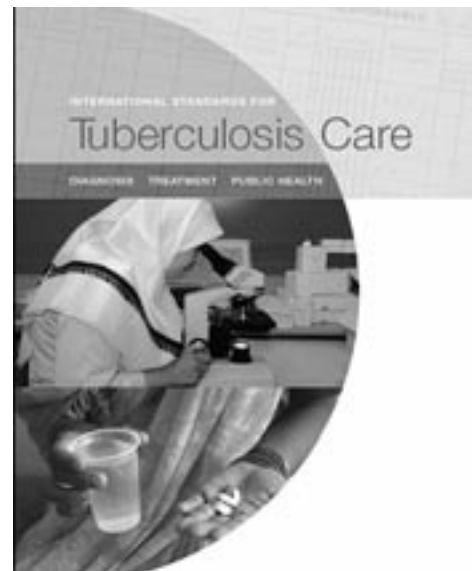
- Pursuing quality DOTS expansion & enhancement
- Addressing TB/HIV and MDR-TB
- Contributing to health system strengthening
- **Engaging ALL care providers**
- Empowering patients and communities
- Enabling and promoting research



International Standards for TB Care

Developed by the TBCTA

- IUATLD, ATS, CDC, WHO, KNCV TB Foundation, Professional Associations etc
- Describes 21 standards for Diagnosis, Treatment and PH aspects of TB Care
- On www.tbctia.org website



Standards for diagnosis

Standards for Diagnosis	
In general	<ul style="list-style-type: none"> The importance of intensified case finding is emphasized A table presenting a succinct summary of the evidence base for the various diagnostic tests has been added
Standard 1	<ul style="list-style-type: none"> Active case finding using symptom-based assessments in high risk populations is emphasized
Standard 2	<ul style="list-style-type: none"> The wording has been changed to recommend collection of at least 2 sputum specimens rather than at least 3 specimens
Standard 3	<ul style="list-style-type: none"> The phrase, "—where facilities for culture are available—," has been deleted to emphasize that cultures for mycobacteria are an important part of the diagnostic evaluation for patients with suspected extrapulmonary tuberculosis
Standard 4	<ul style="list-style-type: none"> This standard is unchanged
Standard 5	<ul style="list-style-type: none"> The phrase, "—where facilities for culture are available—," has been deleted to emphasize that sputum cultures for mycobacteria are an important part of the diagnostic evaluation in patients with negative sputum smears A new algorithm for evaluating persons suspected of having tuberculosis but who have negative sputum smears has been substituted for the previous algorithm The role of liquid culture media and line-probe assays for detecting resistance to isoniazid and rifampicin is described An expanded description of the role of radiography and the importance of quality control for radiography has been added
Standard 6	<ul style="list-style-type: none"> This standard has been re-written to be consistent with the WHO document, <i>Guidance for national tuberculosis programmes on the management of tuberculosis in children</i>

Standards for treatment

Standards for Treatment	
Standard 7	<ul style="list-style-type: none"> This standard is unchanged
Standard 8	<ul style="list-style-type: none"> This standard has been re-written to be consistent with revisions of WHO guidelines
Standard 9	<ul style="list-style-type: none"> The importance of a treatment supporter is emphasized The findings of a systematic review of qualitative research on adherence to tuberculosis treatment are presented
Standard 10	<ul style="list-style-type: none"> The standard has been changed to reflect revisions to treatment recommendations by WHO
Standard 11	<ul style="list-style-type: none"> The original Standard 14 is now Standard 11. The standard has been changed to indicate the need to assess for drug resistance if the sputum smear is positive at completion of 2-3 months of treatment and with treatment failure or relapse. A table describing risk factors for drug resistance has been added to the text. A section on XDR-TB has been added
Standard 12	<ul style="list-style-type: none"> The original Standard 15 is now Standard 12. The standard has been changed to reflect the revised WHO recommendations for programmatic management of DR-TB
Standard 13	<ul style="list-style-type: none"> The original Standard 11 is now Standard 13

