



KINGDOM OF LESOTHO
NATIONAL TUBERCULOSIS PROGRAMME
POLICY AND MANUAL

Draft

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PREFACE

Since the World Health Organization declared tuberculosis (TB) a global emergency in 1993, worldwide efforts to fight the disease have intensified considerably. In Lesotho, TB is associated with HIV and AIDS co-infection, social problems, difficulties in patient adherence and the threat of resistance against anti-tuberculosis drugs. This is of great concern to the country, hence the need for the National Tuberculosis Control Programme (NTP) of Lesotho to be adequately positioned to face the challenges of controlling the disease.

The commitment of the Government of Lesotho to eliminate TB as a public health problem has resulted in strengthening the NTP at both national and district levels and increased allocation of funds to ensure country-wide access to quality TB services. It should be mentioned here, that the efforts of the GOL has been enhanced through 2 grants from the Global Fund to Fight AIDS, TB and Malaria (GFATM), which enabled rapid expansion of access to TB diagnostic and treatment services. Furthermore, a formidable in-country partnership has been built for TB which will ensure sustained action in a synergistic manner.

I note with great sense of fulfillment that Lesotho is among the countries of the world that have reached and even exceeded the 70% target for detection of infectious TB cases. However, the treatment success rate of 73% falls below the set target of 85%, which requires urgent implementation of the African TB emergency declaration to improve treatment outcomes.

The NTP produced the first edition of the Tuberculosis Control manual in 2003 I am convinced that the document has been instrumental to the achievements of the NTP so far.

This 2nd Edition which takes into consideration the most recent developments in TB control especially with respect to TB diagnosis and management under the influence of HIV/AIDS, MDR/XDR-TB management, management of TB in Children and issues of laboratory quality-assurance will no doubt add value to the quality of care for our people. I therefore congratulate the NTP for realizing the publication of this second edition, which is sure a product of considerable hard work.

I would like to reiterate that the Ministry of Health & Social Welfare considers TB control a priority and is strongly committed to the fight against TB, and will continue to play the role of a facilitator to ensure that the MDG targets for TB are achieved in Lesotho by 2015.

Dr. Mphu Ramatlapeng
Minister of Health & Social Welfare
Kingdom of Lesotho

FOREWORD

This manual describes the policy direction as well as guidelines for the diagnosis and management of tuberculosis patients in the Kingdom of Lesotho. It is also meant to serve as a guide for clinicians and other health workers involved in the management of tuberculosis patients with view to providing the optimum quality of care for our people.

The clinical knowledge, policy guidelines and programme organization reflected in this document are based on the TB control strategy recommended by the World Health Organization (WHO) and the Stop TB partnership.

This manual does not intend to provide the kind of comprehensive clinical knowledge on tuberculosis as obtainable from clinical textbooks. The manual, however, does intend to address the major elements relevant to addressing TB as a major public health problem in line with global and regional orientations; and in a user-friendly manner.

While the manual in its entirety is appropriate for TB control programme players at various levels, general practitioners and non-TB specialists may find the manual equally useful for quick reference on specific TB-related topics.

Likewise, some of its chapters are relevant and useful for policy-makers and for our valuable partners who also support TB control as a public health initiative.

Specifically, the manual is composed of 13 chapters which, taken as a whole, provide an overview of TB control. Together, the chapters cover a broad spectrum of topics ranging from epidemiology, pathogenesis, transmission, diagnosis, treatment, TB/HIV co-infection and MDR/XDR-TB management to topics such as TB control policy, TB control programme strategy and organization, health education and TB laboratory networks. Individual chapters may be easily consulted as reference on various topics and subtopics, such as case definitions, extra-pulmonary TB, BCG vaccination, managing TB risk groups and adverse TB drug reactions.

In order to keep the manual to a practical length, repetition of the content has been kept to a minimum, and readers should refer to the index for further reference. Furthermore details of the management of other related conditions e.g. HIV and AIDS and MDR-TB should be sought in their respective guidelines.

It is our hope that all stakeholders in the fight against tuberculosis will find this manual useful in the planning and implementation of their activities within the framework of the national policy.

Dr. M. Moteetee

Director General of Health Services

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The Ministry of Health and Social Welfare appreciates the efforts of the National Tuberculosis Control team in putting together this TB policy manual for Lesotho, which is a comprehensive document that outlined all strategies and activities towards achieving of TB control objectives. Noteworthy are the contributions of Dr. M. Letsie (Head Disease Control Division), Dr. Job R. Ndile (NTP Manager), Dr. Kefas Samson (TB Advisor), Dr. Biggie Mabaera (URC), Dr. Hind Satti (PIH), Dr. Gani Alabi (WHO), Dr. M. Mabathoana (WHO), Mrs. Kekeletso Kao (Director Laboratory Services), Dr. K. Ajay (FIND), Mrs. Mareka Mathabo (Central Laboratory), Ms. Thato Nkuebe (Pharmacist), Mrs. Shoeshoe, Ms. Nthabiseng Ntlama.

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GLOSSARY AND ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
AFB	Acid Fast Bacilli
BCG	Bacillus de Calmette et Guérin
CHAL	Christian Hospital Association of Lesotho
CSF	Cerebrospinal fluid
DOT	Directly Observed Treatment
DOTS	Directly Observed Treatment Short-course
DTBC	District TB Coordinator
DTBO	District TB Officer
DTD	Demonstration and Training District
E	Ethambutol
EPTB	Extrapulmonary tuberculosis
FDC	Fixed Dose Combination
HIV	Human Immunodeficiency Virus
HSA	Health Service Area
IEC	Information, Education and Communication
INH	Isoniazid
IUATLD	International Union Against Tuberculosis and Lung Disease
LFDS	Lesotho Flying Doctors Service
MDR-TB	Multi-drug resistant tuberculosis
MTB	Mycobacterium Tuberculosis
NACP	National AIDS Control Programme
NDSO	National Drug Services Organization
NGO	Non-Governmental Organization
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NTP	National TB Control Programme
PHC	Primary Health Care
PI	Protease Inhibitor
PPD	Purified Protein Derivative
PTB	Pulmonary Tuberculosis
PZA	Pyrazinamide
RR	Recording & Reporting
R	Rifampicin
S	Streptomycin
SCC	Short Course Chemotherapy
SCR	Smear Conversion Rate
TAT	Turn Around Time
VCT	Voluntary Counselling Test
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children Fund
WHO	World Health Organization
Z	Pyrazinamide
ZN Stain	Ziehl – Neelsen Stain

CHAPTER 1 INTRODUCTION

1.1 The country

The Kingdom of Lesotho is completely surrounded by South Africa. The country has an estimated population of 2.1 million people, of whom 39% are aged 0-14 years (male 433,229; female 427,926), 56.3% are aged 15-64 years (male 600,476; female 642,538), and 4.7% are aged 65 years and over (male 43,691; female 60,094). The overall male: female ratio is 0.95. Life expectancy at birth in 2002 was 36 years¹, primarily because of the high HIV/AIDS epidemic.

The country has ten administrative districts namely: Berea, Butha-Buthe, Leribe, Mafeteng, Maseru, Mohales' Hoek, Mokhotlong, Qacha's Nek, Quthing and Thaba-Tseka.

Lesotho obtained its independence from the United Kingdom on 4 October 1966 to become a parliamentary constitutional run by a Prime Minister and His Majesty the King as Head of State. Maseru is the capital city.

More than 80% of the country is higher than 1800 metres above sea level. The major natural resources are water, agricultural and grazing land, some diamonds and other minerals. Only 10% of the land is arable, and population pressure has resulted in overgrazing, severe soil erosion, and soil exhaustion.

TB is a major public health problem in Lesotho. With an estimated prevalence of 696/100,000, the country has the 3rd highest per capita burden in the world. Statistics indicate that about 64% of TB cases are also co-infected with HIV. In 2003, the estimated HIV prevalence among people aged 15-49 years was 28.9%², while the result of the 2005 Sero-prevalence survey gave a prevalence of 23.2%. The high HIV/AIDS prevalence is reversing progress made in poverty alleviation and human development.

1.2 Organization of Health Care Services in Lesotho

Lesotho has a comprehensive, co-coordinated and integrated health system based on Primary Health Care principles. Each of the country's 10 districts has a District Health Management Team (DHMT) which manage, coordinate and oversee the implementation of activities related to health and social welfare services.

The Government of Lesotho (GOL) encourages Public-Private Partnership for provision of quality health care services to the population. The Christian Hospital Association of Lesotho (CHAL) is the main partner of the MOHSW in the provision of health care to the population especially in remote rural areas. CHAL provides one third of health care services through a network of hospitals, clinics and community health workers. CHAL runs 8 out of a total of 20 hospitals; and 75 of the 171 Health Centres in the country. The Lesotho Flying Doctors Service (LFDS) provides emergency medical services to remote mountainous areas, and also supports rural health care programs.

There are 18 General Hospitals in Lesotho, as well as 2 Specialist Hospitals, a Military Hospital and a Private Hospital opened in 1996. Patients requiring specialized care are referred to South Africa.

¹ UNDP Report, 2004

² UNAIDS Report 2004

The Department of Pharmaceutical Services is responsible for the provision of drugs to all hospitals and health centres, while the National Drug Services Organization (NDSO) is responsible for the procurement and distribution of drugs throughout the health system. The Lesotho Pharmaceutical Company, which is a para-statal corporation manufactures and tests a range of drugs and medicines.

The World Health Organization (WHO) is the main technical partner of the MOHSW, providing technical and other forms of assistance for a wide spectrum of health programmes in Lesotho. Other UN agencies including UNICEF, UNFPA and UNDP; international organizations and Non Governmental Organizations (NGOs) are also active in the health sector.

1.3 Organization of TB service delivery

The structure of TB services is based upon the “unit of management” which for Lesotho is the district (responsible for issuing TB numbers for patients in the district), serving an average population of 50,000 to 150,000. The management and organization of TB services at the district level are the responsibilities of the DHMTs discharged through the NTP focal person, which is the District TB Coordinator (DTBCO). Currently each hospital has at least one TB Officer (TBO) under the supervision of the DTBCO and Hospital Management Team (HMT) in general. The TB Officers coordinate and implement the NTP policy at hospital, health center and community levels. Under local government system and the national M&E plan all data and information health information flows from the districts to one focal point in the Health Planning and Statistics Unit (HPSU) of the Ministry of Health from where programs and other department access data for their managerial use.

1.4 Structure of the National TB Control Programme (NTP)

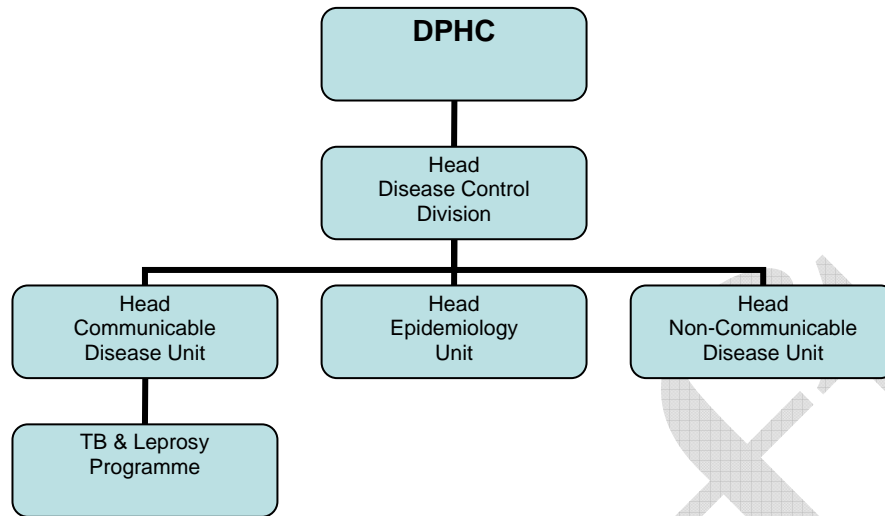
The NTP was established in 1986, and has been fully funded by the Government of Lesotho since 2001. At the national level, it operates under the Disease Control Unit, alongside other communicable and non-communicable disease control programs.

The program is headed by an NTP Manager under the responsibility of the Head of Disease Control Division, who in turn reports to the Director of Primary Health Care, who reports to the Director-General of Health Services.

At the district level, the District TB Coordinators directly supervises the TB Officers who are responsible for TB case registration and treatment in health facilities. At community level the community DOT supporter reports to the TB coordinator.

At community level, various stakeholders including CHWs, CSOs, NGOs, CBOs, TB Treatment Supporters and Traditional Healers etc in their varying capacities deliver TB care in close collaboration with the District team.

Figure 1: Organizational Chart of the Disease Control Division



1.5 Goals, Objectives and targets of the National TB Programme

The Goal of the Lesotho National TB Programme is to reduce TB mortality, morbidity and disease transmission to a level that it no longer constitutes a Public Health Problem, while preventing the development of drug resistance.

The Objectives:

To provide standardized short-course chemotherapy provided under strict supervision to at least all identified sputum smear positive cases.

The targets:

Lesotho subscribes to the global initiative to eliminate TB as a public health problem within the context of the following agreed targets:

- **The World Health Assembly (WHA) targets** to cure at least 85% of newly detected cases of sputum smear-positive TB and to detect 70% of the estimated incidence of sputum smear-positive TB;
- **Millennium Development Goal (MDG) targets:** Target 8 under MDG Goal 6 (to combat HIV/AIDS, malaria and other diseases), To have halted by 2015 and begun to reverse the incidence of malaria and other major diseases, with the following specific for TB:
 - **Indicator 23:** Prevalence and death rates associated with tuberculosis
 - **Indicator 24:** Proportion of tuberculosis cases detected and cured under DOTS
- **The Stop TB Partnership Targets:**
 - **By 2005:** At least 70% of people with infectious TB will be diagnosed (under the DOTS strategy), and at least 85% of these patients will be cured.
 - **By 2015:** The global burden of TB (disease prevalence and deaths) will be reduced by 50% relative to 1990 levels.

CHAPTER 2 TUBERCULOSIS EPIDEMIOLOGY

2.1 Global Epidemiology of TB

TB is still a major cause of death worldwide, but the global epidemic is on the threshold of decline³. WHO estimates that about one-third of the global population is infected with *Mycobacterium tuberculosis* and at risk of developing the disease. In 2005, there were an estimated 8.8 million new TB cases reported, 7.4 million (84%) in Asia and sub-Saharan Africa; and a total of 1.6 million people died of TB, including 195 000 patients infected with HIV.

With the 8.8 million new incident TB cases in 2005, there were 14.1 million prevalent cases (217/100 000) on average (Table 9). An estimated 1.6 million people (24/100 000) died from TB in 2005, including those coinfecting with HIV (195 000).

About 11% of the annual incident cases (about 1 million) are children (under 15 years of age). Of these childhood cases, 75% occur annually in 22 high-burden countries that together account for 80% of the world's estimated incident cases. In countries worldwide, the reported percentage of all TB cases occurring in children varies from 3% to more than 25%. More than 90% of the global TB cases and 98% of TB deaths occur in the developing world and 75% of these cases are in the most economical productive age group (15-50 years). TB deaths comprise 25% of all avoidable adult deaths in developing countries.

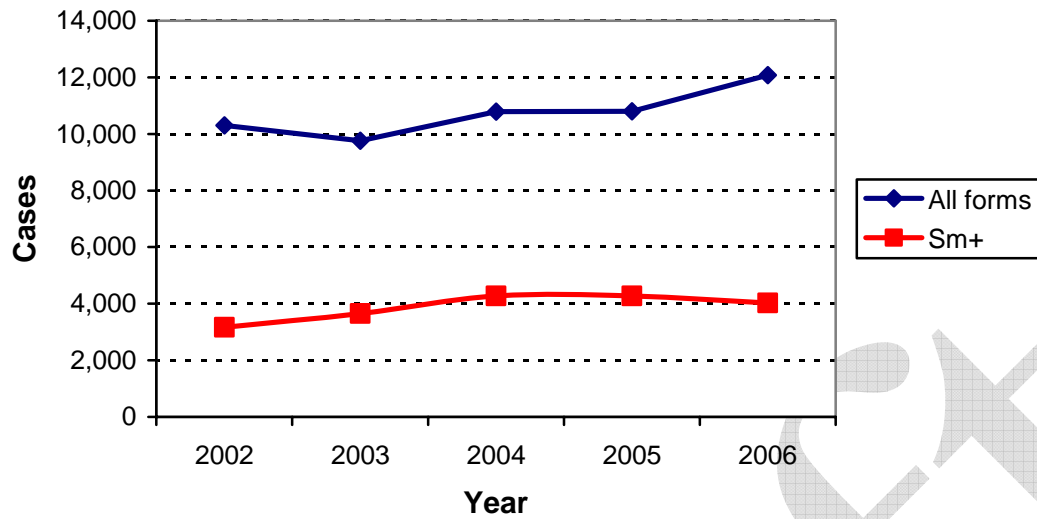
Co-infection with human immunodeficiency virus (HIV) significantly increases the risk of developing TB. Countries with a high prevalence of HIV, especially in the sub-Saharan Africa are witnessing a profound increase in the number of TB cases.

2.2 The Tuberculosis situation in Lesotho

The incidence of TB in Lesotho is one of the highest in the world. In 2006, Lesotho reported 12,074 TB cases (11,436 new and 638 re-treatment) of all forms of TB. The incidence of all cases and new smear positive cases was 635 per 100,000 population and 212 per 100,000 population respectively, with estimated case detection rate of 80% for new sputum smear-positive cases. Out of the 11,436 new cases reported, patients with smear-positive disease accounted for only 35% (4,024) of all notified cases, as opposed to the expected 50%. Figure 1 shows the number of TB cases reported between 1991 and 2006.

Figure 2: Number of tuberculosis cases registered in Lesotho, 2002 – 2006

³ Global Tuberculosis report 2007, Geneva Switzerland



The treatment success rate has witnessed significant improvement from an unacceptable level of 52% in 2002 cohort of smear positive TB patients to 73% among 2005 cohorts. The main factors that negatively influenced the treatment outcomes in 2006 were high death (8%) mostly HIV-related; high transfer rate (6%); default rate (4%), as well as high proportion of patients whose outcomes were not evaluated (7%).

Tuberculosis prevalence surveys conducted by the Ministry of Health and Social Welfare in conjunction with the South African Medical Research Council in 1982 and 1992 showed the Annual Risk of Infection to be 1.2% and 0.8% respectively. Another drug resistance survey has been scheduled for 2007.

CHAPTER 3 STRATEGY AND FRAMEWORK FOR TB CONTROL IN LESOTHO

3.1 The global strategy and framework

Global efforts to control TB were reinvigorated in 1991, when a World Health Assembly (WHA) resolution recognized TB as a major global public health problem. Two targets for TB control were established as part of this resolution – detection of 70% of new smear-positive cases, and cure of 85% of such cases, by the year 2000, 2005. In 1994, the WHO-recommended 5-point policy package referred to as the Directly Observed Treatment Short-course (DOTS) strategy for TB control was launched. The 5 elements of the DOTS Strategy include:

1. **Sustained political commitment** to increase human and financial resources and make TB a nationwide priority integral to the health system.
2. **Access to quality-assured sputum microscopy** for case detection among persons presenting with, or found through screening to have, symptoms of TB.
3. **Standardized short-course chemotherapy for all cases of TB under proper case management conditions, including direct observation of treatment.** Proper case management conditions imply technically sound and socially supportive treatment services.
4. **Uninterrupted supply of quality-assured drugs** with reliable drug procurement and distribution systems.
5. **Recording and reporting system enabling outcome assessment of all patients and assessment of overall programme performance.** This is the basis for systematic programme monitoring and correction of identified problems.

DOTS, which underpinned the First Global Plan to Stop TB, was being applied in 187 countries in 2005; 89% of the world's population lived in areas where the strategy had been implemented by public health services.

The first Global Plan to Stop TB set out the actions that were needed in TB control over the period 2001–2005 and helped to steer global TB control efforts during that period. According to WHO, more than 90 million TB patients were reported between 1980 and 2005; 26.5 million patients were notified under DOTS between 1995 and 2005, and 10.8 million new smear-positive TB cases were registered for treatment by DOTS programmes between 1994 and 2004.

Despite these remarkable achievements, the 2005 WHA targets were not met, and the need to expand the framework of TB control was recognized. This entails placing the task of TB control in the context of health system performance, by encouraging the participation of all health-care providers (not just those working for government health institutions), by empowering TB patients and communities who suffer from TB and by promoting research. This informed the elements of what is termed as the Stop TB Strategy⁷.

The new strategy embraces the fundamentals of TB control originally framed as DOTS, but extends the reach of control activities into other key areas. These include the well-known problems of multidrug-resistant TB (MDR-TB), the now extensively drug-resistant TB (XDR-TB); and of TB associated with the human immunodeficiency virus (HIV).

The second Global Plan to Stop TB (2006–2015), builds on the achievements of the first; is underpinned by the new Stop TB Strategy and aims at attainment of the MDG and related Stop TB Partnership targets for TB control in the next decade. The elements of the New Stop TB Strategy is as follows:

Figure 3: The Stop TB Strategy at a glance

The Stop TB Strategy	
Vision	A world free of TB
Goal	To dramatically reduce the global burden of TB by 2015 in line with the Millennium Development Goals (MDGs) and the Stop TB Partnership targets
Objectives	Achieve universal access to high-quality diagnosis and patient-centred treatment Reduce the human suffering and socioeconomic burden associated with TB Protect poor and vulnerable populations from TB, TB/human immunodeficiency virus (HIV) and multidrug-resistant TB (MDR-TB) Support development of new tools and enable their timely and effective use
Targets	MDG 6, Target 8: "halted by 2015 and begun to reverse the incidence" [of TB] Targets linked to the MDGs and endorsed by Stop TB Partnership – By 2005: detect at least 70% of new sputum smear-positive TB cases and cure at least 85% of these cases – By 2015: reduce prevalence of and deaths due to TB by 50% relative to 1990 – By 2050: eliminate TB as a public health problem (<1 case per million population)
Components of the strategy and implementation approaches	
1. Pursue high-quality DOTSa expansion and enhancement Political commitment with increased and sustained financing Case detection through quality-assured bacteriology Standardized treatment with supervision and patient support An effective drug supply and management system Monitoring and evaluation system, and impact measurement	
2. Address TB/HIV, MDR-TB and other challenges Implement collaborative TB/HIV activities Prevent and control MDR-TB Address prisoners, refugees and other high-risk groups and special situations	
3. Contribute to health system strengthening Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery and information systems Share innovations that strengthen systems, including the Practical approach to lung health (2) Adapt innovations from other fields	
4. Engage all care providers Public–public and public–private mix approaches International standards for tuberculosis care (3)	
5. Empower people with TB, and communities Advocacy, communication and social mobilization Community participation in TB care Patients' charter for tuberculosis care (4)	
6. Enable and promote research Programme-based operational research Research to develop new diagnostics, drugs and vaccines	

3.2 The TB Control Strategy and framework for Lesotho

Lesotho adopted the WHO-recommended DOTS strategy in 1991 and has since 2004 achieved 100% coverage with the strategy by districts. The country has made significant progress in implementing the strategy; and as at 2006 achieved 71% CDR and 73% Treatment success rate for new smear positive cases in 2005 cohort.

The Government of Lesotho is committed to providing the highest possible standard of care for all TB patients regardless of the type through a patient-centred or patient-friendly approach. The service delivery should take into consideration and reflect community participation in TB care, joint TB/HIV care, private-public partnerships, drug susceptibility surveillance and treatment of MDR-TB cases.

The New Stop TB strategy launched in 2006 provides such a framework to help Lesotho realize its TB control objectives. The country therefore adopts the strategy as the framework for TB Control in the country with emphasis on the DOTS as the core element. The country will pursue the objective of institutionalizing the strategy at district and Health Service Area (HAS) levels. To this end, the Planning, Implementation, Monitoring and Evaluation of TB services should be in line with the New Stop TB strategy.

3.2.1 Key Operations for DOTS Implementation in Lesotho:

The Ministry of Health and Social Welfare shall ensure the following key operations for implementation of the DOTS strategy in the country:

- Maintain a National Tuberculosis Control Programme with a strong central unit under Disease Control Unit;
- Ensure development and implementation of a Medium-term Development Plan (Strategic Plan for the TB programme).
- Develop and update TB treatment guidelines based on currently available evidences and best practices endorsed by WHO;
- Ensure a functional microscopy service that meets the requirement of the programme for effective diagnosis of Pulmonary TB with the shortest possible turn-around time for smear results;
- Organize TB treatment services within the PHC system where directly observed short-course chemotherapy is given priority;
- Secure a regular supply of drugs and diagnostic material; and
- Ensure consistent task-oriented supervision of the key operations at the intermediate and district level.
- Strengthen and sustain Advocacy, Communication and Social Mobilization (ACSM), involving private and voluntary health care providers, economic analysis and financial planning, and operational research.

CHAPTER 4 CASE FINDING AND DETECTION POLICIES

4.1 The fundamental basis of case finding

TB is an infectious disease spread through release of droplet nuclei containing virulent human strains of the tubercle bacillus by especially sputum smear positive cases. Infection by *Mycobacterium bovis* through ingestion of unpasteurised cow's milk is less common. An untreated infectious person can infect, on average, between 10-15 persons per year. Finding infectious TB patients and treating them effectively to cure is the best public health approach to break the chain of transmission of tubercle bacilli and improve the epidemiological situation of TB in the country. Therefore Case-finding and treatment are considered to be one entity, because case-finding without effective treatment is pointless. Case-finding can either be passive or active. While Passive case-finding relies on self-referral of symptomatic individuals who consult health institutions, and are subsequently diagnosed as tuberculosis cases, Active case-finding usually involves health services going out to the communities to detect TB suspects among contacts of known pulmonary TB patients.

4.2 The Case finding policy in Lesotho

Detection of TB in health facilities should be an ongoing activity. The main priority is to identify the sources of infection, namely, pulmonary TB cases excreting tubercle bacilli that can be detected by microscopy. Cough is the most common symptom of PTB and present in 95% of smear positive cases. However, it is not a specific sign of TB since it is present in many conditions affecting the lower respiratory tract.

A pulmonary TB suspect is defined as any person who presents with symptoms or signs suggestive of TB, in particular cough for 2 weeks or more). A sputum examination should be done and the suspect is entered into the "Register of TB suspects".

In Lesotho, the priority shall be to provide high quality and effective TB services within the PHC system that will attract the potential beneficiary population. This will include strengthening the management of symptomatic patients at the out-patients and in-patients of all health facilities through implementation of the Practical Approach to Lung Health (PAL). However, it is recommended that active case-finding should be conducted for the following situations:

- HIV infected people (including children) should be screened for TB
- Children who are in close contact with an active TB case, especially those that are under the age of five.

4.2.1 Criteria for identifying TB suspects

A pulmonary TB suspect is defined as any person who presents with symptoms or signs suggestive of TB, in particular cough for 2 weeks or more). A sputum examination should be done and the suspect is entered into the "Register of TB suspects"

4.3 Categorization of TB Cases

The diagnosis of TB refers to the recognition of an active case. Beyond the diagnosis of TB disease, the type of TB case should also be defined to allow appropriate treatment to be given and the outcome of treatment evaluated. Before initiating treatment, health care providers should categorize TB cases based on the following determinants:

- Site of TB disease

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

4.3.1 Site of TB disease

Pulmonary tuberculosis (PTB) refers to disease involving the lung parenchyma. A patient with both pulmonary and extrapulmonary TB should be classified as a case of pulmonary TB. Miliary TB is classified as pulmonary TB because there are lesions in the lungs.