Standards for addressing HIV Infection and other Co-morbid conditions

Standards for Addressing HIV Infection and other Co-morbid Conditions	
In general	<ul style="list-style-type: none"> This is a new category in the standards
Standard 14	<ul style="list-style-type: none"> The original Standard 12 is now Standard 14. It has been rewritten to indicate that all patients with tuberculosis and, in high risk areas or in individuals with risk factors, persons suspected of having tuberculosis should have HIV testing
Standard 15	<ul style="list-style-type: none"> The original Standard 13 is now Standard 15
Standard 16	<ul style="list-style-type: none"> This is a new standard reflecting recommendations for use of isoniazid preventive therapy in persons with HIV infection
Standard 17	<ul style="list-style-type: none"> This is a new standard describing the importance of addressing co-morbid conditions

Standards for Public Health

Standards for Public Health	
Standard 18	<ul style="list-style-type: none"> The original Standard 16 is now Standard 18 and has been rewritten to be consistent with current recommendations for contact evaluation and management
Standard 19	<ul style="list-style-type: none"> This is a new standard describing the use of isoniazid preventive therapy in children and persons with HIV infection who are contacts of an infectious case
Standard 20	<ul style="list-style-type: none"> This is a new standard describing the need for infection control in healthcare facilities
Standard 21	<ul style="list-style-type: none"> The original Standard 17 is now Standard 21 and is unchanged

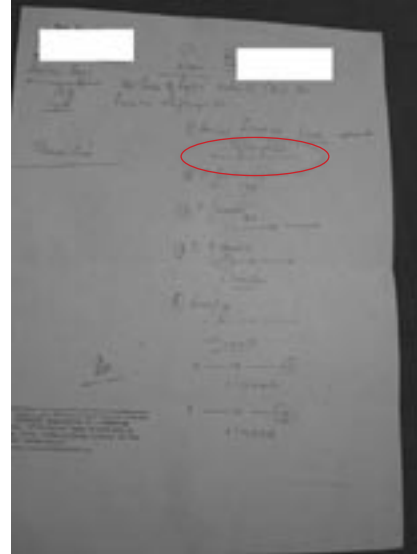
International Commitment

International Standards for TB Care

Eg: Standard - 7

Any practitioner treating a patient for TB is assuming an important public health responsibility.

The practitioner must not only prescribe an appropriate regimen, but also be capable of assessing the adherence of the patient.



Thank You

Rational use of Drugs and Fluoroquinolones

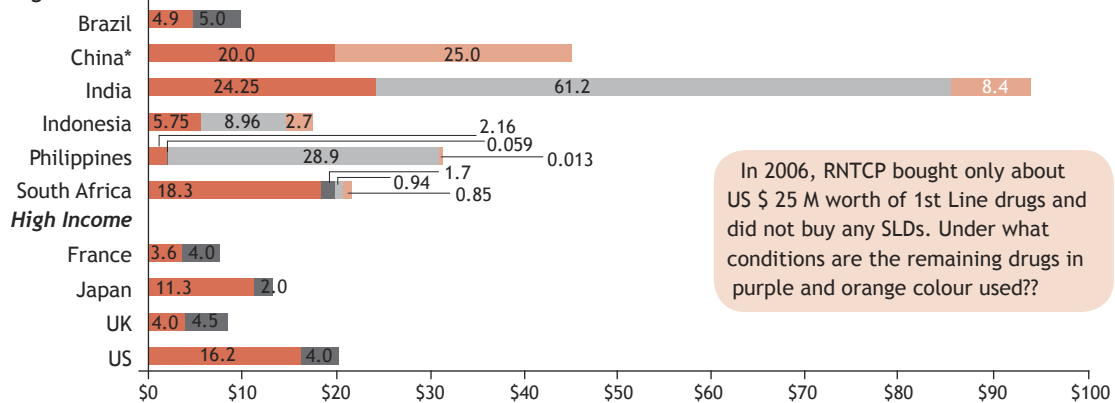
Central TB Division
 Directorate General of Health Services
 Ministry of Health and Family Welfare
 Nirman Bhawan
 New Delhi 110 108



1st and 2nd line TB drug market by country

- First-line Drug (Public Market)
- First-line Drug (Private Market)
- Second-line Drug (Public Market)
- Second-line Drug (Private Market)

High Burden



In 2006, RNTCP bought only about US \$ 25 M worth of 1st Line drugs and did not buy any SLDs. Under what conditions are the remaining drugs in purple and orange colour used??