Extrapulmonary tuberculosis (EPTB) refers to tuberculosis of organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. Diagnosis should be based on one culture-positive specimen, or histological or strong evidence consistent with active EPTB, followed by a decision by a clinician to treat with a full course of tuberculosis chemotherapy.

4.3.2 Bacteriology (result of sputum smear) in pulmonary TB

Defining the smear result in pulmonary cases is important to:

- Identify smear-positive cases, because they are the most infectious cases;
- Record, report and evaluate programme performance (smear-positive cases are the cases for which bacteriological monitoring of treatment progress is most practicable).

Case definitions by site and result of smear

Smear positive PTB case

- At least 1 sputum smears positive for AFBs or
- 1 sputum smear positive for AFBs and chest x-ray abnormalities consistent with active TB or 1 sputum smear positive and culture positive for *M. tuberculosis* or
- One sputum smear examination positive for AFB and laboratory confirmation of HIV infection or strong clinical evidence of HIV infection

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

Smear negative PTB case

- At least two sputum smears are negative for AFBs and
- Chest x-ray abnormalities are consistent with active TB and
- Laboratory confirmation of HIV infection or
- Strong clinical evidence of HIV infection

AND

- Decision by a clinician to treat with a full course of anti-tuberculosis chemotherapy

OR

- A patient with AFB smear-negative sputum which is culture-positive for *Mycobacterium tuberculosis*.

4.3.3 Severity of TB disease

Bacillary load, extent of disease and anatomical site are considerations in determining TB disease severity and therefore the appropriate treatment. Involvement of an anatomical site results in

classification as severe disease if there is a significant acute threat to life (e.g. pericardial TB), a risk of subsequent severe handicap (e.g. spinal TB, or both (e.g. Meningeal TB)). Miliary, disseminated TB is considered to be severe.

4.3.4 History of previous treatment

New

A patient who has never had treatment for TB or who has taken anti-tuberculosis drugs for less than one month.

Relapse

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

Treatment after failure

A patient who is started on a retreatment regimen after having failed previous treatment

Treatment after default

A patient who returns to treatment after having interrupted treatment for two or more consecutive months, and returned to the health service smear-positive (sometimes smear-negative but still with active TB as judged on clinical and radiological assessment).

Transfer in

A patient who has been transferred from another District TB register to continue treatment.

Chronic case

Patient who is sputum positive at the end of a re-treatment regimen.

Other

All cases that do not fit the above definitions. Other previously treated cases include pulmonary cases with unknown result of previous treatment, sputum smear negative pulmonary cases and extrapulmonary cases previously treated.

CHAPTER 5 DIAGNOSIS OF TB

5.1 Basis for the TB diagnosis policy

The highest priority for TB control is the identification and cure of infectious cases i.e. patients with sputum smear-positive PTB. The epidemiological progress in eliminating TB as a public health problem therefore depends on the proportion of the existing infectious cases detected and effectively treated (cured). Therefore all persons (regardless of HIV status) with clinical features suggestive of PTB must submit sputum for diagnostic sputum smear microscopy.

5.2 Approach to TB diagnosis

5.2.1 Identification of Pulmonary TB Suspects:

Over 90% of patients with sputum smear-positive PTB develop a cough soon after disease onset. The most common symptoms of pulmonary tuberculosis are:

- persistent cough for 2 weeks or more; every patient presenting to a health facility with this symptom should be designated a “tuberculosis suspect”
- sputum production which may be blood-stained
- shortness of breath, and chest pain
- loss of appetite and loss of weight
- a general feeling of illness (malaise)
- tiredness and loss of motivation
- night sweats and fever.

The physical signs in patients with PTB are nonspecific. They do not help to distinguish PTB from other chest diseases. There may be general signs, such as fever, tachycardia (fast pulse rate) and finger clubbing. Chest signs (heard through a stethoscope) may include crackles, wheezes, bronchial breathing and amphoric breathing. There are often no abnormal signs in the chest.

A patient presenting with these symptoms and signs who is, or was in contact with a person with infectious tuberculosis should be suspected of having PTB.

All TB suspects who present to health facilities should be recorded on a “Registry of TB suspects”. All health facilities without microscopy should sent suspects sputa to the nearest accredited laboratory within the district.

5.2.1 Sputum Collection, Labeling, Storage and Transport

At least three sputum specimens should be taken from a TB suspect.

At the first encounter with the patient the first specimen is collected on the spot referred to as the “**spot specimen**” is collected; the patient should be provided with a sputum container for collection of the second sample early morning at home (‘**early morning specimen**’).

Sputum collection procedure

- Collection of sputum samples should be performed outside in an open place;
- The person should rinse the mouth with water;

- Explain the steps fully and slowly
- Demonstrate a deep cough from the bottom of the chest, beginning with deep breathing
- Ask the patient to be very careful to direct the sputum into the container not to contaminate the outside of the bottle
- Supervise the collection, but do not stand in front of the patient
- Do it in a well ventilated area or outside without others watching
- Give the patient the container without the lid
- Hold the lid yourself, ready to replace it immediately
- Make sure that the lid is securely closed
- Wash hands after handling the sputum specimen
- The person must be encouraged to produce a specimen after deep coughing even if this is saliva.

Sputum labeling

Correct labeling is essential and will save time and prevent errors.

Label the container first, very clearly with:

- Name of clinic/hospital
- Name of patient and clinic/hospital number
- Indicate whether the specimen is pretreatment, follow-up or end of treatment specimen
- Write clear instructions regarding what investigations are required
- Write the appearance of the sputum (e.g. mucoid, lumpy, green, offensive, etc)
- Date the specimen clearly and time of collection of the specimen

Note:

Labeling should always be done on the body of the container as the lids may easily be mixed up during specimen processing.

Sputum storage

- Place the sputum bottle in a plastic bag if possible to prevent contamination
- Store sputum specimen in a fridge if transport is not available immediately. Do not store in a freezer
- Sputum specimens should not be kept in a fridge for more than a week before transportation, if possible send away as soon as possible
- Record the date on which the specimen has been sent to the laboratory in the “Suspect Register”

Transportation of sputum specimens

- For rural health facilities that are without laboratory services, sputum specimens have to be transported to laboratories at least on a weekly basis;
- The District TB Coordinator should organize a sputum collection schedule for all facilities in the district;
- Transportation of specimens to the laboratory should be in cool sputum transport boxes. High temperatures during transit will kill bacilli;
- During transportation, specimens should be protected from contact with direct sunlight;
- The driver should be properly informed of the reasons for transporting the specimens, thereby ensuring that specimens go direct to the laboratory.

Note: Every working day, a responsible person should check the Suspects Register to see which results are pending and then contact the laboratory to find out where the results are.

Close cooperation with the laboratory will produce quick results, resulting in sputum positive patients being started on the correct treatment as soon as possible.

5.3 Identification of Extra-Pulmonary TB Suspects:

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

Extrapulmonary tuberculosis is more strongly associated HIV infection than pulmonary tuberculosis. HIV-related extrapulmonary tuberculosis is a WHO clinical stage 4 (advanced AIDS) diagnosis, and patients often have disseminated disease and are at high risk of rapid clinical deterioration and death.

The most common types of extra-pulmonary tuberculosis are:

- TB meningitis
- TB lymphadenitis
- Miliary tuberculosis
- TB Pleural effusion
- Tuberculous empyema
- Tuberculous pericardial effusion
- Ascites
- TB of the bones

Table 1: the usual clinical features and diagnostic tests of other forms of extrapulmonary TB

Site of disease	Clinical features	Recommended investigation
Spine	Back pain Gibbus Psoas abscess Radicular pain Spinal cord compression	Plain X-ray Tissue biopsy
Bone	Chronic osteomyelitis	Tissue biopsy
Peripheral joints	Usually monoarthritis especially hip	Plain X-ray Synovial biopsy
Gastrointestinal	Abdominal mass Diarrhoea	Barium X-ray
Liver	Right upper quadrant pain and mass	Ultrasound and biopsy
Renal and urinary tract	Urinary frequency Dysuria Haematuria	Sterile pyuria Urine culture Intravenous pyelogram

	Loin pain/swelling	Ultrasound
Adrenal gland	Features of hypoadrenalism (calcification (hypotension, low serum sodium, not potassium, raised urea, low glucose)	Plain X-ray (calcification) Ultrasound
Upper respiratory tract	Hoarseness and stridor Pain in ear Pain on swallowing	Usually complication of pulmonary disease
Female genital tract	Infertility Pelvic inflammatory disease Ectopic pregnancy	Pelvic examination X-ray genital tract Ultrasound pelvis Tissue biopsy
Male genital tract	Epididymitis	Often evidence of renal/urinary tract TB

5.4 Identification of Child TB Suspects:

Children can present with TB at any age, but the most common age is between 1 and 4 years. Case notifications of childhood TB depend on the intensity of the epidemic, the age structure of the population, the available diagnostic tools, and the extent of routine contact tracing.

The diagnosis of TB in children should be based on careful and thorough assessment of all the evidence derived from a careful history, clinical examination and relevant investigations, e.g. TST, chest X-ray (CXR) and sputum smear microscopy.

Although bacteriological confirmation of TB is not always feasible, it should be sought whenever possible, e.g. by sputum microscopy for children with suspected pulmonary TB who are old enough to produce a sputum sample.

A trial of treatment with anti-TB medications is not recommended as a method to diagnose TB in children. The decision to treat a child should be carefully considered and established by a Medical Officer; and once such a decision is made, the child should be treated with a full course of therapy.

5.5 Diagnosis of PTB

5.5.1 Confirming the diagnosis of PTB

Demonstration of micro-organisms (commonly referred to as acid-fast bacilli or AFB) in a PTB suspects sputum sample by AFB microscopy method proves that individual has smear-positive tuberculosis. However, a laboratory result that does not tie up with other clinical information must be interpreted with caution. The number of bacilli (AFB) seen in a smear reflects the patients infectivity (see 6.6.1).

The laboratory must record the number of bacilli seen on each smear as in table below:

Table 2: Guide for grading results of smear microscopy

Number of bacilli seen on a smear			Fields to examine	Results reported
No	AFB	per 100 oil immersion fields	100	0
1-9	AFB	per 100 oil immersion fields	100	Scanty indicate number (1-9)
10-99	AFB	per 100 oil immersion fields	100	1+
1-10	AFB	per 1 oil immersion field	50	2++
>10	AFB	per 1 oil immersion field	20	3+++

Smear-positive pulmonary tuberculosis

A TB suspect is diagnosed as smear positive TB case if:

- Two sputum smears positive for AFB, **or**
- One sputum smear examination positive for acid-fast bacilli (AFB) with Chest X-ray abnormalities consistent with active TB **and**
 - Laboratory confirmation of HIV infection **or**
 - Strong clinical evidence of HIV infection.

Smear-negative pulmonary tuberculosis

A TB suspect is diagnosed smear negative pulmonary TB if:

- At least two sputum specimens negative for AFB **and**
- Radiographical abnormalities consistent with active tuberculosis **and**
- Laboratory confirmation of HIV infection **or**
- Strong clinical evidence of HIV infection.

and

- Decision by a clinician to treat with a full course of antituberculosis chemotherapy

OR

- A patient with AFB smear-negative sputum which is culture-positive for *Mycobacterium tuberculosis*.

All positive sputum results should be recorded in both the Laboratory and TB District registers in **red** ink for ease of identification. The laboratory identification number and the date the examination was performed should be entered in the column next to that for the result of the examination.

5.5.2 Role of Other Investigations in TB Control

5.5.2.1 Role of Chest x-rays

While chest x-rays are quick and convenient, reliance on chest x-rays as the primary source for confirmation of diagnosis may result in unnecessary treatment. X-rays are necessary in suspects who cannot produce sputum and must be interpreted in the light of their history and clinical findings.

HIV-infection is known to be associated with chest-X-ray abnormalities even without tuberculosis. However, chest X-ray plays an important role in the diagnosis of tuberculosis among people living with HIV. The chest X-ray can also be an important entry point to diagnosing non-tubercular chest diseases, which are common among people living with HIV.

In view of the significant role of chest X-rays in shortening delays in TB diagnosis especially in HIV-infected individuals, the examination could be performed early in the course of investigation of a tuberculosis suspect. The presence of military shadows, unilateral pleural effusion and cavitation can be considered typical of TB and such cases should be initiated on appropriate treatment without delay.

Indications for chest x-ray

When the sputum results are positive

- Suspected complications, e.g. a breathless patient needing specific treatment (pneumothorax or pleural effusion)
- Frequent or severe haemoptysis
- To help in diagnosing other lung diseases
- Only one of the three pretreatment smears is positive.

When the sputum results are negative

- If TB is clinically suspected despite negative smears, the patient should have a chest x-ray to help make a decision regarding diagnosis and treatment.

During and at the end of treatment

It is only necessary to do X-rays during and at the end of treatment if there are specific clinical reasons and the progress is not satisfactory.

Radiographic Abnormalities Seen in PTB

No CXR pattern is absolutely typical of PTB, especially with underlying HIV infection. The table below shows so-called "classical" and "atypical" CXR patterns. The classical pattern is more common in HIV-negative patients, and the atypical pattern in HIV-positive patients.

Table 3: Table showing typical and atypical CXR patterns in HIV positive PTB

Classical Pattern	Atypical Pattern
Upper lobe infiltrates	Interstitial infiltrates (especially lower zones)
Bilateral infiltrates	Intrathoracic lymphadenopathy
Cavitation	No cavitation
Pulmonary fibrosis and shrinkage	No abnormalities

5.5.2.2 Role of culture and susceptibility testing

Culture is more sensitive than smear microscopy, however, it is an expensive and slow diagnostic technique and it takes at least 6 weeks to provide a definitive result. Culture results may therefore not be helpful in making a rapid individual diagnosis. Because culture is expensive and results take a longer time to become available, it is not routinely used under programme conditions.

Indications for sputum culture and DST:

High risk of MDR-TB as in :

- Contacts of known MDR-TB cases with active TB
- Treatment failure
- History of multiple previous treatments in public or private sector

A standardized Category IV regimen should be used as empiric treatment while awaiting DST results.

Moderate risk of MDR-TB as in:

- Treatment default or relapse
- Migrant workers with new TB
- Health workers with new TB

The patient should receive an empiric regimen of first-line anti-TB drugs (Category I or II) while DST is pending.

5.5.2.3 Role of a Tuberculin Skin Test

The tuberculin test measures the body's immune system response to an injection of tuberculin purified protein derivative (PPD). However, the test has limited value in clinical work, especially where TB is common.

- A positive test indicates infection with TB, but not necessarily TB disease.
- In a child under 5 years, a strongly positive skin test indicates recent (6 weeks or more) infection that is a risk factor for progression to disease. In the presence of other features, i.e. history of TB contact, signs and symptoms of TB and x-ray changes, a positive tuberculin skin test is suggestive of TB disease in children.

A positive reaction occurs after previous BCG immunization and should remain positive for several years thereafter. This reaction is usually weaker than the reaction to natural infection with *M. tuberculosis*. A positive reaction is only one piece of evidence in favor of the diagnosis in children.

A negative tuberculin skin test does not exclude TB. Various conditions may cause a negative reaction even if a child has TB. If the chest x-ray is suspicious of TB and the skin test is negative, TB can be diagnosed in children. Conditions that may suppress the tuberculin skin test and give a false negative result include: HIV infection, malnutrition, severe viral infections (e.g. measles, chicken pox), cancer, immuno-suppressive drugs (e.g. steroids), severe disseminated TB.

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Figure 4: Algorithm for the diagnosis of tuberculosis in HIV negative patients

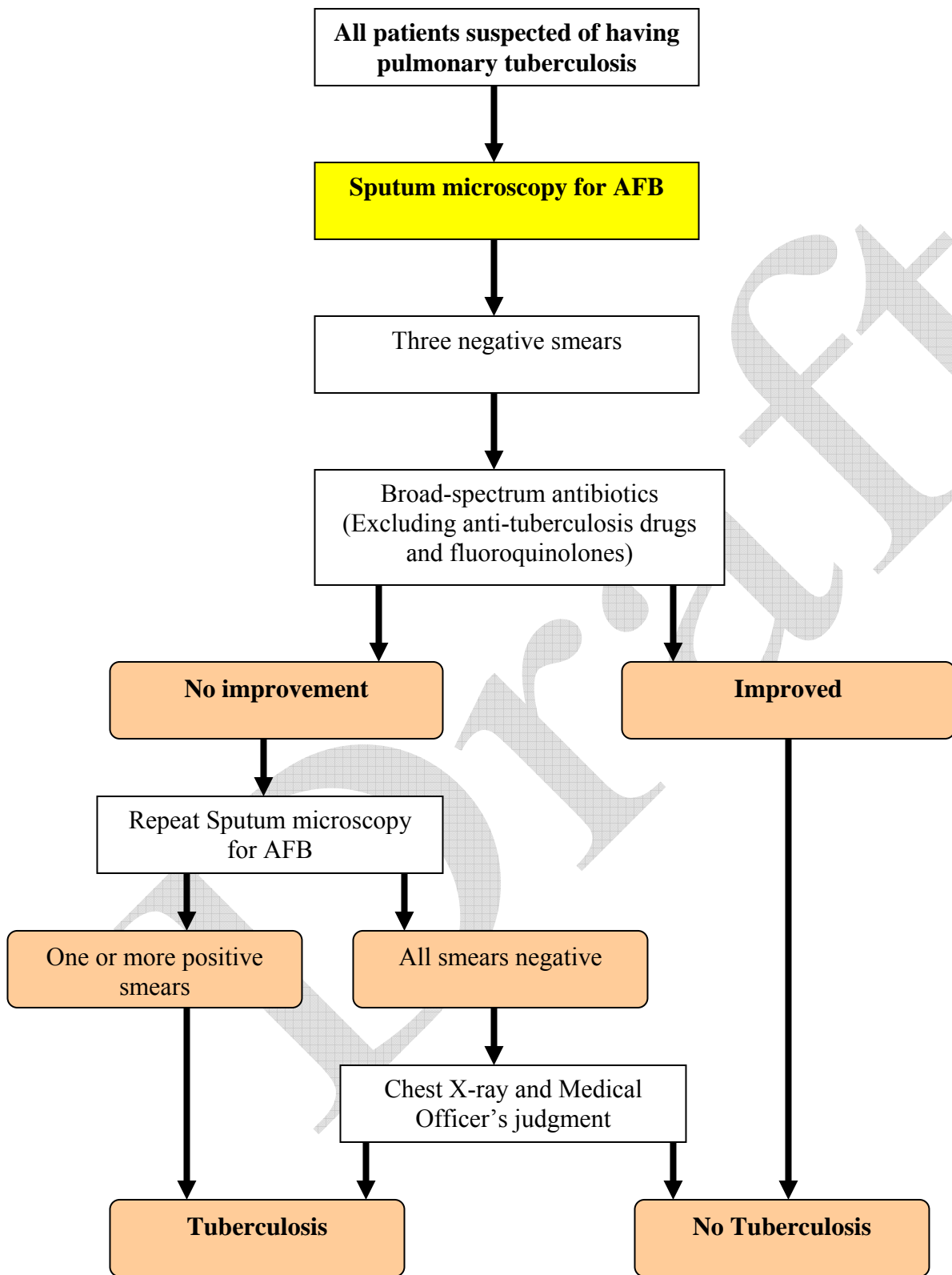
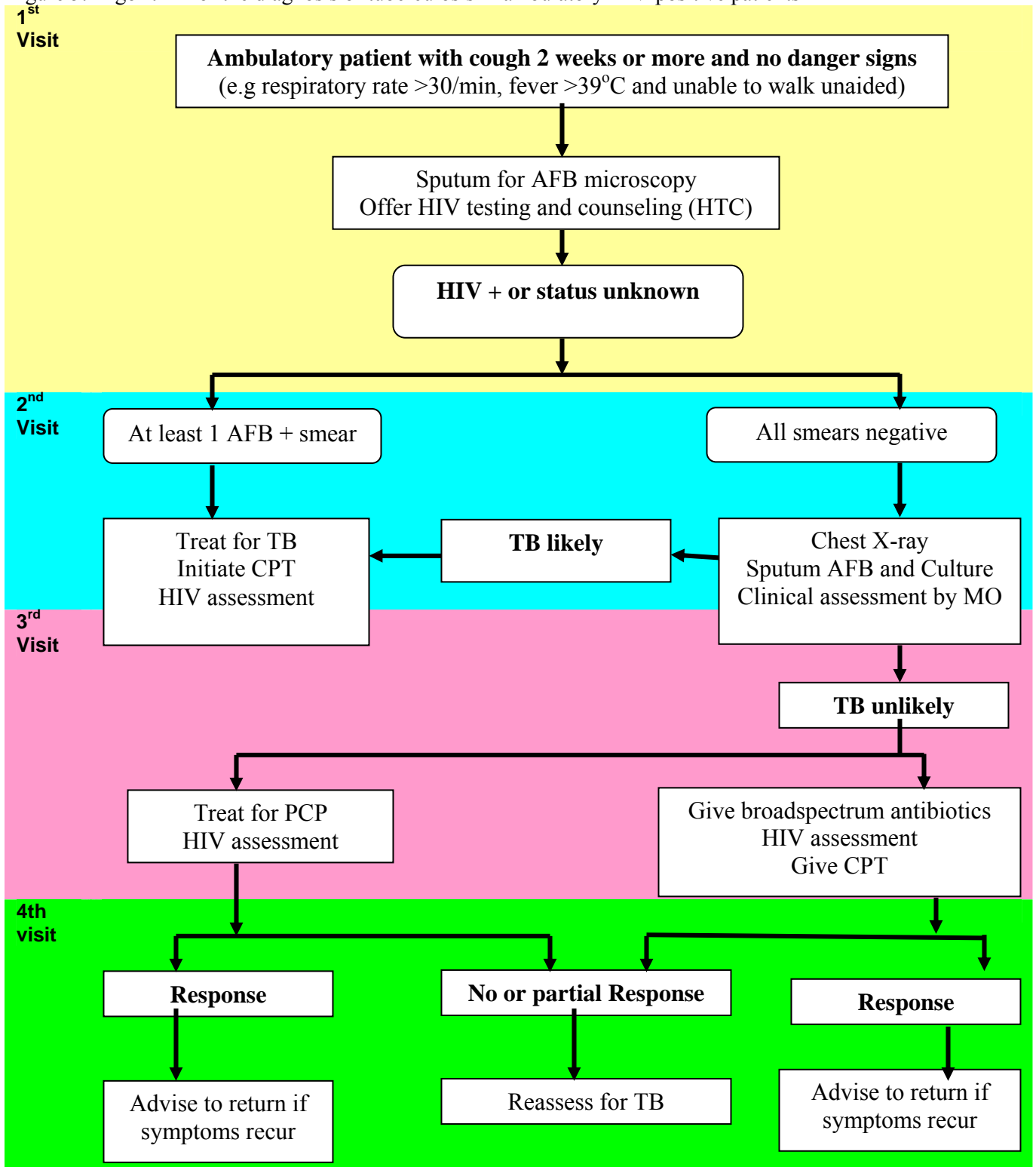


Figure 5: Algorithm for the diagnosis of tuberculosis in ambulatory HIV-positive patients

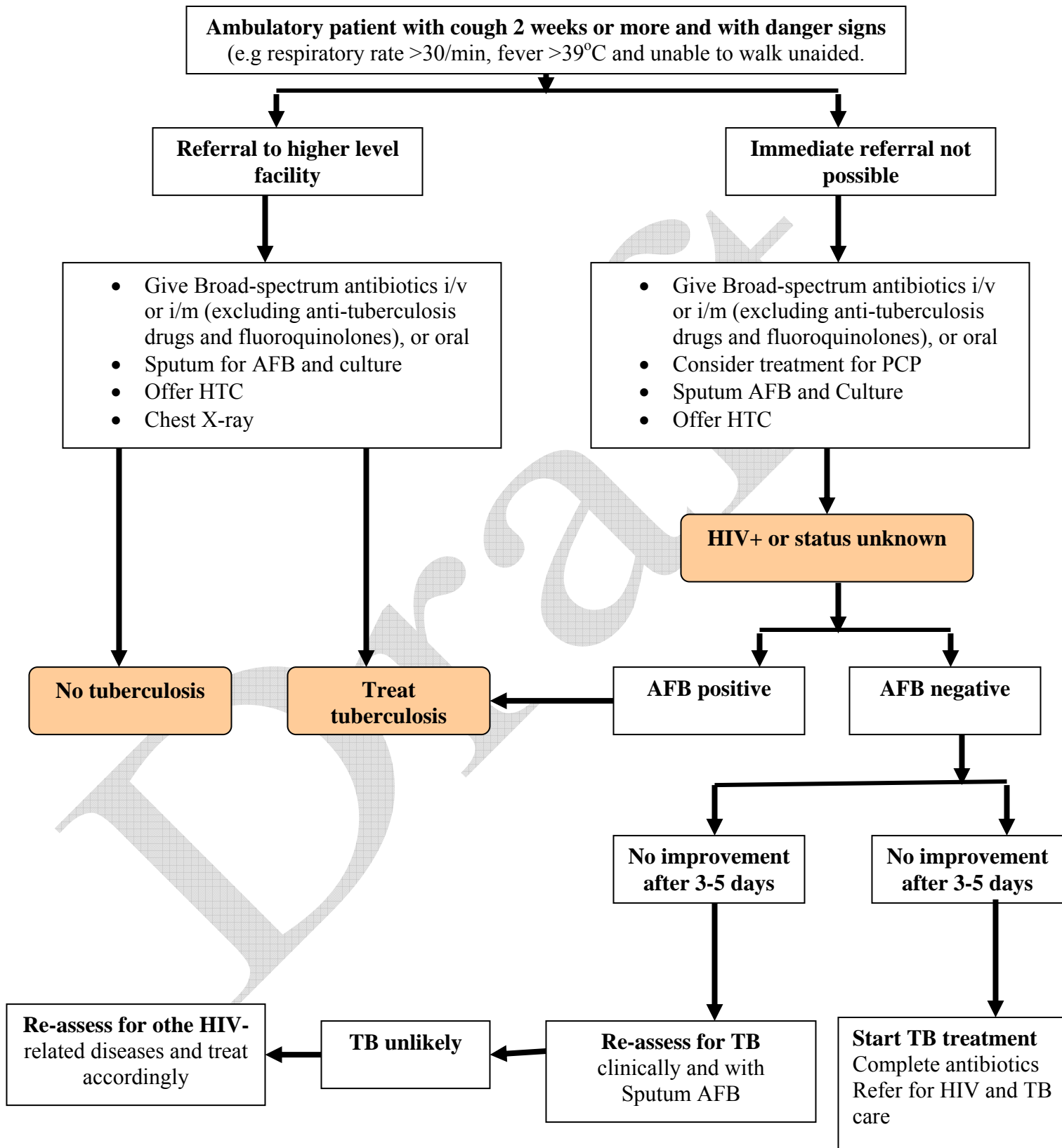


Note:

All investigations should be done at the same time wherever possible to minimize delays, limit the number of visits and speed up diagnosis

There is no fixed duration for interval of the visits.

Figure 6: Algorithm for the diagnosis of tuberculosis in seriously ill HIV-positive patients



5.6 Confirming diagnosis of Extra-Pulmonary TB

Extra-pulmonary tuberculosis diagnosis is confirmed under the following situations:

- One specimen from an extrapulmonary site smear positive for AFB or culture-positive for *M. tuberculosis*;

OR

- Histological or strong clinical evidence consistent with active extra-pulmonary tuberculosis **and**
- Laboratory confirmation of HIV infection **or**
- Strong clinical evidence of HIV infection;

And

- A decision by a clinician to treat with full course of anti-tuberculous chemotherapy.

5.6.1 TB Meningitis

TB meningitis results from rupture of a cerebral tuberculoma into the subarachnoid space or blood-borne. It is a life threatening condition with serious complications if not treated promptly. Diagnosis is confirmed by the demonstrating the relevant clinical signs backed with positive laboratory results:

Clinical Features

- Patients present with gradual onset of headache and decreased consciousness.
- Examination reveals neck stiffness and positive Kernig's sign (flex one of the patient's legs at hip and knee with the patient lying on back, and then straighten the knee - resistance to straightening the knee and pain in the low back and posterior thigh suggest meningeal inflammation).
- Cranial nerve palsies resulting from exudates around the base of the brain.
- Tuberculomas and vascular occlusion may cause focal neurological deficits and seizures.
- Obstructive hydrocephalus may develop.
- Spinal meningeal involvement causes paraplegia (spastic or flaccid)

Laboratory

- Lumbar puncture to examine cerebrospinal fluid and the following features indicate a positive test:
 - Clear CSF
 - Elevated pressure
 - High levels of protein (>1g/l)
 - High lymphocyte count (30-300/mm³)
 - Low glucose
 - AFBs on microscopy in a minority of cases.
 - Some of the CSF findings may be normal, especially in HIV-positive patients.

Patients with suspected TB meningitis should be referred to hospital without delay.

5.6.2 Tuberculous Lymphadenopathy

Tuberculous lymphadenitis should be suspected in any patient with enlarged lymph nodes that are firm, asymmetrical, more than 2 cm in diameter, or where a node has become fluctuant or developed a fistula over several months. It most commonly affects the nodes in the neck (cervical region) and is difficult to distinguish clinically from other causes of enlarged nodes, such as reactive and/or HIV-related lymphadenopathy, malignancies and other lymph node infections, which are also common. Therefore,

needle aspiration using recommended techniques should be carried out at the first outpatient visit for all patients.

Diagnosis can be confirmed by biopsy and demonstration of histological evidence. Where the capacity for histology does not exist, the patient can be started early on anti-TB treatment based on the decision of a Medical Officer to treat as extra-pulmonary TB.

5.6.3 Miliary TB

Miliary TB results from widespread blood borne dissemination of TB bacilli. This is either the consequence of a recent primary infection or the erosion of a tuberculous lesion into a blood vessel.

The patient presents with constitutional features (fever, night sweats and weight loss). Hepatosplenomegaly may be present and choroidal tubercles on fundoscopy. Miliary TB is an under-diagnosed cause of end stage wasting in HIV-positive individuals. Diagnosis should be established using Chest x-ray finding showing diffuse, uniformly distributed, small miliary nodules (“miliary” means “like small millet seeds”) which is pathognomonic of that form of the disease.

5.6.4 Tuberculous pleural effusions

Inflammatory tuberculous effusions may occur in any of the serous cavities of the body, i.e. pleural, pericardial or peritoneal cavities. They are a common form of TB in HIV- positive patients.

- Patients usually have systemic and local features.
- Microscopy of the aspirates from tuberculous serous effusions rarely show AFB because the fluid forms as an inflammatory reaction to TB lesions in the serous membrane.
- Finding of a straw coloured fluid from the pleural tap is highly indicative of TB pleural effusion and should be treated as such.

5.6.5 Tuberculosis of the spine

This is a severe form of tuberculosis when there are neurological sequelae. It is seen both in children, usually within three years following primary infection, and in adults. In many cases more than one intervertebral disc space is involved. As the disease develops, the vertebral body adjacent to the disc space is affected, an abscess is formed and spreads either forward towards the mediastinum or the retroperitoneal space, to the vertebral body with compression of the spinal cord, or back along the vertebral column eventually appearing as a subcutaneous “cold” abscess. Collapse of adjacent vertebral bodies affected by tuberculosis may lead to angulated kyphosis. The sites most commonly involved are the lower thoracic, lumbar and lumbosacral areas.

The main differential diagnoses are malignancy and pyogenic spinal infections. Malignant deposits in the spine tend to erode the pedicles and spinal bodies, leaving the disc intact. Pyogenic infection tends to be more acute than TB, with more severe pain. Diagnosis can be confirmed through X-ray of the spine revealing typical findings consistent with destruction of inter-vertebral disc.

CHAPTER 6 QUALITY ASSURANCE OF LABORATORY SERVICES

6.1 Importance of Laboratory Services in TB Control

A well functioning laboratory is the first requirement for successful management of tuberculosis. This is in view of the fact that a reliable diagnosis and treatment follow-up is necessary to inform treatment decisions that ultimately leads to cure of infectious TB cases; thereby interrupting transmission of the disease. The laboratory also has a major role in surveillance of the TB situation in the community, incidence, prevalence, drug susceptibility patterns, etc).

TB diagnosis should be made as close as possible to the patient's residence, while maintaining the proficiency of the testing procedures. Although sputum smear examination by Ziehl-Neelsen method remains the basic requirement for TB diagnosis, culture and drug susceptibility testing (DST) may be performed depending of the indication. For this reason, it is necessary for the entire population to have access to quality-assured TB laboratory services. Culture should be selectively used in the following circumstances⁴:

1. Surveillance of tuberculosis drug resistance as an integral part of the evaluation of control programme performance
2. Diagnosis of cases with clinical and radiological signs of pulmonary tuberculosis where smears are repeatedly negative
3. Diagnosis of extra-pulmonary and childhood tuberculosis
4. Follow-up of tuberculosis cases who fail a standardized course of treatment and why may be at risk of harbouring drug resistant organisms
5. Investigation of high-risk individuals who are symptomatic, eg. Laboratory workers, health care workers looking after multi-drug resistant patients

Drug susceptibility is mainly of value for epidemiological purposes. Testing of individual patients should be limited to:

- Patients who fail standardized treatment regimens
- High risk individuals who are found to have positive cultures, eg. laboratory workers, health care workers looking after multidrug resistant patients
- Close contacts of multidrug resistant tuberculosis patients who have signs and symptoms of tuberculosis
- Species identification

6.2 TB laboratory Network in Lesotho

Tuberculosis laboratory services in Lesotho forms part of overall laboratory services in the country, and is organized according to the technical complexity, activities performed and functional roles as follows:

1. the peripheral (District) laboratory
2. the intermediate (Supporting a cluster of districts) laboratory
3. the central (National) laboratory

6.3 The Peripheral (District) laboratories

Peripheral laboratories should perform sputum smear microscopy

⁴ WHO Geneva: Laboratory services in TB Control : Culture Part III 1998

utilising Ziehl-Neelsen (ZN) staining of unconcentrated sputum specimens from tuberculosis suspects among other basic investigations. One microscopy centre is recommended per 100,000 population.

6.3.1 The Regional laboratories

Intermediate laboratories should provide supervision, monitoring, training and quality assurance to the peripheral laboratories. Fluorochrome staining of sterilised concentrated specimens should also be performed in addition to ZN procedures, if dictated by the load of specimens. The intermediate laboratory should perform Mycobacterial culture of clinical specimens and differentiation between *M. tuberculosis* and other mycobacterial species. One fluorescence microscopy centre is recommended per 500,000 population. The laboratories in Leribe, Mafeteng, Quithing and Maseru will serve as regional intermediate laboratories that will support the other district ones.

6.3.2 The Central laboratory

The laboratory at Queen Elizabeth II Hospital shall serve as the Central laboratory for Lesotho. The central laboratory should perform microscopy (both ZN and fluorescence), mycobacterial culture, drug susceptibility testing and species identification. Beside the core technical activities, the central laboratory should provide training for laboratory staff, perform quality assurance and proficiency testing, exercise surveillance of primary and acquired tuberculosis drug resistance and participate in epidemiological and operational research. Establishment of tuberculosis culture facilities at intermediate and central level aims to achieve 1 centre per 500 000 to one million population.

6.4 Assuring Quality of Smear Microscopy

The NTP relies on laboratory sputum smear microscopy for diagnosis, categorization of patients; deciding appropriate treatment regimen and assessment of efficacy of treatment. Hence, the credibility, success and sustainability of the programme depend on the capacity of TB laboratory network. Poor quality diagnosis results in failure to detect persons with infectious TB, who will continue to spread infection in the community, or unnecessary treatment of “non-TB cases.” Errors in the reading of follow up smears may result in wrong outcome of patients often with severe consequences to the community. In order to achieve the required technical quality in laboratory diagnosis, a continuous system of quality assurance needs to be established. Intermediate laboratories should supervise the peripheral network, while the central or reference laboratory should supervise the intermediate network.

An effective quality assurance (QA) system of sputum smear microscopy network is of crucial importance for the programme. QA is a comprehensive system consisting of internal quality control (QC), assessment of performance using external quality assessment (EQA) methods, and continuous quality improvement (QI) of laboratory services. To optimize QA, the supervision and monitoring of the laboratory network is essential. This process requires the active support and participation of the respective Central and district levels of the NTP. The definitions of QC, EQA and QI are explained below.

Quality Control (QC) or Internal Quality Control, includes all the 'bench-top' procedures by which the laboratory personnel performing TB smear microscopy control the process, including checking of instrument, new lots of staining solutions, smear preparation, grading etc. It is a systematic internal monitoring of working practices, technical procedures, equipment, and materials, including quality of stains.

External Quality Assessment (EQA) A process to assess laboratory performance. EQA includes 'on-site evaluation' (OSE) of the laboratory to review QC and evaluation of entire process of smear microscopy, and random blinded rechecking of routine smears. EQA also allows participant laboratories to assess their capabilities by comparing their results with those obtained in other laboratories in the network (intermediate and central laboratory) through panel testing and rechecking of patient slides, using both un-blinded and blinded procedures. EQA is also termed "Proficiency Testing" as described by IUATLD.

Quality Improvement (QI) A process by which all components of smear microscopy diagnostic services are carefully analyzed, periodically, with the aim of looking for ways to permanently remove obstacles to success. Appropriate data collection, data analysis, correct interpretation of the results and creative problem solving, are the key components of this process. It involves continued monitoring, identifying defects, followed by remedial action including retraining when

6.4.1 External Quality Assessment (EQA)

External Quality Assessment is one of the most important components of a laboratory QA program. The tuberculosis laboratory network in the country is organized into three levels under the NTP.

Peripheral laboratories must be visited on a regular basis by a supervisor, who has been adequately trained to evaluate the basic functions of the microscopy laboratory.

Intermediate laboratories should be capable of providing supervision, monitoring, training, and quality assurance to peripheral laboratories, including rechecking of smears.

The national TB reference laboratory should play an essential role in the organization and maintenance of the network in terms of developing guidelines, ensuring high quality and standardized smear microscopy, and therefore must have the capacity to provide training and External Quality Assessment, including providing panel testing and rechecking to intermediate and peripheral laboratories.

EQA should focus on identification of laboratories where there may be serious problems resulting in poor performance, and not on the identification of individual slide errors or the validation of individual patient diagnosis. It is also a very important tool for communication with and motivation of laboratory technicians who may otherwise feel isolated in their work. There are three methods that should be combined to evaluate laboratory performance:

- On-site Evaluation
- Panel Testing
- Blinded Rechecking

6.4.2 On-site evaluation of Microscopy Centers:

The on-site evaluation includes a comprehensive assessment of laboratory safety, condition of the binocular microscope, adequacy of supplies as well as the technical components of sputum smear microscopy, including preparation, staining and reading of smears. On-site evaluation should always include macroscopic as well as microscopic examination of randomly selected 5 stained positive and 5 negative smears.

Checklists should be used to assist supervisors during the field visit and to allow for the collection and analysis of standard data for subsequent remedial action. The copies of the checklist, duly completed by the Supervisors, should be handed over to in-charge of the laboratory as well as the Hospital

authorities. This will provide written documentation of the visit, its findings and proposed corrective actions for improvement.

NTP in collaboration with NRL (Central laboratory in Q.E.II hospital at Maseru) is responsible for ensuring that quality-assured laboratory network for sputum smear microscopy is in place and functioning.

A comprehensive checklist for on-site evaluation of Microscopy centers is provided as annexure.

6.4.3 Panel Testing

Panel testing is a method of EQA that evaluates a technician's individual performance in staining and reading, and not the whole laboratory activities. Utilization of panel testing for EQA is considered to be less effective than random blinded rechecking of routine slides because it does not monitor routine performance. Panel testing is administrated to all laboratory supervisors at central and intermediate level using a set of 10 panel slides, including negatives and covering all the positive grades of test smears. These slides should be read and graded within the normal routine programme conditions. Based on the results, remedial actions including training will be employed to address technical skill deficiencies and errors to achieve higher level of proficiency.

6.4.4 Random Blinded Rechecking of Routine Slides

Blinded rechecking is a process of re-reading a statistically valid sample of slides from a laboratory to assess whether that laboratory has an acceptable level of performance. This method provides reliable assurance that NTP is supported by an efficient and reliable sputum microscopy laboratory network.

Random blinded rechecking involves selection of a representative sample of slides from a Microscopy Center (both positives and negatives). The results of the slides are blinded before being read by a supervisor (first controller) in an un-biased manner. The discrepant results are resolved by a higher supervisor (umpire reader). A timely feedback is provided every month to LTs and in-charge of labs for improvement in the quality of microscopy.

The Central and intermediate laboratories would also be supervising the peripheral Microscopy Laboratories on a routine basis; and reports of their visits should be handed over to in-charges at all levels. Corrective actions should be implemented based on findings of these reports.

6.5 Conducting visits to microscopy centres

Microscopy Laboratories are supervised by supervisors from the national and provincial level. The NTP will work with the Supervisors to make sure that tuberculosis-related laboratory services are performed according to national guidelines. Visits to the microscopy centres must be adequately planned, and a checklist should be used.

6.5.1 Preparing for visits:

1. Supervisory visits to be planned in advance such that all MCs are visited at least every quarter from central laboratory supervisor and at least every month by provincial laboratory supervisor; Information should be given in advance about the visit to the microscopy centre.
2. Review the recommendations made during previous visits and the actions taken.
3. Itemize what needs to be checked and decide how frequent they should be checked e.g the Tuberculosis Laboratory Register, should be checked during each visit, while other items including stocks of sputum containers, slides and reagents may be checked periodically.

6.5.2 Conducting the visit

Visiting the laboratory requires good time management to ensure a productive supportive visit without significantly disrupting the daily work schedule of the supervisee. The supervisor should be focused and be systematic in conducting the visit. The following techniques could be employed to check the laboratory operations:

- (i) Review the Tuberculosis Laboratory Register for completeness, consistency and accuracy of recording; and verify that monthly summaries are made correctly.
- (ii) Talk with the laboratory technicians: to verify their understanding of the national guidelines concerning the correct number of sputum specimens required for diagnosis and follow up examinations; the importance of limiting administrative errors and accurately recording the results of sputum smear examinations on the Laboratory Form for Sputum Examination; and storing the examined sputum smear slides of all patients until the EQA purposes.
- (iii) Examine supplies: to determine if there are adequate numbers of sputum containers, slides, reagents, forms and other laboratory supplies for the expected patient turnover.

4. Laboratory supervisory check-lists: given at annexure.

6.5.3 Follow up

The findings of the supervision visit should be discussed with the supervisee with the view to finding solutions to problems detected. This should include on the job capacity building where required.

The supervisor should within one week produce a report of the supervisory visit and forward it to the higher authority. A copy of such a report should also be made available to the head of the Hospital and the laboratory visited.

Adequate follow up should be ensured concerning the recommendations of the report.

6.6 Monitoring documentation related to microscopy examinations

Every TB Microscopy laboratory must have a Tuberculosis Laboratory Register, which should be filled up completely and accurately to ensure that the results are entered for the right persons. In processing sputum for examination, the sputum containers and slides should be marked correctly with Laboratory Serial Number, and accurately record the results of sputum smear examinations on the form. Furthermore, all examined slides should be kept *serially* in the box without segregation of positive and negative slides, until the Laboratory Supervisor reviews them for quality assurance. During the on-site visit, the STLS should select five smear-positive and five smear-negative slides randomly and review them as per QA protocol. Ensure that the Microscopy laboratories and health facilities which collect and transport sputum are visited at least once every month. Other health facilities which collect specimens and transport them to the DMC should assign Specimen Identification Numbers and write it on the side of the containers.

6.6.1 Recording of results of sputum smear examinations

Results of sputum examination should as much as possible be made available within 48 hours after receipt of specimens. The smear results should also be graded according to the following standard NTP protocol: (duplication: refer to a previous chapter with the same information)

Number of AFB seen	Result	Grading	Number of fields to be examined
More than 10 per oil immersion field	Pos	3+	20
1-10 AFB per oil immersion field	Pos	2+	50
10-99 AFB per oil immersion field	Pos	1+	100
1-9 AFB per oil immersion field	Pos	Scanty	100

No AFB in 100 oil immersion fields	Neg		100
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*Record actual number of bacilli seen in 100 fields – e.g. “Scanty 4”

The grading of smear results not only indicates the bacillary load, but also improves the laboratory technician’s attention and facilitates supervision.

All smear-positive (including scanty) results should be recorded in red ink in the Tuberculosis Laboratory Register.

6.6.2 Tuberculosis laboratory register

The Tuberculosis Laboratory Register is used to record the results of sputum smear examinations. The register should contain the patients personal data as well as name of the treatment facility, reason for examination and the results of the examinations. The following information about the patient is then recorded:

- Date of sputum smear examination
- Full name
- Sex
- Age
- Name of the health facility (e.g. primary health centre, private practitioner, NGO, etc.) that requested the examination
- Complete address
- Reason for examination (diagnosis, repeat diagnosis and follow-up of chemotherapy).
- Results of sputum smear examinations (results of specimens 1, 2 and 3 can be recorded).

For patients undergoing repeat sputum examination for diagnostic purposes, the laboratory technician should write RE in the column for diagnosis.

The last two columns of the Tuberculosis Laboratory Register are for the Laboratory Technician’s (LT) remarks and signature.. The remarks column can also mention in brief the action taken for patients belonging to other treatment units or districts, e.g., “Referral.

Every week the in Charge of the MC should review the Tuberculosis Laboratory Register to ensure that correct numbers of sputum smear examinations (i.e. 3 per TB suspect) are being performed for diagnosis. District TB Coordinators should endeavour to compare sputum results mentioned in the Tuberculosis Laboratory Register with those mentioned in the TB Treatment Cards and TB Registers. This can be done by randomly selecting cases from the facilities to cross-check their results in the laboratories.

Up to three-sputum specimen examination results can be recorded for each patient on one line of the Tuberculosis Laboratory Register.

Laboratory staff should not use the Tuberculosis Laboratory Register to record the results of any other laboratory examinations. All results of sputum smear examinations done in a Microscopy Centre should be written only in one Tuberculosis Laboratory Register, and not in any other register.

The laboratory technician should summarize the information on sputum smear examinations done during that month. This information should be summarized in the monthly summary form (See annex) at the end of each month, printed in the Laboratory Register itself. Patients from the following month should be started from the next new page.

Ensure that the patients for diagnosis had three sputum samples examined and follow-up cases had two sputum samples examined

Reasons for False-negative Smear Results:

- Improper storage of sputum specimens
- Inadequate sputum collection
- Too thin or thick smears
- Over-heating the slide while fixing
- Insufficient fixing
- Boiling carbol fuchsin
- Over decolorization with acid-alcohol
- Improper storage of stained slides
- Inadequate examination
- Using saliva for smears
- Reading and reporting errors

Consequences of False-negative smear Results:

- Patients with TB may be missed and thereby patient continues to spread the disease
- Wrong categorization
- Intensive phase treatment may not be extended for the correct duration, resulting in inadequate treatment
- Patients and the community may lose confidence in the programme
- Unwarranted repetition of investigations

Reasons for False-positive Smear Results

- Faulty sputum collection (presence of food particles or fibres)
- Using old scratched slides
- Using unfiltered carbol fuchsin
- Insufficient decolorization with acid-alcohol
- Contamination due to transfer of bacilli from one smear to another
- Not wiping the oil immersion lens after examination of a positive slide
- Reading and reporting errors

Consequences of False-Positive smear Results

- Patients without TB may be unnecessarily put on treatment
- Treatment may continue beyond the recommended duration
- Medicines are wasted
- Patients and the community may lose confidence in the programme

6.7 The Ziehl–Neelsen staining procedure

1. Select a new unscratched slide and label the slide with the Laboratory Serial Number with a marking pencil.
2. Make a smear from yellow purulent portion of the sputum using a wooden stick. A good smear is spread evenly, 2 cms x 3 cms in size and is neither too thick nor too thin. The optimum thickness of the smear can be assessed by placing the smear on a printed matter. The print should be readable through the smear.
3. Allow the slide to air dry for 15–30 minutes.
4. Fix the slide by passing it over a flame 3–5 times for 3–4 seconds each time.
5. Pour 1% filtered carbol fuchsin to cover the entire slide.
6. Gently heat the slide with carbol fuchsin on it, until vapours rise. Do not boil.
7. Leave carbol fuchsin on the slide for at least 5 minutes.

8. Gently rinse the slide with tap water until all free carbol fuchsin stain is washed away. At this point, the smear on the slide looks red in colour.
9. Pour 3% acid-alcohol solution onto the slide.
10. Let the slide stand for 2–4 minutes.
11. Rinse gently with tap water. Tilt the slide to drain off the water.
12. A properly decolourised slide will appear light pink in color .If the slide is still red, reapply acid-alcohol for 1–3 minutes and rinse gently with tap water. Wipe the back of the slide clean with a swab dipped in acid-alcohol,
13. Pour 0.1% methylene blue onto the slide.
14. Leave 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 x40 lens to select the suitable area and then examine under x100 lens using a drop of immersion oil.
18. Record the results in the Laboratory Form and the Laboratory Register.
19. Store all positive and negative slides serially in the same slide-box until instructed by the supervisor.
20. Disinfect all contaminated material before discarding.

6.7.1 Maintain an adequate supply of reagents and other materials

It is necessary to ensure availability of good quality laboratory reagents and consumable supplies for effective un-interrupted functioning of the laboratories. Ideally, reagents should be freshly prepared at the provincial lab or central lab and supplied to the MC labs. In the absence of such an arrangement, the reagents may be purchased from reputed manufactures, as per the NTP specifications for ZIEHL–NEELSEN stains. Batch quality certification should be obtained for the purchased reagents and should be exhausted within the expiry date. It is recommended that quality control testing slides (a set of at least '1+ positive' and a good 'negative' unstained heat-fixed smears) should be used for each batch of new agents before they are used. It should be re-filtered by the laboratory technicians as and when required. Ensure that the binocular microscope is in good working condition and inspect and use the microscope.

The in-charge of the laboratories should determine monthly requirements of reagents and other materials.. The supervisors will make sure these supplies are distributed in a timely manner, usually on a monthly basis. The first in first out (FIFO) principle should also apply, hence the old supplies should be exhausted before starting to use the new ones. Old reagents should not be mixed with the new supplies. They should be kept in separate containers.

The following is a list of laboratory reagents, which should always be available in the laboratory:

- Carbol fuchsin (1%)
- Sulphuric acid (25%)
- Methylene blue (0.1%)
- Synthetic immersion oil
- Methylated spirit

The following is a list of other materials that should always be available in the laboratory:

- Glass slides for microscopy, and slide-boxes for storing slides
- Markers (for marking the slides) and marking pens or grease pencils (for marking the sputum containers)
- Wooden sticks (thick enough to make good smears)

- Transparent glass bottles for reagents (with self-adhesive labels stating date of preparation of reagents)
- Plastic tumblers/mugs
- Glass (or metal) rods (for holding slides during the staining process)
- Staining racks (for drying the slides)
- Sputum containers
- Spirit lamp or bunsen burner
- Lens paper (for wiping the oil immersion lens after examination of each slide)
- 5% phenol or 5% hypochlorite or bleaching powder / liquid bleach (for disinfection)
- Foot-operated bin (for disposal of contaminated materials)
- Timer (stop-watch)
- Laboratory Forms for Sputum Examination, Laboratory Register, “Referral for Treatment” Forms
- Filter Paper
- Fine Silk and Lint cloth

6.7.2 Disposal of laboratory materials.

Sputum specimens examined in the laboratory are potentially infectious. Hence, after examination, they must be disinfected and destroyed so that the risk of infection is avoided. All disposable containers must be used only once.

Sputum cups which contain sputum can be disposed of by any one of the following methods:

- After the sputum smears are examined, all sputum cups should be kept in a bucket containing 5% hypochlorite, or 10% bleach solution (freshly prepared), or 5% phenol solution. Caps of the sputum cups must be removed and the cups, caps and wooden sticks completely submerged in the solution in a secure place for at least 18 hours. After this, the solution, cups, caps and broom sticks can be discarded with other hospital waste. This bin/bucket should have a lid which is foot operated.
- **Incineration:** Wherever incinerators exist, the type specified under Biomedical Waste Management & Handling Rules of the country, with combustion efficiency of 99%, it should be used. Sputum cups made of polypropylene should be used wherever available. (Note: If sputum cups are made of other varieties of plastic, they should be disinfected and destroyed as per the hospital waste management rules). Burning is not recommended.
- **Autoclaving:** The sputum cups and lids, with the lids removed, along with wooden sticks can be autoclaved at the end of each day’s laboratory work. The autoclave cycle should have a holding time of 15 minutes at 121 °C HTAT (Holding time at temperature), 10 minutes at 126 °C HTAT or 3 minutes at 134 °C HTAT. The material can be discarded with other waste after proper cooling.

If none of the above is available, cotton and broom sticks can be disinfected and buried at a safe distance away from inhabited areas in a landfill site ensuring deep burial as specified by the infectious material disposal rules of the country.

Used slides should not be broken. They should be disposed through the hospital waste management system or in a secured pit for sharps in accordance to prevailing guidelines. Slides once used for sputum microscopy should not be reused.

CHAPTER 7 TREATMENT OF TUBERCULOSIS

7.1 The basis for treatment policy

The key to interrupting the spread of TB in the community is early detection and effective treatment of persons who are coughing up living TB bacilli. For treatment to be effective, it is necessary that correct drugs are given at the right doses for the correct duration..

The aims of TB treatment in Lesotho shall be to cure the patient of active TB, prevent death from TB or its complications, decrease transmission of the disease to others, and to prevent the development of drug resistance.

7.2 Essential anti-TB drugs

Anti-tuberculosis drugs have three main properties namely bactericidal, sterilizing activity and the ability to prevent resistance. For anti-TB treatment to be effective, a combination of these properties is required in a treatment regimen. Isoniazid and rifampicin are the most powerful bactericidal drugs, active against all populations of TB bacilli. Pyrazinamide and streptomycin are also bactericidal against certain populations of TB bacilli. Pyrazinamide is active in an acid environment against TB bacilli inside macrophages. Streptomycin is active against rapidly multiplying extra-cellular bacilli. Ethambutol is bacteriostatic and is effective in preventing development of resistance against other anti-TB drugs. The following are the recommended first line anti-TB drugs and the dose range.

Table 4: Essential anti-TB drugs

Essential TB drugs	Recommended Daily Dose (Dose range in mg/kg)
Isoniazid (H)	5 (4-6)
Rifampicin (R)	10 (8-12)
Pyrazinamide (Z)	25 (20-30)
Streptomycin (S)	15 (12-18)
Ethambutol (E)	Children: 20 (15-25) Adults: 15 (15-20)

7.3 Recommended Standard Treatment Regimens for Adults

Treatment of all forms of TB in Lesotho shall be based on the WHO-recommended treatment regimens for the appropriate case definitions. For the purposes of standardization, the WHO category I and Category II regimens shall be used for treatment of new (pulmonary and extra-pulmonary) and previously treated cases respectively. Through the assistance of the Global TB Drug Facility (GDF), the Fixed-Dose Combinations (FDCs) are used in the National TB Programme for both adults and Children. The complete package of required drugs for either Category I or Category II regimen for individual patients is available and therefore to be prescribed as patient kits.

7.3.1 Treatment of New tuberculosis cases

All new TB cases (patients who have never been treated for TB in the past or who has taken anti-tuberculosis drugs for less than one month) shall be treated with WHO Category 1 regimen which involves administration of RHZE in the first 2 months initial phase; and RH in the 4 months of continuation phase. The recommended treatment regimen for new cases is: represented as 2(HRZE)/4(HR).

Note: For Category I patients with particular forms of TB including TB meningitis, miliary TB and spinal TB with neurological signs, the continuation phase may be Category II Regimen (new cases) – Patients on rifampicin (7HR).

Category 1 treatment regimen:

Table 5: Recommended treatment regimen and anti-TB drug dosages for New (category 1) Adult TB cases

Phase of treatment	Drugs	Weight in Kg			
		30-39	40-54	55-70	>70
Intensive phase of 2 months	(RHZE)* (150mg/75mg/400mg/275mg)	2	3	4	5
Continuation phase of 4 months	(RH) (150mg/75mg)	2	3	4	5

*Fixed-dose combination (FDC) drugs

7.3.2 Re-treatment case

Previously treated TB patients (all TB patients who were treated as new cases for more than one month in the past and are now smear or culture positive (failure, relapse, return after default) shall be treated in the first 2 months with isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin. This should be followed by 4 drugs (isoniazid, rifampicin, pyrazinamide, ethambutol) for one month, and 5 months continuation phase with 3 drugs (isoniazid, rifampicin, ethambutol). The recommended regimen is represented as: 2HRZES/1HRZE/5HRE (category II Regimen).

Note: All failures of category 1 treatment should be evaluated for MDR-TB, and be started on category IV treatment if results of DST confirm the diagnosis (See MDR-TB guidelines).

Category II Regimen (re-treatment cases):

Table 6: Recommended treatment regimen and dosages for Re-treatment (category 2) Adult TB cases

Phase of treatment	Drugs	Weight in Kg			
		30-39	40-54	55-70	>70
Intensive phase of 2 months	(RHZE) (150mg/75mg/400mg/275mg)	2	3	4	5
	S (vial 1g)	0.5	0.75	1	1
Intensive phase of 1 months	(RHZE) (150mg/75mg/400mg/275mg)	2	3	4	5
Continuation phase of 5 months	(RHE) (150mg/75mg/400mg)	2	3	4	5

* Streptomycin should **NOT** be given during pregnancy and to those over 65 years.

NB: Switching from intermittent to daily regimen: For patients receiving intermittent regimen from another control area that will continue treatment in Lesotho, the health care worker should determine appropriate recommended dosage for the patient and administer the daily medications from the patient kit.

7.3.3 Treatment regimens in special circumstances

7.3.3.1 Treatment for pregnant women

The benefit of treating an active TB disease in a pregnant woman far outweighs and the risks that the drugs may pose to both the mother and the foetus. Most TB drugs are safe for use in pregnant women with the exception of **streptomycin** which is ototoxic to the foetus and should therefore not be used in pregnancy. Every woman of child bearing age diagnosed with TB should be asked of pregnancy status before starting TB treatment.

7.3.3.2 Treatment for breastfeeding women

A woman who is breastfeeding and has TB should receive a full course of TB treatment. Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to the baby. ***All the TB drugs are compatible with breastfeeding and a woman taking them can safely continue to breastfeed her baby.*** The mother and baby should stay together and the baby should continue to breastfeed in the normal way, but be given prophylactic isoniazid for at least six months (Isoniazid 5mg/ kg). BCG vaccination of the newborn should be postponed until the end of isoniazid prophylaxis.

7.3.3.3 Treatment for women taking the oral contraceptive pill

Rifampicin interacts with the contraceptive pill with a risk of decreased protective efficacy against pregnancy. A woman who is receiving contraception may choose between the following two options while receiving treatment with rifampicin. Following consultation with a physician, she could take an oral contraceptive pill containing a higher dose of oestrogen (50 mcg), alternatively she could use another form of contraception.

7.3.3.4 Treatment for patients with liver disorders

Isoniazid, rifampicin and pyrazinamide are all associated with hepatitis. Of the three, rifampicin is least likely to cause hepatocellular damage, although the drug is associated with cholestatic jaundice, pyrazinamide is the most hepatotoxic. The patients with the following conditions can receive the usual short-course chemotherapy regimen provided that there is no clinical evidence of chronic liver disease: hepatitis virus carriage, a past history of acute hepatitis, excessive alcohol consumption. However, hepatotoxic reactions to TB drugs may be more common in these patients and should be anticipated.

7.3.3.5 Established chronic liver disease

Patients with liver disease should not receive pyrazinamide. Isoniazid plus rifampicin plus one or two non-hepatotoxic drugs such as streptomycin and ethambutol can be used for a total treatment duration of 8 months. Alternative regimens are 9 RE or SHE in the initial phase followed by HE in the continuation phase, with a total treatment duration of 12 months. Therefore recommended regimens are 2 SHRE/ 6HR, 9RE or 2 SHE / 10HE.

In case of acute hepatitis, which may or may not be related to TB or TB treatment, the Medical Officer's clinical judgment is required. In some cases, TB treatment may be deferred until acute hepatitis has resolved. When the Clinician decides to treat TB during acute hepatitis, the combination of (SE) for 3 months is the safest option. If the hepatitis has resolved, the patient can receive a continuation phase of 6 months of (RH). If the hepatitis fails to resolve, (SE) should be continued for a total of 12 months.

7.3.3.6 Treatment of patients with renal failure

Isoniazid, rifampicin and pyrazinamide are either eliminated almost entirely by biliary excretion or metabolized into non-toxic compounds. These drugs can, therefore, be given in normal dosage to patients with renal failure. In severe renal failure, patients should receive pyridoxine with isoniazid in order to prevent peripheral neuropathy. Streptomycin and ethambutol are excreted by the kidney. Where facilities are available to monitor renal function closely it may be possible to give streptomycin and ethambutol in reduced doses. The safest regimen to be administered in patients with renal failure is

2 HRZ/ 4 HR. All patients that fall under the category “special circumstances” should be referred to and managed by to a specialist.

7.4 The Role of Adjuvant Steroid Treatment

Adjuvant steroid treatment is steroid treatment given in addition to anti-TB drug treatment. Studies in the pre-HIV era confirmed the benefit of steroids for TB meningitis and pleural and pericardial TB. Steroids are also of benefit in HIV-positive patients with pericardial TB.

Adjuvant steroid therapy is recommended in the following conditions:

- TB meningitis (decreased consciousness, neurological defects, or spinal block).
- TB pericarditis (with effusion or constriction).
- TB pleural effusion (when large with severe symptoms).
- Hypoadrenalism (TB of adrenal glands).
- TB laryngitis (with life-threatening airway obstruction).
- Severe hypersensitivity reactions to anti-TB drugs.
- Renal tract TB (to prevent ureteric scarring).
- Massive lymph node enlargement with pressure effects.

Rifampicin being a potent inducer of hepatic enzymes that metabolize steroids, the effective dose of prednisolone is half the prescribed treatment dose given to the patient. The suggested treatment doses of prednisolone depending on the condition is as follows:

Table 7: Prednisolone indication and recommended doses in TB management

Indication	Prednisolone treatment (dose for children in brackets)
TB meningitis	60 mg (1–2 mg/kg) daily for weeks 1–4, then decrease over several weeks
TB pericarditis	60 mg (1–2 mg/kg) daily for weeks 1–4 30 mg (0.5–1 mg/kg) daily for weeks 5–8, then decrease over several weeks
TB pleural effusion	30 mg (0.5–1 mg/kg) daily for 1–2 weeks

Steroids are immunosuppressants. Steroids may further depress immunity and increase risk of opportunistic infections in HIV-positive patients. However, on balance, TB/HIV patients are still likely to benefit from the use of steroids in the presence of the above conditions.

7.5 Ensuring compliance to anti-TB therapy

The public health priority of the NTP is to cure smear-positive cases, while preventing the emergence of drug resistance. Ensuring adherence to treatment through Directly Observed Treatment (DOT) is necessary to achieve this goal. Treatment support should be given to TB patients throughout the entire treatment period.

7.5.1 Ensuring patient compliance versus defaulter tracing

Patients’ compliance is a key factor in treatment success. In many parts of the country, a significant proportion of patients stop treatment before the end, for various reasons. The premature interruption of treatment presents a problem for patients, their family members, those who care for them, and for health workers.

Promote compliance through a patient-centered approach. That includes facilitating access to treatment, choosing with the patient the most convenient time and place for direct observation of treatment and, when possible, providing other social and medical services, is much more effective than spending resources on defaulter tracing. Facilitating access includes providing drugs and sputum smears examinations free of charge, reducing the time and cost to the patient to obtain treatment, and providing good and rapid attention.

Convenience to the patient must be balanced with the assurance of regular drug intake and monitoring, important to give the patient the best chances of cure. When patients receive self-administered treatment, patients often take drugs irregularly, and tracing is difficult and often unproductive. In addition, there is a much longer period between interruption of treatment and initiation of treatment after tracing the patient.

It is vital for health staff and community workers to offer polite and efficient attention, and to consider the patient's needs at every contact with the patient.

7.6 Preventive Measures to Decrease Treatment Interruption

At the time of registration of a tuberculosis patient starting treatment, it is important to set aside enough time to meet with the patient (and preferably also with the patient's family members). This is an important opportunity to advise and counsel the patient. During this meeting it is vital to record the patient's physical address and other physical addresses (e.g. partner/spouse, parents, work place, place of study) in order to maximize the probability of locating patients who interrupt treatment.

7.7 Management of treatment interruption

The management of patients who have interrupted treatment is complex and takes into consideration several variables (immune status, degree of remission of the disease with the previous treatment, drug susceptibility) that may be difficult to assess. A simple decision tree is suggested in Table 7.1.

Table 8: Management of TB treatment interruption

Interruption for less than 1 month			
<ul style="list-style-type: none"> Trace patient Solve the cause of interruption Continue treatment and prolong it to compensate for missed doses 			
Interruption for 1 – 2 months			
Action 1		Action 2	
<ul style="list-style-type: none"> Trace patient Solve the cause of the interruption Do 3 sputum smears. Continue treatment while waiting for results 	If smears negative or EPTB	Continue treatment and prolong it to compensate for missed doses	
	If one or more smears positive	Treatment received: < 5 months	Continue treatment and prolong it to compensate for missed doses
		Treatment received: > 5 months	Category I: Start category II Category II: refer (may evolve to chronic)
Interruption for 2 months or more (defaulter)			
<ul style="list-style-type: none"> Do 3 sputum smears Solve the cause of the interruption, if possible No treatment while waiting for results 	If smears negative or EPTB	Clinical decision on individual basis whether to restart or continue treatment, or no further treatment	
		Category I	Start Category II
	Category II	Refer (may evolve to chronic)	

7.8 Monitoring of TB Patients during Treatment

Monitoring patient's clinical as well as bacteriological response to anti-TB therapy is equally important as the treatment itself. Ensuring regular drug intake and identification of adverse drug reactions and side effects should be an integral part of patient's treatment monitoring. Patient's treatment should therefore be monitored as follows:

7.8.1 Bacteriological monitoring:

Serial sputum smear examinations should be performed at recommended intervals to verify the effectiveness of the treatment in killing the bacilli. Two sputum samples should be examined at the end of the second and fifth month and at the end of treatment for all sputum smear positive TB patients. The two samples should be collected as 'early morning samples'.

Table 9: Recommended Schedule for follow up sputum examinations for PTB patients

When to monitor	Category 1 treatment 6-month treatment regimen	Category 2 regimen: 8-month treatment regimen
At time of diagnosis	sputum smear	sputum smear
At end of initial phase	sputum smear (end month 2)	sputum smear (end month 3)
In continuation phase	sputum smear (end month 5)	sputum smear (end month 5)
During last month of treatment	sputum smear (end month 6)	sputum smear (end month 8)

Patients with sputum smear-positive PTB should be monitored by sputum smear examination. These are usually adults and sometimes older children. Routine monitoring of treatment response by CXR is unnecessary and wasteful of resources.

7.8.1.1 New sputum smear-positive pulmonary TB patients (Category I)

Follow up sputum smears should be performed at the end of the second and fifth months, and in the last month of treatment.

If the sputum smears are positive at the end of the second month, the initial phase is prolonged for one additional month after which patient then starts the full continuation phase regardless of the result at the end of the third month.

If the sputum smears are still positive at the end of the fifth month, this constitutes treatment failure. The treatment should be discontinued, and the patient is re-registered as a treatment failure and starts a full course of re-treatment regimen (Category II). A sputum sample is sent for culture and drug susceptibility testing.

7.8.1.2 Previously treated pulmonary sputum smear-positive patients (Category II)

Sputum smear examination is performed at the end of the initial phase of treatment (at the end of the third month), at the end of the fifth month; and at the end of treatment.

If the patient is sputum smear-positive at the end of the third month, the initial phase of treatment with 4 drugs is extended by another month and sputum smears are examined again at the end of the fourth month.

If the patient still has positive smears at the end of the fourth month, and the patient then starts the continuation phase regardless of the smear result. Sputum should however be sent to the laboratory for culture and drug susceptibility testing.

Positive smears at the end of the fifth month indicate failure of the re-treatment regimen and, the patient should be referred for MDR-TB assessment and appropriate management.

7.8.1.3 New sputum smear-negative pulmonary TB patients

Sputum smear-negative patients should be monitored clinically; body weight is a useful progress indicator. Sputum smears should be checked at the end of the second month in case of the following possibilities:

- disease progress due to non-adherence to treatment, or
- an error at the time of initial diagnosis (i.e. a true smear-positive patient misdiagnosed as smear-negative) plus
- drug resistance.

A patient initially diagnosed as sputum smear-negative and treated as a Category I patient who has positive sputum smears (two positive samples, to reduce errors) at the end of the second month should start a full course of Category II treatment. The outcome of the initial treatment should be failure and the patient should be re-registered.

(Note that this is an exception, as failure for initially smear-positive patients is defined as sputum smear-positive at the end of the fifth month of treatment or later.)

7.9 Clinical monitoring:

Monitoring the improvement in the patients' clinical state provides a guide to treatment response. During regular follow up visits, clinical assessment in the form of focused history and physical examination should be conducted and the results documented in the patient's treatment card. Evidence of clinical improvement include reduction or disappearance of symptoms including cough, fever, tiredness and weight loss. One of the key parameters that should be assessed and documented on a regular basis is the patients' weight.

7.9.1 Extra-pulmonary TB

Response to treatment is usually monitored clinically and depending on the organ affected, radiology may play an important role. As in pulmonary smear-negative disease, the weight of the patient is also a useful indicator in monitoring clinical response in extra-pulmonary disease.

7.9.2 Monitoring of TB Patients for Significant Adverse Effects of Anti- TB Drugs

Most TB patients complete their treatment without any significant adverse effects of drugs. However, a few patients do experience adverse effects. It is therefore important that patients be clinically monitored during treatment so that adverse effects can be detected promptly and managed properly. Routine laboratory monitoring is not necessary.

Health personnel can monitor adverse effects of drugs by teaching patients how to recognize symptoms of common adverse effects and to report if they develop such symptoms, and by asking about symptoms when patients report to collect drugs.

7.9.2.1 Prevention of adverse effects of drugs

Health personnel can prevent some drug-induced side-effects, for example Isoniazid-induced peripheral neuropathy. This usually presents as a numbness, tingling or burning sensation of the feet and occurs more commonly in pregnant women and in people with the following conditions: HIV infection, alcohol abuse, malnutrition, diabetes, chronic liver disease. These patients should receive preventive treatment with pyridoxine, 10 mg daily, along with their anti-tuberculosis drugs.

7.9.2.2 Adverse effects of anti-tuberculosis drugs

Adverse effects associated with anti-TB are classified as minor or major. In general, a patient who develops minor adverse effects should continue the TB treatment, sometimes at a reduced dose. The

patient also receives symptomatic treatment. If a patient develops a major side-effect, the treatment or the offending drug is stopped. Further management depends on the nature of the adverse reaction. Patients with major adverse reactions should be managed in a hospital. Table below provides a symptom-based approach to the management of adverse effects.

7.9.2.3 Symptom-based approach to management of drug side-effects

Table 10: Guide to Management of side effects of first-line anti-TB drugs

Side-effects	Drug(s) probably responsible	Management
Minor		Continue anti-TB drugs
Anorexia, nausea, abdominal pain	rifampicin	Give tablets last thing
Joint pains	pyrazinamide	Give aspirin or nonsteroidal anti-inflammatory drug
Burning sensation in feet	Isoniazid	Give pyridoxine 50–75 mg daily
Orange/red urine	rifampicin	Reassurance

Major		Stop drug(s) responsible
Skin itching/rash	most anti-TB drugs	Stop anti-TB drugs (see below)
Deafness (no wax on auroscopy)	streptomycin	Stop Streptomycin, give ethambutol instead
Dizziness (vertigo and nystagmus)	streptomycin	Stop streptomycin, give ethambutol instead
Jaundice (other causes excluded)	most anti-TB drugs	Stop all anti-TB drugs until jaundice resolves
Vomiting and confusion (suspected drug-induced liver function tests pre-icteric hepatitis)	most anti-TB drugs	Stop anti-TB drugs, urgent liver function tests
Visual impairment	ethambutol	Stop ethambutol
Generalized, including shock and purpura	rifampicin	Stop rifampicin

Note that first line drugs cannot be substituted with any second line drug or any other in the event of adverse reaction management.

When to stop anti-TB drugs

Reaction	Drug Responsible
Hearing loss or disturbed balance	Streptomycin
Visual disturbance (poor vision and colour perception)	Ethambutol
Renal failure, shock, or thrombocytopenia	Rifampicin
Hepatitis	Pyrazinamide

7.9.2.4 Management of skin itching and rash

In case of skin itching, it is necessary to determine if the reaction was present before initiation of anti-TB treatment, as many HIV-positive patients have itchy skin lesions as a result of HIV infection.

Other causes of itching should also be excluded, give antihistamines, continue anti-TB treatment and observe closely. In the event that rash develops, anti-TB drugs should be stopped until the rash resolves. In case of severe reaction, supportive treatment should be provided as appropriate.

Reintroduction of anti-TB drugs following drug reaction

Drug challenge should be done to identify the drug responsible for the reaction. The process should start with the anti-TB drug least likely to be responsible for the reaction (i.e. isoniazid). The initial challenge should start with a small dose of the drug.. If a reaction occurs to a small challenge dose, it will not be such a bad reaction as to a full dose. Gradually increase the dose over 3 days. Repeat the procedure, adding in one drug at a time. A reaction after a particular drug is added identifies that drug as the one responsible for the reaction.

Table 11: Guide to performing anti-TB drug challenge and re-introduction

Drug	Likelihood of causing a reaction	Challenge doses		
		Day 1	Day 2	Day 3
Isoniazid	Least likely	50 mg	300 mg	300 mg
Rifampicin	↓	75 mg	300 mg	Full dose
Pyrazinamide		250 mg	1 gr	Full dose
Ethambutol		100 mg	500 mg	Full dose
Streptomycin	Most likely	125 mg	500 mg	Full dose

If the drug responsible for the reaction is pyrazinamide, ethambutol, or streptomycin, resume anti-TB treatment without the offending drug. If possible, replace it with another drug. It may be necessary to extend the treatment regimen. Consider the start of the resumed regimen as a new start of treatment. This prolongs the total time of TB treatment, but decreases the risk of recurrence.

7.10 Determining TB Treatment Outcomes

At the end of the treatment course for each patient with sputum smear-positive PTB, the District TB Coordinator should record the treatment outcome in the District TB Register. The table below (Table 7.3) shows the definitions of standardized treatment outcomes.

Table 12: Definitions of TB treatment outcomes

Cure	Patient who is sputum smear-negative in the last month of treatment and on at least one previous occasion.
Treatment completed	Patient who has completed treatment but who does not meet the criteria to be classified as a cure or a failure.
Treatment failure	Patient who is sputum smear-positive at 5 months or later during treatment. ^b
Died	Patient who dies for any reason during the course of treatment.
Default	Patient whose treatment was interrupted for two consecutive months or more.
Transfer out	Patient who has been transferred to another District and for whom the treatment outcome is not known.

^a Treatment success is defined as the sum of patients cured and those who have completed treatment.

^b Also a patient who was initially smear-negative before starting treatment and became smear-positive after completing the initial phase of treatment.

CHAPTER 8 MANAGEMENT OF CHILDHOOD TUBERCULOSIS

8.1 Introduction

Children can present with TB at any age. Case notifications of childhood TB depend on the intensity of the epidemic, the age structure of the population, the available diagnostic tools, and the extent of routine contact tracing.

The diagnosis of TB in children should be made based on careful and thorough assessment of all the findings from a careful history, clinical examination and relevant investigations, e.g. TST, chest X-ray (CXR) and sputum smear microscopy. As most children with TB have pulmonary TB, bacteriological confirmation of TB should be sought whenever possible, e.g. by sputum microscopy for children with suspected pulmonary TB who are old enough to produce a sputum sample.

The decision to treat a child should preferably be made by a Medical Officer after careful consideration; and once such a decision is made, the child should be treated with a full course of therapy. A trial of treatment with anti-TB medications is not recommended as a method to diagnose TB in children.

The key risk factors for TB include:

- household contact with a newly diagnosed smear-positive case
- age less than 5 years
- HIV infection
- severe malnutrition.

The key features suggestive of TB are:

- chronic symptoms suggestive of TB
- physical signs highly suggestive of TB
- a positive tuberculin skin test
- chest X-ray suggestive of TB.

8.2 Approach to diagnosis of TB in children

The approach to diagnose TB in children follows the usual standard protocol in clinical practice. This includes:

- Careful history (including history of TB contact and symptoms consistent with TB)
- Clinical examination (including growth assessment)
- Tuberculin skin testing
- Bacteriological confirmation whenever possible
- Investigations relevant for suspected pulmonary TB and suspected extrapulmonary TB
- HIV testing (in high HIV prevalence areas)

Note: In most immunocompetent children, TB presents with symptoms of a chronic disease after they have been in contact with an infectious source case. TST can be used to demonstrate infection with *M. tuberculosis* in most cases. The presentation in infants may be more acute, resembling acute severe pneumonia and should be suspected when there is a poor response to antibiotics. In such situations, there is often an identifiable source case, usually the mother.

8.2.1 History taking in childhood TB

The clinician should ensure that careful history is taken including history of TB contact and symptoms consistent with TB.

a. Contact

This refers to a child living in the same household as or in frequent contact with a source case (e.g. the child's caregiver) with sputum smear-positive pulmonary TB or sputum smear-negative but culture-positive TB.

The following actions concerning contact are of importance for diagnosing TB in children.

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

b. Symptomatic children

Children with symptomatic TB often have already developed chronic disease. The commonest symptoms to be considered are as follows:

- **Chronic cough**
 - An unremitting cough that is not improving and has been present for more than 21 days.
- **Fever**
 - Body temperature of $>38^{\circ}\text{C}$ for 14 days, after common causes such as malaria or pneumonia have been excluded.
- **Weight loss or failure to thrive**
 - In addition to asking about weight loss or failure to thrive, it is necessary to look at the child's growth chart.

8.2.2 Clinical examination (including growth assessment)

There are no specific features on clinical examination that are typical of TB in children or can confirm that the presenting illness is due to pulmonary TB. Some signs, although uncommon, are highly suggestive of extra-pulmonary TB (i.e. TB of organs other than the lungs). Other signs are common and should prompt an investigation into the possibility of childhood TB. Important physical signs are:

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

- gibbus, especially of recent onset (resulting from vertebral TB)
- non-painful enlarged cervical lymphadenopathy with fistula formation;

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

- meningitis not responding to antibiotic treatment, with a subacute onset or raised intracranial pressure
- pleural effusion

- pericardial effusion
- distended abdomen with ascites
- non-painful enlarged lymph nodes without fistula formation
- non-painful enlarged joint
- signs of tuberculin hypersensitivity (e.g. phlyctenular conjunctivitis, erythema nodosum).

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

8.2.3 Tuberculin skin test

A positive TST occurs when a person is infected with *M. tuberculosis*, but does not necessarily indicate disease. However, the TST can also be used as an adjunct in diagnosing TB in children with signs and symptoms of TB and when used in conjunction with other diagnostic tests. The TST can be used to screen children exposed to TB (such as from household contact with TB), though children can still receive chemoprophylaxis even if the TST is not available. The TST is useful in HIV-infected children to identify those with dual TB/HIV infection and as an aid in the diagnosis of TB, although fewer HIV-infected children will have a positive TST, as a normal immune response is required to produce a positive test and many HIV-infected children have immune suppression.

TST using the Mantoux method is the recommended test, and should be done using 2 TU of tuberculin PPD RT23. A TST should be regarded as positive as follows:

- in high-risk children (includes HIV-infected children and severely malnourished children, i.e. those with clinical evidence of marasmus or kwashiorkor): >5 mm diameter of induration;
- in all other children (whether they have received a bacille Calmette–Guérin (BCG) vaccination or not): >10 mm diameter of induration.

Note: There can be false-positive as well as false-negative TSTs. Sometimes it is useful to repeat the TST in children once their nutritional status has improved or their severe illness (including TB) has resolved, as they may be initially TST negative, but positive after 2–3 months on treatment. A negative TST never rules out a diagnosis of TB in a child.

8.2.4 Bacteriological confirmation whenever possible

Diagnosis of TB in a child should be confirmed using whatever specimens and laboratory facilities are available. Appropriate specimens from the suspected sites of involvement should be obtained for microscopy and, where facilities and resources are available, for culture (and also histopathological examination). Appropriate clinical samples include sputum, gastric aspirates and certain other material (e.g. lymph node biopsy or any other material that is biopsied). Fine-needle aspiration of enlarged lymph glands – for both staining of acid-fast bacilli and histology – has been shown to be a useful investigation, with a high bacteriological yield.

Bacteriological confirmation is especially important for children who have:

- suspected drug-resistant TB
- HIV infection

- complicated or severe cases of disease
- an uncertain diagnosis.

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

a. Expectoration

Sputum should always be obtained in adults and older children (10 years of age or older) who are pulmonary TB suspects. Although it is difficult to obtain sputum from younger children under 5 and most of them are sputum smear-negative, for those who are able to produce a specimen, it is recommended to send it for smear microscopy (and mycobacterial culture if available).

As with adult TB suspects, two sputum specimens should be obtained: an on-the-spot specimen (at first evaluation) and an early morning specimen (at a follow-up visit).

b. Gastric aspiration

Gastric aspiration using a nasogastric feeding tube can be performed in young children who are unable or unwilling to expectorate sputum. However, this procedure should be performed only on the recommendation and supervision of a Paediatrician. Gastric aspirates should be sent for smear microscopy and mycobacterial culture. A gastric aspirate should be obtained on each of three consecutive mornings.

c. Sputum induction

Several recent studies have found that sputum induction is safe and effective in children of all ages and the bacterial yields are as good as or better than for gastric aspirates. However, training and specialized equipment are required to perform this procedure properly.

8.2.5 Investigations relevant for TB in children

a. Suspected pulmonary TB

Chest radiography is useful in the diagnosis of TB in children. In the majority of cases, children with pulmonary TB have CXR changes suggestive of TB. The commonest picture is that of persistent opacification in the lung together with enlarged hilar or subcarinal lymph glands. A miliary pattern of opacification in HIV-uninfected children is highly suggestive of TB. Patients with persistent opacification which does not improve after a course of antibiotics should be investigated for TB.

Adolescent patients with TB have CXR changes similar to adult patients with large pleural effusions and apical infiltrates with cavity formation being the most common forms of presentation. Adolescents may also develop primary disease with hilar adenopathy and collapse lesions visible on CXR. Good-quality CXRs are essential for proper evaluation. CXRs should preferably be read by a radiologist or a health-care worker trained in their reading. A practical guide for interpreting CXRs has been developed (1).

b. Suspected extrapulmonary TB

The investigations usually used to diagnose the common forms of extrapulmonary TB. In most of these cases, TB will be suspected from the clinical picture and confirmed by histology or other special investigations.

Site	Practical approach to diagnosis
Peripheral lymph nodes (especially cervical)	Lymph node biopsy or fine needle aspiration
Miliary TB (e.g. disseminated)	Chest X-ray and lumbar puncture (to test for meningitis)
TB meningitis	Lumbar puncture (and computerized tomography where available)
Pleural effusion (older children and adolescents)	Chest X-ray, pleural tap for biochemical analysis (protein and glucose concentrations), cell count and culture
Abdominal TB	(e.g. peritoneal) Abdominal ultrasound and ascitic tap
Osteoarticular	X-ray, joint tap or synovial biopsy
Pericardial TB	Ultrasound and pericardial tap

c. Other tests

Serological and nucleic acid amplification (e.g. polymerase chain reaction) tests are not currently recommended for routine diagnosis of childhood TB, as they have been inadequately studied in children and have performed poorly in the few studies which have been done. However, this is an area that requires further research, as such tests may prove to be useful in the future. Other specialized tests, such as computerized chest tomography and bronchoscopy, are not recommended for the routine diagnosis of TB in children.

HIV counselling and testing is indicated for all TB patients as part of their routine management. In areas with lower HIV prevalence, HIV counselling and testing is indicated for TB patients with symptoms and/or signs of HIV-related conditions, and in TB patients having a history suggestive of high risk of HIV exposure.

8.2.6 Standard case definitions of TB in children

Beyond the diagnosis of TB disease, the type of TB case should also be defined to enable appropriate treatment to be given and the outcome of treatment evaluated.

The case definition is determined by the:

- (i) site of disease,
- (ii) result of any bacteriological tests,
- (iii) severity of TB disease, and
- (iv) history of previous anti-TB treatment.

All children diagnosed with TB should be registered with the NTP indicating the type of disease based on the NTPs standard case definitions. It should also be indicated whether they are new cases or previously treated.

The Standard case definitions are as follows:

a) Pulmonary TB, sputum smear-positive

The criteria are:

- two initial sputum smear examinations positive for acid-fast bacilli; **or**
- one sputum smear examination positive for acid-fast bacilli plus CXR abnormalities consistent with active pulmonary TB, as determined by a clinician; **or**
- one sputum smear examination positive for acid-fast bacilli plus sputum culture positive for *M. tuberculosis*.

Adolescents, or children of any age with complicated intrathoracic disease, are more likely to have sputum smear-positive pulmonary TB.

b) Pulmonary TB, sputum smear-negative

A case of pulmonary TB that does not meet the above definition for smear-positive pulmonary TB. Such cases include cases without smear results, which should be exceptional in adults but relatively more frequent in children.

In keeping with good clinical and public health practice, diagnostic criteria for sputum smear-negative pulmonary TB should include:

- 2 initial sputum specimens negative for acid-fast bacilli; **and**
- radiological abnormalities consistent with active pulmonary TB; **and**
- no response to a course of broad-spectrum antibiotics; **and**
- decision by a clinician to treat with a full course of anti-TB chemotherapy.

c) Extrapulmonary TB

Children with only extrapulmonary TB should be classified under this case definition. Children who have both pulmonary and extrapulmonary TB should be classified under the case definition of pulmonary TB.

d) Drug-resistant TB

Children are as susceptible to drug-resistant as to drug-sensitive TB. Drug-resistant TB is a laboratory diagnosis. However, drug-resistant TB should be suspected if any of the features below are present.

1. Features in the source case suggestive of drug-resistant TB:

- Contact with a known case of drug-resistant TB
- Remains sputum smear-positive after 3 months of treatment
- History of previously treated TB
- History of treatment interruption.

2. Features of a child suspected of having drug-resistant TB:

- Contact with a known case of drug-resistant TB
- Not responding to the anti-TB treatment regimen
- Recurrence of TB after adherence to treatment.

The diagnosis and treatment of drug-resistant TB in children should be carried out in line with national MDR-TB guidelines.

8.3 Anti-TB treatment in children

8.3.1 The basis for treatment policy in Children

The DOTS strategy is applicable to all patients with TB, including children. The recommended treatment regimens for the TB diagnostic categories are generally the same for children as for adults. All children satisfying the case definition for categories I and III shall receive category I regimen. The following are the treatment categories for children and their recommended regimens:

Table 13: Classification of Childhood TB and the recommended treatment regimens

TB diagnostic category	Description	Regimen	
		Intensive phase	Continuation phase
I	New smear-positive pulmonary TB New smear-negative pulmonary TB with extensive parenchymal involvement. Other forms of extrapulmonary TB other than TB meningitis	2RHZE	4RH
I	TB meningitis	2RHZS^a 2HRZ(S or Eth)^b 6HRZEth	4RH 7–10HR None^c
II	Previously treated smear-positive pulmonary TB: relapse treatment after interruption treatment failure Other forms of retreatment	2RHZES/1RHZE	5RHE
IV	Chronic and MDR-TB	Specially designed standardized or individualized regimens (see treatment guidelines for MDR-TB)	

E, ethambutol; H, isoniazid; R, rifampicin; S, streptomycin; Z, pyrazinamide.

a In comparison with the treatment regimen for patients in diagnostic category I, streptomycin replaces ethambutol in the treatment of TB meningitis

b Eth = Ethionamide to be prescribed by a specialist.

c No continuation phase as total treatment duration is 6 months.

8.3.2 Treatment of New Child TB case:

A child patient who has never been treated for TB in the past or who has taken anti-tuberculosis drugs for less than four weeks. The recommended treatment regimen for new cases is: 2HRZE/4HR. During the intensive phase lasting 2 months, 4 drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol), are given. Two drugs (isoniazid and rifampicin) during the continuation phase lasting 4 months.

Category I Regimen for Children

Table 14: Anti-TB drugs and dosages for treatment of new Child TB cases

Pretreatment body weight	Intensive (initial) Phase (2 months)		Continuation Phase (4 months)
	RHZ (60/30/150mg)	E (400mg)*	RH (60/30mg)
3-4 kg*	½ tablet		½ tablet
5-7 kg	1 tablet	¼ tablet	1 tablet
8-9 kg	1½ tablets	½ tablet	1½ tablets
10-14 kg	2 tablets	½ tablet	2 tablets
15-19 kg	3 tablets	1 tablet	3 tablets
20-24 kg	4 tablets	1 tablet	4 tablets
25-29 kg	5 tablets	1½ tablets	5 tablets
30-35 kg	6 tablets	1½ tablets	6 tablets

*For the treatment of TB meningitis in children, ethambutol is replaced with streptomycin.

Streptomycin should be avoided when possible in children because the injections are painful and irreversible auditory nerve damage may occur.

Ethambutol not be given to children below 4kg.

8.3.3 Re-treatment regimen for Child TB cases:

A patient previously treated for TB as new case for more than one month in the past and now being treated for TB again. This includes treatment failure, relapse, and return after default cases (smear or culture positive). The recommended regimen is: 2HRZES/1HRZE/5HRE (Category II Regimen). The retreatment regimen has an initial phase of 3 months with 5 drugs (isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin), one month with 4 drugs ((isoniazid, rifampicin, pyrazinamide, ethambutol) and a continuation phase of 5 months with 3 drugs (isoniazid, rifampicin, ethambutol).

Table 15: Anti-TB drugs and dosages for re-treatment of TB children

Pre-treatment body weight	Intensive (initial) Phase (2 months)			3rd Month of Intensive (initial) Phase		Continuation Phase (5 months)	
	RHZ (60/30/150mg)	E (400mg)	S (g)	RHZ (60/30/150mg)	E (400mg)	RH (60/30mg)	E (400mg)
3-4 kg*	½ tablet		0.05	½ tablet		½ tablet	
5-7 kg	1 tablet	¼ tablet	0.1	1 tablet	¼ tablet	1 tablet	¼ tablet
8-9 kg	1½ tablets	½ tablet	0.125	1½ tablets	½ tablet	1½ tablets	½ tablet
10-14 kg	2 tablets	½ tablet	0.2	2 tablets	½ tablet	2 tablets	½ tablet
15-19 kg	3 tablets	1 tablet	0.25	3 tablets	1 tablet	3 tablets	1 tablet
20-24 kg	4 tablets	1 tablet	0.35	4 tablets	1 tablet	4 tablets	1 tablet
25-29 kg	5 tablets	1½ tablets	0.4	5 tablets	1½ tablets	5 tablets	1½ tablets
30-35 kg	6 tablets	1½ tablets	0.5	6 tablets	1½ tablets	6 tablets	1½ tablets

* Ethambutol not be given to children below 4kg.

8.3.2 Management of TB meningitis and miliary TB

TB meningitis and miliary TB are more common in young children and are associated with high rates of death and disability, particularly if the diagnosis is delayed. It is therefore important to consider these diagnoses in young children as early as possible, especially in children who have a history of contact with an adult with infectious TB.

Miliary or haematogenously disseminated TB has a high risk (60–70%) of meningeal involvement and should therefore be managed similarly to TB meningitis. For this reason, many experts recommend that all children with miliary TB (or suspected of having miliary TB) should undergo a lumbar puncture to test for the presence of meningitis. Children with TB meningitis or miliary TB should be hospitalized, preferably for at least the first 2 months or until they stabilize.

Corticosteroids (usually prednisone) are recommended for all children with TB meningitis in a dosage of 2 mg/kg daily for 4 weeks. The dose should then be gradually reduced (tapered) over 1–2 weeks before stopping. The dosage of prednisone can be increased to 4 mg/kg daily (maximum 60 mg/day) in the case of seriously ill children because rifampicin will decrease corticosteroid concentrations, but higher doses carry a risk of greater immune suppression. Other complicated forms of TB, e.g. TB meningitis, complications of airway obstruction by TB lymph glands, and pericardial TB also require corticosteroid therapy.

Children with TB meningitis are at high risk of long-term disability and therefore benefit from specialist care, where this is available.

8.3.3 Administering treatment and ensuring adherence

Treatment of TB in children should be administered on an ambulatory basis. Children, their parents and other family members, and other caregivers should be educated about TB and the importance of

completing treatment. The support of the child's parents and immediate family is vital to ensure a satisfactory outcome of treatment.

Children with severe forms of TB should be hospitalized for intensive management where possible e.g. in:

- TB meningitis and miliary TB, preferably for at least the first 2 months,
- respiratory distress,
- Spinal TB, and (iv) severe adverse events, such as clinical signs of hepatotoxicity (e.g. jaundice).

If it is not possible to ensure good adherence and treatment outcome on an outpatient basis, some children may require hospitalization for social or logistic reasons.

8.3.4 Follow-up of TB treatment in children

Ideally, each child should be assessed by the NTP (or those designated by the NTP to provide treatment) at least at the following intervals: 2 weeks after treatment initiation, at the end of the intensive phase and every 2 months until treatment completion. The assessment should include, as a minimum; symptom assessment, assessment of treatment adherence, enquiry about any adverse events and weight measurement.

Medication dosages should be adjusted to account for any weight gain.

Treatment adherence should be assessed by reviewing the treatment card. A follow-up sputum sample for smear microscopy at 2 months after treatment initiation should be obtained for any child who was smear-positive at diagnosis.

Follow-up Chest X-Rays are not routinely required in children, particularly as many children will have a slow radiological response to treatment. A child who is not responding to anti-TB treatment should be referred for further assessment and management. These children may have drug-resistant TB, an unusual complication of pulmonary TB, other causes of lung disease or problems with treatment adherence.

8.3.4.1 Adverse events

Adverse events caused by anti-TB drugs are much less common in children than in adults. The most important adverse event is the development of hepatotoxicity, which can be caused by Isoniazid, rifampicin or Pyrazinamide. Serum liver enzyme levels should not be monitored routinely, as asymptomatic mild elevation of serum liver enzymes (less than five times the normal values) is not an indication to stop treatment. However, the occurrence of liver tenderness, hepatomegaly or jaundice should lead to investigation of serum liver enzyme levels and the immediate stopping of all potentially hepatotoxic drugs.

Patients should be screened for other causes of hepatitis, and no attempt should be made to reintroduce these drugs until liver functions have normalized. An expert (experienced in managing drug-induced hepatotoxicity) should be involved in the further management of such cases. If treatment for TB needs to be continued for severe forms of TB, nonhepatotoxic anti-TB drugs should be introduced (e.g. Ethambutol, an aminoglycoside and a fluoroquinolone).

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

8.3.5 Re-treatment of child TB cases

In childhood TB cases when anti-TB treatment fails or a relapse occurs, every effort should be made to find the most likely cause for the failure or relapse. Mycobacterial culture and drug susceptibility testing should be performed for all re-treatment cases where possible.

Failure of category III treatment in children is rare but should be managed in the same way that failure in adults is managed, either with a category II or IV regimen, depending on what is known about the risk of MDR-TB in this group of patients. The standard category II regimen is 2HRZES/1HRZE/5HRE.

Category IV regimens are specially designed and may be standardized or individualized. If an adult source case with drug-resistant TB is identified, the child should be treated according to the drug susceptibility pattern of the source case's strain if an isolate from the child is not available.

8.3.6 Children with TB who are co-infected with HIV

Most current international guidelines recommend that TB in HIV-infected children should be treated with a 6-month regimen as in HIV-uninfected children. Most children with TB, including those who are HIV-infected, have a good response to the 6-month regimen. Possible causes for failure, such as non-compliance with therapy, poor drug absorption, drug resistance and alternative diagnoses should be investigated in children who are not improving on anti-TB treatment.

All children with TB and HIV co-infection should be evaluated to determine if ART is indicated during the course of treatment for TB. Appropriate arrangements for access to antiretroviral drugs should be made for patients who meet indications for treatment. Given the complexity of co-administration of anti-TB treatment and ART, consultation with an expert in this area is recommended before initiation of concurrent treatment for TB and HIV infection, regardless of which disease appeared first. However, initiation of treatment for TB should not be delayed. Children with TB and HIV co-infection should also receive cotrimoxazole as prophylaxis for other infections.

In HIV-infected children with confirmed or presumptive TB disease, initiation of anti-TB treatment is the priority. However, the optimal timing for initiation of ART during anti-TB treatment is not known. The decision on when to start ART after starting anti-TB treatment involves a balance between the child's age, pill burden, potential drug interactions, overlapping toxicities and possible immune reconstitution syndrome versus the risk of further progression of immune suppression with its associated increase in mortality and morbidity. Many clinicians start ART 2–8 weeks after starting anti-TB treatment.

8.4 Contact Screening and Management

It is recommended that all household contacts should be screened for symptoms of disease and offer isoniazid preventive therapy (i.e. daily isoniazid for at least 6 months) to children aged less than 5 years and *all HIV-infected children who are household contacts*.

Definitions used in contact screening

Source case: A case of pulmonary TB (usually sputum smear-positive) which results in infection or disease among contacts

Contacts for screening: All children aged under 5 years (whether sick or well) and children 5 years or older if symptomatic, who are in close contact with a source case

Close contact: Living in the same household as a source case (e.g. the child's caregiver) or in frequent contact with a source case

8.5 Assessment and management

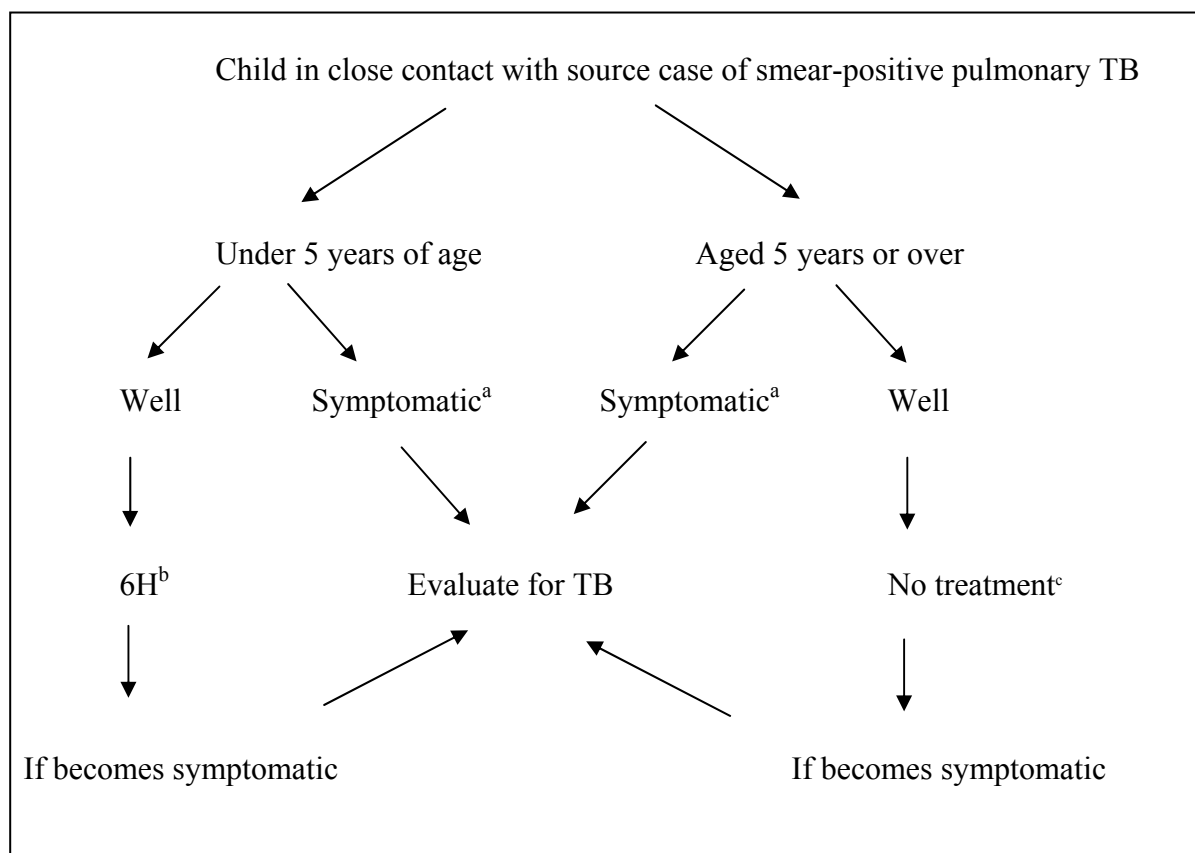
Contacts should be assessed clinically to decide whether the contact is well or symptomatic. Routine assessment of exposed contacts does not require CXR or TST (Figure 8.1). This approach applies to contacts of smear-positive pulmonary TB cases, but screening should also be available for contacts of smear-negative pulmonary TB cases.

If the contact of a source case with smear-negative pulmonary TB is symptomatic, then the diagnosis of TB needs to be investigated as above irrespective of the contact's age.

Recommended treatment for a healthy contact aged under 5 years is isoniazid 5 mg/kg daily for 6 months.

Follow-up should be carried out at least every 2 months until treatment is complete. If TB is suspected at initial assessment or at subsequent follow-up, diagnostic procedures mentioned earlier should be followed. Referral to a district or tertiary hospital may be necessary when there are uncertainties of diagnosis. Contacts with TB disease should be registered and treated

Figure 7: Approach to contact management when chest X-ray and tuberculin skin test are not readily available



^a If TB is suspected, refer to Section 1.

^b Isoniazid 5 mg/kg daily for 6 months.

^c Unless the child is HIV-infected (in which case isoniazid 5 mg/kg daily for 6 months is indicated).

8.6 Special circumstances in child TB management

8.6.1 Child contact is known to be HIV-infected

If the child contact is HIV-infected and asymptomatic, then isoniazid preventive therapy should be considered for all ages, including those 5 years and older. As with other contacts, active disease should be ruled out before providing HIV-infected children with isoniazid preventive therapy. HIV-infected children who have symptoms should be carefully evaluated for TB, and if found to have TB should be started on treatment

8.6.2 Suspected HIV infection of source case and contact

In HIV-endemic countries where HIV prevalence is high among cases with smear-positive pulmonary TB, if the source case is a parent, their children may be at risk of both TB and HIV infection. It is important to ask whether the HIV status of the source case and child contact is known and consider HIV counselling and testing.

8.6.3 Child contacts of infectious MDR-TB cases

The only chemoprophylaxis regimens to have been studied are based on isoniazid and, to a lesser extent, on rifampicin. Since by definition MDR-TB is resistant to both of these drugs, it is unlikely that use of these drugs to treat latent infection caused by an MDR-*M. tuberculosis* strain will prevent the

development of active TB disease. Close contacts of MDR-TB patients should receive careful clinical follow-up for a period of at least 2 years. If active disease develops, prompt initiation of treatment with a regimen designed to treat MDR-TB is recommended. On the basis of the currently available evidence, WHO does not recommend second-line drugs for chemoprophylaxis in MDR-TB contacts.

8.6.4 Management of a baby born to a mother with infectious pulmonary TB

If a mother is found to have pulmonary TB, then the baby, and if possible, the placenta, should be investigated for evidence of congenital TB infection and the baby treated. Once the mother has been on treatment for at least 2–3 weeks, she is generally no longer infectious. If a mother has been on treatment for TB for several weeks before delivery, it is less likely that the baby will become infected. The risk is highest if a mother is diagnosed at the time of delivery or shortly thereafter.

A breastfeeding infant has a high risk of infection from a mother with smear-positive pulmonary TB, and has a high risk of developing TB. The infant should receive 6 months of isoniazid preventive therapy, followed by BCG immunization. Breastfeeding can be safely continued during this period. An alternative policy is to give 3 months' isoniazid, then perform a TST. If the test is negative, isoniazid should be stopped and BCG vaccination given. If the test is positive, isoniazid should be continued for another 3 months, after which it should be stopped and BCG given.

CHAPTER 9 COLLABORATIVE TB AND HIV ACTIVITIES

9.1 Basis for TB/HIV policy

TB and HIV are closely interlinked. TB is a leading cause of HIV –related morbidity and mortality. HIV is the most important factor fuelling the TB epidemic in population with a high HIV prevalence. TB can occur at any point in the course of progression of HIV infection and the risk of developing TB rises sharply with worsening immune status. A person infected with HIV has a 10 times increased risk of developing TB disease. Mortality in HIV+ TB patients is 2-4 times higher (6% to 39% in SSA) than in HIV- TB patients. In Lesotho HIV is considered to be the major factor fueling the TB epidemic, and is estimated to contribute to 54% of TB incidence in adults. Statistics indicate that about 64% of TB cases are also co-infected with HIV, and WHO estimates that HIV contributes to 68% of the deaths of TB patients on treatment. The TB death rates have increased from 10% in 1995 to 13.5% in 2000. In 2003, the estimated HIV prevalence among people aged 15-49 years was 28.9%⁵. The dual TB/HIV epidemic has resulted in overstretch of health delivery services.

Early diagnosis and effective treatment of TB among HIV-infected patients are critical for curing TB, minimizing the negative effects of TB on the course of HIV and interrupting the transmission of *M Tuberculosis* to other persons in the community. Proper case management of TB can significantly prolong the lives of people living with HIV/AIDS. Tuberculosis can occur at any point in the course of progression of HIV infection.

Similarly, early assessment of HIV status of TB patients is necessary to facilitate initiation of care and support interventions.

Initial assessment of HIV Status in TB patients:

- HIV pre-test counseling.
- Serological test (typically, ELISA and/or rapid tests) for HIV antibodies, followed by Western Blot confirmatory test.
- Post-test counseling, including information on reducing risky behaviour, irrespectively whether the HIV test turned to be positive or negative.

Assessment of stage of HIV disease in TB / HIV co-infected patients

- Review of a personal and clinical history for factors that might influence the choice of therapy, (e.g. TB history, contraception methods, liver and renal status, etc).
- A physical examination
- A complete blood count and formula.
- Measurement of CD4 cell count to assess severity of immunodeficiency.
- If HIV RNA testing is available, it can be used to assess the level of viral replication
- Pregnancy test for women if indicated.
- Determination of hepatitis B and C risks and status. Specific serologic testing for hepatitis C and hepatitis B infection, especially, if a patient is current or former IDU.
- Determination of serum of the enzyme alanine aminotransferase (ALT) is important. (A level of ALT exceeding 3 times the normal level will influence the choice of TB and ARV drugs).
- Other tests might be offered based on patient's condition.

⁵ UNAIDS Report 2004

[1] Serum levels of the enzyme aspartate aminotransferase (AST) and bilirubin may also be evaluated, depending upon availability of testing.

9.2 Strategy for collaborative TB/HIV activities in Lesotho

Strengthening collaboration between the National TB Programme and the National AIDS Control Programme is key to addressing the impact of the two diseases in Lesotho. However, collaboration should not be an end in itself, but to improve the TB and HIV care and prevention services provided by the district health systems. There should be a TB/HIV Strategic plan with clear goals and objectives to guide the implementation of joint activities. This should include the following thematic areas:

1. Establishment of Collaborative mechanism
2. Decreasing the burden of tuberculosis in People Living with HIV/AIDS
3. Decreasing the burden of HIV/AIDS in tuberculosis Patients

9.2.1 TB/HIV Coordination mechanism

Both programmes need to ensure joint planning, coordination and monitoring and evaluation system. A functional **TB/HIV working group should be established** that will develop collaborative strategic plans, policy consensus and implement joint TB/HIV activities. The committee should include representatives from both programs, urban and rural district health management teams, from the communities of PLWA and different stakeholders and health partners.

Examples of joint collaborative activities are:

- Joint policy consensus
- Joint advocacy strategies
- Joint IEC activities
- Joint training activities
- Joint monitoring and evaluation
- Joint surveillance
- Joint research

9.2.2 Decreasing the burden of tuberculosis in People Living With HIV/AIDS (PLWHAs)

Decreasing the burden of tuberculosis in PLWHAs should be the core responsibility of the National TB programme but has to be implemented jointly with HIV/AIDS programme. The relevant activities include intensified case finding and treatment, TB preventive therapy, as well as interventions directed towards tuberculosis infection control in health care and congregate settings.

This may require enhancing the capacity of HIV/AIDS care units to screen for TB and administer treatment to detected cases.

Additional interventions beyond effective case finding and treatment

Interventions directed against TB	Interventions directed against HIV and AIDS
<p>a) Increase awareness about TB such that people with symptoms suggestive of TB to seek help at health facilities</p> <p>b) Intensified TB case finding in high risk groups:</p> <ul style="list-style-type: none"> ○ HIV positive clients ○ Patients presenting with STIs 	<p>a) Prevention of HIV transmission</p> <ul style="list-style-type: none"> • Condom promotion • Treatment of STIs • HIV counseling and testing • Sexual behavioral changes • Prevention of mother to child transmission

<ul style="list-style-type: none"> ○ PLHA support groups ○ Home based care patients ○ Prisoners ○ Household contacts of TB patients <p>c) Treatment of latent infection to prevent of new TB disease</p> <ul style="list-style-type: none"> ○ Isoniazid preventive therapy for PLHA 	<ul style="list-style-type: none"> ● IEC activities ● Life skills <p>b) By increasing/ maintaining immune function in PLHA</p> <ul style="list-style-type: none"> ○ Anti retro viral therapy
<p>By providing care for PLHA</p> <ul style="list-style-type: none"> ● (HIV care gives direct opportunities for HIV and TB prevention, and also impacts on prevention by normalizing community attitudes and reducing the stigma of HIV and AIDS) ● Treatment of HIV related diseases ● Prevention of HIV related infections ● Psychological support ● Palliative care ● Nutritional support 	

9.2.2.1 INH Preventive Therapy (IPT)

IPT has been shown to be beneficial in certain settings in preventing morbidity and mortality from TB. INH prophylaxis should be given to all HIV positive individuals in whom TB has been excluded.

IPT should also be given in the following circumstances:

- Children who are contacts of a smear positive TB case
- TB-exposed, HIV-infected children
- TB-exposed health care workers in whom active TB has been excluded;

All TB-exposed, HIV infected children should receive some form of TB treatment – IPT if they are well and active TB is ruled out, or a full course of TB treatment if active TB cannot be ruled out.

IPT prophylaxis for children < 15 years of age who are HIV-infected and TB-exposed

Isoniazid: 5-10 mg/kg daily for 6 months
 Pyridoxine: < 3 years: 12.5 mg daily for 6 months
 > 3 years: 25 mg daily for 6 months

9.2.3 Treatment of TB in HIV positive individuals

Tuberculosis treatment is effective in HIV negative and positive individuals alike. Therefore, treatment of TB should be made available to all diagnosed patients regardless of their HIV status (see 7.2). Treatment of TB should be considered a priority in the event that the patient is dually infected and also requires ART. Strategy for initiation of treatment in HIV infected patients with active TB should be as follows:

9.2.4 Decreasing the burden of HIV/AIDS in tuberculosis patients

Decreasing the burden of HIV/AIDS in tuberculosis patients should be the core responsibility of the National HIV/AIDS programme but has to be implemented jointly with TB programme. The activities include HIV testing and counseling, HIV prevention, Cotrimoxazole preventative therapy, HIV/AIDS care and support including provision of ART.

TB and HIV interventions should be introduced at different levels within the district health system.

LEVEL OF HEALTH CARE	TB/HIV INTERVENTIONS
HOME AND COMMUNITY Community based organizations, non governmental organizations, faith based organizations, government community health programmes	<ul style="list-style-type: none"> • TB, HIV, and STI, IEC activities • Condom promotion • Nutritional advice and support • Psychological support • Community DOT for TB • Community based palliative and terminal care
PRIMARY CARE Government health centers or clinics, mission health centers, NGO health centers, private health centers	<ul style="list-style-type: none"> • HTC • TB case finding and treatment • Intensified case finding • Isoniazid/ Cotrimoxazole provision • Condom promotion • STI Syndromic management • Management of HIV related opportunistic infection and palliative care • Prevention of mother to child transmission
SECONDARY CARE Government hospitals, mission hospitals, private hospitals	<ul style="list-style-type: none"> • Diagnosis and treatment of HIV related diseases • In patient palliative care • Anti retroviral therapy

9.2.4.1 HIV Testing and Counseling (HTC) for TB patients

The risk of having HIV infection being higher among TB patients than in the general population, knowledge of HIV status can help to reduce stigma, promote safe behaviour to reduce HIV transmission and improve access to appropriate care regardless of the their status. Health care workers caring for TB patients need to know the HIV status of their patients to ensure that they are able to provide the most appropriate treatment, care and support during the TB treatment.

HIV Testing and Counseling (HTC) should be offered to all TB patients, before, during or after the TB registration process. This should occur within the context of the TB service provider where the test result can be recorded in the patient record, TB register and reported quarterly with the outcome data. However, where HIV counselling and testing is conducted in a different part of the same facility or even at a distant site, referral should be adequately organized to ensure to keep tract of the patients as well as the test results.

Patient confidentiality must be maintained, and test should be performed based on the patient's informed consent.

9.2.4.2 Cotrimoxazole prophylaxis

UNAIDS and WHO have recommended the use of cotrimoxazole prophylaxis for adults and children living with HIV/AIDS in Africa as part of a minimum package of care. The recommended dosage for trimethoprim-sulphamethoxazole (cotrimoxazole) 160/800mg (960mg) daily for all HIV positive patients (whether they have TB or not) who have symptomatic HIV disease (WHO Clinical stage 2,3 or 4) or have a CD4 count less than 200 cells/mm³ or have already had pneumocystis carinii pneumonia. Lesotho adopted the WHO and UNAIDS recommendation and approves Cotrimoxazole prophylaxis, to be provided at TB clinics/wards by TB staff. This takes into consideration the fact that HIV positive people with TB are all in WHO clinical stage 3 or 4. Thus all TB patients who are HIV positive should get cotrimoxazole prophylaxis irrespective of their CD4 cell count.

Cotrimoxazole should be started after at least two weeks of TB treatment in order to differentiate between side effects from anti-TB drugs and side effects from cotrimoxazole. The dosages for children are 0.625 mg/kg daily.

Cotrimoxazole is contraindicated in the following conditions:

- First trimester pregnancy
- Breastfeeding first 6 weeks post-partum
- History of sulfa allergy
- Clinical renal, hepatic insufficiency
- Bone marrow suppression

(No routine lab test is required)

Treatment should be stopped immediately in the following circumstances:

- Allergy
- Pregnancy
- Development of hematologic abnormalities
- Development of renal/hepatic insufficiency (jaundice)
- Immunosystem restoration

If cotrimoxazole allergy

- Dapsone 100 mg/daily (child 2 mg/kg/day) but this does not protect against toxoplasmosis

Table 16: Cotrimoxazole (CTX) toxicity grading scale for adults and adolescents

Toxicity	Clinical description	Recommendation
Grade 1	Erythema	Continue CTX prophylaxis with careful and repeated observation and follow up. Provide symptomatic treatment, such as antihistamines, if available
Grade 2	Diffuse maculopapular rash, dry desquamation	Continue CTX prophylaxis with careful and repeated observation and follow up. Provide symptomatic treatment, such as antihistamines, if available
Grade 3	Vesiculation, mucosal ulceration	CTX should be discontinued until the adverse effect has completely resolved (usually 2 weeks) at which point reintroduction or desensitization can be considered
Grade 4	Exfoliative dermatitis, Stevens-Johnson or Erythema multiforme, moist desquamation	CTX should be permanently discontinued

Discontinuation of CPT

Setting	Recommendation
CD4 testing not available (clinical assessment only)	Do not discontinue CTX prophylaxis, particularly in settings where bacterial infections and malaria are common HIV-related events
	Consider discontinuation of CTX prophylaxis in those with evidence of good clinical response to ART (absence of clinical symptoms after at least one year of therapy), good adherence and secure access to ART.
CD4 testing available (clinical and immunologic assessment)	If indication is to prevent PCP and toxoplasmosis, CPT can be discontinued in patients with evidence of immune recovery on ART (CD4 \geq 200/mm ³ at least 6 months on

	ART).
	If there is high possibility of bacterial infections, discontinue CTX prophylaxis in those with evidence of immune recovery related to ART (CD4 \geq 350/mm ³ at least 6 months on ART).

9.2.4.3 Antiretroviral treatment

The purpose of ART (anti retroviral therapy) is to achieve maximal and durable suppression of HIV replication, restoration and preservation of immune function, accelerated growth for children, reduction in HIV-related morbidity and mortality as well as overall improvement in quality of life and prolonged survival. As with TB, HIV needs to be treated with a combination of drugs in order to improve efficacy and reduce the development of drug-resistant strains of HIV.

The efficacy of ART is usually manifested by clinical improvement, a reduction in the number and frequency of OIs, enhanced immune status evidenced by gradual and steady rise in the CD4 count and virologically, by a fall in the viral load to undetectable levels six months after the initiation of ART

The choice of ART regimen for TB patients is based on available evidence on effectiveness, drugs availability, overlapping side-effects and toxicity profiles. The ART regimen for TB patients should be based on those recommended in the approved national ART guidelines.

In a treatment-naïve patient (one who has never used ARVs in the past), the first-line regimen should consist of two Nucleoside Reverse Transcriptase Inhibitors (NRTI's) plus one Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI).

Table 17: Recommended NRTI and NNRTI antiretroviral drugs for first-line ART therapy

Nucleoside Reverse Transcriptase Inhibitors (NRTI)	Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI)
Lamivudine (3TC)	Nevirapine (NVP)
Tenofovir (TDF)	Efavirenz (EFV)
Zidovudine (AZT)*	
Stavudine (d4T)*	

Table 18: First Line ART Regimen for Treatment-Naïve Adult Patients

(Treatment-Naïve = those who have never taken HAART or triple therapy previously), for further information on ART, please refer to the National ART guidelines.

Regimen				When to use	When to avoid
1a	Tenofovir (TDF) (300 mg once daily)+	Lamivudine (3TC) (300 mg once daily)+	Efavirenz (EFV) (600 mg once daily; use 400 mg if < 40 kg)	Preferred first-line regimen in adults	Avoid TDF if renal compromise (baseline calculated Creatinine Clearance is < 50 ml/min). Avoid EFV in first trimester of pregnancy*
1b	Tenofovir (TDF) (300 mg once daily)+	Lamivudine (3TC) (300 mg once daily)+	Nevirapine (NVP) (200 mg once daily for the first 2 weeks, then 200 mg twice daily)	NVP should be used in women who expect to become pregnant	Avoid NVP in patients on TB treatment (use EFV-containing regimen) Avoid using TDF if renal compromise (baseline calculated Creatinine Clearance is < 50 ml/min). NVP should be used with caution in those with baseline CD4 between 250-350 due to an increased risk of hepatotoxicity (if used, monitor ALT more frequently)
1c	Zidovudine	Lamivudine	Efavirenz (EFV)*		Avoid AZT in patients with Hb < 8.0

	(AZT) (300 mg twice daily)+	(3TC) (150 mg twice daily)+	(600 mg once daily)		gm/dl Avoid EFV in first trimester of pregnancy*
1d	Zidovudine (AZT) (300 mg twice daily)+	Lamivudine (3TC) (150 mg twice daily)+	Nevirapine (NVP) (200 mg once daily for the first 2 weeks, then 200 mg twice daily)	Preferred regimen in pregnant women, and those who expect to become pregnant	Avoid AZT in patients with Hb < 8.0 gm/dl Avoid NVP in patients on TB treatment (use EFV-containing regimen) NVP should be used with caution in those with baseline CD4 between 250- 350 due to an increased risk of hepatotoxicity (if used, monitor ALT more frequently)
1e	Stavudine (d4T) (30 mg twice daily)+#	Lamivudine (3TC) (150 mg twice daily)+	Efavirenz (EFV)* (600 mg once daily; use 400 mg if < 40 kg)	Use d4T in patients with Hb < 8.0gm/dl	Avoid d4T if at risk of hyperlactatemia#
1f	Stavudine (d4T) (30 mg twice daily)+#	Lamivudine (3TC) (150 mg twice daily)+	Nevirapine (NVP) (200 mg once daily for the first 2 weeks, then 200 mg twice daily)+	Use d4T in patients with Hb < 8.0gm/dl Preferred regimen in those at risk of poor adherence, if 3- in-1 FDC is available	Avoid d4T if at risk of hyperlactatemia# Avoid NVP in patients on TB treatment (use EFV-containing regimen) NVP should be used with caution in those with baseline CD4 between 250- 350 due to an increased risk of hepatotoxicity (if used, monitor ALT more frequently)

* EFV should never be used in the first trimester of pregnancy due to its known teratogenic effects; all women should receive reliable contraceptive methods free of charge if they are on an EFV-based regimen

+ Fixed dose combinations of these medications should be available and used wherever possible

Those at risk of hyperlactatemia when taking Stavudine include:

- Pregnant females
- Females over 70 kg
- those with a body mass index (BMI) > 28

All infants, children, and adults who are already on ARV therapy should remain on their current regimen.

Substituting individual ARVs in first-line regimens

Like all medicines, ARVs also have some side effects. These should be explained to the patient and caregiver prior to initiation of therapy.

Substitutions of individual ARVs within first -line regimens may be due to:

- co-infection with TB: drug-drug interactions exist between NVP and rifampicin; EFV should be substituted in for NVP (exception: children < 3 years or < 10kg) (see **TB co-infection chapter**)
- drug toxicity: see ANNEX 14 for grading and management of ARV toxicity. If *severe or life-threatening toxicity* is related to an identifiable drug, the offending drug can be replaced with another drug from the same class that does not have the same adverse effect.

Drug substitutions should be limited to situations where toxicity is severe or life threatening (Grade 3 or 4 adverse events) (see **ANNEX 14**)

Table 19: Common early adverse effects of 1st line ARV drugs

Common early adverse effects of 1st line ARV drugs

ARV drug	Common associated toxicity
AZT	Gastrointestinal intolerance Anaemia, Neutropenia Lactic acidosis
D4T	Peripheral neuropathy Lactic acidosis
EFZ	CNS toxicity, Teratogenicity Severe skin reaction (Steven Johnson's Syndrome)
NVP	Hypersensitivity Reaction Hepatitis Severe Skin reactions (Steven Johnson's Syndrome)
3TC	Safe drug in children, adolescent and adults
TDF	Renal toxicity
ABC	Hypersensitivity

Guiding Principles in the management of ARV drug toxicity

1. Determine the seriousness of the toxicity.
2. Evaluate concurrent medications and establish whether the toxicity is attributable to an ARV drug or drugs or to a non-ARV medication taken at the same time.
3. Consider other disease processes (eg. viral hepatitis in an individual on ARV drugs who develops jaundice) because not all problems that arise during treatment are caused by ARV drugs.
4. Manage the adverse event according to severity. In general:
 - Grade 4 (severe life-threatening reactions): immediately discontinue all ARV drugs, manage the medical event (i.e. symptomatic and supportive therapy) and reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized.
 - Grade 3 (severe reactions): Substitute the offending drug without stopping ART.
 - Grade 2 (moderate reactions): Consider continuation of ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single-drug substitutions.
 - Grade 1 (mild reactions): Bother some, but do not require changes in therapy.
5. Stress the maintenance of adherence despite toxicity for mild and moderate reactions.
6. If there is a need to discontinue ART because of life-threatening toxicity, all ARV drugs should be stopped until the patient is stabilized.

When severe or life-threatening (Grade 3 or 4 adverse events) occur due to antiretroviral medications, it must be reported to HAHPKO, using the appropriate form (If there really is a form for this, then it can be added as an ANNEX)

Table 20: Potential significant adverse events associated with 1st -line ARVs and recommended substitutions

First-line ARV drug	Most common significant adverse events	Suggested first-line ARV drug substitution
	Pancreatitis	AZT
	Peripheral neuropathy	
	Lipodystrophy	

	High lactate or hyperlactatemia	AZT*
	Lactic acidosis (if hyperlactatemia was not recognized early)	TDF+
AZT	Severe anaemia	D4T
	Severe neutropenia	
	Severe gastro-intestinal intolerance	
3TC	Well-tolerated	
EFV	Persistent and severe CNS toxicity	NVP
	Potential teratogenicity (EFV should be avoided in first trimester of pregnancy)	
NVP	Hepatitis	EFV
	Less-severe rash (Grades 1 through 3)	Protease inhibitor#
	Severe or life-threatening rash (Stevens-Johnson syndrome)	
TDF	Renal toxicity	AZT (or D4T)

(Modified from WHO Guidelines, 2006)

* also consider Tenofovir (TDF) in adults and post-pubertal children

+ TDF is not recommended in pre-pubertal children; call Specialist Site for advice on complicated paediatric cases

EFV should be avoided since there is a potential for NNRTI class-specific toxicity; Protease inhibitor can be either Lopinavir/ritonavir (Kaletra) or Atazanavir/ritonavir

Table 21: Severe toxicities associated with specific 1st line ARVs and recommended substitutions

First-line ARV drug	Most frequent significant toxicity for the ARV drug*	Suggested first-line ARV drug substitution
TDF#	Renal Toxicity	AZT
AZT	Severe anemia or neutropenia	d4T or ABC or TDF#
	Lactic acidosis	TDF#
	Severe gastrointestinal intolerance	d4T or ABC or TDF#
d4T	Lactic acidosis	TDF#
	Peripheral neuropathy	AZT or ABC or TDF#
	Pancreatitis	
	Lipoatrophy/metabolic syndrome	
EFV**	Persistent and severe central nervous system toxicity, psychologic abnormalities	NVP
	Potential teratogenicity **	
NVP***	Acute symptomatic hepatitis	EFV
	Hypersensitivity reaction	ABC--(disadvantage: triple NRTI is less potent) Lop/r-- (disadvantage: premature start of second-line ARV drug)
	Severe or life threatening rash (Stevens-Johnson Syndrome)	
ABC	Hypersensitivity reaction	AZT

*Definitions for toxicities can be found in Annex 14; substitutions should occur for grade 3 or 4 adverse effects

**All women should receive reliable contraceptive methods free of charge if they are on an EFV-based regimen.

***All TB patients should be switched from NVP to EFV (except for children < 3 years or < 10kg).

TDF should not be used in children < 16 years of age due to effect on bone mineral density;

#if possible, reserve use of TDF (use other NRTIs first)

Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006. Antiretroviral therapy of HIV infection in adults and adolescents in resource-limited settings. WHO 2006

- AZT and d4t should **NEVER** be used together.
- Efavirenz should be used instead of Nevirapine as it causes less liver damage. Another alternative to Nevirapine is Abacavir.
- PIs can be used during rifampicin-containing TB treatment regimens while boosted with Ritnovir.No drug modification need it for patients on second line ARVs.

In view of the above, all HIV infected patients should be asked about antiretroviral use, especially whether they are currently using PIs or NNRTIs before anti-TB drugs are prescribed. Table 4 summarizes the indications for starting ARV therapy in patients with TB.

Use of fewer than 3 ARVs increases the chances for development of resistance of HIV to individual ARVs, which may eventually result in treatment failure.

1st line regimen for children should be chosen using the following considerations:

Table 22: Considerations for choice of 1st line ART for children

AZT or d4T*	+	3TC	+	EFV or NVP
Use d4T for Hb < 8.0 gm/dl or no Hb readily available Use d4T 3:1 fixed dose combination (d4T-3TC-NVP) for patients at risk for poor adherence		Always part of 1st line regimen		Use EFV for any child > 3 years and > 10 kg Use NVP for any child < 3 years or < 10 kg EFV cannot be used for children < 3 years or < 10kg Use EFV in children > 3 years and >10kg for those with elevated LFTs (> 2.5 times the upper limit of normal) Use EFV for those on concurrent anti-tuberculous therapy**

*AZT and d4T should **NEVER** be used together

** For children < 3 years of age or < 10kg who are also on concurrent anti-tuberculous therapy,

9.2.4.4 Administering ART in TB patients

Patients co-infected with TB and HIV should be initiated on antituberculous therapy as a matter of priority to prevent death from active TB. Due to the high mortality rates even among persons receiving antituberculous therapy and the risk of development of other OIs, it is recommended that the need for ART should also be assessed immediately. The guideline for timing of initiation of ART in a dually infected patient is presented in table below:

Table 23: protocol for initiating first-line ART in adults/adolescents already on anti-TB

CD4 Count	When to Initiate ART
Extrapulmonary TB (Irrespective of CD4 count)	Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months)

< 200	2-8 weeks after starting antituberculous therapy
201-350	After 8 weeks of antituberculous therapy
>350	Re-evaluate at completion of antituberculous therapy

*All first-line treatment regimens should use 2 NRTIs and Efavirenz. Both nevirapine and the PIs should be avoided due to drug-drug interactions with the rifamycins.

9.2.4.5 Concurrent DOTS and ART administration in Children:

For concurrent HAART and Ant-TB therapy, the following regimen should be used:

Children < 3 years of age:

AZT or d4t + 3TC + NVP (at standard dose)

Children > 3 years of age:

AZT or d4t + 3TC + EFV

The protocol for initiation of 1st line ART in children already on TB treatment is as in table below:

Table 24: Initiating first-line ART in children already on anti-TB treatment

WHO Clinical Stage	Immunodeficiency	CD4 Available	No CD4
4	Any	2-4weeks	2-4weeks
3	Severe	4-8weeks	4-8weeks
	Mild	8weeks -completion	
	No immunodeficiency	completion	

Although the use of nevirapine is not ideal due to its interaction with rifampicin, it was chosen due to its clinical efficacy demonstrated thus far as well as current familiarity with its use among health care providers. Abacavir was not chosen due to the known inferior potency of triple NRTI therapy, especially in the setting of a young child diagnosed with both TB and HIV, as well as the potential difficulty of diagnosing hypersensitivity reaction in rural setting.

9.2.4.6 Developing tuberculosis while on HAART

If pulmonary TB is diagnosed after a patient has already been initiated on HAART, then anti-tuberculous treatment must be started. Adults and children > 3 years and > 10 kg, who are on Nevirapine based regimens must be switched to Efavirenz. Children < 3 years of age and < 10kg, can be maintained on their nevirapine based regimen.

Kaletra and other PI's have significant interactions with rifamycins, and they should not routinely be used together. There may be cases when Kaletra is the only option for patients on concomitant TB treatment. Kaletra should be used in these cases only in consultation with a pediatric HIV expert.

9.2.4.7 Managing side effects in concurrent TB/HIV treatment

Patients on concurrent antituberculous therapy and ART may experience overlapping toxicities due to both treatments. These patients should therefore be closely monitored especially for hepatic evidence of hepatic damage through monthly ALT assay. Due to the high risk of peripheral neuropathy associated with the use of INH, and D4T regimens, it is recommended that patients be placed on

pyridoxine (vitamin B6) as a routine part of antituberculous therapy in co-infected patients. Dosing is as follows:

Pyridoxine:

Adults and Children > 3 years of age: 25mg po daily

Children < 3 years of age: 12.5mg po daily

9.2.4.8 Directly Observed Therapy for concomitant TB/HIV treatment

Due to the difficulties of taking antituberculous therapy and ART as well as the risk of developing drug-resistance, it is recommended that all patients receive directly observed therapy (DOT) during the course of their TB treatment. DOT should be provided by a paid treatment supporter who fills out the DOT card. The importance of patient education and empowerment around medication taking is a key part in improving adherence as is addressing socioeconomic barriers.

9.2.4.9 Drug-Resistant TB and HIV

Drug-resistant forms of TB (such as MDR-TB and XDR-TB) have been reported to be more common among HIV infected populations in some studies. Thus, any patient not clinical or bacteriologically responding to antituberculous therapy after 2 months who is receiving good DOT should have a culture sent for drug susceptibility testing (DST). For management of patients with suspected or confirmed drug-resistant TB, please refer to the national MDR guidelines.

9.2.4.10 Infection Control in HIV

The importance of infection control in settings of high HIV prevalence cannot be underestimated. All efforts should be put into place to ensure that proper administrative, environmental and personal protective controls are practiced. Under no circumstances should patients receiving TB therapy or with suspected TB be referred to the ART clinic for testing. HIV testing should be routine for all TB patients and suspects given the high rate of co-infection (approximately 90% in Lesotho) and this persons to provide testing and counseling should be available at all TB treatment centers, including the inpatient hospital wards. TB treatment should be available at health centers. Finally, ART can be provided by staff at TB treatment sites if they are trained and certified. Further details on Infection Control is provided in Chapter 10.

9.2.4.11 Nutritional Support for TB/HIV patients

Both TB and HIV are wasting diseases and patients have been shown to have improved outcomes when nutritional support is provided. Thus, every effort should be made to ensure that co-infected patients receive nutritional support whenever possible. Education and counseling is a necessary but insufficient step in assisting with nutritional support in co-infected patients, especially given the levels of malnutrition in Lesotho. Health centers should pair with partner organizations where needed to provide actual food supplements to patients.

9.2.4.12 Monitoring patients on concurrent ART and DOTS

Clinical Monitoring

Clinical assessment should be the primary tool for monitoring adults both before and after initiation of ART.

After starting ART, clinical assessments should take place by a doctor or nurse at 2 weeks, 1 month, 2 months, 3 months, 6 months, and at least every 6 months thereafter

A focused history and physical should be performed during routine visits. Important features of regular clinical assessments should include:

- monitoring of
 - weight (done at every visit)
 - height (in children, done every 3 months)
 - head circumference (in children < 3 years of age, measured every 3 months)
 - developmental status in children;
 - nutritional status in children;
- diagnosis and management of interim or new illnesses
 - OIs that may suggest immune reconstitution syndrome or treatment failure;
 - other co-morbidities, including STIs, Hepatitis B, substance abuse, psychiatric illness
- medication review
 - side effects
 - adherence and dosing
 - other medications, including traditional medicines and other medications that may interact with ARVs
- early diagnosis of pregnancy
- changes in social situation that might affect adherence to ART

Laboratory Monitoring

Laboratory monitoring should complement the clinical assessments. Baseline laboratory tests will help to determine which regimen a person should be initiated on. However, the absence of the capacity to perform laboratory testing should not preclude a person from starting ART.

Baseline Laboratory Investigations

Where possible, the following baseline laboratory investigations should be obtained prior to starting ART:

- CD4 count, or percentage (in children ≤ 5 years)
- Full blood count (FBC)
- ALT
- Serum Creatinine when Tenofovir (TDF) is being considered in adults, followed by calculation of the rate of Creatinine Clearance (*for details of calculation method for Creatinine clearance, please refer to the National ART guidelines*)
- Pregnancy test in all women of child-bearing age

Routine Laboratory Investigations

The following laboratory tests should be performed routinely depending on the specific ARVs that are included in the patient's regimen:

- If on AZT, Haemoglobin (Hb) should be checked at 1 month, 2 months, 3 months, 6 months, and every 6 months thereafter.
- If on NVP, ALT should be checked at 1 month, 2 months, 6 months, and every 6 months thereafter. If the CD4 count at initiation is between 250-350, there is an increased risk of hepatotoxicity, so additional ALT testing is recommended at 2 weeks and 3 months.
- If on Tenofovir (TDF), serum creatinine (and rate of Creatinine Clearance) should be checked 6 months after initiation, and every 6 months thereafter.
- CD4 counts should be checked every 6 months, to help determine efficacy of treatment

Additional laboratory tests can be requested depending on the results of the clinical assessments, but should only be done if the result is required to further guide management. These include, but are not limited to:

- Lactate measurement, if the patient is on a NRTI (especially D4T or ddI) for > 4 months and losing weight, and/or having other symptoms that suggest hyperlactatemia⁶
- Glucose and lipid measurements, if the patient is taking a Protease Inhibitor, such as Lopinavir/ritonavir (Kaletra) or Atazanavir/ritonavir

Point-of-care testing machines should ideally be available in all clinics to measure Haemoglobin (Hb), glucose, and lactate. Not only do such machines allow for immediate results, but they also take some pressure off the district hospital laboratories, which are faced with an ever-increasing number of requests.

Viral load testing is an excellent method to determine efficacy of treatment in the first 6 months. However, it is not recommended for systematic monitoring of patients on ART in resource-limited settings such as Lesotho at the current time. Instead, efficacy should be determined by regular clinical and CD4 count monitoring as described above.

9.2.4.13 Immune Reconstitution Inflammatory Syndrome among patients with HIV-related TB

- Fever
- New or worsening adenitis - peripheral or central nodes
- New or worsening pulmonary infiltrates, including respiratory failure
- New or worsening pleuritis, pericarditis, or ascites
- Intracranial tuberculomas, worsening meningitis
- Disseminated skin lesions
- Epididymitis, hepatosplenomegaly, soft tissue abscesses

Table 25: Overlapping Side effect adverse reactions to First-line anti-TB and ART drugs

Side Effects	Possible causes	
	Anti-TB Drugs	ARV Drugs
Skin rash	PZA, RIF, INH	NVP, EFZ, ABC
Nausea, vomiting	PZA, RIF, RBT, INH	ZDV, RTV, AMP, IDV
Hepatitis	PZA, RIF, RBT, INH	NVP, PIs, Immune reconstitution
Leukopenia, anemia	RBT, RIF	ZDV

Reasons to delay ART

- Overlapping side effects from ART and anti-TB therapy
- Complex drug-drug interactions
- Immune reconstitution inflammatory syndrome (paradoxical reactions)
- Difficulties with adherence to multiple medications

⁶ High lactate (hyperlactatemia) is a potentially serious side effect resulting from mitochondrial toxicity in patients who have been on NRTIs (especially d4T and ddI) for > 4 months. If hyperlactatemia is not recognized early, it will progress to lactic acidosis, which carries a significant risk of mortality. A point-of-care lactate machine should ideally be available in all sites where ART is being made available. Any patient developing symptoms of hyperlactatemia (weight loss, fatigue, nausea, vomiting, abdominal pain, and/or shortness of breath) should have a lactate level checked the same day, and be immediately managed by a trained clinician.

CHAPTER 10 INFECTION CONTROL

10.1 Rationale

Persons with undiagnosed, untreated and potentially contagious TB are often seen and managed in Health care settings; and such frequent exposure to patients with infectious TB disease may put the health worker at risk. Furthermore Health care workers and staff may themselves be immunosuppressed due to HIV infection and be at higher risk of developing TB disease once infected.

Nosocomial transmission of *M. tuberculosis* has been linked to close contact with persons with TB disease during aerosol-generating or aerosol-producing procedures, including bronchoscopy, endotracheal intubation, suctioning, other respiratory procedures, open abscess irrigation, autopsy, sputum induction, and aerosol treatments that induce coughing.

All health facilities should be made aware of the need for preventing transmission of *M. tuberculosis* especially in settings where persons infected with HIV might be encountered or might work. All HCWs should be sufficiently informed regarding the risk for developing TB disease after being infected with *M. tuberculosis*.

All health-care settings should develop a TB infection-control plan designed to ensure prompt detection, airborne precautions, and treatment of persons who have suspected or confirmed TB disease. TB infection control measures can be divided into three categories namely: Administrative, Environmental (or engineering) and Personal respiratory protection controls.

10.2 Administrative Controls

The first and most important level of infection control is the use of administrative measures to prevent droplet nuclei from being generated, thus **reducing the exposure** of HCWs and patients to *M. tuberculosis*. These measures include:

- Each health facility implementing effective written policies and protocols to ensure the rapid identification, isolation, diagnostic evaluation, and treatment of persons likely to have TB;
- Designating an Infection Control Officer in key health facilities with responsibility and authority for the implementation of the infection control plan.
- Risk assessment for TB transmission in the facility should be conducted periodically,
- Ensuring the timely processing of patients screening, laboratory testing, and reporting of results to the ordering clinician;
- Implementing effective work practices among health care workers (HCWs) for the management of patients with suspected or confirmed TB disease
- Educating, training, and counseling HCWs about TB, with specific focus on prevention, transmission, and symptoms
- Screening and evaluating HCWs who are at risk for TB disease or who might be exposed to *M. tuberculosis* for TB infection and disease.
- Ensuring that HIV-positive HCWs do not work in areas of high TB transmission or with MDR-TB patients

10.3 Environmental control measures

The following environmental control methods should be used in the above-mentioned high-risk areas to prevent the spread and **reduce the concentration of droplet nuclei in the air**.

- Maximising natural ventilation e.g., keeping windows open (even in winter and at night)
- Controlling the direction of airflow e.g. strategically placed fans

Ventilation maintains air quality by both air dilution and removal of airborne contaminants. Uncontaminated supply air mixes with contaminated room air (dilution), and air is subsequently removed from the room.

10.4 Personal respiratory protection

HCWs need to be protected from inhaling infectious droplets by the use of personal respiratory protective devices designed to fit over the mouth and nose and filter out infectious TB particles. The emphasis of infection control rests on maximising the environmental control and personal caution. Therefore, personal respiratory protection using **N95** is only indicated in specialized settings, e.g., referral facilities nursing MDR-TB and XDR-TB patients, and only when all other infection control measures have been fully implemented

10.4 Control of TB Transmission in Prisons

Tuberculosis occurs up to 100 times more commonly in prisons than in civilian populations.

- The spread of tuberculosis is worsened by late diagnosis and treatment of infectious cases, and poor prison living conditions such as overcrowding
- The main strategies for achieving these goals of TB control are the early diagnosis of TB cases and their prompt and effective treatment.
- It is thus vitally important to screen new inmates by history and sputum smear microscopy if the inmates are symptomatic for TB.
- Penal reforms and improvement in prison living conditions are also important strategies for early case detection, rapid effective treatment which will reduce morbidity and mortality in prisons and so interrupt the chain of transmission
- There should be “Equivalence” of care in the prisons, i.e., all prisoners have the right to the same standard of health care as the state provides for the general community
- There should be particular attention on integrating prison and civilian TB services

CHAPTER 11 MANAGEMENT OF MULTI-DRUG AND EXTENSIVELY RESISTANT TUBERCULOSIS

11.1 The basis for MDR policy

Multi-Drug-resistant TB is said to be present only through laboratory confirmation of in vitro resistance to one or more first-line antituberculosis drugs. Although Lesotho currently has a very low combined primary HR resistance (Multidrug resistance TB or MDRTB) of 0.4 % in 1995, the emergence of XDR-TB in South Africa and other countries in the region makes it imperative to ensure adequate MDR-TB policy.

Antituberculosis drug resistance is classified according to the following three definitions:

- **Confirmed mono-resistance.** Tuberculosis in patients whose infecting isolates of *M. tuberculosis* are confirmed to be resistant in vitro to one first-line antituberculosis drug.
- **Confirmed poly-resistance.** Tuberculosis in patients whose infecting isolates are resistant in vitro to more than one first-line antituberculosis drug, other than both isoniazid and rifampicin.
- **Confirmed MDR-TB.** Tuberculosis in patients whose infecting isolates are resistant in vitro to at least isoniazid and rifampicin.
- **Confirmed XDR-TB.** The existence of MDR-TB with additional resistance to any fluoroquinolone, and at least one of three injectable second-line drugs (capreomycin, kanamycin, and amikacin)..

The emergence of multi-drug resistant (MDR) TB and lately extensively drug resistant (XDR-TB) is the most serious aspect of the TB epidemic. MDR TB is difficult and expensive to treat, whilst XDR-TB is almost untreatable. It is therefore essential to prevent the development of MDR TB. As with other forms of drug resistance, MDR TB is a largely man-made problem, being the consequence of human error in any of the following:

- prescription of chemotherapy
- management of drug supply
- patient management
- patient adherence.

11.2 When to Suspect MDR TB

The occurrence of MDR should be suspected clinically in the following situations:

- Without prior history of TB treatment
 - Health care worker with new tuberculosis
 - Household contact of known MDR-TB case
 - Patients who have a history of migrant work
- With prior history of TB treatment:
 - Treatment after relapse or default
 - Treatment failure in HIV-negative patients (sputum smear positive after five months of therapy)
 - Treatment failure in HIV-positive patients (sputum smear positive or lack of clinical improvement after two months)
 - Patients with history of multiple previous treatments in public or private sectors

The above cases should be investigated by *M. TB* Culture and Drug Susceptibility Testing (DST). The clinician should obtain two new sputum samples from the suspect using standard operating procedures and send a request for culture and DST. See Annex for the Request Form for Smear, Culture and DST.

Two sputum samples are needed in view of high contamination rates when transporting raw sputum samples over long distances.

The clinician may initiate treatment with second-line anti-tuberculosis drugs in some of while DST results are being awaited.

11.3 Laboratory Confirmation of MDR

The ability of the national and regional laboratories to perform sputum culture and DST for the first line anti-TB drugs must be maintained as part of the overall National TB programme. In addition, the national reference laboratory should have the capacity to perform DST for 2nd line drugs.

Diagnosis of MDR should only be established on the basis of **sputum culture and drug susceptibility testing result**.

11.4 Eligibility for Drug Susceptibility (DST)

Patients in whom MDR is strongly suspected should have sputum sent for culture and DST. The type of such patients include;

- Patients who remain or turn positive after 3 months of TB treatment
- Patients previously treated for TB
- Patients who had contact MDR TB cases
- Patients who had a contact that died while on DOT for TB
- Hospital and health care workers developing signs and symptoms of TB
- TB patients with HIV
- Prisoners from facilities with high MDR rates

11.5 Management of MDR TB

The management of MDR should focus both on improving the quality of case management for TB patients on first line treatment to prevent emergence of resistance as well as appropriate management of the diagnosed resistant cases.

The first step to undertake, once a decision has been made to treat MDR TB cases is to identify a specialized unit where all cases will be referred to in order to assess them and decide whether to treat or not. The Main referral centre for MDR TB in Lesotho will be based in Botshabelo hospital.

Adequate arrangement should be made to arrange for continuation of treatment at the designated district and designated clinic. The patient's drugs will be transferred to the designated district that will in turn transfer them to the designated clinic.

A specialized management team comprising of a physician or specially trained medical officer, a dedicated MDR TB trained nurse, and a social worker should be established. The purpose of this team is to oversee all aspects of management including counseling of the patients.

A community-base care approach for MDR management should be considered where feasible and with adequate steps taken to ensure infection control.

The following basic principles should be observed in the treatment of MDR cases⁷:

- Treatment regimen should consist of at least 5 drugs with proven to which the organisms have proven susceptibility. More than 5 drugs may be started when the susceptibility pattern is not yet known or in the presence of an extensive bilateral pulmonary disease;
- The drugs should be administered for at least 6 days per week, usually twice daily to minimize side effects,
- The treatment should be started preferably with the high ended recommended doses;
- An injectable agent (aminoglycoside or capreomycin) should be used for at least 6 months after culture conversion;
- Each dose must be given under direct observation by a treatment supporter;
- A ‘consent to treatment’ should be obtained prior to initiation of treatment;
- All treatment records should be properly documented and preferably kept in a database.
- Patients should not be admitted with other normal TB patients at all or admitted in general medical wards. Patients will have to be admitted for at least a period of four months or until they have produced two consecutive monthly culture-negative sputa.

It must be emphasized that the priority of the programme is to ensure that all new patients complete their first line TB treatment. **“With good standard treatment meticulously prescribed and meticulously administered, multidrug resistance should not occur”**(pg 14 of the “Guidelines for the Management of Drug-Resistant Tuberculosis. WHO:TB:96.210(Rev1) 1997, World Health Organization”).

The key to this approach includes:

- use of the approved standardized regimen
- rational drug susceptibility testing of specimens from MDR tuberculosis patients
- provision of a social worker for counselling and support
- provision of key nursing staff to provide continuity during the treatment period
- direct observation of treatment throughout the course
- keeping updated registers
- monitoring compliance
- developing measures for rapid recall if patients interrupt their treatment
- increasing education and motivation of patients
- tracing and evaluating contacts rapidly.

11.5.1 MDR Treatment options:

Table 26: Recommended treatment approach for mono or poly resistant TB

Resistance Pattern	Suggested regimen
H	Option 1: 9R-E-Z Option 2: 9R-E-Z-FQ Option 3: 6S-R-E-Z/3R-E-Z
E	Option 1: 2S-H-R-Z/4H3R3 Option 2: 3S-H-R-Z/6H3R3
Z	6S-H-R-E/6H3R3E3
HE	6S-R-Z-FQ/6R-Z-FQ
HZ	6S-R-E-FQ/6R-E-FQ

⁷ The PIH Guide to the Management of Multi-Drug Resistant Tuberculosis, International edition 2003

EZ	6S-H-R-FQ/6H-R-FQ
HEZ	6S-R-FQ-Ethio-CS/12R-FQ-Ethio-CS
R	Option 1: 9S-H-Z-E (regimen not proven for other aminoglycosides or capreomycin) Option 2: 6S-H-E-Z/12S3-H-E-Z Option 3: 6S-H-E-Z-FQ/12H-E-Z-FQ
RE	6S-H-Z-FQ-Ethio/12H-Z-FQ-Ethio
RZ	6S-H-E-FQ-Ethio/12H-E-FQ-Ethio
REZ	6S-H-FQ-Ethio-CS/12H-FQ-Ethio-CS

Note:

- Some DST patterns have more than one option for treatment.
- Option 1 should only be used if there is not extensive disease and there is high confidence in the DST results, while options 2 and 3 are more aggressive and should be used for patients with more extensive disease.
- If the strain is resistant to streptomycin, then a sensitive aminoglycoside or capreomycin should be substituted in the regimen.
- Prothionamide can be substituted for ethionamide.

11.5.1.1 Empiric MDR treatment

Any patient suspected of having MDR-TB or failing a Category II treatment should be placed on an empiric regimen while awaiting DST. The empiric regimen should be based on the patient’s previous drug exposure, the sensitivity pattern of known MDR-TB contacts, or the surveillance data of other patients in a similar setting who have failed therapy.

Table 27: Examples of empirical regime for MDR cases without DST results

Clinical situation	Recommended empirical treatment
Failures of Category II	E, Z, CM (or KM), FQ, Ethio, CS
Contacts of MDR-TB patients with active disease:	Empiric treatment regimen should be based on the DST of the MDR-TB patient.

11.5.1.2 Standardized MDR treatment regimen

The use of standardized regimens should be based on a reliable Drug Resistance and DST survey conducted in the country or region. The regimens should be well designed to cover adequately the possible resistance patterns. Patients should be placed on them early, before extensive parenchymal damage occurs to the lungs. If a patient fails a standardized regimen designed for the treatment of MDR TB, DST should be performed and the patient placed on an individualized regimen.

11.5.1.3 Definitive treatment regimen

When the results of DST are available, a definitive individualized treatment regimen (ITR) can be designed for the patients. If the resistance pattern does not prove the existence of MDR TB, the regimen should be designed based on the treatment of mono or poly-resistant TB. If the DST reveals MDR TB, the regimen can be designed using the following approach.

Discontinuation of the injectables

The decision to stop the injectable should be made upon review of the cultures, smears, X-rays, and clinical status of the patient. The following criteria are used to consider cessation of the injectable agent:

- Patient has completed a minimum of six months of documented culture-negativity.

- Surgery is not planned.
- There are four remaining drugs to which the isolate has documented sensitivity.

When the regimen contains only four drugs including the injectable, the injectable is used for a minimum of 12 months of documented culture negativity and may be used for the entire course of treatment in patients with extensive lung damage or high-grade resistance.

11.5.2 Recurrence/persistence of positive cultures after four months of treatment

For cultures or smears that remain positive or become positive after conversion, the clinical evidence must be weighed to determine the course of action.

- DST should be compared to determine if the newly positive culture has the same susceptibility pattern as the initial strain or whether amplification of the resistance pattern has occurred.
- Re-appearance of single or multiple smears or cultures should be considered as possible evidence for treatment failure, and the patient should in all cases be evaluated for the possibility of changing therapy or of surgery.
- If the culture(s) or smear(s) are thought to reflect active disease, then the treatment should be adjusted and extended for 18 months of consecutive negative cultures. Preferably two or more drugs can be added while waiting for DST results.
- If the resistance pattern is completely different, it may represent either contamination or, less likely, a new infection.
- A culture that has fewer than 10 colonies may represent a contaminant; a repeated culture should
- be performed two or three times and documented to be negative before it is determined to be a contamination.

11.5.3 Completion of MDR therapy

Bacteriological, clinical, and radiological data are all considered when determining the duration of therapy for MDR TB. The guidelines are:

- A minimum of 18 months of negative cultures past conversion.
- For patients with extensive damage on chest X-ray, therapy may be extended to 24 months negative cultures past conversion.

The final outcome of treatment should be recorded in the MDR TB registry. Final outcomes consist of cure, treatment completed, death, treatment default, treatment failure, and transfer out.

11.5.4 Follow-up after completion of MDR therapy

Treatment follow-up should be done for a minimum of two years after cure. The following are guidelines for surveillance of the cured MDR TB patient:

- Follow-up visits (months 6, 12, and 24) to assess for symptoms and signs of relapse.
- Smear and culture every three months for the first year, and then every six months for the second year.
- Clinical and radiographic evaluation as needed for development of respiratory symptoms.

Due to the high prevalence of residual lung disease, it may be helpful to continue ancillary medicines, such as bronchodilators, in patients after antituberculosis therapy is completed.

11.5.5 Interruption and re-initiation of treatment

The clinician should reinitiate treatment in patients for whom therapy has been suspended due to noncompliance or in patients who have defaulted during therapy. The following is recommended:

Have the patient sign a new adherence contract.

- Perform a full history and physical exam.
- Obtain a smear and culture.
- If positive, culture should be sent for DST.
- Obtain a radiograph and repeat the initial laboratory data.

The treatment regimen and duration to be used for patients restarting therapy should be based on the month at which the patient abandoned therapy and the clinical state at which the patient returns to therapy (see MDR management guidelines).

Patients who have been off therapy for longer than six months should be evaluated for active disease, and, if it is present, the patient should be started on a completely new course of treatment.

If no active disease is present, clinical judgment should be used to decide whether to reinstitute therapy. If therapy is not restarted, the patient should be followed regularly for signs of relapse.

11.5.6 Indications for surgery:

Surgery as an adjunct to chemotherapy for patients with localized disease can significantly improve outcomes where skilled thoracic surgeons and excellent postoperative care are available. It is clear that the respiratory function of the healthy lung should be sufficient to compensate for resection of the affected lobe or lung.

When resectable disease is present, surgery should be considered for the following cases:

- Failure to demonstrate clinical or bacteriologic response to chemotherapy after three to six months of treatment.
- High likelihood of failure or relapse, due to high degree of resistance or extensive parenchymal involvement, regardless of smear and culture status.
- Morbid complications of parenchymal disease, e.g., hemoptysis, bronchiectasis, bronchopleural fistula, or empyema.
- Recurrence of positive culture status during MDR-TB (or second line) therapy.
- Relapse after completion of MDR-TB (or second line) therapy and under consideration for further individualized chemotherapy.

11.5.7 MDR TB Treatment in Special Situations.

11.5.7.1 MDR-TB treatment in Children:

Children with MDR TB generally have primary resistance transmitted from an adult contact with MDR TB. When DST is available, it should be used to guide therapy; however, because children have paucibacillary tuberculosis, they are often culture-negative. In culture-negative children who have clinical evidence of active TB and a contact with documented MDR TB, the child's treatment should be guided by results of DST of the contact.

Careful consideration of the risks and benefits of each drug should be made in designing a regimen. Frank discussion with the patient and family members is critical, especially at the outset of therapy. Given the life-threatening aspects of MDR TB, there are no drugs that are absolutely contraindicated in children. Drugs should be dosed according to the child's weight (see MDR clinical management guidelines). Monitoring monthly weights is therefore especially important in pediatric cases, with adjustment of doses as the child gains weight.

11.5.7.2 MDR TB treatment and pregnancy

All female patients of childbearing age should be tested for pregnancy upon initial evaluation; birth control is strongly recommended for all women receiving MDR TB therapy. The efficacy of oral contraceptives may be decreased due to potential drug interactions, and therefore other contraceptive options should be

considered. All patients are encouraged to use condoms to protect against sexually transmitted diseases.

Pregnant patients should be carefully evaluated, taking into consideration gestational age and severity of MDR TB. The risks and benefits of MDR TB treatment should be considered carefully, with the primary goal being smear conversion in order to protect the health of the mother and child, both before and after birth.

- Since the majority of teratogenic effects occur in the first trimester, therapy may be delayed until the second trimester unless life-threatening symptoms occur.
- Patients in the third trimester have reduced risk of teratogenicity, although aminoglycosides may still damage the fetal ear. For the most part, aminoglycosides are not used in the regimens of pregnant patients.
- If possible, begin treatment in the second or third trimester with three or four oral drugs with demonstrated efficacy against the infecting strain, and then reinforce the regimen with an injectable agent and possibly other drugs immediately postpartum.

Newborn infants are at high risk of developing disseminated tuberculosis. If possible, smear-positive mothers should avoid close contact with infants, leaving the care of the infant to a family member until the mother is smear-negative.

11.5.7.3 MDR TB treatment and diabetes

The treatment of TB in the diabetic will result in poorer outcomes if glucose is not well controlled. The responsibility often falls on the physician treating the patient for tuberculosis to ensure proper diabetic care. In addition, diabetes may potentiate adverse effects, especially renal dysfunction and peripheral neuropathy. The following guidelines are suggested to assist in the management of the diabetic with MDR TB.

11.5.7.4 MDR TB and renal insufficiency

Renal insufficiency due to longstanding tuberculosis disease is not uncommon. Great care should be taken in the administration of second-line drugs in patients with renal insufficiency, and the dose and/or the interval between dosing should be adjusted according to recommended guideline (See guidelines on MDR clinical management).

11.5.8 Extensively Drug Resistant Tuberculosis (XDR-TB)

XDR-TB is defined as resistance to at least Isoniazid and Rifampicin (which is the definition of MDR TB), in addition to any fluoroquinolone, and at least one of the three following injectable used in anti-TB treatment: Capreomycin, Kanamycin and Amikacin⁸.

⁸ Report of the meeting of the WHO Global Task Force on XDR-TB, Geneva 9-10 October 2006

CHAPTER 12 MONITORING AND EVALUATION

12.1 The basis for the M&E policy

A key element of the DOTS Strategy is the establishment and maintenance of a system to monitor case detection and treatment outcomes. It is essential for efficient programme management since it provides a basis for evaluating the progress made in achieving programme targets, supervision of staff and for monitoring and surveillance.

12.2 Programme supervision

The Lesotho NTP should ensure sustenance of task-oriented supervision at all levels to increase the efficiency of health workers by developing their knowledge, perfecting their skills, improving their attitudes towards their work and increasing motivation. The NTP Central Unit should provide technical supervision support to the district level, while the districts provide same to the health facility level.

The emphasis of supervision to the district level should be on supporting the District officers in technical and managerial functions, while that of facilities should focus on identification of TB cases and administration of treatment including follow up of cases.

Supervisory visits must be planned carefully. Before each visit the supervisor should review the health centre's reports, the correspondence about the reports, the findings of the last supervisory visit and corrective actions already taken.

Supervision should be conducted using the appropriate supervision tools that assesses the relevant tasks. The facilities to be visited should be notified in advance of the date and purposes of the supervisory visit. The number of supervisory visits should be planned before the start of the fiscal year, for inclusion in the annual-programme budget.

12.3 Programme monitoring

Monitoring programme performance to ascertain whether activities are accomplished as planned, and identification of problems should be conducted periodically in collaboration with partners. Monitoring should be conducted preferably on annual basis, but could be at a mid-term of the Medium term plan.

12.3.1 Programme indicators:

Table 28: Standard indicators for monitoring and evaluation of the TB programme

Indicator	Description	International target	Baseline	Target
Impact Indicators				
TB prevalence rate.	Estimated number of all active TB cases per 100,000 population at a given point in time.	Halving of prevalence by 2015, relative to 1990	544	
TB incidence rate	Estimated number of TB cases occurring per year, per 100,000 population		696	
TB mortality rate	Estimated number of deaths due to TB (all cases) per year, per	Halving of mortality by 2015, relative to 1990	107	

Indicator	Description	International target	Baseline	Target
	100,000 population			
Outcome indicators				
Case detection	New smear positive TB cases detected (diagnosed and reported to the national health authority), among the new smear-positive TB cases estimated to occur countrywide each year (number and percentage)	70% under DOTS, nationally by 2005	80%	70%
Treatment success rate	New smear positive TB cases that successfully complete their treatment among the new smearpositive TB cases registered during a specified time period. Successful completion entails clinical success with or without bacteriological evidence of cure (number and percentage)	85% under DOTS nationally for the cohort of new smear-positive patients by 2005	73%	85%
Smear conversion rate	New smear positive TB cases that convert to smear-negative at the end of the initial phase of treatment, among new smear positive TB cases registered during a specific time period (can also apply to any treatment cohort of cases) (number and percentage)	No international target. As a proxy (but not a replacement for) the treatment success indicator, above, the 85% level is nevertheless a general target	To be established.	90%
Specific programme indicators				
DOTS expansion:				
Proportion of Districts implementing the DOTS Strategy:	Percentage of districts having at the capacity for diagnosis and treatment of TB under DOTS.	100%	100%	100%
Population having access to DOTS.	Proportion of the population living in areas where DOTS services are available	100%	To be established	100%
Proportion of Health Care facilities providing DOTS.	Proportion of the health care facilities having at least 1 health staff trained in DOTS.	100%	70%	100%
Identification of infectious TB cases				
Smear positivity	# or percentage of			15%

Indicator	Description	International target	Baseline	Target
rate among TB suspects	persons found to be sputum smear positive cases of TB, among persons identified as TB suspects clinically during a specified time period.			
Intensified case finding among PLWAs:				
Proportion of PLWHAs screened for TB	Number of PLWHA, receiving HIV testing and counseling or HIV treatment and care services, who were screened for TB symptoms expressed as a proportion of all PLWHA attending HIV testing and counseling or HIV treatment and care services.	Numerator: Number of PLWHA seen at HIV testing and counseling or HIV treatment and care services who were screened for TB symptoms, over a given time period Denominator: Total number of PLWHA seen at HIV testing and counseling or HIV treatment and care services, over the same given time period.		
Proportion of PLWHAs with TB	Number of cases of newly-diagnosed TB identified in PLWHA attending for HIV testing and counseling or HIV treatment and care services (who were screened for TB symptoms), expressed as a proportion of all PLWHA attending HIV testing and counseling services and HIV treatment and care services (who were screened for TB symptoms).	Numerator: The number of cases of newly-diagnosed TB identified in PLWHA attending HIV testing and counseling or HIV treatment and care services who were screened for TB symptoms, over a given time period Denominator: Total number of PLWHA attending HIV testing and counseling or HIV treatment and care services who were screened for TB symptoms over the same given time period.		
Prevention of TB disease among PLWHAs				
Proportion of eligible PLWHAs on INH prophylaxis	Number of newly-diagnosed HIV-positive clients who are given treatment for latent TB infection (TB preventive therapy) expressed as a proportion of the total number of newly-diagnosed HIV-positive people.	Numerator: Total number of newly-diagnosed HIV-positive clients in whom active TB has been excluded who start (given at least one dose) treatment of latent TB infection Denominator: Total number of newly-diagnosed HIV-positive clients		
Prevention of HIV in TB patients				
Proportion of TB patients counseled and tested for HIV	Number of registered TB patients who are tested for HIV, after giving consent, as a proportion	Numerator: Total number of TB patients, registered over a given time period, who are tested for HIV (after giving		

Indicator	Description	International target	Baseline	Target
	of the total number of registered TB cases.	consent) during their TB treatment Denominator: Total number of TB patients, registered over the same given time period.		
Proportion of TB patients that tested positive for HIV.	Number of registered TB patients who are tested for HIV (after giving consent) and who test HIV-positive, expressed as a proportion of the total number of all registered TB patients who are tested for HIV.	Numerator: Total number of all TB patients registered over a given time period who test HIV-positive (after giving consent) during their TB treatment Denominator: Total number of TB patients registered over the same given time period who are tested for HIV (after giving consent)		
Prevention of opportunistic infection in HIV positive TB patients				
Proportion of HIV positive TB patients on CPT	Number of HIV-positive TB patients who receive (given at least one dose) CPT during their TB treatment as a proportion of the total number of HIV-positive TB patients.	Numerator: Number of HIV-positive TB patients, registered over a given time period, who receive (given at least one dose) CPT during their TB treatment Denominator: Total number of HIV-positive TB patients registered over the same given time period		
HIV Care and Support for HIV-positive TB patients				
Proportion of HIV positive TB patients receiving care and support)	Number of HIV-positive TB patients referred to HIV care and support services (as defined in local or national HIV/AIDS policy) during TB treatment, expressed as a proportion of the total number of HIV-positive TB patients.	Numerator: Number of HIV-positive TB patients, registered over a given time period, who are referred to HIV care and support services during their TB treatment* Denominator: Total number of HIV positive TB patients registered over the same given time period		
Provision of anti-retroviral therapy for TB patients.				
Proportion of eligible HIV-Positive TB patients receiving ART	Number of HIV-positive registered TB patients who are started on or continue previously initiated ART, during or at the end of TB treatment, as a proportion of all HIV-positive registered TB patients.	Numerator: All HIV-positive TB patients, registered over a given time period, who receive ART (are started on or continue previously initiated ART) Denominator: All HIV-positive TB patients registered over the same given time period		
HIV prevalence among TB patients				
HIV sero-prevalence rate among TB patients	Number of all newly-registered TB patients who are HIV-positive, expressed as a proportion	Numerator: Total number of newly-registered TB patients who are HIV positive, over a given time period		

Indicator	Description	International target	Baseline	Target
	of all newly-registered TB patients.	Denominator: Total number of newly-registered TB patients (registered over the same given time period) who were tested for HIV and included in the surveillance system		

12.4 Programme evaluation

Programme Evaluation should be conducted at the end of a plan period to assess progress towards operational targets and epidemiological objectives. The evaluation should ensure measurement of all programme indicators, such as percentage of patients cured, to assess progress in achieving targets and objectives.

12.5 Reporting and Recording system

The adequate care of tuberculosis cases requires that records be kept on each individual patient, with periodic reporting of the results of case-finding and of treatment. This is essential to ensure that the patient is correctly treated and that adequate supplies of essential materials are provided. In addition, the information that is routinely collected and reviewed allows problems that may arise with the management of the patients and of the system to be identified. The documents used to record and report the care of the patients should be simple, clear and kept to the absolute minimum that is required for adequate care. The following description provides a guide for the recording of patients as they appear to the health facility, and comprises the minimum number of records and reports necessary to ensure the proper care of the patients.

Table 29: Recording and reporting formats used in the National TB Programme

S/No.	M&E format	Data requirement	Level	Responsible	Frequency of entry
1	TB Suspects (chronic cough) register	Records of patients presenting with chronic cough	Health facility	General Health Care staff	Daily
2	Sputum Examination request form	Results of AFB smear microscopy	Health facility	General Health Care staff	Daily
3	TB Laboratory register	Results of AFB smear microscopy	Laboratory	Laboratory Scientist or technician	Daily
4	TB Culture/ Sensitivity Request/Report	Request for DST	Laboratory	Laboratory Scientist or technician	Based on need.
5	TB Treatment Card	Patients treatment records and progress	Health facility	General Health Care staff	Daily
6	TB appointment Card	Daily patient's treatment records	Health facility Home	General Health Care staff	Daily
7	TB referral/ Transfer Form	Patient's up to date treatment status	Health facility Home	General Health Care staff	Based on need.
8	TB Treatment Register	Patient's daily treatment records	Health facility	General Health Care staff	Daily
9	District TB Central register	Records of all TB cases in an district	District	District TB Coordinator	Weekly /Monthly

S/No.	M&E format	Data requirement	Level	Responsible	Frequency of entry
10	District Quarterly Report on TB Case finding form	Report on TB cases detected in a quarter by category.	District/National	District TB Coordinator	Quarterly, Annual
11	District Quarterly Report on Sputum Conversion form.	Report on treatment outcome of TB cases started on treatment 3-6 months earlier.	District/National	District TB Coordinator	Quarterly, Annual
12	District Quarterly TB Cohort Report form.	Report on treatment outcome of TB cases started on treatment 12-15 months earlier.	District/National	District TB Coordinator	Quarterly, Annual
13	District TB drugs Returns form.	Quarterly district or State drug utilization and request	District/National	District TB Coordinator	Quarterly, Annual

CHAPTER 13 SUPPLIES AND LOGISTICS MANAGEMENT

12.1 Rationale

Availability of TB drugs and other supplies is essential for provision of effective TB services on a continual basis, and hence must be procured and distributed in adequate quantities, at the appropriate time. Within the context of TB control, supply and logistics refers to the maintenance of a system that guarantees un-interrupted supply of drugs, laboratory materials and reporting and recording forms.

12.1.1 Estimating Drug Needs and Preparing Procurement Plan

Before estimating drug requirements, the lead time (length of time between placing an order and receiving it) must be known. If the lead time is 6 months or more, the procurement plans should cover the drug needs for one year plus the reserve stock. Estimates of drug requirements are based on the expected number of cases to be treated vis-à-vis the recommended standard regimen for chemotherapy.

12.1.2 Estimate the expected number of cases in each treatment category and the drugs needed next quarter

Sufficient stock of drugs should be available in the country for all TB cases expected to started on treatment during a whole year. Drug supply to the district level will be carried out on quarterly basis based on need. The number of patients detected in a particular quarter is used to determine the requirements for the next. The District TB Coordinator will determine these numbers from records of current cases and will order drugs to be sent to your health facility to meet the expected need including a provision for buffer stock. The reserve stock allows for possible increases in the number of cases and extra supplies in case of delay in drug delivery. These regimens are packaged in patient drug boxes (patient kits), which makes calculation and accounting easier.

12.1.3 GDF patient kits

WHO advocates the use of FDCs for first-line TB treatment because these medicines significantly reduce a patient's pill burden and can significantly improve adherence levels.

In Lesotho, patient kits for Category I (and Category III), and for Category II retreatment regimen are used, containing blister packs with fixed dose combination (FDC) tablets. There are 4FDCs for the intensive phase, and 2FDCs for the continuation phase. In addition, there are pediatric FDC formulations..

Advantages of patient kits	Limitations
<p><i>Standardized treatment:</i> allows health workers to select a single container that has the predetermined medicines, strengths, and quantities (the TB patient kit for administering to the patient), limiting confusion and wastage.</p> <p><i>Quantification for procurement or ordering:</i> improves ease of estimating medicine needs whereby 1 patient = 1 patient kit.</p> <p><i>Distribution of TB medicines:</i> improves ease of logistics in that fewer items are being transported.</p> <p>Stock management and inventory control: improves ease of</p>	<ul style="list-style-type: none">• Larger storage space may be needed in central and local warehouses.• Personnel should be trained in the adjustment of kits according to body weight, inventory methods, and repacking.• If TB packs are reconstituted, loose medicines must be collected, packing materials must be available, an area should be available for reconstitution in the

Advantages of patient kits	Limitations
<p>managing stocks and documentation of stock movement because one product is being handled.</p> <p><i>Patient adherence:</i> Whereas medicine stock-outs cause patients to lose confidence in the health system, the patient kit assures the TB patient that his or her medicines will be available from start to finish of treatment. In addition, the patient may feel ownership of the patient kit and will likely complete the full course of treatment since he or she can see how many medicines must still be taken to achieve cure during visits to the health center or dispensary</p>	<p>warehouse, and procedures such as “Good Storage Practices” should be in place and followed.</p>

Management of patient kits is as follows:

- All Health facilities should have patient kits in store to cater for at least two new category I and one category II patients;
- *In-patients.* The personalized patient kits should be supplied to the Ward Nurse who will dispense to the patient on daily basis .When a patient is discharged before completing treatment, the Patient Kits should be transferred to the nearest Health Facility to the patient’s home or a treatment supporter.
- *Patients who die, default or fail treatment:* The remaining complete blisters will be put in a “Supply Box”, as indicated on the GDF-leaflet, for re-packaging of a new Patient Kit. The repackaging is done by the Pharmacy staff, and the number of repackaged Patient Kits is entered on the Quarterly Patient Kit Ordering Form.
- *Patients who are transferred:* in principle, the patient kit follows the patient. Advantage is the transparent accountability, because Patient Kits orders are based on registered cases, which exclude transfers in. When a patient is diagnosed in a health facility and subsequently transferred to another near home, the TB Coordinator. Writes a transfer form for the patient. The patient gets blisters from the “supply box” to cover the period for him/her to reach the health facility. In the health facility a new patient kit is opened for the patient.. When a patient is already on treatment using his/her patient kit and then transferred , the TB Officer arranges the already opened patient kit to follow the patient. In this case, the patient is supplied enough blisters from his or her own patient kit to reach the health facility.
- *Quarterly Patient Kit Ordering Form:* is filled out quarterly within one week after ending of the quarter, together by Pharmacy staff and TB Officer. The form is sent to the NTP Central Unit, who then forwards a complete set of Order Forms to NDSO. NDSO will then take care of distribution to all Districts/HSAs.
- *“Porter” problem:* The Pharmacy staff needs to be vigilant that no TB drugs and blisters penetrate in the local markets.

Some additional tablets will be needed for patients who need one extra month of initial-phase treatment (about 10% of patients in treatment Categories I and II) and for heavier adults who need larger than standard doses. Some loose tablets will be needed for patients who develop side effects on the fixed dose combinations.

The Category II regimen includes streptomycin, therefore a supply of streptomycin (56 doses of streptomycin, 5 ml sterile water per gram of streptomycin, sterile needles and syringes) should be available in reserve for each patient on Category II treatment. All these items, including self-destruct syringes with needles, are packaged in the Category II patient kits.

Adjustment of the GDF patient kits.

The patient kits for **category I and category III** are the same: 2[RHZE]/4[RH].

- For 2 months intensive phase patient kit contains 6 blisters of RHZE in FDC.
- For 4 months continuation phase the patient kit contains 12 blisters of RH in FDC.

The kits are prepared for the middle weight patient, one that weighs between 40-54 kg., since most TB patients weigh within this range when they begin treatment.

Note that treatment regimen requires 28 doses to be given in a month instead of 30 or 31 doses, and that blisters for all medicines contain 28 tablets.

The patient kits for **category II treatment** is 2S[RHZE]/1[RHZE]/5[RHE].

- For 3 months intensive phase (for tablets) the patient kit contains 9 blisters of RHZE in FDC.
- For 5 months continuation phase (for tablets) the patient kit contains 15 blisters of RHE in FDC.
- The patient kit contains 56 doses of streptomycin. No adjustment is needed for streptomycin since 56 doses are given to all category II patients

Separate containers should be prepared and labelled “**Supply Box RHZE**” “**Supply box RH**” and “**Supply Box RHE,**” to place the blister sheets removed from a patient kit for a lighter weight patient. These same supply boxes should be used to get the additional blister sheets needed for the heavier weight patient. When a supply box is empty and additional tablets are required a patient, the supply box should be replenished with a new patient kit from which the required tablets could be obtained. Discard the now empty patient kit unless required to keep it for accountability purposes to be checked by the district supervisor.

Note: When using medicines from the supply box always check the expiry dates and never give expired medicines to patients; if expired, remove the medicines and store away from the good medicines for later disposal.

Adjustments for category I (and III) regimen

Patient weighs	RHZE blisters	RH blisters
30-39 kg	remove 2 blister sheets	remove 4 blister sheets
40-54 kg	no changes	no changes
55-70 kg	add 2 blister sheets	add 4 blister sheets

Adjustments for category II regimen

Patient weighs	RHZE blisters	RHE blisters
30-39 kg	remove 3 blister sheets	remove 5 blister sheets
40-54 kg	no changes	no changes
55-70 kg	add 3 blister sheets	add 5 blister sheets

Note: in some cases the treatment of a category I patient may need to be extended in the intensive phase by an additional 1 month for a total of 3 months of RHZE, rather than the normal 2 months. For these patients do the following:

Additional one month treatment for Category I

Patient weighs	RHZE blisters
30-39 kg	add 2 blister sheets
40-54 kg	add 3 blister sheets
55-70 kg	add 4 blister sheets

12.2 Logistics for laboratory materials

The health units require an adequate supply of sputum containers to collect and transport sputum specimens to microscopy service. **All health facilities that see TB suspects should have sputum containers.** The laboratories themselves need a regular supply of slides, reagents and other materials to perform the tests required.

12.2.1 Estimating Laboratory Materials Requirements

The sputum containers and laboratory supplies required for microscopy examinations are estimated on the basis of the expected prevalence of TB among the respiratory symptoms who attend Health Care facilities. Generally, prevalence of smear-positive cases among respiratory symptomatics at health facilities ranges from 5-15%.

A large number of sputum containers are needed to identify and investigate TB suspects and to follow up patients. A shortage of sputum containers can constitute a major barrier to the TB diagnostic process; and must be avoided.

Estimation of the quarterly requirements for sputum containers should be based on the expected number of sputum examinations to be done for diagnosis plus the expected number to be done for follow-up. Estimates can be based on the number of new cases treated in the previous quarter.

Example methodology for calculating the number of sputum containers needed

The number of sputum containers needed for diagnosis may be calculated as follows:

- number of new pulmonary sputum smear-positive cases previous quarter
- multiplied by 10 (because on average, 10 TB suspects have been investigated for each new pulmonary sputum smear-positive case detected).
- Multiplied by 3 (because 3 sputum samples are needed from each TB suspect)

The number of sputum containers needed for follow up of treatment is calculated as follows:

- number of new sputum smear-positive cases detected in the previous quarter
- multiplied by 6 (3 follow-up examinations of sputum samples each time)
- number of retreatment cases enrolled in the previous quarter;
- multiplied by 6 (3 follow-up examinations of sputum samples each time)
- number of sputum smear negative cases enrolled in the previous quarter;
- multiplied by 2 (one follow-up examination of 2 sputum samples)

The total number of sputum containers to order is calculated as follows:

- number needed for diagnosis, plus
- number needed for follow-up examinations, plus
- 10% for additional investigations, plus
- 20% for reserve stock, minus
- the number of sputum containers in stock at the end of last quarter

The National Reference TB Laboratory is responsible for determining and advising on the specifications for laboratory equipment and supplies.

Suggested specifications for sputum containers are:

- The container mouth should measure at least 50mm to facilitate sputum collection
- The container should have a watertight screw cap permitting full hermetic closure to prevent leakage during transportation

- The container should be made of disposable material (plastic) that can be destroyed easily by burning.
- The container should be made of translucent material so that the level of sputum in the interior can be clearly seen.

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CHAPTER 13 HUMAN RESOURCE DEVELOPMENT

The purpose of DOTS training sufficiently build capacity of programme as well as general health care staff to effectively deliver quality TB care to patients. Detailed planning is crucial if sufficient public and private sector personnel are to be trained effectively and within the time frame needed. Central and District staff must be trained in both technical and managerial aspects of TB control to equip them with the necessary skills to adequately support the general health care staff. To this end, a well articulated Human Resource Development (HRD) plan based on the needs at various levels is required. One of the strategies to strengthen HR is through in-service training.

13.1 Planning Issues

The planning of training should cover a number of issues:

- How to organize training activities;
- Who should be trained (i.e. the many different types of staff to be trained and their training needs;
- How many staff to be trained;
- Training methods and materials;
- Selection of trainers and training sites
- The schedule of training activities
- Supporting and maintaining training activities
- Monitoring and evaluation of training activities
- Introducing the revised national policy on TB control into the curricula of laboratory, nursing and other health-related schools.

13.2 How to Organize Training

At the central level, an HRD focal point should be identified and assigned the responsibility of preparing the plan for training, coordinating with other programmes and institutions, and evaluation of training activities. The HRD focal point is also responsible for identifying all resources required for the training sites (overhead projectors, slide projectors, flip charts, course and facilitators guides) and for the workshop participants (modules, answer sheets, recording and reporting forms, manuals).

To estimate the cost of training, basic information is needed on:

- Per diem and travel of participants;
- Per diem and travel of facilitators
- Quantity and cost of printed materials, stationery and refreshments

The decision on the staff to be trained should take into account the calibre of staff required to implement the revised strategy. This should include managerial staff, the private sector, CHAL, the leadership of professional health associations, and individual private practitioners who can provide care for TB patients.

Table 30: Analysis of training needs at various levels of the NTP

Level	Type of personnel	Training Needs
Central	TB Central Unit Staff	Basic TB epidemiology. How to plan, provide, support and

		evaluate the programme, how to coordinate with other programmes and training institutions, assist and supervise the districts, establish linkages with NGOs and health institutions and undertake advocacy
District	District TB Coordinator	Information about the revised NTP strategy and goals so that s/he can support its implementation. How to establish DTDs, how to use the reporting and recording system, evaluate quarterly district reports, and supervise health centre staff.
District hospitals, health centres, Private sector and NGO hospitals	Doctors, nurses, community health workers	Knowledge and skills regarding how to: <ul style="list-style-type: none"> • Identify TB suspects • Collect, handle and transport sputum specimens • Prescribe TB treatment • Provide DOT • Provide health education to patients and families • Register and report data • Examine contacts of infectious cases • Manage TB/HIV/AIDS

13.3 Monitoring and evaluation of training activities

Training activities should be monitored in terms of quantity and quality. The quantity of training should be guided by training targets, while the quality should be assessed with respect to the corresponding quality of service delivery at the health facility level. In particular, programme managers should monitor:

- The number of health staff of different categories who have been trained as a percentage of the training target for each district;
- The number of health centres and laboratories of each category that have sufficient trained staff
- Completion of training activities in relation to the training schedule
- The number of health units that have at least 1 staff member trained in the DOTS strategy.
- The number of staff at health units who are trained in the DOTS strategy.
- The number of laboratories that have at least one technician trained in microscopy.
- The number of doctors in the public sector that have been trained on the DOTS strategy
- The number of private practitioners who are able to provide correct TB diagnosis and treatment.

The immediate assessment of quality of training should be conducted by comparing participants knowledge at the beginning and end of each course through pre and post tests. It should be recognized that the impact of a training course on TB control is limited unless it is reinforced by supervision where performance is evaluated and support provided to ensure optimum quality of care. However, evaluation of performance should also take note of the context (logistics, supervision and communication) within the trainees work.

CHAPTER 14 ADVOCACY, COMMUNICATION, SOCIAL MOBILISATION

14.1 Introduction

Advocacy, communication, and social mobilization (ACSM) strategies can be most effectively concentrated to help address four key challenges to TB control **at country level**:

- Improving case detection and treatment adherence
- Combating stigma and discrimination
- Empowering people affected by TB
- Mobilizing political commitment and resources for TB.

14.2 Communication as an overarching theme

The term “communication” is an overarching one meaning the process people use to exchange information about TB. All communication activities make use of some form of media or channel of communication (e.g. mass media, community media, interpersonal communication). While much of the communication effort on TB is concerned with transmitting a series of messages to people affected by TB, nearly all communication practitioners stress that to be effective, communication should be understood as a two-way process, with “participation” and “dialogue” as key elements.

Programme communication to inform and empower

In the context of TB control, *programme communication* is concerned with informing and creating awareness among the general public or specific populations about TB, and empowering people to take action. Programme communication also works to create an environment through which communities, particularly affected communities, can discuss, debate, organize, and communicate their own perspectives on TB. It is aimed at changing behaviours (such as persuading people with symptoms to seek treatment) but can also be used to catalyze social change (such as supporting community or other communication-for social-change processes that can spark debate, and other processes to shift social mores and barriers to behaviour change).

14.3 Advocacy to change political agendas

Advocacy denotes activities designed to place TB control high on the political and development agenda, foster political will, increase financial and other resources on a sustainable basis, and hold authorities accountable to ensure that pledges are fulfilled and results achieved.

Policy advocacy includes data and approaches to advocate to senior politicians and administrators about the impact of TB at the national level, and the need for action.

Programme advocacy is used at the local, community level to convince opinion leaders about the need for local action.

Media advocacy generates support from governments and donors, validates the relevance of a subject, put issues onto the public agenda, and encourage the media to cover TB-related issues regularly and in a responsible manner.

14.4 Social mobilization to build partnerships

Social mobilization is the process of bringing together all feasible and practical intersectoral allies to raise awareness of and demand for a particular programme, to assist in the delivery of resources and services and to strengthen community participation for sustainability and self-reliance.

“Allies” include decision - and policy - makers, opinion leaders, nongovernmental organizations (NGOs) such as professional and religious groups, the media, the private sector, communities and individuals. Social mobilization generates dialogue, negotiation and consensus, engaging a range of players in interrelated and complementary efforts, taking into account the needs of people.

To achieve TB control advocacy objectives, the main obstacles to TB control and the tools available for overcoming them should be identified. Some of the constraints in Lesotho are:

- The DOTS strategy is not being implemented
- Financial and human resources are lacking
- Prevalence of MDR TB is increasing
- Prevalence of HIV/AIDS is increasing and directly affecting TB morbidity and transmission of TB infection.

There is a need to identify ways of overcoming these constraints and why do they exist?

14.5 Selection of Advocacy Strategies and Tactics

According to the WHO⁹; there are four priority advocacy strategies. They are:

- A media strategy
- A publications strategy
- Coalition-building and working with NGO's
- An insider strategy

Deciding which strategy or which combination of strategies to use should take into account the benefits and risks, the time frame, and the expertise and financial resources needed for effective implementation.

14.5.1 Media strategy

Media coverage should focus on the country's most important media (press, radio and television).

Tactics might involve:

- Using World TB Day as an opportunity for a media event;
- Holding news conferences
- Conducting media tours to DTDs.
- Developing background materials for the media such as fact sheets
- Purchasing advertising space and placing newspaper supplements
- Using articulate and eloquent TB patients as speakers in media interviews and visits.

14.5.2 NTP Publications strategy

Activities should include:

- Publishing attractive TB programme reports;
- Publishing TB programme brochures including reading materials for the community
- Producing a newsletter
- Disseminating WHO TB reports

⁹ Tuberculosis Handbook WHO. 1998

- Developing and distributing Information, Education and Communication (IEC) materials for the community and patients

14.5.3 Coalitions and working with NGOs

Activities could include:

- Encourage grassroots participation in TB control efforts
- Involve community organizations
- Coordinate education, communication, training and advisory activities with those of organizations working on related issues such as AIDS, asthma, anti-smoking and diabetes;
- Approach corporations, professional associations and workers unions for political and financial support for TB control;
- Conduct a preparatory World TB Day workshop for NGOs and professional associations;
- Request prestigious personalities from scientific circles and performing arts celebrities to serve as advocates.
- Establish an advocacy steering committee that should include representatives from the Health Education Unit.

14.5.4 Insider strategy

The “Insider strategy” refers to making direct contact with the principal “targets” of advocacy activities, particularly politicians, government officials at decision making level.

Activities should include:

- Networking and lobbying
- Arranging meetings, workshops and seminars to reach key people
- Maintaining regular and frequent communication with international cooperation and technical agencies.

14.6 Message Development and Presentation

Messages should take into account the audience, i.e. the key persons for whom they are intended.

Message content:

- Ensure that the message is technically sound and defensible;
- Always emphasize the severity of the TB problem and that DOTS is the best solution;
- Provide examples of DOTS successes and demonstrate its advantages;
- Emphasize the threat of MDR TB

Resource mobilization

Advocacy implies some budgetary risk. But failure to undertake any advocacy activity will probably mean that the NTP continues to operate at the same or even a lower level of funding.

In order to secure financial resources:

- Assign regular budget funds for advocacy activities;
- Investigate and understand potential donors.

In order to secure human resources:

- Involve those MOHSW departments (e.g. AIDS programme, Health Education) that have expertise in advocacy and related issues;
- Use WHO to guide the programme

CHAPTER 15 ROLE OF NGOS, PRIVATE SECTOR AND COMMUNITIES IN TB CONTROL

The government of Lesotho encourages Public-Private Partnership (PPP) especially in the health sector with the aim of complementing the government efforts to expanding access to quality health care to the population. The guiding principle for the partnership and collaboration is to strengthen ownership, ensure transparency and social responsibility. The involvement of the private sector and NGO's in TB control activities is very crucial. However, there is need for strong coordination to ensure synergy and complementarity in implementation of activities. It is necessary to ensure that partners are adequately oriented in the Stop Strategy, follow the national policy with respect to standard case management as well as the NTP information system.

Stakeholders in diagnosis and treatment of TB patients should also be involved in all activities of tuberculosis control, including training, monitoring and evaluation. The main output indicators of the involvement of other partners is the number and proportion of private hospitals, clinics and individual doctors, who notify new cases, implement DOTS and report treatment outcomes in a collaborative agreement with the MOH.

At the community level, Community-based organizations (CBOs) have a significant role to play with respect to:

- Supporting patients throughout treatment until cure
- Patient, family and community education
- Case finding
- Lobbying for government commitment to TB control
- Increasing accountability of local health services to the community.
-

Based on the available information on the key lessons learned from community contribution as documented by WHO¹⁰, the determinants for success includes:

- Good collaboration between the general health services, NTP and the community groups;
- Good education of the TB patients and their family members;
- Training of community members and the health services staff;
- A system of regular supervision of community members by NTP staff.

The main challenges identified include: identification of the leadership responsible for managing the change process and of the appropriate community group; maintaining adequate level of community motivation; and ensuring good communication links between the different elements of service provision.

NGOs often play an important role in mobilizing community contribution, as they are usually closer to the community than the formal health care sector. However, regular supervision and monitoring is still required to achieve the desired impact. Before the programme decides to involve the community in TB

¹⁰ Community Contribution to TB Care: Practice and Policy. WHO. 2003.

care, it is necessary to ensure that a system of follow-up is established. Regular monitoring and evaluation of treatment outcomes needs to be conducted. The key areas that communities can contribute in TB care are:

- Direct Observation of Treatment
- Support and motivation of patients
- General support and home visits
- Case detection
- Default tracing
- Increasing community awareness

It is recommended that the NTP develops a training programme for communities before engaging them.

SUGGESTIONS FOR FURTHER READING

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