Ref: Global alliance for TB drug development, May 2007.
 Pathway to patients: Charting the dynamics of the global TB Drug Market.

Irrational prescriptions of drugs and diagnostics

Levofloxacin!! For TB suspect

TB Elisa!! Prescribed for diagnosis of PTB



Fluoroquinolone resistance

- Only 4 (1.8%) out of 216 MDR-TB patients detected in the state wide DRS survey in Gujarat (2005-06) had XDR-TB
- But, as many as 60 (28%) out of these 216 MDR-TB patients had ofloxacin resistance

Rational use of fluoroquinolones

- “Empiric fluoroquinolone monotherapy has been associated with delays in the initiation of appropriate anti-tuberculosis therapy, and also resistance in *M. tuberculosis*.”
Int J Tuberc Lung Dis 2004;8(12):1396-400.
- Chennai Consensus Statement (Sep. 2007): “The fluoroquinolone group of drugs..... their use should be restricted only to the treatment of confirmed MDR-TB cases.”
- National Task Force for Medical Colleges (2006): “Fluoroquinolones as a class are critical for the successful treatment of MDR-TB, and should not be used in any first-line regimen.”

Thank You

Appendix 8

MoU and Application Format

To,
The Chairperson,
District / Corporation Health Society,

.....

Date:

Subject: Application for the NGO / PP Schemes under RNTCP

Respected Madam/Sir,

I/We have gone through the Revised Schemes for NGOs and Private providers under Revised National TB Control Program. I/We are herewith applying for the following scheme:

(Please tick the appropriate scheme. If a NGO/PP opts for more than one scheme, tick accordingly. Strike out whichever is not applicable).

- i. TB Advocacy, Communication, and Social Mobilization Scheme
- ii. Sputum Collection Centre/s Scheme
- iii. Sputum Pickup and Transportation Scheme
- iv. Designated Microscopy Centre Scheme
- v. Laboratory Technician Scheme
- vi. Culture-DST Scheme
- vii. Treatment Adherence Scheme
- viii. Urban Slum Scheme
- ix. Scheme for Tuberculosis Unit
- x. TB-HIV Scheme

The MoU and required documents, if any, is herewith attached.

Signature:

(Mr / Ms / Dr)

Designation:

Name of PP / NGO:

Address:

Revised National Tuberculosis Control Programme

Memorandum of Understanding (MoU) for the participation of Non-Governmental Organisations (NGOs)/Private Providers

1. Parties

This is to certify that _____
[Name of NGO/Private Provider] hence forth referred to as NGO/PP, has been enrolled as an NGO/Private Provider in the District of _____ [Name of District] for performance of the following activities in accordance with RNTCP policy; under the schemes listed below:

(Please tick the appropriate scheme. If a NGO/PP opts for more than one scheme, tick accordingly on a single MoU. Strike out whichever is not applicable).

- i. TB advocacy, communication, and social mobilization scheme
- ii. Sputum collection centre/s Scheme
- iii. Sputum pickup and transportation Scheme
- iv. Designated Microscopy Centre Scheme
- v. Laboratory Technician Scheme
- vi. Culture-DST Scheme
- vii. Treatment Adherence Scheme
- viii. Urban Slum Scheme
- ix. Scheme for Tuberculosis Unit
- x. TB-HIV Scheme

2. Period of Cooperation:

The NGO/Private Provider agrees to perform all activities outlined in the RNTCP NGO/Private Provider schemes. The duration of cooperation will be from ___/___/____ (dd/mm/yyyy) to ___/___/____ (dd/mm/yyyy). In case of poor performance and non-diligence, the contract can be terminated by the DHS at any time without prior notice.

3. Terms, conditions and specific services during the period of the MoU.

- A. The District/State Health Society shall (please strike out which ever is not applicable)
 - i. Provide financial and material support to the NGO/Private Provider for carrying out the activities as mentioned in the NGO/Private Provider scheme
 - ii. Provide relevant technical guidelines and updates (manuals, circulars, etc.)
 - iii. Provide RNTCP medicines and laboratory consumables for use as per RNTCP policy as outlined the scheme
 - iv. Periodically review the activities being undertaken by the NGO/Private Provider
- B. The NGO/Private Provider will: -
 - i. Perform all activities as mentioned under the scheme for which MoU is signed.
 - ii. Submit utilization certificate indicating expenditure during the quarter and available unspent balance to the respective State/District Health Society on quarterly basis.
 - iii. Maintain adequate documentation of as per RNTCP policy which is mentioned under the scheme.
 - iv. Get commodity assistance as per the scheme.

C. Grant-in-Aid

Funds - Rs. will be released bi-annually by the respective health society in the name of the NGO/Private Provider.

The NGO/Private Provider will submit utilization certificate indicating expenditure during the particular quarter and available unspent balance to the respective State/District Health Society on quarterly basis. The subsequent release will depend on the unspent balance and committed liability (if any).

In case services of NGO are discontinued, unspent balance, if any will be refunded.

Necessary approval from the Central TB Division/ State Health Society has been obtained:
Yes/ No/ Not applicable.

Enclosures: Copy of the NGO/Private Provider schemes.

Signature of STO/DTO:
(On behalf of the
respective SHS/DHS)
Seal:

Signature of authorised signatory:
(on behalf of the NGO
/Private Provider)
Seal:

Duplicate

To,
The Chairperson,
District / Corporation Health Society,
.....

Date:

Subject: Application for the NGO / PP Schemes under RNTCP

Respected Madam/Sir,
I/We have gone through the Revised Schemes for NGOs and Private providers under Revised National TB Control Program. I/We are herewith applying for the following scheme:

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- x. TB-HIV Scheme

The MoU and required documents, if any, is herewith attached.

Signature:

(Mr / Ms / Dr)

Designation

Name of PP / NGO:

Address:

Revised National Tuberculosis Control Programme

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- viii. Urban Slum Scheme
- ix. Scheme for Tuberculosis Unit
- x. TB-HIV Scheme

2. Period of Cooperation:

The NGO/Private Provider agrees to perform all activities outlined in the RNTCP NGO/Private Provider schemes. The duration of cooperation will be from ___/___/____ (dd/mm/yyyy) to ___/___/____ (dd/mm/yyyy). In case of poor performance and non-diligence, the contract can be terminated by the DHS at any time without prior notice.

3. Terms, conditions and specific services during the period of the MoU.

- A. The District/State Health Society shall (please strike out which ever is not applicable)
 - i. Provide financial and material support to the NGO/Private Provider for carrying out the activities as mentioned in the NGO/Private Provider scheme
 - ii. Provide relevant technical guidelines and updates (manuals, circulars, etc.)
 - iii. Provide RNTCP medicines and laboratory consumables for use as per RNTCP policy as outlined the scheme
 - iv. Periodically review the activities being undertaken by the NGO/Private Provider
- B. The NGO/Private Provider will: -
 - i. Perform all activities as mentioned under the scheme for which MoU is signed.
 - ii. Submit utilization certificate indicating expenditure during the quarter and available unspent balance to the respective State/District Health Society on quarterly basis.
 - iii. Maintain adequate documentation of as per RNTCP policy which is mentioned under the scheme.
 - iv. Get commodity assistance as per the scheme.

C. Grant-in-Aid

Funds - Rs. will be released bi-annually by the respective health society in the name of the NGO/Private Provider.

The NGO/Private Provider will submit utilization certificate indicating expenditure during the particular quarter and available unspent balance to the respective State/District Health Society on quarterly basis. The subsequent release will depend on the unspent balance and committed liability (if any).

In case services of NGO are discontinued, unspent balance, if any will be refunded.

Necessary approval from the Central TB Division/ State Health Society has been obtained:
Yes/ No/ Not applicable.

Enclosures: Copy of the NGO/Private Provider schemes.

Signature of STO/DTO:

(On behalf of the
respective SHS/DHS)

Seal:

Signature of authorised signatory:

(On behalf of the NGO
/Private Provider)

Seal:

