Republic of Botswana
Ministry of Health

NATIONAL TUBERCULOSIS PROGRAMME MANUAL

Sixth edition
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Preface

The Botswana National Tuberculosis Programme has prepared this sixth edition of the national guidelines on the management of tuberculosis with the help of the World Health Organization and the BOTUSA Project of the US Centers for Disease Control and Prevention, with critical input from experts worldwide. The fundamental principle underlying the material in this manual is that it is evidence-based.

The purpose of this revision is to update the guidelines in light of developments in TB control since the publication of the previous manual in 1995. Many changes have occurred in tuberculosis control, necessitated mainly by the continuing challenges posed by the intersection of the HIV and tuberculosis epidemics and the growing threat of drug-resistant tuberculosis. Recent programme data indicate that the level of HIV co-infection among TB patients is approximately 80%. Successive drug susceptibility surveys have shown a progressive increase in the prevalence of multidrug-resistant tuberculosis (i.e., resistance to both rifampicin and isoniazid) in new cases in Botswana from 0.2% in 1995 to 0.5% in 2001 to 0.8% in 2002. To facilitate progress towards global, regional and national TB control targets, the Stop TB Partnership has developed new global and regional strategies and interventions.

These developments have influenced revision of the manual. The most cost-effective public health measure for tuberculosis control remains the identification and cure of infectious TB cases, i.e. patients with smear-positive pulmonary TB. Because the goal of the BNTP is to reduce morbidity and mortality, this manual addresses the treatment of adult and childhood TB, including smear-positive and smear-negative pulmonary TB and extrapulmonary TB, and presents updated information on the management of drug-resistant and HIV-co-infected TB patients.

The objectives of the revised manual are to describe:

- The TB burden in Botswana, BNTP policies and strategy for effective TB control
- Standardised treatment regimens according to TB case definitions and categories, including MDR-TB cases
- Clinical monitoring practices, and recommendations to ensure treatment adherence including the role of community-based TB care
- Special considerations in treating HIV-infected TB patients
- Surveillance and monitoring tools on all aspects of TB prevention and control in Botswana

This manual sets the national policy for TB prevention and treatment and will guide the training of health staff, providing guidance on issues of policy and practice to all health workers at all levels of health care. It also promotes uniformity in the effective management of TB in the country. Attempts have been made to make the text simple and user-friendly while including sufficient evidence-based material to enable its use as a reference book for medical and nursing schools in Botswana.

Foreword

In 1975, The Ministry of Health launched the Botswana National Tuberculosis Control Programme (BNTP), which has achieved appreciable progress over the years. The BNTP achieved a high level of efficiency in its operations as demonstrated by the high success rate, the universal adoption of short-course chemotherapy and the use of directly observed therapy for all patients for the entire treatment period.

Today we witness a serious threat to this achievement. The unwelcome association of tuberculosis and HIV is eroding the gains made by the control programme. The annual number of reported TB cases has increased markedly since 1990, despite a noticeable decline during the preceding decade. Fortunately, tuberculosis is still a preventable and curable disease, despite its association with HIV. With proper management, it is possible to achieve cure rates greater than 95% among TB patients. Tuberculosis treatment remains one of the most cost-effective public health interventions in the world, being far cheaper than many preventive services. The cost of ignoring TB would be extremely high as it kills over 50% of its victims if they are not effectively treated.

However, even as we appreciate that prevention of TB is cheaper than many other public health interventions, it is important to note that running TB services exerts a considerable burden in an already overburdened health system. This manual therefore provides guidelines to improve TB control through case finding, case holding, contact tracing and effective application of chemotherapy. The revision of this manual is necessary to keep up with the emerging challenges; the need to adjust our strategies according to the new information that has evolved over time is crucial if we are to use the resources more effectively to provide comprehensive services to TB patients.

Botswana subscribes to the new Stop TB Strategy, a six-point strategy whose components address the key challenges facing TB control in improving access to the prevention, treatment, care and support of TB, TB/HIV and MDR-TB. The Directly-Observed Treatment, Short-course ("DOTS") strategy remains the '*sine qua non'* of TB control. These guidelines are based on recommendations made by the World Health Organization (WHO), the International Union Against Tuberculosis and Lung Disease (IUATLD) and the United States Centers for Disease Control, and have been adapted to suit our local situation.

Health care workers at all levels of practice in both the public and private sectors are encouraged to follow the guidelines outlined in this manual. I wish to commend the editors of the sixth edition, as well as external reviewers, for the hard work that they put into the production of this manual. TB control must continue to receive the highest priority from all health workers because TB is still the single highest cause of mortality among adult people living with HIV and AIDS in Botswana.

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List of Abbreviations and Acronyms

AFB	Acid-Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
Am	Amikacin
ARI	Annual Risk of Infection
ART	Anti-Retroviral Therapy
ARV	Anti-Retrovirals
ATT	Anti-tuberculosis Therapy
BCG	Bacille Calmette Guérin vaccine
BNTP	Botswana National Tuberculosis Programme
BOTUSA	Botswana USA Project
CDC	United States Centers for Disease Control and Prevention
Cfx	Ciprofloxacin
CHBC	Community Home-Based Care Coordinator
CHN	Community Health Nurse
Cm	Capreomycin
CMO	Chief Medical Officer
CNS	Central Nervous System
CPT	Cotrimoxazole Preventative Therapy
Cs	Cycloserine
CSF	Cerebrospinal fluid
CT	Computer-aided Tomography
CXR	Chest X-Ray
DHT	District Health Team
DOT	Directly Observed Treatment
DOTS	Directly Observed Therapy, Short-course strategy
DST	Drug Susceptibility Testing
E	Ethambutol
EFV	Efavirenz
EPTB	Extrapulmonary Tuberculosis
EQA	External Quality Assurance
ESR	Erythrocyte Sedimentation Rate
Eto	Ethionamide
ETR	Electronic Tuberculosis Register
FDC	Fixed-Dose Combination
FNA	Fine Needle Aspiration
FWE	Family Welfare Educator
GFATM	Global Fund to fight AIDS, Tuberculosis and Malaria
GOB	Government of Botswana
H	Isoniazid
HAART	Highly Active Anti-Retroviral Therapy
HIV	Human Immunodeficiency Virus
INH	Isoniazid
IPT	Isoniazid Preventative Therapy
IRIS	Immune Reconstitution Inflammatory Syndrome
IUATLD	International Union Against Tuberculosis and Lung Disease
LJ	Lowenstein-Jensen (media)

LP	Lumbar Puncture
MDR-TB	Multidrug-resistant TB
MO	Medical Officer
MOH	Ministry of Health
MOTT	Mycobacteria Other Than Tuberculosis
MRI	Magnetic Resonance Imaging
TMP	Trimethoprim
NGO	Non-governmental Organisation
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRL	Nyangabgwe Referral Laboratory
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NTM	Non-Tuberculous Mycobacteria
NTRL	National Tuberculosis Reference Laboratory
Ofx	Ofloxacin
PCP	*Pneumocystis Jiroveci (Carinii)* Pneumonia
PGL	Persistent Generalised Lymphadenopathy
PHC	Primary Health Care
PHS	Public Health Specialist
PI	Protease Inhibitor
PLWHA	Person Living With HIV/AIDS
PPD	Purified Protein Derivative
PTB	Pulmonary Tuberculosis
PZA	Pyrazinamide
R	Rifampicin
RIF	Rifampicin
S	Streptomycin
SMX	Sulphamethoxazole
THZ	Thioacetazone
TB	Tuberculosis
TMP	Trimethoprim
TBC	Tuberculosis Coordinator
TST	Tuberculin Skin Test
UNAIDS	Joint United Nations Programme on AIDS
WHO	World Health Organization
XDR-TB	Extensively Drug Resistant Tuberculosis
Z	Pyrazinamide
ZN	Ziehl-Neelsen

1. INTRODUCTION

1.1 What is Tuberculosis?

1.1.1 Cause and transmission

TB is a communicable disease caused by *Mycobacterium tuberculosis* (also known as the tubercle bacillus) that is spread primarily by tiny airborne particles (droplet nuclei) expelled by a person with infectious TB during coughing or sneezing. If another person inhales these droplet nuclei, transmission may occur. Some bacilli reach the alveoli, where they are ingested by macrophages. Infection begins with the multiplication of tubercle bacilli within these alveolar macrophages. Some of the bacilli spread through the bloodstream when the macrophages die; however, the immune system response usually contains the bacilli and prevents the development of disease.

M. tuberculosis is very common in Botswana and is responsible for almost all the TB cases seen in the country. *M. tuberculosis* and three very closely related mycobacterial species (*M. bovis, M. africanum,* and *M. microti*) cause tuberculous disease and form the *M. tuberculosis* complex. *M. bovis* also causes TB in cattle. Clinically, disease caused by *M. bovis* is difficult to distinguish from disease caused by *M. tuberculosis*; there are little data on the prevalence of *M. bovis* infection in Botswana. No cases of *M. africanum* infection have been confirmed in Botswana.

Mycobacteria other than those comprising the *M. tuberculosis* complex are called Non-Tuberculous Mycobacteria ("NTM") or Mycobacteria Other Than Tuberculosis ("MOTT") (Annex 1). These mycobacteria may cause pulmonary disease resembling TB. Increasingly, cases from these organisms are being reported in patients with weakened immune systems, especially due to HIV. It is important to note that infection with MOTT also may produce AFB-positive sputum smear results and positive Mantoux skin test readings mimicking *M. tuberculosis*. Culture can distinguish between *M. tuberculosis* and MOTT. Disease due to MOTT is usually unresponsive to first-line anti-TB drugs.

1.1.2 Infection and disease

It is important to distinguish between TB infection and TB disease. Persons who are infected by *M. tuberculosis* but have no TB symptoms have latent TB infection. Such persons may have a positive reaction to the tuberculin skin test. In most individuals infected with the TB bacilli, a few organisms remain dormant in the lungs as latent TB. These may later escape from the control of the immune systems and reactivate any time in the future if the function of the immune system is compromised and cause either pulmonary TB or disseminated tuberculosis. Active TB disease occurs when the bacilli cause signs or symptoms.

Many factors influence the progression from infection to disease, which is greatly dependent upon the strength of the body's cell-mediated immunity. Important factors include HIV infection, malnutrition, alcoholism, diabetes mellitus, silicosis, smoking and some malignancies. HIV is by far the most powerful factor affecting disease progression. In the absence of HIV, lifetime risk of progression to disease after infection is 10%; in HIV-infected individuals, there is a 7-10% *annual* risk of disease, Despite the challenges posed by the impact of HIV on the TB epidemic, eventual TB control and elimination throughout the world is possible because:

- The source of infection is almost exclusively a person with the disease who is usually easy to identify.

- Transmission can be limited if infectious persons are put on proper treatment.
- Technology involved in the control is relatively simple and can be applied efficiently even in less sophisticated settings.
- Human beings are the only reservoir for *M. tuberculosis*.

1.2 Global Tuberculosis Epidemiology

The World Health Organization (WHO) declared TB a global emergency in 1993 in recognition of the growing importance of TB as a worldwide public health problem. A third of the world's population, or approximately two billion people globally, is infected with tuberculosis. In 2004, there were approximately 9 million new cases and two million TB deaths. Developing countries bear a disproportionate burden of TB, with 95% of cases and 98% of deaths that occur each year. More than two thirds of cases occur in the economically productive 15- to 50- year age group and TB is responsible for 25% of all avoidable deaths in developing countries.

Countries with a high prevalence of HIV, particularly those in sub-Saharan Africa, have witnessed a profound increase in the number of TB cases, with incidence rates in some countries increasing three-fold over the last decade. In 2004, approximately 741,000 new TB patients were co-infected with HIV, the majority in sub-Saharan Africa.

1.3 Tuberculosis in Botswana

Botswana has one of the highest TB notification rates in the world and has consistently reported in excess of 590 cases per 100,000 population annually since 2000. Three annual risk–of- (TB) infection, or ARI surveys, have been carried out in Botswana since 1956. The annual risk of infection declined from 5.8% in 1956, to 0.1% in 1989. This decline paralleled a major decline in TB notification rates from 506/100,000 in 1975 to 199/100,000 in 1989. However, during the early 1990s, TB rates began to rise again, and reached a peak in 2002 with a notification rate of 623/100 000. The total number of cases rose from 5655 in 1995 to 10228 in 2005.

Based on subsequent studies of TB and HIV co-infection, it has become clear that the increase in TB incidence is a result of the increasing prevalence of HIV in Botswana, as shown in Figure 1.1 below.

Figure 1.1: TB Notification Rate and HIV Prevalence among adult pregnant women in Botswana, 1990 – 2005

Sources: BNTP Annual Reports and ANC Sentinel Surveillance Reports

The proportion of TB patients who are co-infected with HIV in Botswana has been shown by several studies to range from 60% to 86%. Tuberculosis is responsible for 13 % of all adult deaths and 40% of deaths among people living with HIV/AIDS.

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CHAPTER 2 TUBERCULOSIS CONTROL FRAMEWORK IN BOTSWANA

2.1 Organisation of Health Services in Botswana

The Ministry of Health (MOH) provides leadership on health matters by formulating health policies and ensuring their correct interpretation and implementation throughout the health care delivery system. There are six departments in the Ministry of Health: Department of Policy, Planning, Monitoring and Evaluation, Department of Health Sector Relations and Partnership, Department of Ministry Management, Department of HIV/AIDS Prevention and Care, Department of Clinical Services and Department of Public Health. All government hospitals are under the Department of Clinical Services.

There are 24 health districts in Botswana, which are responsible for delivery of PHC services such as preventive services, curative services and programmes for the control of major public health diseases. The Ministry of Local Government provides policy direction and guidance at the local level, while day-to-day management of some functions of PHC is the responsibility of local authorities (e.g., city councils, town councils and district councils). An inter-ministerial Primary Health Care Co-coordinating Committee ensures adequate coordination of PHC activities conducted by both ministries. Annex 2 outlines the organisation of health services and the roles of the two ministries.

2.2 Organisation of the Botswana National Tuberculosis Control Programme

The MOH established the Botswana National TB Control Programme (BNTP) in 1975, with technical assistance from WHO. The programme introduced short-course chemotherapy for treatment of TB in 1986 and adopted the “DOTS” strategy in 1993. The BNTP is part of the Disease Control Division that, in turn, is under the Department of Public Health. The Isoniazid Preventive Therapy Programme is an activity within the BNTP.

Management of tuberculosis is fully integrated into the PHC system, and services are provided in each of the 24 health districts through district hospitals, clinics and health posts. Trained health care workers and a network of lay community volunteers carry out these tasks. In each district, a Public Health Specialist (PHS) leads the district health team. The PHS has the overall responsibility for TB services in the district. District TB Coordinators (TBCs) are responsible for reporting and recording TB surveillance data and coordinating programme activities at the district level.

Annex 2 presents the Ministry of Health organogram and the relationship of TB control-relevant departments in the Ministry of Health and the Ministry of Local Government.

2.2.1 Programme Objectives

The major objective of the BNTP is to eliminate tuberculosis, bearing in mind the financial constraints pertaining to the medical services in the country. More specifically the programme aims to:

1. Strengthen integration of TB control into the health system and safeguard the government commitment to TB control.
2. Detect 70% of expected new cases of infectious TB and cure at least 85% of these (i.e., smear negative at the end of treatment).
3. Ensure standardised short-course chemotherapy on an ambulatory basis under direct observation whenever possible.

4. Strengthen standardised case notification based on case finding and confirmation by effective AFB smear microscopy.
5. Provide timely and reliable TB laboratory services with respect to microscopy and TB culture and sensitivity.
6. Ensure effective integration of TB and HIV treatment services.
7. Strengthen programme supervision based on performance indicators, standardised recording and reporting, and monitoring and evaluation.
8. Ensure quality and client-oriented TB control services.
9. Maintain a reliable and regular TB drug supply and distribution.

2.3 The "DOTS" Strategy

Botswana adopted the WHO-recommended "DOTS" strategy in 1993 and reports 100% geographical "DOTS" coverage. The strategy remains at the heart of TB control strategy; its five components are:

1. Political commitment with increased and sustained financing:

The Government of Botswana's demonstrates its commitment to TB control by supporting TB control activities, maintaining a continuous and sustained supply of high quality TB drugs, and providing free treatment to all TB patients. GOB also participates actively in national and international partnerships for TB control; the US Centers for Disease Control (CDC), the Global Fund to fight AIDS, TB and Malaria (GFATM), and the WHO are some of the Government's important partners, and offer new opportunities for TB control.

2. Case detection through quality-assured bacteriology:

Bacteriological examination is recommended for TB case detection. There are 48 laboratories with TB microscopy services (equivalent to one diagnostic centre per 35,000 population). Laboratories at district, mission, primary and mine hospitals perform only smear microscopy while the National TB Reference Laboratory (NTRL) in Gaborone performs smear microscopy, culture, drug susceptibility testing. The Nyangabgwe Reference Hospital Laboratory in Francistown performs mycobacterial culture only. The NTRL also supervises the national External Quality Assurance (EQA) network for microscopy.

3. Standardised treatment, with supervision and patient support:

TB control in Botswana is based on standardised short-course treatment regimens for adults and children, which is supervised throughout the course of treatment. Treatment support is provided at health facilities and by community volunteers under the supervision of the TB control programme.

4. Uninterrupted supply of quality-assured drugs

An effective and reliable national drug supply and management system has ensured a regular supply of quality-assured anti-TB drugs and prevented stock-outs.

5. Monitoring and evaluation system and impact measurement:

The BNTP has a well-organised standardised recording and reporting system using individual patient data. Paper registers are used at facility level, while at district levels, both paper and electronic

registers are used. Data from each district are sent to national level electronically on a quarterly basis where they are recorded in an electronic register (ETR). At the national level, quarterly and annual reports are produced. National and district-level TB coordinators conduct regular supervision and monitoring visits.

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CHAPTER 3: PREVENTION

3.1 Bacille Calmette Guérin Vaccine

The Bacille Calmette Guérin (BCG) vaccine consists of attenuated live bovine tubercle bacilli. Injection of this vaccine into the body stimulates protective immunity, particularly against development of TB in persons who become infected with *Mycobacterium tuberculosis* in high prevalence countries where children are exposed to TB at a very early stage. Therefore, BCG protects young children against disseminated and severe forms of tuberculosis such as TB meningitis and miliary TB.

3.1.1 BCG Vaccination and HIV

The HIV pandemic has implications for BCG vaccination. HIV reduces the immune response to BCG vaccination. The conversion to a positive TST after BCG is less frequent in HIV-infected individuals.

WHO had previously recommended that in countries with a high burden of TB, a single dose of BCG vaccine should be given to all healthy infants as soon as possible after birth, unless a child presented with symptomatic HIV infection. However, recent evidence shows that children who were HIV-infected when vaccinated with BCG at birth and who later developed AIDS were at increased risk of developing disseminated BCG disease. Among these children, the benefits of potentially preventing severe TB are outweighed by the risks associated with the use of BCG vaccine.

The revised WHO recommendation is that children known to be HIV-infected, even if asymptomatic, should no longer be immunized with BCG vaccine. In countries with a high prevalence of HIV infection and TB, such as Botswana, HIV-uninfected children will particularly benefit from the use of BCG vaccine The following guidance, summarised in Table 3.1, facilitates decisions on the use of BCG vaccine in infants at risk for HIV infection:

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- **Benefits outweigh risks for BCG vaccination for certain infants. The following infants should be immunized:**
    - Infants with no signs or symptoms suggestive of HIV infection who are born to women of unknown HIV status.
    - Infants of unknown HIV infection status with no signs or symptoms suggestive of HIV infection but who are born to known HIV-infected women.
- **Risks outweigh benefits for BCG vaccination for certain infants. The following infants should not be immunized:**
    - Infants with known HIV infection with or without signs or symptoms suggestive of HIV infection.
    - Infants of unknown HIV infection status but who have signs or symptoms suggestive of HIV infection and who are born to HIV-infected mothers. However, this guideline will be applicable only to children who have not yet received BCG in the first few weeks of life, since clinical manifestations typically occur after three months of age. If infection status can be established with early virological testing, BCG may then be administered once HIV infection has been ruled out.
    - Infants of unknown HIV infection status but who have signs or symptoms suggestive of HIV infection and who are born to women of unknown HIV infection status. If infection

status can be established with early virological testing, BCG may be administered once HIV infection has been ruled out.

Table 3.1 Summary of guidance on BCG vaccination and HIV infection

Give BCG vaccine	Do not give BCG vaccine
Known HIV negative children	*Known HIV positive* children with or without signs or symptoms of HIV infection
Children of *unknown HIV* status without signs or symptoms of HIV infection, regardless of HIV status of mother	Children of *unknown HI*V status with signs or symptoms of HIV infection present, regardless of HIV status of mother

3.1.2 BCG Administration

In Botswana, the intra-dermal injection is applied into the outer aspect of the left forearm. Table 3.2 below shows the administration schedule and dosages of BCG.

Table 3.2: BCG administration schedule and dosing

Age	Dose	Site
At birth	0. 05 ml	Intra-dermal
Above 1 year	0.10 ml	Intra-dermal

Further detailed instruction on vaccination technique, vaccine handling, etc. is contained in the "Health Workers manual for EPI" issued by the Family Health Division as BCG is integrated within the Expanded Programme of Immunization strategy.

3.1.2 Contraindications for BCG vaccination. Do not administer the BCG vaccination:

- to infants/children who are known or suspected to have HIV infection (see section 3.1.1 above) because of the high risk of disseminated BCG disease.
- when other factors suppressing the immune system such as, e.g. congenital immune deficiency, leukaemia, lymphomas, and steroid treatment are present.
- simultaneously with measles vaccine. There should be a period of at least one month between the two vaccines.
- BCG during or within 24 hours after discontinuation of isoniazid therapy.

3.1.2. BCG reactions

Normal reaction:

- The wheal caused by the injection of vaccine will disappear in about half an hour.
- Two to three weeks after vaccination a small, red, indurated and slightly tender nodule develops, which then increases in size to about 10 mm diameter.
- A small superficial abscess forms which will later ulcerate, crust and finally heal, leaving behind a scar 5-7 mm in size.
- The normal reaction takes about 12 weeks from injection to development of the scar

Accelerated reaction:
The nodule appears earlier, the ulcer is larger and the resultant scar is larger, 10-15 mm in diameter.

3.1.3 Complications of BCG

- Swelling of lymph nodes adjacent to the vaccination site usually requires no specific treatment and anti-TB treatment is not indicated. The swelling can persist for several weeks or months
- Babies may develop subcutaneous abscesses if injected subcutaneously rather than intradermally. The abscess may only require pain relief. Aspiration is recommended rather than incision and drainage.
- Excessive ulceration (duration and/or size) may occur. First-line treatment is daily cleaning and a simple dressing. After one week, many such ulcers will show healing. If secondary infection occurs, give a broad-spectrum antibiotic.
- Local ulcers and BCG adenitis persisting for more than eight weeks should be treated with a two- months course of isoniazid 5 - 10mg/kg given once daily.

re-insert bullet and indentation hereSystemic complications due to generalized BCG infection are very rare but may be controlled with a full course of anti-TB treatment. Note that PZA is ineffective because it does not kill *M. bovis,* the attenuated pathogen in BCG. Offer HIV testing and counselling when extensive or systemic complications of BCG develop.

3.2 Isoniazid TB Preventive Therapy Programme

Isoniazid Preventive Therapy (IPT) is an intervention recommended by WHO and the Joint UN Programme on AIDS (UNAIDS) since 1998 for people living with HIV/AIDS. Isoniazid is administered for six months to eligible HIV-infected individuals to prevent the development of active TB. Studies in several African countries demonstrated the effectiveness of INH as a TB preventive therapy. INH decreased the incidence of TB among HIV-infected persons by about 40%, and the protection period ranged from less than one year to three years. When patients are properly screened, the risk of inducing INH resistance through IPT is thought to be small.

Following a successful pilot study on the usefulness and feasibility of implementing IPT in Botswana, the National IPT Programme was introduced in 2001 as one of the components of the BNTP. Currently, all districts offer IPT to HIV infected individuals, who must be evaluated thoroughly for active TB before commencing IPT. It is expected that the IPT strategy will reduce the burden of TB among PLWHA.

3.2.1 Eligibility criteria for enrolling clients on IPT

1. Confirmed HIV infection
2. Exclusion of active tuberculosis to avoid monotherapy, which could lead to the development of INH resistance
3. 16 years of age and above
4. Not currently pregnant[1]
5. No terminal AIDS
6. No history of hepatitis and no active hepatitis at enrolment
7. No prior history of isoniazid intolerance
8. No history of TB in the previous three years
9. Not a habitual treatment defaulter

[1] IPT is a non-urgent preventative intervention that can be deferred until after the delivery of the child

3.2.2 Screening algorithm

A comprehensive algorithm is employed to ensure that each client meets the eligibility criteria above. This includes proof of HIV status, history and physical examination, full evaluation of persons with cough and fever (TB suspects). BNTP advises extensive patient counselling on side effects and the importance of treatment adherence. Chest radiography is not recommended for routine screening in Botswana.

3.2.3 Drugs and Dosages of drugs used in IPT programme (adult)

The recommended daily adult dosage of INH is 300 mg (maximum), for six months by mouth; patients under 30 kg, should receive 10mg/kg with the same frequency and duration. Pyridoxine (B6) is co-administered (25 mg orally, daily).

3.2.4 Monitoring on subsequent visits

Patients returning for monthly INH refills should be seen by a nurse. At each visit, nurses should evaluate patients for unintentional weight loss, drug intolerance and side effects of INH (e.g., jaundice, hepatitis), signs or symptoms of active TB disease. Patient adherence to therapy should be assessed via pill count and recorded in the IPT register. Any patient with signs of active TB disease should receive a full medical exam and sputum smear-examination.

3.2.5 Reasons for termination of IPT by HCWs

IPT clients who miss at least two consecutive monthly refill/monitoring visits, develop INH intolerance (jaundice, hepatitis, etc), or become terminally ill should be discontinued from IPT. Female clients who become pregnant after three months of IPT may continue with INH; clients who have completed less may be discontinued. Any client developing active TB should discontinue therapy immediately.

3.2.6 Suggested approach to person with active TB who is on IPT or completed IPT

All TB suspects confirmed by smear should commence a full-course of Category I anti-TB treatment; medical officers are advised to submit sputum specimens for culture & drug sensitivity testing. If the DST results demonstrate low-level INH mono-resistance, continue with HR in the continuation phase; if high-level INH mono-resistance is confirmed, stop INH and use three drugs (RZE) for the continuation phase. If there is no drug susceptibility result after two months of anti-TB treatment (ATT), continue with the four drugs while awaiting the results. Table 7.1 details suggested regimens for different DST patterns.

3.3 Infection Control

3.3.1 Background

HCWs are at increased risk of TB infection. The risk can be as much as 7- to 24-fold, even among staff such as auxiliary nurses, ambulance drivers, laboratory staff and cleaners. Patients with undiagnosed or untreated smear-positive pulmonary TB present the highest risk for nosocomial transmission. Patients with smear-negative TB are generally less infectious, while extra pulmonary TB is, with some rare exceptions (discharging abscesses etc.), not infectious. The risk of TB infection

depends on the frequency and amount of time of direct patient contact, as well as individual factors in the health worker. For example, in HCWs infected with *M. tuberculosis*, concomitant HIV infection will strongly increase the risk of progression from infection to active disease. Several countries have documented nosocomial outbreaks of multidrug resistant TB in HIV- infected persons. Most recently, an outbreak of extensively drug-resistant TB (XDR-TB) among patients and HCWs was reported in South Africa.

It is important to note that patients with fully drug-sensitive strains of TB become non-infectious after 1-2 weeks of standard anti-TB treatment. Patients with drug-resistant strains, particularly patients with MDR-TB, may take considerably longer to become non-infectious.

3.3.2. Tuberculosis infection control in Health Care settings

TB infection control in health facilities has two main objectives: to prevent transmission of TB from patients to health workers, and to prevent patient-to-patient transmission.
There are three levels of infection control measures:

1. Administrative controls
2. Environmental controls
3. Personal respiratory protection

There is a consensus that the first two levels are the most important. Use of personal respiratory protection cannot compensate fully for missing administrative and environmental controls.

Administrative controls:
These measure include

- Early diagnosis of potentially infectious TB patients
- Prompt separation or isolation of infectious TB patients from other patients, particularly patients at increased risk of infection (HIV-positive)
- Prompt initiation of appropriate treatment.

Patients suspected of having TB should be assessed promptly. Sputum should be collected outside or, alternatively, in well-ventilated empty rooms. Patient waiting areas should be well ventilated. If possible, non-diagnosed patients with cough should be separated from other patients and consideration should be given to prioritising them to minimize their contact with other patients and HCWs.

Hospitalised patients with PTB, especially smear-positive disease, should be kept in an isolation ward or in a room separate from other patients. Hospitalised MDR-TB patients should remain in isolation until sputum conversion has been demonstrated. They should be separated from all patients, especially HIV- infected patients.

As far as possible, HIV-infected HCWs should avoid working in high-risk areas or in performing high-risk procedures such as sputum induction, bronchoscopy, etc.

Environmental controls:
Environmental controls are measures used to reduce the number of infectious droplet nuclei in the health facility environment. Some examples are:

- Maximizing natural ventilation through open windows in waiting rooms, examination rooms and patient wards
- Using mechanical ventilation in isolation rooms or wards
- More costly methods such as ultraviolet germicidal irradiation to kill *M. tuberculosis*, or air filtration

Good ventilation is particularly important in high-risk areas such as TB isolation rooms, TB wards, intensive care units with TB patients, and specialised rooms such as sputum induction rooms, bronchoscopy rooms, and autopsy rooms.

Personal respiratory protection:
This is the last line of defence against infection and should not be used instead of adequate administrative and environmental controls.

Only respirators (N95 masks) give adequate protection against inhalation of infectious droplet nuclei that may contain mycobacteria. Surgical masks and other masks do not offer good enough protection. Widespread use is expensive and impractical. Respirators are indicated for:

- Staff who care for patients with smear-positive PTB, particularly patients in isolation rooms and/or patients with MDR-TB
- Staff performing high-risk procedures with TB patients such as bronchoscopy, sputum induction, spirometry or autopsy
- Staff performing surgery on potentially infectious TB patients

Respirators are issued for individual use and may be re-used by the same person for up to a month. Respirators should not be shared and must be stored in a clean dry location between uses.

Surgical masks may be used by patients with known or potential smear-positive or drug-resistant TB, for example, if they are leaving isolation rooms for diagnostic or other procedures. This limits the spread of micro-organisms from the wearer to other persons.

Infection control plan:
Health facilities, in particular hospitals, should have infection control plans/guidelines and TB control should be an integral part of such plans. The designated infection control officer is responsible for the development and implementation of this plan.

3.4 Contact tracing and examination

When a new case of smear-positive pulmonary tuberculosis has been discovered, the TB focal person at the health facility should initiate investigations within three working days from the date of registration to identify infected contacts. All close contacts (e.g., household members or co-workers) should be evaluated. Particular attention should be given to children under five years of age.

If the index case is a child, the source of the disease will be a person with PTB, usually smear-positive. If the source is unknown, ask household contacts for symptoms and investigate any contact with symptoms of PTB. Contact tracing is not necessary for smear-negative PTB or EPTB unless the index case is a child.

A contact examination form should be completed for each confirmed case's contacts. Should tuberculosis suspects be found, their names are to be entered into the "Suspect and Sputum Dispatch Register", until confirmed.

3.5 Protection of Child Contacts

Tracing of children who are household contacts of infectious adults is part of the national TB control policy. Clinical assessment alone is sufficient to decide whether a paediatric contact is well or symptomatic. Routine assessment of exposed contacts does not require CXR or TST.

Young children living in close contact with a source case of smear-positive pulmonary TB are at particular risk of TB infection and disease. The risk of infection is greatest if the contact is close and prolonged such as the contact an infant or toddler has with a mother or other caregivers in the household. The risk of developing disease after infection is much greater for infants and young children under five years than it is for children aged five years or older. If disease does develop, it usually does so within two years of infection, but in infants, the time lag can be as short as a few weeks. Isoniazid preventive therapy for young children with infection who have not yet developed disease will greatly reduce the likelihood of developing TB during childhood.

The International Union Against Tuberculosis and Lung Disease (IUATLD) and WHO therefore recommend isoniazid (5mg/kg daily for six months) as preventive treatment for all children under five years of age who are household contacts of sputum smear-positive PTB patients, and in whom active TB disease has been excluded. The Botswana National TB programme has also adopted this recommendation, which should be implemented by all health workers.

A *newborn* baby (less than one month old) of a mother with smear-positive TB should not be given BCG at birth. The child should be given isoniazid (INH) prophylaxis (5mg/kg daily) for 6 months, followed by BCG. If the child shows signs of TB, he/she should be started on full TB treatment. An *infant* (one month and older) of a mother with smear-positive PTB is at high risk of infection and of developing TB. The infant should receive six months of isoniazid, followed by a second BCG immunization if there is no scar from the BCG given at birth.

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CHAPTER 4: CASE DEFINITIONS

A case definition is a standardised way to identify what type of TB case a patient is. Standardised case definitions permit:

- Appropriate choice of treatment regimens and correct assessment of treatment outcomes
- Proper patient registration and case notification
- Evaluation of the frequency of each case type
- Effective recording and reporting of case statistics

4.1 Determinants of case definitions

Table 4.1: Determinants of case definitions

Determinant of Case Definition	Example(s)	Importance
Site of TB disease	Pulmonary Extrapulmonary	• Choice of treatment regimen • Recording and reporting in TB register
Results of bacteriology tests (sputum smear)	Smear-positive Smear-negative	• Give priority to patients who are most infectious or most at risk of death • Recording and reporting in TB register • Monitoring treatment progress and outcome
History of previous TB Treatment	New Retreatment after relapse Retreatment after failure Retreatment after default	• Previously treated patients may have a high risk of drug-resistant TB and may require a different treatment regimen
Severity of TB disease	Bacillary load on smear Anatomical site (such as meningeal, spinal, military)	• May influence choice of regimen • Influences duration of treatment

4.2 Case Definitions

4.2.1 Site of TB disease

The diagnosis of TB means that a patient has symptomatic disease due to *M. tuberculosis*. The disease site may be either pulmonary, extrapulmonary or both.

Pulmonary TB (PTB): Any TB disease that involves the lung parenchyma. Therefore, disease that involves *only* the intrathoracic lymph nodes or pleural effusion is **not** considered pulmonary TB.

Extrapulmonary TB (EPTB): Any TB disease involving organs other than the lung parenchyma (such as pleura, pericardium, kidneys, lymph nodes, bones or meninges)

Note: A patient having *both* pulmonary and extrapulmonary disease is classified as a case of **pulmonary** TB.

4.2.2 Results of bacteriology tests

For **PTB** cases, it is important to determine the presence of acid-fast bacilli (AFB) in sputum when the patient is first diagnosed. The sputum smear result may be *positive* or *negative* based on whether AFB are seen.

Smear-positive cases: Any patient with at least one positive smear result (irrespective of quantity of AFBs seen on microscopy)
Smear-negative cases: Any pulmonary TB case that does not meet the definition of being smear-positive. This includes:

1. Patients with three negative smear results and radiological findings and doctor's decision to treat for TB
2. Patients with negative smear results and a positive culture result for *M. tuberculosis*
3. Patients who are unable to produce sputum and with highly suspicious radiological and clinical findings and doctor's decision to treat for TB

EPTB patients include:

1. Patients with extrapulmonary histological and/or laboratory and clinical evidence and a doctor's decision to treat for TB
2. Patients with one culture positive or positive AFB smear from the extrapulmonary site

4.2.3 History of previous TB treatment

It is important to ask every patient with pulmonary or extrapulmonary TB about a history of previous TB treatment, which increases the likelihood of drug-resistant TB. Recording a patient's history of previous TB treatment also allows epidemiological monitoring within the region and country.

Definitions included within the history of previous TB treatment category are:

- New: A patient who has never had treatment for TB, or who has taken anti-TB treatment for less than one month
- Retreatment after relapse: A patient previously treated for TB who has been declared cured or treatment completed, and is diagnosed with sputum smear-positive or culture-positive TB
- Retreatment after failure: A patient who is started on a re-treatment regimen after having failed previous treatment, i.e., sputum positive after 5 months of treatment. This is also a patient who was initially smear negative and was smear positive at the end of two month's treatment
- Retreatment after default: A patient who returns to treatment following interruption of treatment for two or more **consecutive** months, with smear or culture positive TB (sometimes smear-negative but still with active TB as judged on clinical and radiological assessment)

Smear-negative PTB and EPTB cases may also be classified as retreatment after relapse, treatment failure and default.

4.2.4 Severity of TB disease

The patient's bacillary load and anatomical site of TB disease partly determine the severity of disease. Meningeal, spinal, pericardial or miliary TB are severe forms of TB because of the greater threat to

the patient's life. By contrast, TB of the lymph nodes, bones (excluding the spine) or skin, are considered less severe forms of TB.

References

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5. DIAGNOSIS OF TUBERCULOSIS

In line with the national routine HIV testing policy, all persons with symptoms or signs of TB should be tested for HIV. Rapid HIV testing is available in all public health facilities in Botswana.

5.1 Case finding

The highest priority in TB control is the identification and cure of infectious cases, i.e. those patients with sputum smear-positive PTB. There are two ways to identify TB: passive and active case finding.

Passive case finding means that the illness is diagnosed when a patient attends a health facility to seek medical help. **Active case finding** refers to health workers actively searching for patients in the community. The most common method of active case finding in Botswana is contact investigation. Other methods of active case finding can be special surveys, either in certain geographical areas or in defined populations (e.g. schools, prisons). The most common tools in case finding (passive or active) are history taking, physical examination, sputum examination, X-ray examination and tuberculin skin testing.

5.2 Clinical Presentation

5.2.1 History

Common symptoms of pulmonary TB:

- Prolonged cough for 2 - 3 weeks. Any person with such a symptom is classified a **TB suspect**
- Shortness of breath, chest pain or haemoptysis
- General symptoms such as fever, loss of appetite, loss of weight, malaise, night sweats

Symptoms of extrapulmonary TB:
Apart from the general symptoms described above, patients may also complain about the following depending on the affected organ.:

- Swollen glands (TB lymphadenopathy)
- Headache (TB meningitis), severe backache, sometimes with difficulties in walking (TB of spine), swollen joints (TB arthritis)
- Abdominal pain and distension (TB peritonitis), intermittent diarrhoea, sometimes with blood (TB bowel)
- Recurrent urinary infections which are sterile on ordinary culture and do not respond to antibiotics (renal TB)

Medical and Social History:

- Previous exposure to a PTB case (e.g. history of TB illness in family or household)
- History of previous TB treatment
- HIV status
- Occupational history, especially in the mining industry
- History of diabetes mellitus, smoking, alcoholism or prolonged treatment with steroids

5.2.2 Physical examination

General examination:

- Signs are often non-specific, and may be related to chronic illness or concomitant HIV infection, e.g., fever, wasting, enlarged lymph nodes, skin changes, etc

Pulmonary TB:

- There may be crepitations and diminished breathing sounds over apexes, and amphoric breath sounds may be heard over cavities
- However, auscultation may be entirely normal, even in advanced cases of PTB

Extrapulmonary TB:

- Signs will depend upon the site.

5.3 Investigations

5.3.1 Sputum smear microscopy

Microscopic examination of sputum is an essential test in TB diagnosis; TB culture is definitive. Patients with smear-positive PTB are the main sources of new infections in the community, thus finding and treating the smear-positive PTB patients has the highest priority in every TB program. **Health workers should always obtain specimens for sputum microscopy if PTB is suspected**.

Collection and dispatch of sputum specimens:

- Obtain sputum (not saliva, which is unsuitable for smear microscopy) as described in Annex 3. Collect three sputum specimens as follows:

For outpatients – the "spot, early morning, spot" method:
One **"spot"** specimen is submitted under the supervision of a health worker at the first interview. The patient takes the second "early morning" specimen the next day, before cleaning the mouth or eating. This specimen normally yields the highest load of AFB. The third specimen is collected on the **"spot"** when the patient returns with the 2nd sputum specimen.

For inpatients:
Three early morning specimens collected on three consecutive days

Sputum Results:

- The number of bacilli (AFB) seen in a smear reflects the patient's infectivity. Every laboratory should therefore quantify the results of sputum smear microscopy as shown in Table 5.1 below.
- A laboratory result that is not consistent with the clinical picture must be interpreted with caution
- Laboratory results are subject at times to human and material error. Some of the errors are clerical errors, reagents problems, bad quality specimens, process errors and lack of quality control.

Table 5.1: Recording the results of sputum smear microscopy

Number of acid-fast bacilli (AFB)	Number of oil immersion fields examined	Reported as
No AFB	per 100 fields	**No AFB seen** *(No AFB per 100 fields)*
1 – 9 AFB	per 100 fields	**Scanty.** Record exact figure *(1 – 9 AFB per 100 fields)*
10 – 99 AFB	per 100 fields	**1+** *(10 – 99 AFB per 100 fields)*
1 – 10 AFB	per field	**2+** *(1 – 10 AFB per field in 50 fields)*
More than 10 AFB	per field	**3+** *(>10 AFB per field in 20 fields)*

Facilities equipped with the Meditech computer system should submit requests for TB investigations on the computer. Clinicians should be pro-active in obtaining results and contacting the laboratory if results are not immediately forthcoming.

5.3.2 Mycobacterial culture

Examination by mycobacterial culture is the "gold standard" of TB diagnosis. However, culture is more costly and time-consuming than microscopy, and requires specialised media and skilled laboratory personnel. Given these constraints, culture is less suitable for routine case detection in Botswana.

Indications for culture:

- Patients with a history of previous anti-TB treatment (e.g., retreatment after relapse, failure or default)
- Patients who are sputum smear-positive at the end of the intensive phase of treatment and/or at the end of treatment
- Investigation of symptomatic individuals at high risk of MDR-TB (e.g. laboratory workers, contacts of MDR-TB patients and HCWs caring for such patients)
- Investigation of fluids suspected to be infected by *M. tuberculosis*, e.g., abscesses, gastric fluid, pleural fluid, cerebrospinal fluid and urine.
- Patients with suspected cryptogenic TB should have blood taken for TB culture. The blood specimens should be collected in special culture bottles available from the NHL.
- Investigation of patients who develop active PTB during or after IPT
- Children who have suspected drug-resistant TB, complicated or severe cases of disease or an uncertain diagnosis

With the Lowenstein-Jensen (L-J) method, a positive result (growth of mycobacteria) is usually apparent after three weeks. If there is no growth by eight weeks, the result is negative.

5.3.3 TB Drug Susceptibility Testing (DST)

The National TB Reference Laboratory (NTRL) performs DST on all positive cultures, testing for isoniazid, rifampicin, ethambutol and streptomycin. DST for pyrazinamide is technically difficult and results are difficult to interpret, consequently the NTRL does not perform the test.

The mycobacteriology request and report form (MH2011) should be completed for all specimens

submitted for culture and susceptibility testing. With the LJ method, DST results are available approximately four weeks after growth of a culture. Therefore, the period from reception of a specimen in the NTRL to availability of susceptibility results is at least 7 – 8 weeks. If the NTRL confirms MDR TB, it sends the resistant specimens to a regional supranational reference laboratory (usually in South Africa) for susceptibility testing for second-line drug resistance.

5.3.4 Radiography

Radiography has more than 90% sensitivity but only 65 – 70% specificity for detecting PTB. A chest X-ray is an important tool in supporting the diagnosis of PTB in symptomatic individuals whose sputum smears are negative for AFB, but it is not possible to diagnose PTB using chest X-rays **only.** Therefore, always request sputum smear examination for all TB suspects. Radiography is also useful in diagnosing other types of TB, particularly disease of the bones, joints and spine.

The following radiographic appearances suggest active TB:

- Shadows in one or both upper zones
- Cavities in one or both upper zones
- Miliary pattern
- Persistent shadows after pneumonia treatment
- Pleural effusion
- A combination of any of the above, especially in HIV-infected patients

5.3.5 Other tests and procedures for diagnosing TB

- Biopsy of lymph nodes and the pleura
- Fine needle aspiration of lymph nodes
- Lumbar puncture for obtaining cerebrospinal fluid (CSF) in suspected cases of TB meningitis
- Echocardiography with aspiration if TB pericarditis is suspected
- Abdominal ultrasound may reveal ascites and/or enlarged intestinal lymph nodes
- Bone marrow aspirates and blood for *M. tuberculosis* culture for investigating suspected miliary or cryptic TB (use special TB blood culture bottles)
- Tuberculin skin test (Mantoux) in diagnosing TB in children

Molecular methods for diagnosis and strain identification of *M. tuberculosis* (Polymerase Chain Reaction, Ligase Chain Reaction amplification) are not available in Botswana for routine investigation of TB

5.4 Diagnosis of extrapulmonary tuberculosis

Pleural effusion is the most common HIV-related form of extrapulmonary TB, followed by lymphadenitis, pericarditis and meningitis. Always request sputum smear microscopy for any patient with suspected or confirmed EPTB who also has a chronic cough. Register any patient with concurrent PTB and EPTB as a case of PTB.

5.4.1 Pleural Effusion

Patients often present with respiratory symptoms, and may have dullness to percussion and diminished breath sounds on the affected side. Suspected pleural effusion should be confirmed by chest radiography and immediate aspiration of fluid whenever possible. If visible clots form in the

aspirate within a few minutes of being placed in a plain tube, then the fluid has a high protein content, which suggests TB. Pleural biopsy (using an Abram's needle) gives a high diagnostic yield. This is invasive but can be a safe and useful procedure in experienced hands. Though AFB yield from pleural effusions is low, the fluid should still be sent for smear and culture.

Failure of the aspirate to clot does not exclude TB. Laboratory analysis of the fluid will show protein >30 g/L (lower in very wasted patients) and >50% lymphocytes if due to TB. Start ATT within seven days, particularly if the patient is HIV-infected, unless there are clinical or radiological features suggestive of a diagnosis other than TB.

There is no need to give broad-spectrum antibiotics before anti-TB treatment to patients with unilateral effusions if the pleural fluid is clear and clots on standing, unless bacterial pneumonia is a strong possibility. Patients with unusual findings, such as bilateral effusions and cloudy or bloody aspirates, should be investigated for causes other than TB.

5.4.2 Tuberculous lymphadenitis

Suspect TB lymphadenitis in any patient with enlarged nodes that are firm, asymmetrical, more than 2 cm in diameter, or with a fluctuant or discharging sinus. TB lymphadenitis most commonly affects the cervical nodes and is difficult to distinguish from other causes of enlarged nodes such as HIV-related lymphadenopathy, malignancies or other infections of the lymph nodes.

Fine needle aspiration (described in Annex 5) with microscopy and cytology of the aspirated material has a high diagnostic yield. If a fistula has formed, then microscopy of discharging pus is likely to show AFB. Cytology, if available, can identify most other important causes of enlarged lymph nodes. An excision biopsy for gross examination, Z-N microscopy, histological examination, and if indicated, culture, can be considered.

Start ATT immediately if the patient is HIV-infected and has clinical features of disseminated tuberculosis (such as marked weight loss, rapid clinical deterioration or multiple sites of suspected TB) or if TB lymphadenitis is considered the most likely clinical diagnosis but excision biopsy is likely to be delayed for two weeks or longer.

5.4.3 TB pericarditis

Tuberculosis is the cause of pericardial effusions in about 90% of HIV-infected individuals and in 50% to 70% of HIV-uninfected individuals. Patients may present with fever, chest pain, breathlessness, hypotension, tachycardia, raised jugular venous pressure, hepatomegaly and ascites. The chest X-ray shows an enlarged globular heart shadow and echocardiography will show pericardial fluid. If there are any clinical features of cardiac tamponade (e.g., pulsus paradoxus or distended neck veins), perform urgent pericardiocentesis.

5.4.4 TB meningitis

TB meningitis presents as chronic meningitis with gradual onset of fever, headache, neck stiffness and altered consciousness. In addition, there may be cranial nerve palsy, focal neurological signs, paraplegia or seizures. Lumbar puncture (LP) is essential for diagnosis. The CSF typically shows moderately raised white cell count, predominantly lymphocytes, with elevated protein, reduced glucose (usually not as low as in pyogenic meningitis) with negative AFBs on microscopy. The most important differential diagnosis in our setting is cryptococcal meningitis and so the CSF should always

be examined with India ink for cryptococci. TB of the central nervous system may also occur as space-occupying lesions (tuberculomas). Diagnosis is by Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scans.

TB meningitis is most often a presumptive diagnosis and there is an urgency to start treatment as soon as possible because of the associated high morbidity and mortality. Steroids have been shown to improve mortality.

5.4.5 TB of bones and joints

This is more common in children than in adults, and most frequently affects the spine. Other common sites included the large joints of the lower and upper limbs. Multiple lesions may occur. Spinal TB presents with chronic back pain, usually of the lower thoracic spine, often associated with stiffness and restricted movement. Delayed diagnosis of spinal TB can lead to paraplegia. Clinical examination may show deformity, sinuses and abscesses, the latter may be some distance away from the site of the disease (e.g. psoas abscess). X-ray shows narrowing of the intervertebral space and osteolytic lesions in the anterior parts of the adjacent vertebrae. There will often be an anterior wedge-shaped collapse of the vertebral body with narrowing of the disc space and a postero-anterior view may show a shadow of a paravertebral abscess. By contrast malignant lesions of the spine show preservation of the disc space and compression or collapse of the entire vertebral body. TB of other bones and joints usually presents with painful swellings, sometimes with sinus formation; X-ray may reveal osteolytic lesions.

5.4.6 Abdominal tuberculosis

Abdominal TB can affect the bowel or the peritoneum, both diseases may present with fever, anorexia, loss of weight, night sweats and diarrhoea, which may be bloody. There may be a palpable mass in the right iliac fossa due to involvement of the iliocaecal region. Peritoneal disease may occur because of lymphatic or haematogenous spread of bacteria from another focus, usually the lungs, or as a complication to intestinal disease, e.g. perforation. Abdominal ultrasound may show ascites, thickened intestinal walls or enlarged lymph nodes. Microscopic examination of peritoneal fluid is usually negative for AFBs, while histology of peritoneal biopsy specimens will usually show typical granulomatous lesions.

5.4.7 Genitourinary TB

Renal TB often presents with frequency, dysuria, nocturia, suprapubic pain and haematuria. Patients may also present with renal failure. Radiology and/or ultrasound may show loss of calyceal architecture and/or signs of obstruction. Diagnosis is by culture of early morning urine specimens. TB of the female genital tract usually spreads from the fallopian tubes to the peritoneum or endometrium, and may present as infertility, pelvic pain or irregular bleeding. Histological examination or culture of endometrial specimens aid diagnosis.

5.4.8 Tuberculosis of the skin

Tuberculosis of the skin may present as chronic ulcerating/granulomatous lesions or as nodular or verrucous plaques. Diagnosis is by histological examination of biopsy specimens.

5.4.9 Cryptic tuberculosis

High rates of undiagnosed disseminated TB have been consistently identified in febrile, HIV-positive inpatients and in post-mortem series. In cryptic (i.e., hidden) disseminated TB, sputum smears may be negative, the chest X-ray normal and liver function tests elevated, while bone marrow aspirates and mycobacterial blood culture may be positive.

5.5 Differential diagnosis of TB

The main differential diagnoses of *PTB* are bacterial pneumonia and PCP. Patients with PCP typically have a history of progressive breathlessness and a dry cough. Chest X-ray commonly shows bilateral infiltrates/shadows, but may be atypical and may even be normal. Blood gas analysis may show hypoxemia.

Persons who have worked in gold mines and quarries may have silicosis. Symmetrical shadows in the middle lobes are typical on chest X-ray, and breathlessness is common in advanced silicosis. Patients with silicosis have a higher risk of TB and the two diseases may coexist. Kaposi's sarcoma may have extensive lung involvement that can be mistaken for PTB.

The main differential diagnoses of *miliary TB* are septicaemia, AIDS wasting syndrome and disseminated carcinoma. The main differential diagnosis of *TB lymphadenopathy* is HIV-associated persistent generalized lymphadenopathy (PGL), which usually presents with small, symmetrical, non-tender nodes and is often one of the earliest manifestations of HIV infection occurring years before other systemic HIV related disease occurs. Non-Hodgkin's Lymphoma is another differential diagnosis for TB lymphandenopathy, specifically in HIV-infected patients with low CD4 counts.

5.6 Algorithms for the diagnosis of PTB

The diagnosis of PTB is influenced by the severity of the patient's illness, the HIV infection status, and on the level of care services available at facilities that patients present to. The key symptom is a chronic cough (2-3 weeks), which should always alert every health care worker about the possibility of TB as a cause. The management of ambulatory patients is described in Figure 5.1, and of seriously ill patients in Figure 5.2. The presence of danger signs (respiratory rate >30/minute; fever >39°C, pulse rate >120/minute; inability to walk unaided) should spur more aggressive interventions, especially in HIV-infected patients. In seriously ill patients with a chronic cough, diagnosis may be difficult when the sputum smear result is negative for AFB. A number of such patients may die with undiagnosed TB if diagnosis is delayed, and it is sometimes necessary to treat these for TB based on a high level of suspicion.

Figure 5.1: Algorithm for the diagnosis of PTB in ambulatory patients

Ambulatory patient with cough for 2 -3 weeks and no danger signs*

Sputum microscopy for AFB
HIV test

AFB positive

HIV positive

Treat for TB
CPT (if HIV positive)

TB likely

HIV negative

Treat for PCP if likely***

Response

No response or partial response

Reassess for TB

AFB negative or no result

HIV positive

CXR**
Clinical assessment

TB unlikely

Treat for bacterial infection

Response

HIV negative

Treat for bacterial infection

No response or partial response

CXR
Repeat AFB

No TB

Reassess for other diseases

TB likely

Treat for TB

* Danger signs: Respiratory rate >30/minute; Fever >39°C, Pulse rate >120/minute; Unable to walk unaided
**CXR may be done earlier but ALWAYS submit sputum for AFB examination as well
***PCP is unlikely if patient is HIV negative

Figure 5.2: Algorithm for the diagnosis of PTB in seriously ill patients

Seriously ill patient with cough for 2 -3 weeks and danger signs*

Admit
Parenteral antibiotics for bacterial infection
Sputum microscopy for AFB
HIV test
CXR

HIV positive

Treat for PCP

HIV negative

AFB negative or no result

AFB negative or no result

AFB positive

Improvement after 3 – 5 days

No improvement after 3 – 5 days

No response or partial response

Response

Treat for TB
Continue antibiotics

Advise to return if symptoms recur

Refer if no improvement

Treat for TB

Reassess for TB
Refer if necessary

Advise to return if symptoms recur

* Danger signs: Respiratory rate >30/minute; Fever >39°C; Pulse rate >120/minute; Unable to walk unaided

5.7 Diagnosis of TB in children

The diagnosis of TB in children relies 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. Most children with TB have pulmonary TB. 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 of diagnosing TB in children.

In most immunocompetent children, TB presents with symptoms of a chronic disease after they have been in contact with an infectious source case. The key risk factors for TB are outlined in Figure 5.3 below:

Figure 5.3 Key risk factors for TB

1. Household contact with a newly diagnosed smear-positive case
2. Age less than 5 years
3. HIV infection
4. Severe malnutrition.

The key features suggestive of TB are shown in Figure 5.4. In the great majority of children, infection with *M. tuberculosis* can be demonstrated by a TST. 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.

Figure 5.4 Key features suggestive of TB

The presence of three or more of the following should strongly suggest a diagnosis of TB:

1. Chronic symptoms suggestive of TB
2. Physical signs highly of suggestive of TB
3. A positive tuberculin skin test
4. Chest X-ray suggestive of TB

Existing diagnostic tests for TB in children have shortcomings, and the full range of tests (including bacteriological culture and TST) is often not available in settings where the vast majority of TB cases are diagnosed. The development of affordable diagnostic tests for TB in children in low-resource settings should be a priority for researchers and policy-makers. In some countries, score charts are used for the diagnosis of TB in children, although they have rarely been evaluated or validated against a "gold standard". Therefore, they should be used as screening tools and not as the means of making a firm diagnosis. Score charts perform particularly poorly in children suspected of pulmonary TB (the most common form) and in children who are also HIV-infected.

5.7.1 Recommended approach to diagnose TB in children

The decision to treat a child should be carefully considered and once such a decision is made, the child should be treated with a full course of anti-TB therapy. The proposed approach to diagnose TB in children (Figure 5.5) is based on limited published evidence and rests heavily on expert opinion.

Figure 5.5 Recommended approach to diagnose TB in children

1. Careful history (including history of TB contact and symptoms consistent with TB)
2. Clinical examination (including growth assessment)
3. Tuberculin skin testing
4. Bacteriological confirmation whenever possible
5. Investigations relevant for suspected pulmonary TB and suspected extrapulmonary TB
6. HIV testing

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

a. Contact

Close contact is defined as living in the same household as or in frequent contact with a source case (e.g., the child's caregiver) with sputum smear-positive PTB. Source cases that are sputum smear-negative but culture-positive are also infectious, but to a much lesser degree. The following points concerning contact are of importance for diagnosing TB in children.

- All children with respiratory symptoms who have been in close contact with a smear-positive TB case must be screened for TB.
- When any child younger than 15 years is diagnosed with TB, efforts should be made to detect the source case (usually an adult with sputum smear-positive PTB) and any other undiagnosed cases in the household.
- If a child presents with infectious TB (sputum smear-positive PTB or cavitary TB on CXR), child contacts must be sought and screened, as for any smear-positive source case.

b. Symptoms

The specificity of symptoms for the diagnosis of TB depends on how strict the definitions of the symptoms are. In most cases, children with symptomatic TB develop chronic symptoms. The commonest are:

- Chronic cough*:* An unremitting cough that is not improving and has been present for more than 21 days
- Fever*:* Body temperature of >38 °C for 14 days, after common causes 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.

2. Clinical examination (including growth assessment)

There are no specific features on clinical examination that can confirm that the presenting illness is due to pulmonary TB. Some signs, although uncommon, are highly suggestive of extrapulmonary 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 extrapulmonary 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 extrapulmonary TB:

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

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

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 or symptoms of TB and when used in conjunction with other diagnostic tests. There are a number of TSTs available but the Mantoux method is the recommended test.

The TST should be standardised for each country using either five tuberculin units (TU) of tuberculin purified protein derivative (PPD)-S or 2 TU of tuberculin PPD RT23, as these give similar reactions in TB-infected children. Health-care workers must be trained to administer, read and interpret a TST (described in Annex 6).

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 BCG vaccination or not) : >10 mm diameter of induration

Value of the TST

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.

There can be false-positive as well as false-negative TSTs. Possible causes for these results are shown in Table A6.1 in Annex 6. 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.

4. Bacteriological confirmation whenever possible

It is always advisable to confirm diagnosis of TB in a child 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 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 staining of acid-fast bacilli and histology, is a useful investigation, with a high bacteriological yield. In addition to increasing the yield of confirmed TB cases, mycobacterial culture is the only way to differentiate *M. tuberculosis* from other non-tuberculous mycobacteria. 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 (ten years of age or older) who are pulmonary TB suspects. Among younger children, especially children under five years of age, sputum is difficult to obtain and most children are sputum smear-negative. However, in children who are able to produce a specimen, it is worth sending it for smear microscopy (and mycobacterial culture if available). Bacterial yields are higher in older children (more than five years of age) and adolescents, and in children of all ages with severe disease. As with adult TB suspects, three sputum specimens should be obtained.

b. Gastric aspiration
Gastric aspiration using a nasogastric feeding tube can be performed in young children who are unable or unwilling to expectorate sputum. Gastric aspirates should be sent for smear microscopy and mycobacterial culture. A gastric aspirate should be obtained on each of three consecutive mornings. The procedure for gastric aspiration is described in Annex 7.

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 specialised equipment are required to perform this procedure properly. In developing and improving laboratory services for TB diagnosis, the priority is to ensure there is a network of quality-controlled microscopy laboratories for staining acid-fast bacilli in clinical samples.

5. Investigations relevant for suspected PTB and suspected EPTB in children

a. Suspected PTB

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 that 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. A radiologist or a suitably trained HCW should read CXRs.

b. Suspected EPTB

Table 5.2 shows the investigations usually used to diagnose the common forms of EPTB. In most of these cases, the clinical picture suggests TB and histology or other special investigations will confirm the diagnosis.

Table 5.2 Common forms of extrapulmonary TB in children

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

Specialised tests, such as computerised chest tomography and bronchoscopy, are not recommended for the routine diagnosis of TB in children. 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 that have been done.

6. HIV testing

In Botswana, HIV counselling and testing is indicated for all TB patients as part of their routine management.

5.7.2 Standard case definitions of TB in children

The case definition of TB in children is determined as in adults, i.e., by the site of disease, result of any bacteriological tests, severity of TB disease, and history of previous anti-TB treatment. All children with TB should be registered with the NTP using the standard case definitions described in Chapter 4.

Adolescents, or children of any age with complicated intrathoracic disease, are more likely to have sputum smear-positive pulmonary TB. Children with only extrapulmonary TB should be classified under this case definition, and those with both PTB and EPTB should be classified under the case definition of PTB.

5.7.3 Drug-resistant TB in children

Children are as susceptible to drug-resistant as to drug-sensitive TB. Drug-resistant TB is a laboratory diagnosis. However, suspect drug-resistant TB in the presence of any of the following features:

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 three 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 is complex and should be carried out at referral centres. Annex 9 provides additional information on choosing a suitable category IV regimen.

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CHAPTER 6: TREATMENT OF TB

6.1 Principles of treatment

The main objectives in TB treatment are to:

1. Cure the patient of TB (by rapidly eliminating most of the bacilli)
2. Prevent death from active TB or its late effects
3. Prevent relapse of TB (by eliminating the dormant bacilli)
4. Prevent the development of drug-resistance (by using a combination of drugs)
5. Prevent the transmission of TB to others

6.1.1 Curing the patient of TB

Rifampicin is essential for obtaining high cure rates, Directly Observed Treatment (DOT) greatly increases cure rates. Resistance or contraindications to rifampicin significantly reduce cure rates.

6.1.2 Prevention of death from active TB or its late effects

Delayed diagnosis and treatment contribute to a high mortality among TB patients, with or without concomitant HIV infection. Prompt and effective treatment reduces the risk of death during TB treatment. In TB patients infected with HIV infection, cotrimoxazole prophylaxis and antiretroviral therapy reduce the risk of death from opportunistic infections.

6.1.3 Prevention of relapse of TB

An intensive phase of treatment with a combination of at least rifampicin, isoniazid and pyrazinamide makes it possible to have a relatively short (four months) continuation phase. Absence of these three drugs during the first two months of treatment is associated with a much greater risk of recurrence, unless the continuation phase is prolonged.

6.1.4 Prevention of the development of drug-resistance

Appropriate treatment taken for the correct duration maximises cure rates and reduces the development of drug resistance, especially to isoniazid and rifampicin, the most effective drugs. Every dose of rifampicin should be taken under direct observation. Fixed dose combination (FDC) tablets, containing two or more anti-TB drugs, provide extra protection against the development of drug resistance. These will most probably be introduced into the Botswana National TB Programme in 2008.

6.1.5 Decreasing transmission of TB to others

Chemotherapy is the most effective means of reducing transmission by sputum smear-positive patients. Provided the tubercle bacilli are sensitive to the drug combination used, they are rapidly sterilised by the drugs, especially rifampicin, and the sputum typically becomes non-infectious after 2 weeks of treatment even though AFB might still be found in the sputum for several more weeks.

6.2 Anti-tuberculosis drugs

6.2.1 First-line Anti-TB Drugs

These are drugs for treating new and retreatment cases of TB (Table 6.1). Anti-TB drugs possess three main properties: bactericidal action, sterilizing action and the ability to prevent resistance.

Table 6.1: First-line anti-tuberculosis drugs

Essential drug (abbreviation)	Recommended daily dose in mg/kg body weight (range)
Isoniazid (H)	5 mg (4-6) Maximum 300mg daily
Rifampicin (R)	10 mg (8-12) Maximum 600mg daily
Pyrazinamide (Z)	25 mg (20-30)
Ethambutol (E)*	Adults 15 mg (15-25)
Streptomycin (S)	15 mg (12-18) Maximum for <40 years = 1g Maximum for ≥ 40 years = 0.75g

*Ethambutol is safe in children at a dose of 20 mg/kg (range 15-25 mg/kg) daily, which is higher than in adults (15mg/kg) because peak serum concentrations are lower in children than in adults receiving the same mg/kg dose. Its use in Botswana in children is reserved for specialist care

6.2.2 Fixed-Dose Combination Tablets

These medications contain up to four different anti-tuberculosis drugs in fixed dose combinations. The WHO strongly recommends the use of FDC tablets for the treatment of tuberculosis.

FDCs offer several advantages. First, treatment is simplified and prescription errors reduced because of clearer dosage recommendations and easier dose adjustments. Second, the patient has fewer tablets to swallow, which may encourage patient adherence. Third, FDCs eliminate patient selection of which drugs are taken in the event of unobserved treatment. Fourth, FDCs remove the risk of monotherapy, reduce the risk of rifampicin misuse and development of drug resistance. Fifth, FDCs facilitate improved drug procurement, distribution, dispensing and handling at all levels.

There are some disadvantages to FDCs however. These include risk of prescription errors, raising the risk of excess dosage (leading to toxicity) or under-dosage (leading to development of drug resistance). Although there is no guarantee of treatment adherence, health care workers may be tempted to avoid DOT because of ease of treatment. Additionally, there may be poor rifampicin bioavailability in some FDCs, particularly in 3- and 4-drug combinations, necessitating stringent quality assurance measures. FDCs are unsuitable if drug resistance develops to one or more of the components, or when adverse effects occur.

The use of FDCs does not remove the need for single drugs, which are essential in certain situations, e.g., for persons with adverse drug reactions. Table 5 describes different recommended fixed-dose combination tablets.

Table 6.2: Recommended Fixed-Dose Combination drugs in Botswana

Formulations	Abbreviation
Rifampicin 150mg/ Isoniazid 75mg/Pyrazinamide 400mg/Ethambutol 275mg	$R_{150}H_{75}Z_{400}E_{275}$
Rifampicin 150mg/Isoniazid 75mg	$R_{150}H_{75}$
Rifampicin 150 mg/Isoniazid 75 mg/ Ethambutol 275 mg	$R_{150}H_{75}E_{275}$
Ethambutol 400mg/Isoniazid 150mg	$E_{400}H_{150}$
Rifampicin 60mg/Isoniazid 30mg (paediatric formulation)	$R_{60}H_{30}$

6.2.3 Phases of treatment

Anti-TB treatment consists of an **intensive phase (also described as an initial phase)** of at least four drugs for at least two months, and a **continuation phase** of at least two drugs for at least four months. The intensive phase is a very important part of treatment and is effective in eliminating infectious bacilli and minimising the development of resistant strains. The continuation phase is necessary to minimise relapse.

6.2.4 Tuberculosis treatment in HIV-infected individuals

The treatment of TB is the same for HIV-infected as for non-HIV infected patients. All patients with dual TB/HIV infection should receive cotrimoxazole preventative therapy (CPT) while on TB treatment regardless of their CD4 cell count. All HIV co-infected TB patients are eligible for antiretroviral therapy; timing of initiation of ART is contingent upon several factors including CD4 count (refer to section 6.5.1 for details).

6.3 Drug regimens for Tuberculosis

6.3.1 Rationale for standardised regimens:

There is one main treatment regimen, consisting of standardised combinations of the five first line drugs, namely, Isoniazid (H), Rifampicin (R), Ethambutol (E), Pyrazinamide (Z) and Streptomycin (S).

Standardised regimens have the following advantages over individualised prescription of drugs:

1. Reduced errors in prescription thus reducing the risk of development of drug resistance
2. Improved estimation of drugs needs, purchasing, distribution and monitoring
3. Improved training of staff on treatment of TB
4. Reduced costs of anti-TB treatment
5. Improved drugs supply when patients move from one area to another

6.3.2 Standardised treatment regimens

The standard code for TB treatment regimens uses an abbreviation for each anti-TB drug. The number in front of each phase represents the duration of that phase in months. Letters in brackets indicate fixed-dose combination tablets. The only recommended schedule in Botswana is daily dosing.

Example 1: 2HRZE/4HR

The *initial phase* is 2HRZE. The duration of the initial phase is 2 months with daily treatment with isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E), given as single formulation tablets.
The *continuation phase* is 4HR. The duration of the continuation phase is four months with daily treatment with isoniazid and rifampicin, given as single formulation tablets.

Example 2: 2 (HRZE)/4(HR)

The *initial phase* is 2(HRZE). The duration of the initial phase is 2 months with daily treatment with isoniazid (H), rifampicin (R) and pyrazinamide (Z) and ethambutol (E), given in four-in-one fixed-dose combination tablets.
The *continuation phase* is 4(HR). The duration of the continuation phase is four months with daily treatment with isoniazid and rifampicin, given as two-in-one fixed-dose combination tablets.

Table 6 shows the recommended treatment regimens for each diagnostic category.

Table 6.3: Recommended Treatment Regimens in Botswana

TB Diagnostic Category	TB Patients	TB Treatment Regimens	
		Initial Phase (daily)[a]	Continuation Phase (daily)
I	All new adult cases of TB regardless of site, bacteriology or severity of disease, and severe TB in children	2HRZE[b]	4HR
II	Previously treated cases of TB[c]: - Retreatment after relapse - Retreatment after default - Retreatment after treatment failure	2 HRZES/1 HRZE	5 HRE
III	Less severe cases of TB in children	2HRZ	4HR
IV	Chronic and MDR-TB cases (still sputum-positive after supervised re-treatment)[d]	Specially-designed standardised or individualized regimens are recommended	

a. Direct observation of drug intake is always required in treatment that includes rifampicin
b. Streptomycin is an alternative to ethambutol. In meningeal TB, replace ethambutol with streptomycin
c. Whenever possible, perform drug sensitivity testing before prescribing Category II treatment. Patients with proven MDR-TB should use Category IV regimens (see Chapter 7)
d. Consider early culture and sensitivity testing in contacts of patients with culture-proven MDR-TB

6.3.3 Category I: *For all new cases of tuberculosis in **adults**, regardless of site, bacteriology or severity of disease*

2HRZE + 4HR

Duration of treatment course: 6 months

1. **Intensive phase:** 2HRZE: (i.e., isoniazid, rifampicin, ethambutol and pyrazinamide) given daily for two months.

In smear-positive cases, if the sputum is still positive at the end of two months, continue the intensive phase for one more month and then start the continuation phase at the end of three months, irrespective of sputum status. Submit an additional specimen for culture and DST.

2. **Continuation phase:** 4HR

Because the regimen contains rifampicin, give the continuation phase under DOT. If the sputum smear result is positive at 5 – 6 months, stop treatment, submit sputum specimens for culture and susceptibility testing and commence the retreatment regimen. Prolong the continuation phase to six months, i.e., 2HRZE/6HR, for patients with tuberculous meningitis or pericarditis, disseminated or spinal disease with neurological complications.

For children with severe disease, e.g., TB meningitis or disseminated TB, use Category I regimen. For children with less severe disease, use Category III regimen.

6.3.4 **Category II:** *For smear-positive or culture positive retreatment cases (after relapse, default or treatment failure)*[2]

These patients are at risk of having drug-resistant strains. Patients with pulmonary TB in Category II should submit a pre-treatment sputum specimen for culture and drug susceptibility testing to ensure the most effective treatment regimen. Because of the increased risk of multidrug-resistance, ensure DOT for the full treatment course.

Thoroughly investigate children with treatment failure or relapse to find the most likely cause, including cultures and drug susceptibility testing where possible. Failure of category I regimen is most commonly due to non-adherence with treatment. Culture and drug susceptibility testing are useful in preventing the addition of a single drug to a failing regimen.

Manage children who fail Category I treatment with either a Category II or a Category IV regimen, depending on the risk of MDR-TB (resistance to at least isoniazid and rifampicin).

2SHRZE + 1HRZE + 5HRE (directly observed)

Duration of treatment course: 8 months

1. **Intensive phase: 2SHRZE/1HRZE**

Isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin for the first two months, followed by isoniazid, rifampicin, ethambutol and pyrazinamide for another month (under direct observation)

If at the end of the initial three months the sputum is smear negative, start the continuation phase. If the smear is positive at three months, continue with the four drugs for a further month. If the patient is still smear positive after four months of treatment, stop all drugs for three days and send

[2]Smear-negative pulmonary and extrapulmonary cases may also be relapses, failures, returns after default or chronic cases. However, this should be a rare event and should be supported by pathological or bacteriological evidence (culture).

a sputum specimen for culture and sensitivity testing. The patient should then start the continuation phase while awaiting results. Further extension of the intensive phase will not increase the chances of cure.

2. **Continuation phase: 5HRE**

Five months of daily isoniazid, rifampicin and ethambutol (under direct observation)

Patients who remain smear positive after the end of a fully supervised continuation phase will derive no benefit from another retreatment regimen, and should be classified as chronic cases and referred for specialist care.

6.3.5 **Category III:** *For less severe cases of tuberculosis in* ***children***

2HRZ + 4HR

Duration of treatment course: 6 months

1. **Intensive phase:** 2HRZ: (i.e., isoniazid, rifampicin and pyrazinamide) given daily for two months.

This regimen contains no ethambutol. In smear-positive cases, if the sputum is still positive at the end of two months, continue the intensive phase for an additional month and then start the continuation phase at the end of three months irrespective of sputum status.

2. **Continuation phase:** 4HR

Ensure DOT for this rifampicin-containing phase.

6.3.6 **Category IV:** *For all patients who remain or become smear positive after completing a fully supervised retreatment regimen.*

This category is for chronic and MDR-TB cases, and consists of specially designed standardised or individualized regimens, as described in Chapter 7.

6.5 Treatment regimens in special cases

6.5.1 HIV-infected TB patients

Case definitions and anti-TB treatment regimens are the same for HIV-positive and HIV-negative TB patients, as are drug dosages in mg/kg. It is important to remember that HIV-positive children often have a gravely ill parent, who may be unable to care for the child. Therefore, HCWs should be aware of a child's family circumstances for optimum TB treatment.

In HIV-infected patients with confirmed or presumptive TB, initiation of TB treatment is the priority. The clinician should decide the optimal timing for initiation of ART during TB treatment, as described below. The decision on when to start ART after starting TB treatment involves a balance between the 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.

Response of HIV-positive patients to anti-TB Treatment:

- HIV-positive patients who complete standardised short-course chemotherapy show the same clinical, microbiological and radiological response as HIV-negative patients, though on average, they gain less weight.
- TB patients with advanced HIV disease have a much higher case-fatality during and after anti-TB treatment compared to HIV-negative patients, especially if diagnosed with smear-negative TB.
- Excess deaths in HIV positive TB patients are commonly due to TB and concomitant HIV-related conditions such as septicaemia, diarrhoea, pneumonia, Kaposi's Sarcoma (KS), cryptococcal meningitis, etc
- Relapse of TB after completion of short-course chemotherapy may be higher in HIV-positive patients.

Assess the eligibility of all HIV-infected TB patients for antiretroviral therapy (ART) during anti-TB treatment and ensure that all eligible TB patients can access ARVs. The determinants for starting ART include the level of CD4+ cell counts and assessment of the clinical stage of HIV. Start anti-TB treatment immediately and give cotrimoxazole preventative therapy to all patients with dual TB and HIV infection.

Patients on anti-TB treatment who require ART:

For many patients, it is possible to defer ART until the end of the intensive or even the continuation phase of treatment. In all cases, treat active TB immediately because of the high risk of disease progression and death. The national ART recommendations for the timing of initiation of ART in HIV-infected persons on anti-TB treatment are:

- Within 1 – 2 weeks if CD4 count is <100/mm^3 (high risk of HIV disease progression and death during anti-TB treatment)
- Within 2 – 4 weeks if CD4 count is 100 – 200/mm^3
- At the end of TB treatment if CD4 is >200/mm^3 (and remains above 200/mm^3).

Patients on ART who develop active TB disease:

Patients on first line ART can continue with the first line anti-TB treatment regimen, with normal ARV doses. Patients on second or third line ART regimens should receive anti-TB treatment under the care of a specialist physician.

Patients on second or third line ART:

Doses and/or regimens may need to be changed. Discuss with specialist or refer before starting anti-TB treatment.

TB Immune Reconstitution Inflammatory Syndrome (TB-IRIS):

TB-IRIS can present as an "unmasking" of active TB by ART in asymptomatic or minimally symptomatic patients due to the recovery of the immune system soon after ART initiation. The second

presentation is paradoxical TB-IRIS, when patients on anti-TB treatment prior to starting ART develop signs and symptoms of deteriorating TB, such as enlargement of lymph nodes, cold abscesses or effusions, or worsening of pulmonary infiltrates, after ART initiation. There may be life-threatening complications but death is rare.

Paradoxical TB-IRIS occurs in 8-45% of TB patients who commence ART, usually after a median interval of 2-4 weeks after ART initiation. The main risk factors are a shorter interval between the initiation of anti-TB treatment and ART, the presence of disseminated TB, a combination of low baseline CD4 and high baseline VL, and a vigorous CD4/VL response to ART.

Table 6.4: Paradoxical TB-IRIS

Case definition	Major clinical criteria	Minor clinical criteria
• Diagnosis of HIV and TB according to WHO case definitions • Improvement or stabilisation of TB with anti-TB treatment • Documented response to ART (>1 log decrease in HIV RNA) • Onset within 3 months (up to 6) of starting/changing ART • Exclusion of alternative causes, e.g., failed anti-TB treatment, other opportunistic infections, neoplasms, drug toxicity or reaction, complete non-adherence to ART	• New or enlarging lymph nodes, cold abscesses or other focal tissue involvement • New or worsening radiological features of TB • Breakthrough TB meningitis or new or enlarging focal CNS lesion • New or worsening serositis	• Constitutional symptoms, e.g., fever, night sweats • Respiratory symptoms, e.g., cough, dyspnoea, stridor • Abdominal pain and/or hepatomegaly • Resolution of clinical and/or radiological findings without change in anti-TB treatment
One major OR **two minor** clinical criteria = **Paradoxical TB-IRIS**		

Treatment of paradoxical TB-IRIS

Many cases of TB-IRIS are self–limiting. Therefore, continue anti-TB treatment in such patients. The role of steroids and non-steroidal anti-inflammatory drugs in TB-IRIS has not been clearly defined. The potential hazards of steroids such as the development of Kaposi's sarcoma, reactivation of herpes virus infections and other steroid side effects must be balanced against the severity of the TB-IRIS. If in doubt, refer the patient to the next level of care.

6.5.2 Pregnant women

Ask every woman of childbearing age whether she is pregnant before commencing anti-TB treatment. Most anti-TB drugs are safe in pregnancy but do not give streptomycin because it is ototoxic to the foetus. The successful outcome of pregnancy greatly depends on the successful completion of TB treatment.

6.5.3 Breastfeeding women

All first-line anti-TB drugs are safe for use in breastfeeding women as their concentration in breast milk is relative low. If the mother has smear-positive TB, give the baby INH 5mg/kg for 6 months, followed by BCG vaccination. As far as possible, do not separate the mother and child for the entire duration of treatment.

6.5.4 Women using hormonal forms of contraception

Rifampicin reduces the efficacy of the contraceptive pill. A female TB patient wishing to prevent pregnancy while on rifampicin can use a high-dose (50 mcg) oestrogen pill or non-hormonal contraceptive methods such as the condom.

6.5.5 Patients with liver disorders

Provided there is no clinical evidence of chronic liver disease, anti-TB treatment is safe in patients with hepatitis virus carriage, a history of acute hepatitis or excessive alcohol consumption. In the last case, strongly advise the patient to reduce or stop drinking alcohol.

6.5.6 Patients with established chronic liver disease

Do not give pyrazinamide to patients with chronic liver disease. INH, rifampicin, ethambutol and streptomycin are safe in these patients.

6.5.7 Acute hepatitis (e.g., acute viral hepatitis)

It is rare to get concomitant TB and acute hepatitis unrelated to TB. The decision whether to stop or continue anti-TB treatment requires good clinical judgment. The safest option in acute hepatitis not due to TB is to give streptomycin and ethambutol until the hepatitis has resolved (for a maximum of three months) followed by a continuation phase of INH and rifampicin for 6 months.

6.5.8 Patients with renal failure

The hepatobiliary system and general metabolism are responsible for the breakdown of isoniazid, rifampicin and pyrazinamide into non-toxic compounds. The kidneys excrete streptomycin and ethambutol. Avoid streptomycin and ethambutol unless specialist care is available. The safest regimen in renal failure is 2HRZ/4HR. In severe renal failure, give pyridoxine to prevent INH-induced peripheral neuropathy.

6.6 Cotrimoxazole Preventative Therapy

Cotrimoxazole (trimethoprim [TMP]/Sulphamethoxazole [SMX]) prevents several secondary bacterial and parasitic infections, particularly *Pneumocystis jiroveci* pneumonia (also known as PCP) and toxoplasmosis, in adults and children living with HIV/AIDS. The reduction in mortality ranges from 29-46%. Cotrimoxazole is also active against pneumococcus, salmonella, nocardia and malaria. Cotrimoxazole preventative therapy (CPT) reduces hospitalisation and mortality among HIV-positive TB patients.

All HIV-positive TB patients should receive CPT regardless of the CD4 count, for at least the duration of anti-TB treatment.

Table 6.5: Recommended Cotrimoxazole Doses

Age (weight) of child	Recommended daily dose	Suspension (5ml syrup = 200mg/40mg)	Child tablet (100mg/20mg)	Single strength adult tablet (400mg/80mg)	Double strength adult tablet (800mg/160mg)
6 wks – 6 mo (<5kg)	100mg sulfamethoxazole/ 20mg trimethoprim	2.5ml	One tablet	-	-
6 mo – 5 yr (5-15kg)	200mg sulfamethoxazole/ 40mg trimethoprim	5ml	Two tablets	Half tablet	-
6 yr – Post - pubertal	400mg sulfamethoxazole/ 80mg trimethoprim	10ml	Four tablets	One tablet	Half tablet
Post-pubertal Adolescents Adults	800mg sulfamethoxazole/ 160mg trimethoprim	-	-	Two tablets	One tablet

Extend CPT beyond the end of anti-TB treatment if the CD4 cell count is less than 200 cells/mm^3.

6.7 Role of adjuvant steroid therapy

Corticosteroids may be beneficial in the management of tuberculous meningitis and pericarditis, irrespective of the HIV status of the patient, where they can increase survival and decrease morbidity.

Indications for steroids

- TB meningitis (decreased consciousness, neurological deficits, and spinal block)
- TB pericarditis (with effusion or constriction)
- Massive lymphadenopathy with pressure effects such as airway obstruction
- Severe hypersensitivity reactions to anti-TB drugs
- More rarely: hypo-adrenalism; renal tract TB (to prevent ureteric scarring); TB laryngitis with life-threatening airway obstruction

The drug most frequently used is prednisolone 2 mg/kg/day (maximum 60mg/day) for four weeks. Taper off the dose over several weeks before stopping.

Table 6.6: Recommended doses of adjuvant steroid therapy

Indication	Prednisolone treatment
TB meningitis	60 mg/d for 4 weeks then taper off over several weeks
TB pericarditis	60 mg/d for 4 weeks, then 30 mg/d for 4 weeks then taper off over several weeks

6.8 Side effects of anti-TB-drugs

Patients need to be educated about the possibility of side effects, and encouraged to report any unusual sign or symptom that might occur after start of anti-TB-treatment, as side effects are common with anti-TB drugs (see Annex 10). Although most side effects are minor, 3-6% of patients develop severe side effects that may warrant stopping the offending drug or changing the regimen. All health workers involved in TB treatment should know the most common side effects of the anti-TB-drugs. HIV-infected patients have a higher incidence of side effects than HIV-uninfected TB patients do. Second-line anti-TB drugs have more side effects than first-line drugs.

Desensitisation schedule:

If a major side effect occurs during treatment and anti-TB drugs are the most likely cause, stop all drugs, unless there is strong evidence that a single offending drug is responsible, such as hearing loss or severe dizziness due to streptomycin. When symptoms have subsided, wait another two weeks and reintroduce the TB drugs, as described below.

Table 6.7: Schedule for reintroduction of anti-TB drugs

Day	Drug and dose
1	INH 25 mg
2	INH 50 mg
3	INH 100 mg
4	INH 200 mg
5	INH 300 mg*
6	INH 300 mg + R 150 mg
7	INH 300 mg + R 300 mg
8	INH 300 mg + R 450 mg
9	INH 300 mg + R 600 mg*
10	INH 300 mg + R 600 mg + E 400 mg
11	INH 300 mg + R 600 mg + E 800 mg
12	INH 300 mg + R 600 mg + E 1200 mg*
13	INH 300 mg + R 600 mg + E 1200 mg + Z 500 mg
14	INH 300 mg + R 600 mg + E 1200 mg + Z 1000 mg
15	INH 300 mg + R 600 mg + E 1200 mg + Z 1500 mg
16	INH 300 mg + R 600 mg + E 1200 mg + Z 2000 mg*

*All doses are weight-dependent and the highest dose might not be indicated for low-weight patients or children.

If a patient is on fixed-drug combination (FDC) pills, stop the FDC and use single-drug formulations for the reintroduction of the drugs to identify the offending drug.

6.9 Drug interactions

Rifampicin has interactions with a number of drugs which are metabolised in the liver and lowers the serum concentrations of a number of drugs such as antiretroviral drugs (ARVs), hormonal contraceptives, anti-epileptic drugs (e.g., phenytoin, carbamazepine), steroids, oral hypoglycaemic agents, oral anticoagulants (e.g., warfarin) and digitalis glycosides. Antacids (e.g. Aluminium

hydroxide) may significantly decrease the absorption of rifampicin. Do not give simultaneously with this drug.

6.9.1 Rifampicin and ARVs

Rifampicin increases the metabolism of protease inhibitors and non-nucleoside reverse transcriptase inhibitors, lowering the levels of nevirapine and efavirenz. Protease inhibitors such as ritonavir increase the level of rifampicin, further complicating concomitant anti-TB and anti-HIV treatment.

6.9.2 Rifampicin and hormonal contraceptives

Rifampicin increases the metabolism of most hormonal contraceptives, as shown in the table below.

Table 6.8: Interaction between rifampicin and hormonal contraceptives

Contraceptive	Effects	What to do
Oestrogen/progesterone combination pills	Increased metabolism and lower concentration of hormones	Advise use of dual protection (condoms) while on rifampicin. Alternatively: High-dose oestrogen pills will probably still be effective
Progesterone-only pills	Increased metabolism of progesterone	Use dual protection
Depo-Provera	Probably little effect on metabolism	Continue Depo-Provera
Hormonal implant (Norplant)	Probably some effect on metabolism	Use dual protection

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CHAPTER 7: DRUG RESISTANT TUBERCULOSIS

7.1 Background

The incidence of drug-resistant TB has increased globally since the introduction of the first drug treatment for TB in 1943. Three studies performed to establish the level of drug resistance in Botswana indicate that drug-resistant TB is a growing problem. The prevalence of MDR-TB was 0.2% among new TB cases and 6.1% in retreatment cases in a survey conducted from 1994-1997, rising to 0.6% and 9.0% respectively in 1999 and to 0.8% and 10.4% respectively in 2002. These data represent slight but statistically significant increases.

Drug-resistance may only be diagnosed through culture and drug susceptibility testing. Any patient in whom chronic TB or drug-resistant TB is diagnosed requiring treatment with second-line drugs falls under WHO diagnostic Category IV and will need specialised regimens. In Botswana, only specialists trained in the care of MDR-TB patients and designated by the BNTP are permitted to initiate treatment and make management decisions for MDR patients. Non-specialists are required to refer all MDR patients, once identified through drug susceptibility testing, to the appropriate specialists at Princess Marina or Nyangabgwe Hospitals.

7.2 Definitions

Primary resistance and acquired resistance[3]: Primary resistance refers to infection by isolates of *M. tuberculosis* that are confirmed to be resistant in vitro to one or more anti- TB drugs before the initiation of any anti-TB treatment. Acquired resistance refers to the development of in vitro resistance to anti-TB drugs during anti-TB therapy.

Confirmed mono-resistance: Tuberculosis in patients whose infecting isolates of *M. tuberculosis* are confirmed to be resistant in vitro to one first line anti- tuberculosis drug

Confirmed poly-resistance: Tuberculosis in patients whose infecting isolates are resistant in vitro to two or more first line anti- tuberculosis 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.

Extensively drug resistant TB (XDR-TB): Tuberculosis resistant to the two most potent anti-tuberculosis drugs (INH and rifampicin) and to a fluoroquinolone (ciprofloxacin, ofloxacin, etc.) and one or more of the following injectable drugs: kanamycin, amikacin and capreomycin.

Culture conversion: is defined as two consecutive negative cultures taken at least 30 days apart in patients with initially culture-positive TB.

[3]Primary" and "acquired" drug resistance cannot be distinguished under programmatic conditions in most countries. Any resistance identified by drug susceptibility testing (DST) before the start of the patient's first anti-tuberculosis treatment is primary resistance. If new resistance is then found in the same patient when DST is later repeated and genetic testing confirms that it is the same strain, only then can it be concluded that the strain has acquired resistance.

7.3 Causes of drug resistant TB

Microbial resistance is caused by genetic mutation that makes a drug ineffective against the mutant bacilli. Although its causes are microbial, clinical and programmatic, drug resistance is a man-made phenomenon. An inadequate or poorly administered treatment regimen allows a drug resistant strain to become the dominant strain in a patient infected with TB. Exposure to a single drug, whether because of poor adherence to treatment, inappropriate prescription, irregular drug supply or poor drug quality, suppresses the growth of bacilli that are susceptible to that drug but permits multiplication of pre-existing drug resistant mutants. Subsequent transmission of such bacilli to other persons may lead to a disease that is drug resistant from the outset (primary resistance), which can be a significant source of new drug-resistant cases in the general population.

There is a link between poor programme performance, or insufficient coverage of a good programme, and drug resistance. Previously treated cases, worldwide, are more likely to be drug-resistant and to have resistance to more drugs than untreated patients.

7.4 Diagnosis of MDR-TB

MDR TB is diagnosed through culture and sensitivity of sputum collected from patients suspected to have drug resistant TB. Routine drug susceptibility testing (DST) is indicated in TB patients with risk factors for developing drug resistant TB such as:

1. Failure of re-treatment regimen and chronic TB cases. These patients have the highest number of MDR-TB rates of any group, often exceeding 80%.
2. Exposure to a known MDR-TB case: close contacts of MDR-TB patients have high rates of MDR-TB.
3. Failure of first-line regimen: These are patients who are sputum smear-positive at 5 months or later during the course of treatment.
4. Patients who remain sputum smear-positive at 2 or 3 months of short course chemotherapy, or patients who were initially smear-negative who become smear-positive at the end of the intensive phase.
5. Retreatment after relapse, treatment failure or treatment default
6. Exposure in institutions that have MDR-TB outbreaks or a high MDR-TB prevalence.
7. Residence in areas with high prevalence of MDR-TB.
8. History of using anti-TB drugs of poor or unknown quality.

It must be emphasized that confirmation of the diagnosis of MDR-TB can only be made by culture and sensitivity of sputum specimens. Chronic cases in particular have a very high likelihood of having multidrug-resistant or extensive-drug resistant tuberculosis and should be referred to specialists as soon as possible. Although smear negative PTB and extra-pulmonary cases may also be treatment failures, relapses or chronic cases, this is a rare event and should be supported by pathological and/or bacteriological evidence.

7.5 Pre-treatment evaluation and infection control

The required initial pre-treatment clinical investigation includes a thorough medical history and physical examination. The recommended initial laboratory evaluations include an HIV test, sputum

smear microscopy and culture, DST, chest x-ray, serum creatinine, serum potassium, thyroid stimulating hormone, liver enzymes and a pregnancy test.

The initial evaluation establishes a baseline and may identify patients who are at increased risk for adverse effects or poor outcomes. Monitoring of treatment and management of adverse effects may have to be more intensive in patients with pre-existing conditions or conditions identified at the initial evaluation, such as diabetes mellitus, renal insufficiency, acute or chronic liver disease, thyroid disease, mental illness, drug or alcohol dependency, HIV infection, pregnancy, lactation and others. The management of MDR-TB when these conditions exist is beyond the scope of this manual. Specialists should manage such patients. Discuss methods to avoid pregnancy during treatment in women of childbearing age.

7.6 Hospitalisation and ambulatory treatment of MDR-TB patients

MDR-TB treatment can be given as in-patient care, clinic-based treatment or as community-based care. Whichever method is used, effective management of MDR-TB depends on an uninterrupted supply of quality drugs provided to patients free of charge through a reliable network of educated providers. Therefore, all centres initiating MDR-TB treatment should communicate all relevant patient information to the receiving unit or district, ensuring that second-line drugs are available at the peripheral level before discharging MDR-TB patients. Refer immediately to the MDR-TB specialist any MDR-TB patient whose condition worsens or who needs any medication changes.

The choice between hospitalisation and ambulatory treatment depends on many factors, such as severity of disease, availability of hospital beds, adequacy of infection control measures, and availability of trained HCWs in hospitals and clinics to administer treatment and manage adverse drug reactions. Other factors include the availability of a social support network to facilitate adherence to ambulatory treatment and the presence of other clinical or social conditions in patients. Home-based care provided by trained lay and community health workers can achieve comparable results and, in theory, may result in decreased nosocomial spread of MDR-TB.

In each setting, care should be delivered by a multidisciplinary team of providers, including MDR-TB specialists, nurses, TB coordinators, social workers and community health workers or volunteers, each with roles and responsibilities that will vary depending on the needs and resources available in specific settings. Health education to patients and family and community is essential.

7.7 Essential assessments before designing a treatment strategy

Treatment strategies for MDR-TB depend on data obtained from national drug resistance surveys and the availability and use of anti-tuberculosis drugs in the country. The prevalence of drug resistance in new patients as well as in different groups of re-treatment cases (failure, relapse, return after default and other cases) varies, and thus a complete and accurate treatment history is imperative.

It is essential to determine which second-line drugs a patient may have been exposed to prior to diagnosis of the current episode. Some second-line drugs may have been used only rarely and will likely be effective in treatment regimens for drug-resistant TB, while others may have been used extensively (e.g., fluoroquinolones) and will therefore have a higher probability of ineffectiveness in patients with resistant strains.

7.8 Treatment of drug-resistant TB

7.8.1 Mono- and poly-resistant TB other than MDR

Treatment of patients infected with mono- or poly-resistant strains using standardised short-course chemotherapy has been associated with increased risk of treatment failure and further acquired resistance, including the development of MDR-TB. While the likelihood of poor outcomes is relatively low with many types of mono- and poly-resistance (i.e. the majority of patients with mono- or poly-resistant strains will be cured with short-course chemotherapy), providers may choose alternative regimens based on DST patterns as described below. Always submit sputum for culture and drug sensitivity testing if there is any suspicion of drug resistance.

7.8.2 Treatment of patients with mono- and poly-resistant strains

Table 7.1 gives suggested regimens for different DST patterns. When using this table, it is essential to consider whether resistance has been acquired to any of the drugs that will be used in the recommended regimen. Pyrazinamide drug susceptibility is not performed in Botswana. Therefore, the regimens in Table 7.1 assume that there is PZA resistance. However, some clinicians would add PZA to those regimens because a significant percentage of patients could benefit from the drug.

Table 7.1: Suggested regimens for mono- and poly-drug resistance (when further acquired resistance is not a factor and laboratory results are highly reliable)

DRUG RESISTANCE PATTERN	SUGGESTED REGIMEN	MINIMUM TREATMENT DURATION (months)	COMMENTS
H (± S)	R, Z, E	6–9	A fluoroquinolone may strengthen the regimen for patients with extensive disease.
H and Z	R, E, fluoroquinolones	9–12	A longer duration of treatment should be used for patients with extensive disease.
H and E	R, Z, fluoroquinolones	9–12	A longer duration of treatment should be used for patients with extensive disease.
R	H, E, fluoroquinolones + at least 2 months of Z	12–18	An injectable agent may strengthen the regimen for patients with extensive disease.
R and E (± S)	H, Z, fluoroquinolones + injectable agent for at least the first 2-3 months	18	A longer course (6 months) of the injectable agent may strengthen the regimen for patients with extensive disease.
R and Z (± S)	H, E, fluoroquinolones + injectable agent for at least the first 2-3 months	18	A longer course (6 months) of the injectable agent may strengthen the regimen for patients with extensive disease.
H, E, Z (± S)	R, fluoroquinolones +	18	A longer course (6 months) of the

H = isoniazid; R = rifampicin; E = ethambutol; Z = pyrazinamide; S = streptomycin
Adapted from *Drug-resistant tuberculosis: a survival guide for clinicians*

- **Development of further resistance.** Further resistance should be suspected if the patient was on the functional equivalent of only one drug for a significant period (usually considered as one month or more, but even periods of less than one month on inadequate therapy can lead to resistance). Sometimes resistance develops if the patient was on the functional equivalent of two drugs, depending on the drugs concerned. For example, pyrazinamide is not considered a good companion drug to prevent resistance. If a patient was receiving *functionally* only rifampicin and pyrazinamide in the initial phase (i.e., s/he was resistant to isoniazid and ethambutol), resistance to rifampicin may have developed during the initial phase. Thus, it is crucial to consider which *functional* drugs the patient received between the time of DST specimen collection and the time of the new regimen design (i.e. consider whether resistance has developed to any of the functional drugs).
- **DST results**. The DST result that prompts a change in treatment may not accurately reflect the bacterial population at the time it is reported since it reflects the bacterial population at the time the sputum was collected. The regimens in Table 7.1 are based on the assumption that the pattern of drug resistance has not changed during this interval. It is also important to note that a high level of confidence in the laboratory is needed for effective use of Table 7.1.

7.8.3 Treatment strategies for MDR TB

The following terms describe the treatment strategies for MDR-TB:

- **Standardised treatment:** Regimens are designed according to representative DRS data in well-defined patient populations. All patients in a patient group or category receive the same regimen. However, suspected MDR-TB should always be confirmed by DST results.

- **Standardised treatment followed by individualised treatment:** Initially, all patients in a certain group receive the same regimen based on DST survey data from representative populations. The regimen is then adjusted when individual DST results become available

- **Empirical treatment followed by individualised treatment:** Each regimen is individually designed based on patient history of anti-tuberculosis treatment. The regimen is then adjusted when individual DST results become available

The management of MDR-TB patients requires purpose-designed treatment cards and registers.

7.8.4 Classes of anti-tuberculosis drugs

Anti-tuberculosis drugs are classified as first- and second-line drugs, with isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin being the primary first-line drugs. These guidelines often refer to this classification but also use a group system based on efficacy, experience of use and drug class. These groups are referred to in the following sections and are very useful for the design of treatment regimens (see Table A9.1 in Annex 9).

7.9 Regimen design

The following basic principles are involved in any regimen design:

- Regimens should be based on the history of drugs taken by the patient.
- Consider the drugs and regimens commonly used in Botswana and the prevalence of resistance to first-line and second-line drugs when designing a regimen
- Regimens should consist of at least four drugs with either certain, or almost certain, effectiveness. If the evidence about the effectiveness of a drug is unclear, the drug can be included in the regimen but it should not be depended upon for success. Often, more than four drugs may be started if the susceptibility pattern is unknown, if effectiveness is questionable for an agent(s) or if extensive, bilateral pulmonary disease is present.
- Drugs are administered seven days a week. When possible, pyrazinamide, ethambutol and fluoroquinolones should be given once per day because the high peaks attained in once-a-day dosing may be more efficacious. Once-a-day dosing is permitted for other second-line drugs, depending on patient tolerance. However, ethionamide/prothionamide, cycloserine and PAS have traditionally been given in split doses during the day.
- The drug dosage should be determined by weight, as shown in Table A9.1.
- An injectable agent (an aminoglycoside or capreomycin) is used for a minimum of 6 months.
- Treatment is for a minimum duration of 18 months past culture conversion.
- Each dose is given as DOT throughout the treatment. A treatment card is marked for each observed dose.
- DST should be used to guide therapy. It should be noted that the full assessment of DST for some first-line and most of the second-line drugs in terms of reliability and clinical value has not been determined. DST does not predict the effectiveness or ineffectiveness of a drug with complete certainty. Nonetheless, regimens should include at least four drugs that are highly likely to be susceptible, based on DST and/or the drug history of the patient.
- Pyrazinamide can be used for the entire treatment if it is judged effective. The intensive phase should extend a minimum of four to six months following culture conversion, defined as two consecutive negative monthly cultures. Many MDR-TB patients have chronically inflamed lungs that theoretically produce the acidic environment in which pyrazinamide is active.
- Early MDR-TB detection and prompt initiation of treatment are important factors in achieving successful outcomes.

7.10 Standardised treatment regimens

A standardised Category IV treatment regimen has been developed for Botswana that may be used until the DST results are available, as shown in Table 7.2 below.

Table 7.2: Standardised Category IV treatment regimen for MDR-TB in Botswana

Treatment Phase	Recommended dose (mg/body weight/day		
	<50kg	50 – 65kg	>65kg
Intensive Phase (minimum 6 months, or 4 months post- culture conversion)			

Amikacin	750	1000	1000
Ethionamide	500	750	750
PZA	1000	1500	1500
Ciprofloxacin	1000	1500	1500
Continuation Phase (minimum 18 months post-intensive phase)			
Ethionamide	500	750	750
Ciprofloxacin	1000	1500	1500

Use ethambutol in both phases of treatment if the strains are still susceptible
If ethambutol resistance is detected, use cycloserine in both phases of treatment

It is strongly recommended to confirm MDR-TB by DST in all patients enrolled on a standardised Category IV regimen. Otherwise, misclassification of patients can occur, which will either deny isoniazid and rifampicin to those patients who would benefit from these drugs, or unnecessarily expose others to potentially toxic first- or second-line drugs. To ensure a standardised regimen that will treat the vast majority of patients with four effective drugs, it is often necessary to use five or six drugs to cover all possible patterns of resistance. An injectable agent and a fluoroquinolone form the core of the regimen.

7.11 Individualized treatment regimens based on DST

Standardised treatment regimens are commonly used in specific groups of patients while DST is pending, as described above. The design of an individualized regimen differs from that of standardised treatment regimens in that it uses the resistance pattern of the infecting strain of the individual patient as another source of data, in addition to the patient's treatment history and the prevailing resistance patterns in the community. The method for designing the individualized regimen is described in Table A9.2 in Annex 9.

Standardised treatment regimens are strongly recommended since most DST methods have a turnaround time of several months. This helps to avoid clinical deterioration and prevent transmission to contacts while waiting for the DST results. Note however that is some cases it may be prudent to defer Category IV treatment while waiting for the DST results, for example in patients with chronic disease who have been treated several times with second-line drugs, as long as the patient is clinically stable and **appropriate infection control** measures are in place.

A detailed clinical history can help to indicate which drugs are likely to be ineffective. The probability of acquired resistance to a drug increases with the length of time it has been administered. If a history of previous anti-tuberculosis drug use suggests that a drug is likely to be ineffective because of resistance, this drug should not be relied upon as one of the four core drugs in the regimen even if the strain is susceptible in the laboratory. However, if the strain is resistant to a drug in the laboratory, but the patient has never taken it and resistance to it is extremely uncommon in the community, this may be a case of a laboratory error or a result of the limited specificity of DST for some second-line drugs.

A patient may receive months of a standardised regimen before DST results return from the laboratory. The possibility of further acquired resistance during this time must be considered. If there

is a high probability of acquired resistance to a drug after the specimen for DST was collected, this drug should not be counted as one of the four drugs in the core regimen.

7.12 Duration of administration of the injectable agent (intensive phase)

The recommended duration of administration of the injectable agent, or the intensive phase, is guided by culture conversion. The injectable agent should be given for at least six months and should be continued for at least four months after the patient first becomes and remains culture negative.

An individualized approach that takes account of the results of cultures, smears, X-rays and the patient's clinical status may also help in deciding whether to continue an injectable agent longer than the recommended period. This would apply particularly in the case of patients for whom the susceptibility pattern is unknown, the effectiveness of a drug(s) is uncertain or extensive or bilateral pulmonary disease is present. Intermittent therapy with the injectable agent (thrice weekly after an initial period of 2–3 months of daily therapy) can also be considered for patients in whom the injectable agent has been used for a prolonged period and when the risk of toxicity increases.

If the patient has been on an empirical regimen containing five or six drugs, discontinuation of drugs other than the injectable agent can be considered once the DST results are available and provided the patient continues with at least three of the most potent agents.

7.13 Duration of treatment

The recommended duration of treatment is guided by culture conversion. Treatment should continue for at least 18 months after culture conversion. Extension to 24 months may be indicated in patients defined as "chronic cases" with extensive pulmonary damage.

7.14 Extrapulmonary MDR-TB and MDR-TB treatment

The treatment strategy is the same for patients with pulmonary and extrapulmonary MDR-TB. If the patient has symptoms suggestive of central nervous system involvement and is infected with MDR-TB, the regimen should use drugs that have adequate penetration into the central nervous system (CNS). Pyrazinamide, ethionamide/prothionamide and cycloserine have good CNS penetration; kanamycin, amikacin and capreomycin penetrate effectively only in the presence of meningeal inflammation; PAS and ethambutol have poor or no penetration.

7.15 Adjunctive therapies in MDR-TB treatment

A number of other measures can be used to lessen adverse effects and morbidity as well as improve MDR-TB treatment outcomes. These include corticosteroid therapy (described in Chapter 6) and nutritional support.

Nutritional support

In addition to causing malnutrition, MDR-TB can be exacerbated by poor nutritional status, low body mass index and severe anaemia. Without nutritional support, patients can become enmeshed in a vicious cycle of malnutrition and disease, especially those already suffering from baseline hunger. Second-line drugs may also further decrease the appetite, making adequate nutrition a greater challenge. Nutritional support can take the form of providing free staple foods, and whenever possible should include a source of protein.
Vitamin B6 (pyridoxine) should also be given to all patients receiving cycloserine or terizidone to prevent neurological adverse effects. Vitamin (especially vitamin A) and mineral supplements can be given in areas where a high proportion of the patients have deficiencies to them. If minerals are given (zinc, iron, calcium, etc.), they should be administered at a different time from the fluoroquinolones, as they can interfere with the absorption of these drugs.

7.16 Monitoring of MDR TB treatment

Patients should be seen by a clinician on a monthly basis, and monitored closely for signs of treatment failure through regular history taking and physical examination. Symptoms of TB such as cough, fever weight loss and loss of appetite generally diminish during the first months of treatment, and should be monitored by HCWs. Recurrence of TB symptoms after sputum conversion may be the first sign of treatment failure. For children, weight and height should be monitored regularly to ensure that they are growing normally. A normal growth rate should resume after the first months of treatment.

Sputum smears and culture should be monitored monthly (defined as 30 days apart) throughout treatment. Even after conversion, monthly smears and cultures are recommended. For patients who remain culture positive, DST can be repeated.

The most important objective evidence of improvement is conversion of sputum smear and culture to negative. Several studies have found that the time to culture conversion for patients on an effective regimen is approximately two months, although this may vary depending on the severity of disease. Paucibacillary culture should not be automatically regarded as negative when treating MDR-TB as acquired drug resistance can begin with one or two colonies on a sputum culture. Culture conversion should not be considered equivalent to cure as a proportion of patients may initially convert and later revert to culture positive status.

Chest x-ray may be unchanged or only show slight improvement especially in re-treatment patients with chronic pulmonary TB lesions. Chest x-ray should be taken every six months, particularly if the patient’s clinical condition has worsened.

7.17 Monitoring for side effects

Adverse effects due to MDR-TB treatment are more common within the first 6 months of treatment. Medical officers and nurses should screen patients regularly for symptoms of common adverse effects: rashes, gastrointestinal symptoms (nausea, vomiting and diarrhoea), psychiatric symptoms (psychosis, depression, anxiety and suicidal ideation), jaundice, ototoxicity, peripheral neuropathy and

symptoms of electrolyte imbalance (muscle cramping, palpitations). Refer all patients to specialists for anything more than minor adverse effects.

Table 7.3: Monitoring during treatment of drug resistant TB

Monitoring evaluation	Recommended frequency
Evaluation by clinician	At baseline and at least monthly until culture conversion, then every 2-3 months
Review by treatment caregiver	At every DOT encounter
Sputum smear and cultures	Monthly until the end of treatment
Weight	At baseline then monthly
Drug susceptibility testing	At baseline and every three months for patients who remain culture positive.
Chest x-ray	At baseline and then at the end of treatment unless indicated
Serum creatinine	At baseline and then monthly when receiving injectable agent
Serum potassium	At baseline and then monthly when receiving injectable agent
Thyroid stimulating hormone	Every six months if receiving ethionamide and /or PAS; and monitor monthly for signs and symptoms of hypothyroidism
Liver serum enzymes	Every 1-3 months in patients receiving pyrazinamide for extended periods or for patients at risk for or with symptoms of hepatitis
HIV testing	At baseline, and repeat if initially negative and signs and symptoms of HIV infection develop
Pregnancy test	At baseline for women of childbearing age and repeat if indicated.

7.18 Management of Contacts of MDR-TB Patients

Opportunities to halt the spread of resistant mycobacteria in communities and to treat MDR-TB in a timely fashion are often squandered. The main reasons are lack of investigation of contacts of MDR-TB patients, failure to ask patients presenting with active TB disease about any history of exposure to MDR-TB, and lack of access by national treatment programmes to second-line regimens and/or no access to DST.

Close contacts of MDR-TB patients are defined as people living in the same household, or spending many hours a day together with the patient in the same indoor living space. As with contacts of drug-sensitive TB patients, contacts of MDR-TB patients are at risk of acquiring infection and developing active disease, therefore all family and workplace contacts should be identified and assessed for signs and symptoms of active TB disease. The available data indicate that close contacts of MDR-TB patients who develop active TB most commonly have drug resistant disease.

As with any TB suspect, symptomatic contacts of MDR TB patients should receive a physical and sputum-smear examination. Smear-positive specimens should be send for culture and DST. While awaiting DST results, start the patient on an empiric regimen based upon the DST pattern of the index case or upon the most common resistance pattern in the community. Studies from high-burden TB areas have shown that approximately one half to two thirds of household members had the same strain of TB, as determined by genetic testing. The degree of strain concordance could be higher in

contacts that are children aged less than five years because they have less exposure to strains circulating outside the household.

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 these drugs, it is unlikely that treatment of latent infection caused by an MDR-TB strain with isoniazid and rifampicin will prevent the development of active TB disease. **Close contacts of MDR-TB patients should receive careful clinical follow-up for at least two years.** In line with current WHO recommendations, the BNTP does not recommend the use of second-line drugs for chemoprophylaxis in MDR-TB contacts.

7.18 Treatment outcome definitions for category IV treatment

The following treatment outcomes rely on laboratory culture results as a monitoring tool, and should be applied to patients who are receiving Category IV regimens.

Cured: A patient who has completed treatment according to the national MDR-TB protocol and has been consistently culture-negative (with at least 5 results) for the last 12 months of treatment. If only one positive culture is reported during that time, and there is no concomitant clinical evidence of deterioration, a patient may still be considered cured, provided that this positive culture is followed by a minimum of three consecutive negative cultures taken at least 30 days apart.

Treatment completed: A patient who has completed treatment according to the national MDR-TB protocol but does not meet the definition for cure because of insufficient bacteriological results (i.e. fewer than five cultures were performed in the final 12 months of treatment).

Died: A patient who dies for any reason during the course of MDR-TB treatment.

Failed: A patient with two or more positive results among the five cultures in the final 12 months of therapy, or with a positive culture result from the final three specimens. (Treatment will also be considered to have failed if a clinical decision has been made to terminate treatment early because of poor response or adverse events. These latter failures can be indicated separately for the purposes of sub-analysis).

Defaulted: A patient whose treatment was interrupted for two or more consecutive months for any reason.

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

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8. MONITORING TREATMENT RESPONSE

8.1 Monitoring treatment response

Treatment monitoring is an important element of effective tuberculosis control and enables the assessment of the infectivity of a patient, the response to treatment and the outcome treatment. Treatment response is assessed by clinical, laboratory, and radiological methods. Clinical assessment enables the monitoring of response to treatment. Sputum conversion is an important indicator in assessing the quality of TB control, and enables the calculation of conversion and cure rates, while patients with complicated PTB may require X-ray examination. Sputum culture and drug susceptibility testing is indicated for all retreatment patients (relapse, treatment failure or default) as well as new patients who remain smear-positive after three months of directly observed treatment .

8.1.1 Category I: New sputum-positive PTB

i. At the end of 2 months of treatment (2 smears):

More than 85% of these patients have a negative smear result after two months and can proceed to the continuation phase of treatment. A positive smear result may indicate one of the following:

a. Poor treatment adherence;
b. Inadequate supervision of treatment;
c. Slow rate of smear conversion, e.g. if a patient has a heavy initial bacillary load ; or
d. Presence of TB strains resistant to first-line drugs.

If the patient remains AFB smear-positive at the end of two months, prolong the intensive phase for a third month and repeat the smear examination at the end of three months. If these smears are negative, stop the intensive phase and begin the continuation phase. If the smears remain positive, submit additional specimens for culture and drug susceptibility tests. Stop the intensive phase and begin the continuation phase pending DST results, which will guide the selection of an appropriate regimen.

ii. At 5 – 6 months (2 smears):

Treatment outcome of smear positive patients depends on the result of smear microscopy at this time.

a. If the smear is negative at 5 – 6 months and was negative at the end of the intensive phase, the treatment outcome is “Cured”
b. If the smear is positive at 5 – 6 months, the treatment outcome is “Treatment Failure”. Stop Category I treatment, re-register the patient as “Retreatment after failure”, send sputum for culture and drug sensitivity testing and start Category II treatment.

8.1.2 Category II: Previously treated sputum-smear positive PTB

i. At the end of 3 months of treatment (2 smears):

a. If the sputum smears are positive, stop streptomycin and continue with the remaining four drugs for another month. Repeat smear examination at the end of four months.
b. If the result is positive at the end of four months, send a sputum specimen for culture and drug sensitivity testing, and start the patient on the continuation phase.

c. Repeat smear microscopy at five months (whilst waiting for the culture and DST results). Positive smear results indicate failure of the retreatment regimen.
d. If results show resistance to any of the drugs used in the continuation phase, refer the patient to a specialist physician for assessment and consideration of second-line treatment.

ii. At the end of 8 months (2 smears):

a. If the smears are negative for AFB, record the treatment outcome as "Cured"
b. If the smears are positive at the end of 8 months, this indicates failure of the re-treatment regimen. Send sputum for culture and sensitivity testing. Refer the patient to a specialist physician, who should start a standardised category IV treatment regimen whilst awaiting results.

8.1.3 New sputum smear-negative pulmonary TB patients

Most smear-negative TB patients need only clinical assessment, and the body weight is a useful progress indicator. Order sputum microscopy if the patient has an unremitting or worsening cough at the end of the intensive phase. If the sputum was negative at the beginning of treatment and subsequently became positive at the end of the intensive phase, record this as "Treatment Failure." Stop Category I treatment, submit sputum specimens for culture and drug susceptibility testing and commence the patient on Category II treatment whilst awaiting the results. Register the patient as "Retreatment after failure."

8.1.4 Extrapulmonary TB

Most patients with extrapulmonary TB need only clinical assessment. Again, body weight is a useful indicator. Occasionally, other investigations such as radiology may be necessary during follow-up.

8.2 Adherence to treatment

8.2.1 Admission Policy

Tuberculosis treatment should be ambulatory, and whenever possible, started, carried out and completed at the same treatment unit (health facility). Admit patients who present with the following:

a) TB meningitis and miliary TB, preferably for the first two months
b) Danger signs, e.g., respiratory distress, temperature of 39º C or more, inability to walk unaided
c) Spinal TB
d) Severe adverse events, e.g., hepatitis

Strict infection control and isolation procedures should be observed for all PTB patients admitted for in-patient treatment. Particular care should be taken to separate PTB patients from other in-patients, particularly those who may be HIV-infected.

Some patients may require hospitalisation if it is not possible to ensure adherence to treatment for social or logistical reasons. In-patients who improve on treatment may transfer to a health unit of their choice for ambulatory, directly observed treatment. Transferring patients between facilities presents a high risk of treatment interruption. Minimise transfers as much as possible, and when necessary, strictly adhere to the procedures described in Chapter 12 on "Transfer" or "Moved" of patients.

8.2.2 Involuntary Isolation

Occasionally, a TB patient may refuse treatment at the outset or refuse to restart treatment after default, failed treatment or relapse. In such cases, make every effort to obtain the patient's voluntary compliance with anti-TB treatment, e.g., by discussing benefits of treatment to the patient, the family and the community, highlighting the risks of inadequate treatment to the patient and others. Enlist the help of appropriate members of the family or respected community members such as dikgosi, church elders, etc. If distance to a health facility or difficulties in getting time off work to receive DOT are part of the problem, offer community TB care, workplace DOT or any other innovative method of ensuring that an adequate course of treatment is taken.

Should all options be exhausted and the patient is infectious (smear or culture positive), then involuntary isolation would be the last resort. The Public Health Act (Chapter II, Sections 10 and 11) authorises any registered medical practitioner to order the detention of any person at risk of spreading disease until *the patient is free from infection or can be discharged without danger to the public health.* This mechanism should **only** be used as a last resort to protect the community from the results of irresponsible behaviour of an infectious patient.

It is vital for clinicians to exhaust every option of enlisting the patient's voluntary adherence to anti-TB treatment before invoking this law. Its inappropriate or exuberant use can lead to TB suspects and patients alike delaying or avoiding health care out of fear of compulsory isolation.

8.2.3 Administering directly observed treatment and ensuring adherence

The priority of TB control is to reduce morbidity and mortality and to prevent the emergence of drug resistance. Successful treatment depends on obtaining the patient's cooperation in adhering to the prescribed treatment and on the early and effective tracing of any patient who interrupts treatment.

Directly observed treatment (DOT) means that a health worker or trained caregiver watches the patient swallow the drugs, either at health facilities or in the community. The best way to ensure treatment compliance is a patient-centred approach, which includes facilitating access to treatment, deciding with the patient the most convenient time and place for DOT and, when possible, providing other care and support services. Balancing the patient's need for convenience with the provider's need to assure regular drug intake and patient monitoring, gives the patient the best chance for a successful outcome.

Be polite and attentive to the patient's needs at every contact. Where there is difficulty in managing certain cases, e.g. treatment failures, relapses or patients with other serious medical conditions, refer the patient for specialty care. Educate TB patients, including children and their parents, about TB and the importance of completing treatment. Patient treatment cards are essential for documenting treatment adherence. The support of the immediate family is vital to ensure a satisfactory outcome of treatment, especially for children.

8.2.4 Treatment follow-up

A medical officer should assess each TB patient monthly during treatment. It may be necessary to see patients more frequently depending on their condition. Monthly assessment of TB patients should include at least the following:

- A symptom assessment (cough, weight loss, fever, adverse effects)
- An assessment of adherence (by reviewing the treatment card)

- Enquiry about any adverse events and
- Weight measurement (adjust dosages to account for any weight change)

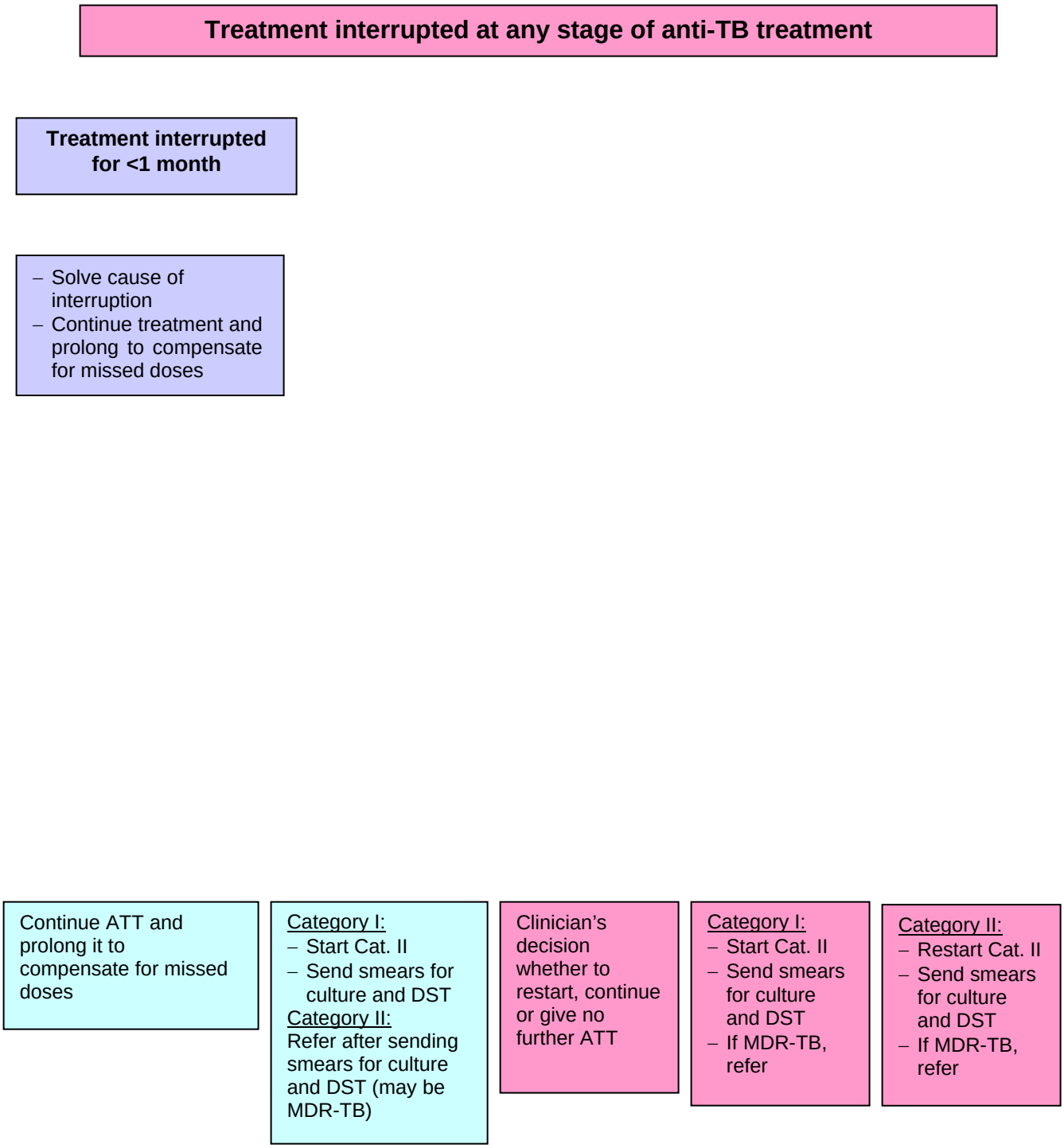
Obtain a follow-up sputum smear for microscopy at two months from any patient who was smear-positive at diagnosis, and from any initially smear-negative patient who does not improve on treatment, e.g., has a persistent or worsening cough, continuing weight loss, etc.

Follow-up chest X-rays are not routinely required, particularly for children. Many children show a slow radiological response to treatment. Refer any child who is not responding to TB treatment for further assessment and management. Such children may have other causes of lung disease, a complication of TB, drug-resistant TB, or non-adherence with treatment.

8.2.5 Actions to take when treatment is interrupted

Patient-centred DOT is the best way of avoiding treatment interruption, but treatment interruption may still occur. Figure 8.1 illustrates the management of treatment interruption at any stage of treatment.

Figure 8.1: Actions to take when TB treatment is interrupted



Adapted from Treatment of tuberculosis – guidelines for national programmes (WHO/CDS/TB/2003.313)

8.3 Follow-up after treatment

Once a patient has completed or cured Category I or Category II treatment, there is no need for formalised follow-up unless the attending clinician feels further review(s) are necessary. Category IV (MDR) patients, should receive bi-annual examinations for at least one year following treatment completion or cure.

8.4 Recording standardised treatment outcomes

At the end of treatment, the facility should record the patient's outcome on the treatment card, and in the facility TB register, as described below.

Table 8.1: Definitions of standardised treatment outcomes

OUTCOME	DEFINITION
Cure	Patient who was initially sputum positive, is sputum smear-negative in the last month of treatment and on at least one previous occasion.
Treatment completed	Patient who completed treatment but does not meet the criteria of a cure or a failure
Treatment success	The sum of smear-positive patients cured and those who have completed treatment. This is a cohort definition
Treatment Failure	Patient who is sputum smear-positive at 5 months or later during treatment - Also includes any patient who was smear-negative before starting treatment and became smear-positive at the end of the intensive phase
Died	Patient who dies for any reason during the course of treatment
Default	Patient who interrupts treatment for two consecutive months or more
Transfer out	Patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known

References

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CHAPTER 9: COMMUNITY TB CARE INITIATIVE

9.1 Background

In many places, health care is not easily accessible and there is need to look at other approaches of providing TB control interventions outside the clinic and hospital setting. Providing TB care in the community, so-called community-based TB care, is one such approach. Community TB care is a component of the Stop TB strategy and an integral part of the BNTP strategy. Its primary objective is to decentralise TB services beyond health facilities into the community so that TB care is more effective, acceptable, affordable and available. Community TB care complements facility-based "DOTS," and embraces the principles of the PHC approach.

Pilot projects in several countries including Botswana, showed that community-based TB care is feasible, acceptable and cost-effective. The approach can improve treatment adherence and treatment outcomes in a variety of settings. Most patients prefer to be cared for in their homes. One approach is for community members to act as DOT supporters while in another setting, family members observe treatment, resulting in high cure rates. Community participation in TB care can foster a spirit of community and family support for TB patients, which may ultimately result in the reduction of the stigma associated with TB.

9.2 Rationale for Community TB care in Botswana

Botswana is a vast and sparsely populated country. Access for many Batswana to health facilities is difficult, and daily-observed TB treatment is not feasible in many parts of the country, which leads to treatment interruption. The combination of resource constraints (especially human resources for health) and the rise in TB cases fuelled by HIV is straining the ability of public health services to cope. Some TB patients are too sick to attend daily ambulatory TB services at a health facility. Because of the high rate of dual TB and HIV disease, many TB patients receive care under the home-based care programmes in place in many parts of the country.

9.3 Organisation of Community TB care

The country is scaling up the implementation of community TB care, which is currently available in limited settings. Consultation between the TB focal person at health facilities, community representatives and individual TB patients, results in the selection of community volunteers. Through the health facility teams, the district TB coordinator is responsible for training these volunteers to provide varied TB services like facilitating early diagnosis of TB, direct observation of treatment and education of TB patients and the community. The TB coordinator supervises and supports the community volunteers. Monitoring of community care remains the responsibility of the BNTP. Effective community-based TB care depends on effective facility-based TB care services.

Districts that are scaling up the care of TB patients in the community should ensure that there is good communication and collaboration between health facility staff, the community and community-based organisations, with clear roles and responsibilities for all partners, including community volunteers. Education and counselling of TB patients and their families is essential, as is quality training of health workers and community volunteers, with regular supervision and monitoring of by BNTP staff.

Districts intending to introduce community TB care should carefully plan the introduction. The steps include identifying and mobilising appropriate community organisations, scaling up the health education of TB patients and the community, with targeted training of community members contributing to TB care. The BNTP will introduce recording and reporting forms to monitor and evaluation the implementation of community TB care.

9.4 Who is eligible for Community TB Care?

Community TB care is currently optional for patients, but is particularly suitable for very sick patients or those living in remote areas who are therefore unable to attend daily ambulatory TB services at the health facility. Patients on category II (with daily injections of streptomycin) or with a history of repeated non-adherence are unsuitable for community-based care.

9.5 Supervision

Community TB care volunteers are supervised from the health facility (clinic, health post) which covers the area where they work. The district TB coordinator has the overall responsibility for supervision and coordination of community TB care in the district.

References

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CHAPTER 10: HEALTH EDUCATION

Health education of patients and communities is a vital component of the national TB control strategy. Every HCW who diagnoses, registers or initiates treatment for any patient should provide health education.

10.1 Patient Education

Every patient should receive clear and accurate information about TB and its management before commencing ATT. Patient education leads to a better understanding of the problem and better adherence to treatment; effective educational strategies include individual face-to-face talks, group discussions, e.g., in the outpatient DOT clinic or in the wards, or through pamphlets, posters and other media. Communities can be educated through commemorative events, at meetings of health teams and community members, or by community volunteers.

Who should educate TB patients?

All HCWs in contact with TB patients throughout the course of their treatment are responsible for providing health education. Patient education is a continuous process throughout treatment, therefore it is important to emphasize appropriate health education messages at different phases of treatment.

How to communicate with patients

At each patient encounter, the health care worker should choose an appropriate message to teach or reinforce. Demonstrate a caring, respectful attitude through actions, words, body language, tone of voice and eye contact. Praise, encourage and motivate the patient to continue treatment. Be non-judgmental if the patients' views or lifestyles differ from your own. Use simple non-medical terms and words that are familiar to the patient, in the appropriate language and at the appropriate level of understanding. Repeat important information.

10.2 Topics for discussion with patients

It is important to give accurate information about the definition, cause, and mode of transmission of TB, including drug-resistant TB, by addressing any myths. At the first visit, discuss what TB is, how it is transmitted, and treated. Describe the relationship between TB and HIV and explain Botswana's routine HIV testing policy. Emphasize the importance of knowing one's HIV status, and reinforce HIV prevention messages. Reassure the patient about the curability of TB even among HIV-infected patients.

Describe the drugs that will be used and show the patient the tablets. Be clear about the duration of each phase treatment and the importance of daily DOT throughout treatment. Explain what Directly Observed Therapy is, what potential side effects s/he should expect, and the need to minimize travel (e.g., to cattle posts) until after treatment completion. At subsequent visits, reinforce description of treatment (amount and frequency of drugs, possible side effects of drugs), treatment during continuation phase, importance of adherence, good nutrition and abstinence from tobacco and alcohol, and the frequency and importance of follow-up sputum collection.

Ensure that the patient's close contacts, particularly children, present themselves for screening. Instruct the patient on limiting transmission, especially cough hygiene and adequate ventilation, and about the importance of a balanced diet and abstinence from alcohol and smoking. If appropriate, inform the patient about transfer procedures.

10.3 Topics for discussion with communities and treatment supporters

Most of the content of individual patient health education is appropriate for educating treatment supporters and communities. It may be necessary to emphasise some areas such as the myths or the mode of transmission of TB, the TB and HIV link, infection control measures, contact tracing and early detection of TB, and the need for DOT. Encourage communities to develop a supportive attitude towards TB patients.

10.4 Some questions and answers about DOT

10.4.1 What is Directly Observed Treatment?

Directly observed treatment means that an observer watches the patient swallowing the tablets, in a way that is sensitive and supportive to the patients needs. This ensures that a TB patient takes the right drugs, in the right doses, at the right intervals for the required treatment period. The observer may be a health worker or a trained and supervised community member. It is important to ensure confidentiality. The TB drugs should remain with the treatment observer and only given to the patient at the time of intake.

10.4.2 Why directly observed treatment?

DOT is necessary to ensure treatment adherence. It motivates the patient to continue treatment and reduces treatment interruption, and facilitates prompt action should patients miss their doses. DOT places the responsibility of ensuring that patients complete their treatment upon HCWs. By reducing treatment interruption and thereby improving treatment outcomes, DOT prevents the development of drug resistance.

CHAPTER 11: DRUG SUPPLY AND MANAGEMENT

To achieve a continuous and sustainable supply of drugs, health care facilities should have control systems for maintaining drug stocks. A successful TB programme depends on a regular supply of anti-TB drugs. Poor quality drugs and irregular TB treatment contribute to poor treatment outcomes and increase the risk of the development of drug resistance.

The MOH has long-established procedures for the procurement and management of anti-TB drugs. The pharmacy technician or pharmacist, in consultation with the Public Health Specialist and the district TB coordinator, orders the anti-TB drugs required by all the facilities in the district, including hospitals. The order forms part of the combined annual drug order of the District Health Team, which submits it to the Central Medical Stores. The CMS purchases and distributes the drug supplies at regular intervals to the districts during the course of the year. This system has eliminated anti-TB drug stock outs.

Pharmacy personnel maintain records of the drugs issued to health facilities, and monitor quantities and expiry dates. Districts normally keep maintain a 3 – 4 month supply. Drugs for treating MDR-TB are special order drugs. If a district has an MDR TB patient, the PHS can make a special order to the CMS for the relevant drugs. A letter from the specialist physician at the referral hospital where treatment was initiated should accompany the order. Fixed drug combination (FDC) tablets will be introduced in 2008 and will replace single anti-TB drugs.

CHAPTER 12: RECORDING AND REPORTING

12.1 Importance of programme administration

A simple but effective recording and reporting system is essential for the purpose of TB programme monitoring and evaluation as well as for further planning (Ninth report group of experts IUATLD/WHO). Such a system has been long established in Botswana. Due to the increasing role of the TB/HIV co-epidemic, several changes have been made to the existing reporting and recording system to improve reporting and provide more detailed information on the extent of TB/HIV co-infection. The updated system is described below in some detail.

12.2 Reporting Forms

The BNTP utilises nine forms. The application and instructions for completion of each form are provided below. The forms are listed according to the natural sequence in which they would be completed by the HCW. Additional forms will be introduced in 2007-2008 – for Community TB Care and for MDR-TB management.

1. Suspect and Sputum Dispatch Register (MH 2028)
2. Mycobacteriology Request and Report form (MH2011)
3. Tuberculosis Laboratory Register (MH 1041)
4. Unit Tuberculosis Register (MH 2003)
5. Tuberculosis Treatment Card (MH 1050)
6. Patient's Tuberculosis Card (Appointment and DOT Card) (MH 1022/1)
7. Tuberculosis Contact Examination Form (MH 1028).
8. Notice of Transfer of a Patient (MH 1024)
9. District Tuberculosis Register (MH 2003)

Form 1: Suspect and Sputum Dispatch Register (MH 2028)

The 'Suspect and Sputum Dispatch Register' (SSD Register) is to be maintained by all health facilities and completed by health workers requesting sputum-smear examination.

The SSD Register combines:

- The registration of all patients presenting at the health unit with symptoms suggestive of tuberculosis (“TB suspects”); and
- Sputum specimens submitted for direct smear examination (both for suspects and for bacterial monitoring of treatment progress at two months, end of treatment, or as otherwise indicated) ;
- All specimens submitted, whether for smear microscopy, culture, or drug sensitivity testing, should be registered in the SSD Register for tracking purposes.

All patients suspected of having active TB are classified as TB suspects and therefore, should be:

- Recorded in the register (patient’s name)
- Investigated (sputum, X-ray where necessary)

The SSD Register enables staff to ensure that:

- Required sputum specimens for TB suspects are dispatched to the appropriate district laboratory for examination;

- Results are received back from the laboratory for all specimens sent, and recorded in one central location;
- All the suspects for whom a positive sputum smear result is obtained are registered and started on TB treatment;
- All bacteriology results for treatment evaluation are received and centrally recorded so that they then be transcribed onto the TB treatment card, the Patient TB card (Appointment/DOT Card), and the Facility TB register**.**

The SSD Register contains the following data elements, which must be completed to correctly track bacteriology specimens:

- Date of suspect registration and specimen collection;
- Suspect number (a serial number for a newly identified TB suspect) or the TB ID number (consisting of the District number/Facility number/Serial registration number/Year) as appropriate
- Patient name
- Sex, age and detailed address (to be filled in for suspects only)
- Dates of specimen collection and dispatch date that the result is received by the clinic, and the result of the bacteriological examination.

When the decision has been made as to whether or not the patient has tuberculosis, complete the last ("Decision") column with the allocated Unit TB Number or with the words "Not TB". **Until the 'Decision' column has been completed in one or other of the two ways, the entry serves as a reminder that an important decision is outstanding**.

In some cases, this decision may have to be postponed, e.g. in the event that the patient's condition strongly suggests tuberculosis but three sputum smear results are negative. In such cases, enter in the Decision column the date of proposed re-examination (e.g. To Come Again 12/6/05). When the patient does return, re-register under date of return (say, 12/6/05) but using the original serial number. If the patient does not return, a home visit should be made.

Form 2: Mycobacteriology Request and Report Form (MH 2011)

The Mycobacteriology Request and Report Form must be completed for each specimen submitted for any mycobacteriology laboratory service. This includes smear microscopy, TB culture and drug sensitivity testing; each specimen must be accompanied by this request form. Once the specimen has been processed, laboratory staff will complete the "REPORT" section on the lower half of the form and return to the requesting HCW or treatment unit. Some facilities have an electronic request system (Meditech) for all laboratory investigations, including mycobacterial investigations. The MH2011 form will be revised to ensure that all relevant information is captured by both systems.

Currently, the Mycobacteriology Request and Report Form requires completion of the following descriptive elements by the **requesting HCW**:

- Patient name, Facility Registration Number and Omang/ID Number
- Sex, age and address
- Dates of specimen collection and request
- District, Hospital and Ward
- Requesting MO's Name and Signature

The health care worker must then check off the following

- Type of specimen (Sputum, Other)
- Investigation required (AFB microscopy, or culture and DST)
- Patient Category (new, retreatment (and type), chronic)
- Treatment Regimen at time of specimen collection (none, standard, reserve, second line other)
- Request Specimen Collection Period (0 months, i.e., diagnostic specimen, 2 months, 5 – 6 months)
- Any previous DST results

Once the requested laboratory results have been completed, the laboratory technician will complete the results section on the lower half of the form. The results section should indicate whether the results are preliminary or final, and should be signed and dated by the technician.

Receipt of laboratory results in clinic. Once received back in the clinic, the receiving HCW should record the results in the **Suspect and Sputum Dispatch Register and the Facility TB Register as appropriate.**

Form 3: Tuberculosis Laboratory Register (MH 1041)

The 'Tuberculosis Laboratory Register' is kept at all laboratories. For each smear to be examined, the microscopist or laboratory technician who carries out the smear examination must enter the following information:

- Specimen serial number
- Date of examination
- Patient name
- TBID (which contains the facility number where the patient is registered)
- Name of MO/staff requiring examination
- Result of examination.

The District TBCO must check regularly whether patients with positive smears in the Tuberculosis Laboratory Register are entered into the Facility and District Tuberculosis Registers.

Form 4: Unit Tuberculosis Register (MH2003)

The 'Unit Tuberculosis Register' is the backbone of the national TB reporting and recording system. All health facilities are required to maintain a Facility Tuberculosis Register. The register contains the particulars of all detected cases of tuberculosis, registered at the facility, and patients who, after registration, continue to receive their treatment there. The register records bacteriological status at registration and during the course of treatment, patients' compliance and the outcome of treatment. The disposition of patients who may transfer to another facility for their care is also recorded in the Facility TB Register. The following section describes the purpose of each part of the register, and how to complete the register.

'Unit TB Number'
The 'Unit TB number' consists of four parts:

‘A’ - District Number
‘B’ - Facility Code number
‘C’ - Specific serial number of the patient starting with 01 at the beginning of each year
‘D’ -Year of registration

For detailed information on the district facility code numbers, see the Master Health Facility List.

The first two parts of the number ('A' and 'B') are common to all patients registered in one facility. Therefore it appears only once on the top of each page in the "Facility TB Register'. The parts 'C' and 'D' are particular to any one patient: they appear, therefore, at the beginning of a line of the register allocated to a particular patient.

Example: In 2004 ("D" =2004), Francis Mulenga was the first registered patient ('C' = 01) at Lobatse Hospital ('B = 01) in District 6 ('A' = 06). Similarly, Eva Mpho was the second patient in 2004 at the same health unit (Table XX)).

A new number should be assigned to any subsequent patient coming for treatment to this unit, be it a "new case" or "retreatment" (after relapse, failure or return from default) as well as to any patient "transferred in" to this health unit from elsewhere while on treatment (be it from outside or from within district). If a serial number is duplicated, or a patient is registered twice by mistake, simply draw a line through the incorrect entry. NEVER RENUMBER the patients once registered. Errors or numbering issues will be addressed by the District TB Coordinator when transferring information from the Facility register to the District TB Register.

'Date of registration': This is the date on which a patient first attended for TB treatment at the given health facility. In the instance of "Transferred in" or "Moved in" patients, this date does not necessarily coincide with the date on which treatment was started.

'Transfer in' or 'moved in': Mark "T" or "M" for those transferred or moved in from elsewhere, outside or within the district.

'Name in full': Write the full name of the patient.

'Sex': Insert M (ale) or F (emale) according to the patient's sex

'Age': Express in years of age (e.g. 37). If the patient or family member does not know the patient's age, ask for an approximate age or date of birth.

'Address': Give the full residential address. Please note that, on the *new* "TB Treatment Card", space is provided for alternate addresses (e.g. physical address).

'Date treatment started and regimen': For the abbreviations of the regimen in use, see bottom of page of the register.

'Disease classification': Enter "P" for pulmonary, "EP" for extra-pulmonary. In case of "EP", indicate the site affected.

'Category of patient': Mark "x" or " ✔ " in the column for the appropriate option.

- *New:* Patient who has never been previously treated for tuberculosis, or received therapy for less than <u>one</u> month.
- *Retreatment after:*
  - Relapse: Patient previously treated and considered cured or "treatment completed" who now has smear-positive PTB or other bacteriologically-confirmed TB.

- Failure: A patient who is started on a retreatment regimen after having failed previous treatment.
- Default: A patient who returns to treatment, bacteriologically positive, following interruption of treatment for two consecutive months or more.

'Dates and results of sputum examinations': For all sputum-smear results, the date of the sputum collection and the result Positive (P) /Negative (N) should be recorded in the space provided.

- Pre-treatment: before start of treatment, three sputum-smear examinations should be conducted in all cases, other than young children.
- At 2 months: two sputum specimens should be collected for examination at the end of second month of treatment.
- At 5 – 6 months: two sputum specimen should be collected for examination after 5 – 6 months of treatment.
- At eight months: two sputum specimen should be collected for examination for patients on an extended or retreatment regimen with an eight-month duration
- Later than eight months: If no sputum examinations were done at 5 – 6 and/or 8 months, two specimens should be examined as soon as possible thereafter.
- Culture or biopsy results should be recorded as such.

'Compliance with treatment': Compliance is expressed as the proportion of "days of treatment attended" over "days of treatment expected" for each calendar month (e.g., (e.g., a patient scheduled to receive treatment for the entire month of February who only received 22 doses would be recorded as 22/28)

'Date treatment stopped': Treatment phase is complete when the patient has taken all the doses for the phase. The treatment regimen is complete when the patient has taken the correct number of doses for both phases. For these cases, treatment should be stopped, and the date of "treatment completed" should be entered in the appropriate column.

Smear negativity/positivity at the end of the treatment is based on "the last" sputum result, i.e. on the six- and eighth- month results, as below. If either or both of these results are not available (NA), extra specimens should be examined as soon as possible thereafter.

- "Smear-negative" = Two smear-negative sputum results at end of treatment (5 – 6 or 8 months as appropriate).
- "Smear-positive" = One smear-positive sputum result at 5 – 6 months and/or at 8 months)
- "Smear results NA" = No specimen obtained

Treatment should also be stopped automatically if a patient interrupts treatment for two consecutive months. Record these patients as “Defaulters”.

A treatment end date should be recorded for patients that die during treatment of any cause (record the date of death), or who transfer/move out to another facility to continue treatment.
The entry in the date column should correspond with the date on which treatment was stopped.

'Remarks': In case of a "transferred out" or “moved out" patient, the location to where the patient has gone should always be specified.

Form 5: Tuberculosis Treatment Card (MH 1050)

All health facilities should keep the 'Tuberculosis Treatment Card' for each patient on anti-TB treatment. The card includes the following details:

- Patient's name, age, sex, and address(es)
- Unit TB number and data concerning patient's transfer
- Classification of type of disease and category of patient
- Treatment regimen(s)
- Results of sputum examinations
- Dates of supervised drug administration (DOT) and initials of administering HCWs
- Patients' weight record
- Clinical notes
- Drug reactions, if any
- HIV status of the patient
- Receipt of concurrent ART and start date of ART
- Receipt of IPT prior to TB diagnosis and start date of IPT
- Number of contacts identified and screened

The cards of all patients should be filed serially in chronological order in a ring binder provided by the TB Programme, so they can be easily retrieved and reviewed, even after the patient has completed treatment.

Form 6: Patient's Tuberculosis Card (Appointment and DOT Card) (MH 1022/1)

Each registered TB patient should have form MH 1022 distributed at the first treatment visit. This form contains all of the patient's relevant demographic and registration information, sputum exam results and treatment regimen. Most important to the patient, this form has space to record the administration dates of all DOT, as well as all future scheduled monitoring visits (e.g., at two months, etc.).

Form 7: Tuberculosis Contact Examination Form (MH 2035)

The 'Tuberculosis Contact Examination Form' is kept at all health units and is used for contact screening. This screening form should be used to interview all household and prolonged close contacts of any patient with infectious TB.

Form 8: Notice of transfer of a patient (MH 1024)

The 'Notice of Transfer of a Patient' is kept at all health units and is used to communicate all the relevant registration and treatment information for patients who may transfer their TB care patients to another facility within or outside the district.

When sent, the form should contain the following information:

- Date sent
- Sending health facility
- Receiving health facility
- Patient's name, sex, age
- Patient's unit TB number
- Name and signature of sender

Response to a transfer slips must be completed by the receiving clinic and sent back to the original (sending) health facility.

Form 9: District tuberculosis register

The District TB co-ordinator (TBCO) keeps the 'District Tuberculosis Register'. It consists of all the Facility Tuberculosis Registers. Data on patients contained in the Facility Tuberculosis Register are transferred to the District Tuberculosis Register regularly, every month, in the following way:

Maintaining the District TB register:
The District TB coordinator visits all facilities under his supervision at the end of each month and updates his District Tuberculosis Register to coincide with the Unit Tuberculosis Registers. This is certainly feasible in (geographically) smaller districts where the number of health facilities is not too big and where transport is readily available.

In larger districts, with bigger number of facilities or transport difficulties, the above procedure may not be feasible. In those cases it is essential, however, that each facility be visited at least once in a quarter by the TBCO to check and advise on the maintenance of quality documentation of the programme activities.

12.3 Newly Registered TB Cases

Each quarter, District TB coordinators must report all newly registered tuberculosis. This report is one of the pre-programmed functions found in the electronic TB register computer programme (ETR). Data from the District Tuberculosis Register are entered monthly into the ETR; the ETR is then used to generate quarterly reports. It is obvious that reliable reports can be produced only if the District Tuberculosis Register is kept up-to-date. District TB co-ordinators must therefore visit the health facilities once a month or at least quarterly to update this register since information entered into the computer is dependant on it.

12.3.1 Treatment Outcomes

Table 12.1: Examples of schedule for assessment and reporting of outcomes

Patients registered during	Will have reached assessment date by	And should be reported on in early
1st quarter 2007	September 31, 2007	December 31, 2007
2nd quarter 2007	December 31, 2007	March 31, 2008
3rd quarter 2007	March 31, 2008	June 30, 2008
4th quarter 2007	June 30, 2008	September 31, 2008

The Quarterly Report of Treatment Outcomes (also computer generated) should also be prepared.

12.3.2 Forwarding of the reports

Quarterly Reports should reach the MOH before the end of the first month of the quarter in which prepared. The Quarterly Report should be copied onto a diskette, CD or sent by e-mail and should reach Disease Control unit, MOH by the following date:

For first quarter	- before April 30, same year
For second quarter	- before July 31, same year
For third quarter	- before October 31, same year
For 4th quarter	- before January 31, following year

12.4 Administrative Procedures

Description of the various forms used, their content and functions has been given above. Following is the summary of necessary actions required from the health staff when dealing with BNTP.

12.4.1 Initial investigation of tuberculosis suspects

When a person presents with features of active pulmonary TB, the following procedure must be adopted:

- Make an appropriate entry into "Suspect and Sputum Dispatch Register."
- Fill in "Sputum Request Form" and send it as soon as possible, together with the required number of sputum samples, to your laboratory.
- When results are received, make an appropriate entry into the "Suspect and Sputum Dispatch Register". If the sputum result(s) is positive, the appropriate treatment should be started at once. If the sputum result(s) is negative, the patient will be referred to the medical officer for further investigation(s) and a final decision "TB, or Not TB".

12.4.2 Registration and treatment

When a diagnosis of TB has been made, the patient will be registered and start treatment.

- Enter all required details into the Unit Tuberculosis Register: allocate Unit TB Number, consisting of the code of district ('A'), code for health unit ('B'), consecutive number of register ('C') and the year of registration ('D').
- Issue a Tuberculosis Treatment Card. (This card is kept at the health unit)
- Issue a Patient's Tuberculosis Card. (This card was formerly known as the "Appointment card" and is kept by the patient)
- If the patient has smear-positive TB, issue a Contact examination form and plan for a home visit to be done within three days of registration.
- Monitor patient's compliance by making an entry into the Tuberculosis Treatment Card and the Patient's Tuberculosis Card whenever the medication has been taken.
- Check all cards of patients on treatment at the end of each day to discover those who have not come for treatment. Follow-up immediately (the same day or, at the latest, the following day) those who defaulted.
- Check patients' weight at the end of each month and enter into the Tuberculosis Treatment Card in the space provided. Adapt treatment dosages, accordingly.
- Collect sputum specimens for review (at two, six, and in some instances eight months) as indicated in the Tuberculosis Treatment Card. Use the "Suspect and Sputum Dispatch Register" to keep record of all sputum specimens sent for examination. Record all sputum results into the Unit Tuberculosis Register, and patient treatment card also.
- Refer patients for check-up. Each short-course chemotherapy TB patient must be reviewed at least once a month by the PHS/MO.

- At the end of each month fill in number of days "treatment attended" over number of days "treatment expected" in the "Compliance with treatment" column of your Unit TB Register.

12.4.3 Transfer of a patient

Transfer OUT:
When a patient is being transferred to another health facility, a duplicate of the original card is prepared and marked on top in bold letters with "DUPLICATE".

The receiving facility returns the bottom section "Response to a transfer of a TB patient", the appropriate column ("Transfer out") in the Unit Tuberculosis Register will be marked. This indicates that the patient has arrived, and that the responsibility for his/her follow-up is, from now on with the new unit.

- Prepare a duplicate of the patient's original Tuberculosis Treatment Card. Write on top of the card in bold letters "DUPLICATE". It is important that the section "Transfer out" to "moved out" on the original card is completed and that the original card be filed at the appropriate place in the transferring out unit. The duplicate card is forwarded to the receiving facility.
- Prepare the "Notice of transfer of a patient", that will accompany the duplicate Tuberculosis Treatment Card, when sent to the receiving health facility.
- Send both, the duplicate 'Card' and the 'Notice of Transfer' of a patient to the receiving unit. Also, add the 'Contact Examination Form', if applicable.
- When the receiving unit returns to you the tear-off slip "Response to a transfer of TB patient", make an entry under the appropriate column "Transfer out" in your Unit Tuberculosis Register.
- If a patient was sent to another health facility, but no "Response to a transfer of TB patient" was received, it would be advisable to contact the facility over the phone or radio and to enquire.

Transfer IN:

- Enter all details of the newly arrived patient into the Facility Tuberculosis Register and issue a new facility TB Number, as appropriate to **your** facility TB Register. Make sure you indicate that the patient is "transferred in" or “Moved in”, by putting an "x" or a “✔”mark in the appropriate column.
- Enter your Facility TB Number into the second line on the duplicate Tuberculosis Treatment Card and on the Patient's Tuberculosis Card in the spaces provided (the first line should already contain the number of the sending facility).
- Keep the duplicate Tuberculosis Treatment Card for monitoring the continued treatment at your unit. Make corresponding entries as regards compliance with treatment also into Patient's Tuberculosis Card (former "Appointment Card"), which is retained by the patient.
- Return the bottom tear-off section "Response to a transfer of a TB patient" to the unit, which sent the patient to you, as soon as the patient has come to your unit.
- If a Tuberculosis Treatment Card was sent to you, but no patient arrived, it is advisable to contact the sending health facility over the phone or radio and to enquire.

12.4.4 Contact examination

In case of a smear-positive tuberculosis patient being diagnosed at your unit

- Prepare Contact Examination Form.
- Initiate contact screening.
- Once a tuberculosis suspect is discovered, register him/her in the Suspect Sputum Dispatch Register.

In case of a tuberculosis patient being diagnosed outside your facility

- A completed Contact Examination Form will be sent to you.
- Initiate contact screening.
- Once a tuberculosis suspect is discovered, register him/her in the Suspect and Sputum Dispatch Register.

12.4.5 Discharge from treatment

Categorisation of patients at the end of treatment is described in Chapters 7 and 8, and on the inside of the cover of each Facility Tuberculosis Register.

12.5 Recording and reporting in the IPT programme

The IPT programme uses the following forms:

12.5.1 Facility IPT Register and Compliance Record

This is the backbone of the national IPT recording and reporting system. The record should be maintained by all facilities and be completed each time an HIV-positive client is screened for IPT, irrespective of whether they are found eligible or not.

The register contains particulars of all clients screened for IPT. A new serial number is given to each client who is screened for eligibility for IPT. A client can only be registered once in a calendar year. A client initially found to be ineligible on registration who later becomes eligible within the same year should keep the same serial number given at registration. Should the client return the following year, a new serial number should then be given.

The compliance section of the register contains records of all clients' visits and should be completed each time the client comes for review and refill of tablets. It is also very important to record the client's completion status on the appropriate section in the register, including the date treatment stopped and the reasons for failure to complete treatment.

12.5.2 District Facility Register

This is similar to the facility register except that it has more pages. Data from all facility IPT registers are transferred from the facility registers into the district registers before entry into the electronic IPT database. This transfer of clients' data is done monthly by the TB coordinator who visits all health facilities under his/her supervision at the end of every month to update the district register.

12.5.3 Dispensary Tally Sheet

The dispensary tally sheet is used to monitor the number of tablets issued to IPT clients and should be maintained at all clinic dispensary units. The serial numbers and other particulars of clients in the tally sheet should match those in the facility registers. The tally sheet indicates:

- The dosage and the number of tablets dispensed at the initiation of treatment
- The refill date as well as the tablets issued (at the bottom of the slash refill date/no. tablets)

12.5.4 IPT Transfer Form

This is kept in all facilities and is used to communicate all relevant registration and treatment information for clients who may transfer to another facility within or outside the district. This form contains the following information about the client:

- Transferring district and facility
- Receiving district and facility
- Patient's name, sex and age
- Local IPT number
- Date of transfer
- Name and signature of sender

The response to a transfer slip must be completed by the receiving clinic and sent back to the original (transferring) health facility.

12.5.5 Monthly Report Form

This form must be used by all health facilities. It should be filled every month end, indicating the status of IPT performance in respective facilities. It contains the following information:

- Number of clients who were screened for IPT
- Number of clients enrolled onto IPT
- Number of clients excluded from IPT
- Number of clients who completed therapy
- Number of clients who fail to complete therapy
- Number of clients who transferred to other facilities
- Reasons for not completing therapy
- Name and signature of reporting officer

The filled-out form should be sent to the district where all such forms are sent for summarisation into one report, which will then be transmitted to the national level.

12.6 Cohort Report in the IPT programme

A cohort report shows a report for a group of individuals with some characteristics in common, such as those who started IPT Treatment. The report shows the total number of people registered, those who started and so on. The cohort report also has percentages to show the proportions from one category to the other, e.g. 61.47% of the registered clients started IPT in 2004 in the Bobirwa district. The total completed refers to the clients who completed treatment in 2004 and they constitute 62.67% of those that started the IPT treatment. The clients who did not complete (Incomplete) the IPT are subdivided into eight categories i.e. Missing incomplete reason, Active TB, Terminal AIDS, Hepatitis/ Severe side effects, lost to follow up, IPT discontinued by health worker, voluntary withdrawal from the programme by patient and other.

CHAPTER 13: TASK DISTRIBUTION

13.1 Importance of task distribution

The Botswana National Tuberculosis Programme can only function effectively if all stakeholders are aware of their role in the prevention and management of TB, and execute their roles well.

Most health workers, especially doctors, nurses, TB coordinator's and Family Welfare Educators (FWE), have important roles to play in the BNTP and therefore need to have a broad knowledge of the different components of the programme.

In addition to a broad knowledge about the BNTP, each individual health worker must know in detail how he or she should function within the programme, which tasks to perform, how to perform them and how the various categories of health workers involved in TB relate to each other.

13.2 Public Health Specialist

The Public Health Specialist (PHS) is responsible for all TB work in the health district and should ensure that policies and procedures regarding diagnosis, registration and treatment of TB patients are known and followed by health personnel within the district. Where possible, the PHS should actively participate in clinical TB work.

The PHS must ensure that all drugs for TB are ordered for all health facilities and that a record of all anti-TB drugs in stock is maintained, including those issued to health facilities.

The establishment of good personal relations between the patient, the staff at the health facility and the TB coordinator is crucial in preventing default, which most often takes place immediately after the patient is discharged from hospital or as soon as the patient is diagnosed in the health facility.

The PHS must ensure that TB and the BNTP are permanent agenda items for seminars and workshops to keep health staff and other community leaders well informed and up to date on TB matters.

13.3 Chief Medical Officer in charge

The Chief Medical Officer (CMO) in charge of a hospital is responsible for ensuring that all other hospital doctors, family nurse practitioners and other nursing personnel in that hospital involved in TB work are familiar with the TB Programme and follow the guidelines and principles of the BNTP. The CMO should work closely with the PHS in all questions regarding the BNTP.

- Firstly, the CMO in charge should emphasise to all staff that sputum smear examination is the prime diagnostic procedure for diagnosing pulmonary tuberculosis and that sputum smears should be obtained for all suspected cases of pulmonary TB.
- Secondly, doctors and nurses must be familiar with the different TB drugs and their possible side effects and correct dosages according to the weight and age of the patient.
- Thirdly, doctors and nurses must know and follow the procedures for registration of TB patients and procedures involved at time of discharge from hospital to daily supervised outpatient treatment, including correct filling of the TB treatment card and the patient's card. The TB-coordinator must always be informed in advance when a TB patient is to be discharged, so that he/she can make sure that arrangements are being made for outpatient

treatment whenever possible.

- The CMO will appoint a focal point for TB control in hospitals

13.4 Matron and other supervising staff

The senior nursing staff must be familiar with the TB programme in order to be able to supervise and give advice.

13.5 TB Coordinator

The TB Coordinator is the TB focal person in the district responsible for coordinating all aspects of the BNTP work in the district and is directly responsible to the PHS. The TB coordinator is also responsible for managing the community TB care in the district, and teaches FWEs and nurses in the proper filling of TB cards and registers, treatment support and tracing of contacts and defaulters.

The TB Coordinator should visit the hospital (TB wards), including the laboratory, at least once a week. The TB co-ordinator participates in seminars and workshops where TB is a subject and addresses *kgotla* meetings on TB as frequently as possible. He/she should follow the PHS/MOs on clinic visits on a regular basis.

The TB Coordinator is responsible for the maintenance of the District TB Register, the Electronic TB Register, compiling analysis and reporting to the BNTP on a regular basis. The coordinator should maintain records of TB drugs at the district level and ensure that new supplies are ordered, unless the DHT has a pharmacist/pharmacy technician attached.

13.6 Community Health Nurse

The main functions of the Community Health Nurse (CHN) will be:

- To co-ordinate home based care for patients, in the respective district, with AIDS related diseases, including TB
- To complement the efforts of the Community Home Based Care (CHBC) Coordinator and the TB Co-ordinator in data-collection, reporting, and training of CHBC staff.
- To assist the CHBC Coordinator, TB Coordinator in the coordination of the day-to-day TB control activities of all health workers
- Together with the TB Coordinator, to compute and analyse the district data on TB notification and TB treatment outcome, and to interpret the data to re-enforce the control strategies
- To ensure that the national TB policies are being adhered to in the district
- To co-ordinate and supervise the implementation of IPT

13.7 Community Home-Based Care Coordinator

A CHBC should be a CHN trained in TB work to complement the efforts of the TB Coordinator, especially in the treatment, care and support of home-based patients with dual TB and HIV infection. In addition, the CHBC Coordinator is responsible for:

- Providing data to the TB Co-ordinator on patients treated at home
- Supervising/coordinating TB treatment at community level

13.8 Health facility nurses and Family Welfare Educators

Nurses and FWEs working in clinics and health posts must know in detail the procedures for passive case-finding, i.e. how to keep a suspect-register, when and how to collect sputum for smear microscopy, when and how to send samples to the laboratory, how and when to refer a case to a higher level facility. They should also know how to keep the local TB register, procedures for transfer of a patient to another facility, how to record and give daily supervised treatment, and what to do in case a patient does not turn up for his treatment. The clinic nurse will supervise the local CTBC volunteers. Nurses can register patients and start treatment if patients have smear-positive PTB.

One FWE should be assigned to the TB Programme to complement the efforts of doctors and nurses in the procedures for registration of TB patients, discharge from the hospital to daily supervised out patient treatment especially those receiving DOT at OPD. The FWE will report all defaulters tracing efforts to the facility as well as the TB Coordinator for further action.

13.9 Medical, paediatric and surgical specialists

Hospital-based specialists should attend to referred cases, advise and initiate treatment when indicated. Proper feedback to referring facility/MO is essential, as well as information to TB Coordinator if a patient is started on TB treatment. Follow-up can usually be done by PHS/District health staff. Cases of MDR-TB should be referred to specialist physicians at the two referral hospitals. Specialists are expected to participate in the training of doctors and nurses on all aspects of TB control.

13.10 Private medical practitioners and private hospitals

Private medical practitioners should adhere to the diagnostic criteria described in this manual, and refer TB patients to public health facilities for treatment. Private hospitals are also expected to follow guidelines for diagnosis and treatment and to liaise with PHS/TB Coordinator on a regular basis and submit regular reports to the DHT.

It cannot be too strongly emphasised that private practitioners are not authorised to manage TB patients outside the framework of the National TB programme. Once a diagnosis of TB has been made the patient must be referred to the public sector for full documentation and supervision of their treatment under DOT. Patients who are diagnosed as having TB whilst admitted to a private hospital should have their TB treatment commenced immediately in accordance with national guidelines. Upon discharge to continue treatment on an outpatient basis, they should be transferred to the government public health system.

13.11 Pharmacy staff at clinic and hospital level

Responsibilities:

- Ordering all anti-TB drugs and maintaining adequate stocks at DHT (ensures a regular supply of drugs and checks on expiry dates)
- Maintaining good records of all anti-TB drugs in stock at health facilities
- Providing daily treatment to TB patients in coordination with other staff and correctly recording treatment on the treatment cards
- Reporting defaulters to the relevant staff for further action

13.12 District Health Education Officer.

The District Health Education Officer will promote Health Education activities related to TB, and will mobilise the community on matters related to TB control.
Responsibilities:

- Facilitating the organisation of World TB Day commemorations on an annual basis
- Assisting the TB Coordinator in convening TB-related seminars for staff and communities

13.13 Botswana National Tuberculosis Programme

The BNTP is part of the public health department of the MOH, and is responsible for tuberculosis control in the whole country. An epidemiologist/PHS is in charge of the entire BNTP management, assisted by several epidemiological and technical staff.

Main responsibilities:

- Updating BNTP policies and strategies
- Updating and publishing the BNTP manual
- Coordinating the implementation of the BNTP with other sections of the MOH and with the Ministry of Local Government
- Training (or assist in training) personnel involved in the BNTP
- Liaising with CMS to ensure adequate supply of drugs, laboratory reagent, equipment and documents needed in the implementation of the BNTP.
- Ensuring that the requested reports on case finding, sputum conversion and results of treatment out comes are completed and dispatched by each district
- Maintaining and managing a national TB health information system
- Supervising, monitoring and evaluating the implementation of BNTP strategies throughout the country, including TB preventive therapy and community TB care implementation
- Coordinating scientific and operational research in the field of TB in collaboration with partners

ANNEXES

Annex 1: Mycobacteria Other Than Tuberculosis (MOTT)

Mycobacteria Other than Tuberculosis, also known as Non-tuberculous Mycobacteria (NTM) or Atypical Mycobacteria refers to all the species in the family of mycobacteria that may cause human disease, but do not cause tuberculosis (TB). In Botswana these organisms are commonly referred to as MOTT and our laboratories use this term when reporting them from culture results.

The most common MOTTs that require treatment are *M. avium complex, M. kansasii, M. absussus, M. chelonae, M. fortuitum, M. terrae, M. xenopi,* and *M. simiae.*

Unlike TB, MOTT infections are **not** considered contagious. There is no evidence that the infection can be transmitted from one person to another. These organisms are commonly present in water and soil but do not normally cause disease in individuals with normal lungs and a normal immune system. People who have damaged lungs from diseases such as emphysema, bronchiectasis or previous TB infection appear to be at greater risk for developing a MOTT infection. People who are immunocompromised are particularly at risk of developing a MOTT infection which may affect not only the lungs but all major organs.

MOTT organisms take up the ZN stain in the same way as the TB bacilli and so if present in sputum will appear as acid fast bacilli (AFB) in sputum smears. They will consequently be reported as AFB positive even though they are not tuberculous. There is no way of distinguishing MOTT from TB mycobacteria in a sputum smear. However culture of sputum will differentiate TB bacilli from MOTT organisms and the laboratory will therefore report a positive culture result as either showing TB or MOTT.

Unfortunately our laboratories are not able to determine precisely which of the above MOTT species is present but it is assumed that the most common MOTT to infect patients with severe immune deficiency is the group known as Mycobacterium Avium Complex or MAC.

Before ARTwas available MAC was the most commonly reported bacterial infection among people with AIDS. With CD4 counts less than 100 cells/mm^3, and often below 20 cells/mm^3, MAC can disseminate throughout the body, affecting almost any organ, but especially the liver, spleen, bone marrow and lymph nodes. The resulting disease is debilitating and often fatal without treatment. Since the introduction of HAART, the incidence of MAC has fallen significantly and the disease can be cured using appropriate antibiotics providing the CD4 count increases to above 200/cmm in response to ART.

Symptoms

The widespread dissemination of the organisms may cause high fevers, severe anaemia, night sweats, chills, weight loss, loss of appetite and weakness. If the gut is involved, symptoms can include chronic diarrhoea with malabsorption of nutrients, and abdominal pain due to ulcers. There may also be lymphadenopathy, hepatomegaly and splenomegaly. Respiratory symptoms similar to those caused by PTB may also occur.

No information is available on the incidence of MOTT in Botswana though a small number of cases are diagnosed each year as a result of sputum culture. MOTT may also be diagnosed from blood cultures and if these were done more frequently more cases might be detected.

Treatment

MOTT do not respond to standard anti-TB treatment. There is a common misperception that MOTT are a type of MDR-TB. This is clearly not the case as the organisms causing MOTT are from a different species and require different treatment regimens from those used for MDR-TB.

Treatment for MOTT is empirical and based on information from studies in other countries, as Botswana does not perform drug susceptibility testing on these organisms. Regimens to treat MOTT should consist of a combination of two or more drugs, including at least clarithromycin and ethambutol. A third drug can be added from one of the following: rifampicin, gentamicin, amikacin or ciprofloxacin. Treatment should continue until blood cultures are negative and there is evidence of sustained recovery of the immune system (sustained CD 4 count >200). Treatment of MOTT should be initiated and continue under the supervision of a physician specialist.

Annex 2: Organograms

Figure A2.1: Organogram of the Ministry of Health

Figure A2.2: Organogram of Ministry of Health and Ministry of Local Government relevant to TB control

Annex 3: Sputum collection

Sputum collection:

- Use sterile glass or plastic containers, 5 - 6 cm deep with screw caps. The containers must be leak-proof and rigid to avoid crushing during transport to the laboratory.
- Sputum collection should be done in the open air or in an empty room with good ventilation. Where this is not possible or the patient is too ill to be taken outside, the health worker assisting with the sputum collection should wear an N95 respirator mask.
- The health worker should explain the procedure fully and slowly.
- The health worker should supervise, but should not stand in front of the patient.
- Only sputum (2 – 5 ml) should be accepted as a good specimen. Saliva (white, watery, frothy) should not be accepted, with the exception of induced sputum which resembles saliva and should therefore not be rejected

Sputum collection technique:

1. Rinse the mouth before producing the specimen and drink some warm water to wet the throat.
2. Open the container and keep it near the mouth.
3. Keep the body inclined to the front.
4. Take two deep breaths, holding the breath for a few seconds after each inhalation and then exhaling slowly.
5. Breathe in a third time and forcefully blow the air out.
6. Breathe in again and then cough, producing viscid sputum that should be carefully ejected into the container
7. Close the lid securely.
8. Wash hands after handling the sputum container.

Transportation of sputum specimen:

1. Label the specimen appropriately: Patient's name, clinic name and date of sputum collection. Label the container and NOT the lid.
2. Place the sputum container in a leak-proof plastic bag to prevent contamination, together with the requisition form. The specimens should then be placed into a rigid container with cooler bags to prevent higher temperatures (which may kill bacteria) during transportation.
3. Enter the specimen data into the Suspect and Sputum Dispatch Register before dispatch
4. Send the specimens to the laboratory as soon as possible.
5. If dispatch is delayed, store specimens in a fridge (do not freeze) or in a cool dark corner of the room until they can be sent.
6. During transportation, specimens should be protected from exposure to direct sunlight.

Annex 4: Quantifying fluorescent smear results

Fluorochrome staining methods require much lower magnifications (typically 250x to 630x) by Ziehl-Neelsen staining methods (oil immersion field = 1 000x). Thus, a fluorochrome-stained smear examined at 250x may contain much larger numbers of bacilli than a similar specimen stained with Ziehl-Neelsen and examined at 1 000x. To avoid confusion, a method using magnification factors was devised to enable comparison of reports between laboratories regardless of the stain or magnification used.

Table A4.1: Quantification of fluorescent smear results

1 Ziehl-Neelsen 1 000x	2 Report	3 Fluorescent microscopy magnification		
		250x	450x	630x
0	No AFB seen	0	0	0
1-9/100 fields	Report exact count	Divide observed count by **10**	Divide observed count by **4**	Divide observed count by **2**
10-99/100 fields	+1			
1-10/field	+2			
>10/field	+3			

Modified from: Laboratory Services in Tuberculosis Control – Part II: Microscopy (WHO/TB/98.258)

To adjust for altered magnification of fluorescent microscope, divide the number of organisms seen (under fluorescent microscopy) by the factor provided and refer to column 1 for range and column 2 for what to report.

Example:
Suppose 20 acid-fast bacilli are observed per field using the 450x magnification. If this number is divided by the magnification factor of 4 according to the table, the comparable number of bacilli that would have been observed under 1 000x is 5 per field. The laboratory result should therefore read 2+, and not 3+, as originally indicated by 20 acid-fast bacilli per field.

Annex 5: Performing Fine Needle Aspiration

Fine needle aspiration is a very useful way of diagnosing tuberculosis when enlarged lymph nodes are present. Perform as follows:

- Connect a 19G needle to a 10ml syringe and insert it into a selected node, avoiding any visible blood vessels.
- Apply constant suction through the syringe and gently move the needle in and out of different parts of the node without exiting the skin.
- Remove the syringe, leaving the needle in situ, and draw in some air.
- Remove the needle and re-attach it to the syringe.
- Expel the air in the syringe through the needle onto a slide.
- Send the slide to the laboratory for Ziehl-Neelsen staining. The specimens can also be submitted for culture.

Annex 6: Administering, reading and interpreting a Tuberculin Skin Test

A TST is the intradermal injection of a combination of mycobacterial antigens which elicit an immune response (delayed-type hypersensitivity), represented by induration, which can be measured in millimetres. The TST using the Mantoux method is the standard method of identifying people infected with *M. tuberculosis*.

Administration:

1. Locate and clean injection site 5–10 cm below elbow joint.
   - Place forearm palm-side up on a firm, well-lit surface.
   - Select an area free of barriers (e.g. scars, sores).
   - Clean the area with 70% alcohol or methylated spirit and then dry with a sterile swab.

2. Prepare syringe.
   - Check expiration date on vial and ensure vial contains tuberculin PPD-S (5 TU per 0.1 ml).
   - Use a single-dose tuberculin syringe with a short (5mm to 10mm) 27-gauge needle with a short bevel, which must fit very tightly on the syringe.
   - Fill the syringe with 0.1 ml tuberculin.

3. Inject tuberculin.
   - Insert the needle slowly, bevel up, at an angle of 5–15° lengthwise of the arm, while lightly stretching the skin in the direction of the needle.
   - The needle bevel should be visible just below skin surface.
   - Hold the syringe by the barrel only and do not touch the plunger until the needlepoint has been satisfactorily inserted.
   - Slowly inject the 0,1 ml tuberculin.
   - Remove the finger from the end of the plunger before withdrawing the needle.

4. Check injection site.
   - The injection should raise a flat, anaemic weal with pronounced pits and a steep borderline, 6 mm to 10 mm in diameter.
   - If not, the injection was too deep. Repeat the injection at a site at least 5 cm away from the original site.
   - The weal disappears within 10-30 minutes.
   - The injection is only very slightly painful and gives a sensation comparable to that of an insect bite, which lasts for one or two minutes.

5. Record information.
   - Record all the information required by your institution for documentation (e.g. date and time of test administration, injection site location, lot number of tuberculin).

Reading:

Read the test between 48 and 72 hours after administration. A patient who does not return within 72 hours should be rescheduled for another TST. Measure the reaction with a small transparent ruler calibrated in millimetres, or preferably by callipers with a dial.

1. Inspect site.

- Visually inspect injection site under good light, and measure induration (thickening of the skin), not erythema (reddening of the skin).
- Sometimes a small red spot the size of a pinpoint remains at the site of the entry of the needle. When the reaction is negative, it is sometimes very difficult to determine where the injection was made. This may easily be avoided by drawing a circle in red ink on the skin at the time of inoculation.

2. Palpate induration.
   - Carefully palpate the test site with fingertips to find the margins of induration.
   - The induration may vary from a firm, well-circumscribed density in the skin to a soft, ill-defined swelling. The latter type may easily escape notice unless the test site is palpated with a light touch.
   - The reaction may be intense with a large papule 10-20 mm in diameter, surrounded by a pinkish rosette, which may be several centimetres wide. In these cases, the reaction is often accompanied by itching. In a few cases, the centre of the papule may look like a blister.

3. Mark induration.
   - Use fingertips as a guide for marking widest edges of induration across the forearm (transverse to the arm).
   - If the reaction is positive, the zone all around the injection site is red, infiltrated and elevated. The redness is <u>not</u>sufficient indication of a positive reaction. The essential factor is the induration, which is always easy to feel.

4. Measure diameter of induration using a clear flexible ruler.
   - Place “0” of ruler line on the inside-left edge of the induration.
   - Read ruler line on the inside-right edge of the induration (use lower measurement if between two gradations on mm scale).

5. Record diameter of induration.
   - Do not record as “positive” or “negative”.
   - Only record measurement in millimetres.
   - If no induration, record as 0 mm.

Interpretation of the test:

The TST should be regarded as positive as follows:
- In high-risk children (including HIV-positive children and severely malnourished children) ≥5 mm diameter of induration.
- In all other children (whether they have received BCG vaccine or not) ≥10mm diameter of induration.

Table A6.1: Causes of false-negative TST and false-positive TST

Causes of false-negative TST	Causes of false-positive TST
- Incorrect administration or interpretation of test - HIV infection - Improper storage of tuberculin - Viral infections (e.g. measles, varicella) - Vaccinated with live viral vaccines (within 6 weeks)	- Incorrect interpretation of test - BCG vaccination - Infection with MOTT

Annex 7: Gastric Aspiration

Background:
Gastric aspiration is used to collect gastric contents to try to confirm the diagnosis of TB by microscopy and mycobacterial culture in young children when sputum cannot be spontaneously expectorated nor induced using hypertonic saline. It is most useful for young hospitalized children.

Because of the distress caused to the child, and the generally low yield of smear-positivity on microscopy, this procedure should be used only where culture and microscopy are available..

During sleep, the lung's mucociliary system sweeps mucus up into the throat where it is swallowed and remains in the stomach until the stomach empties. Therefore, the highest-yield specimens are obtained first thing in the morning. Gastric aspiration on each of three consecutive mornings should be performed for each patient.

Performing the test properly usually requires two people (one doing the test and an assistant). Children with a low platelet count or bleeding tendency should not undergo the procedure.

Required equipment:
1. Gloves
2. Nasogastric tube (usually 10 French or larger)
3. 5, 10, 20 or 30 cm3 syringe, with appropriate connector for the nasogastric tube
4. Litmus paper
5. Specimen container
6. Pen (to label specimens)
7. Laboratory requisition forms
8. Sterile water or normal saline (0.9% NaCl)
9. Sodium bicarbonate solution (8%)
10. Alcohol/chlorhexidine

Procedure:
The procedure can be carried out as an inpatient first thing in the morning when the child wakes up, at the child's bedside or in a procedure room on the ward (if one is available), or as an outpatient (provided that the facility is properly equipped). The child should have fasted for at least four hours (infants for three hours) before the procedure.
1. Prepare all equipment before starting the procedure.
2. Position the child on his or her back or side. The assistant should help to hold the child.
3. Measure the distance between the nose and stomach, to estimate distance that will be required to insert the tube into the stomach.
4. Attach a syringe to the nasogastric tube.
5. Gently insert the nasogastric tube through the nose and advance it into the stomach.
6. Withdraw (aspirate) gastric contents (2–5 ml) using the syringe attached to the nasogastric tube.
7. To check that the position of the tube is correct, test the gastric contents with litmus paper: blue litmus turns red (in response to the acidic stomach contents). (This also can be checked by pushing some air (e.g. 3–5 ml) from the syringe into the stomach and listening with a stethoscope over the stomach.)
8. If no fluid is aspirated, insert 5–10 ml sterile water or normal saline and attempt to aspirate again.

    a. If still unsuccessful, attempt this again. (Even if the nasogastric tube is in an incorrect position and water or normal saline is inserted into the airways, the risk of adverse events is still very small.)
    b. Do not repeat more than three times.
9. Withdraw the gastric contents (ideally at least 5–10 ml).
10. Transfer gastric fluid from the syringe into a sterile container (sputum collection cup).
11. Add an equal volume of sodium bicarbonate solution to the specimen (to neutralize the acidic gastric contents and so prevent destruction of tubercle bacilli).

After the procedure:

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

Safety:

Gastric aspiration is generally not an aerosol-generating procedure. As young children are also at low risk of transmitting infection, gastric aspiration can be considered a low risk procedure for TB transmission and can safely be performed at the child's bedside or in a routine procedure room.

Annex 8: Treatment Categories

Table A8.1: Category I Treatment for Adults: 2(HRZE)/4(HR)

Weight (kg)	Intensive Phase for 2 months	Continuation Phase for 4 months
	$R_{150}H_{75}Z_{400}$ E_{275}[1]	$R_{150}H_{75}$[2]
30 – 39	2 tabs	2 tabs
40 – 54	3 tabs	3 tabs
55 – 70	4 tabs	4 tabs
>70	5 tabs	5 tabs

[1] $R_{150}H_{75}Z_{400}$ E_{275} = fixed-dose combination of rifampicin 150mg, isoniazid 75mg, pyrazinamide 400mg and ethambutol 275mg

[2] $R_{150}H_{75}$ = fixed-dose combination of rifampicin 150mg and isoniazid 75mg

[3] $E_{275}H_{75}$ = fixed-dose combination of ethambutol 275mg and isoniazid 75mg

Table A8.2: Category I Treatment for Children: 2(HRZ)/4(HR)

Weight (kg)	Intensive Phase for 2 months	Continuation Phase for 4 months
	$R_{60}H_{30}Z_{150}$[1]	$R_{60}H_{30}$[2]
3 - 4	½ tab	½ tab
5 - 7	1 tab	1 tab
8 – 9	1½ tabs	1½ tabs
10 – 14	2 tabs	2 tabs
15 – 19	3 tabs	3 tabs
20 – 24	4 tabs	4 tabs
25 – 29	5 tabs	5 tabs

[1] $R_{60}H_{30}Z_{150}$ = fixed-dose combination of rifampicin 60mg, isoniazid 30mg and pyrazinamide 150mg

[2] $R_{60}H_{30}$ = fixed-dose combination of rifampicin 60mg and isoniazid 30mg

Table A8.3: Category II Treatment for Adults: 2S(HRZE)/1(HRZE)/5(HRE)

Weight (kg)	Intensive Phase for 2 months		Intensive Phase for 1 month	Continuation Phase for 5 months
	Streptomycin (mg)	$R_{150}H_{75}Z_{400}$ E_{275}[1]	$R_{150}H_{75}Z_{400}$ E_{275}	$R_{150}H_{75}E_{275}$[2]
30 – 39	500	2 tabs	2 tabs	1.5 tabs
40 – 54	750	3 tabs	3 tabs	2 tabs
55 – 70	1000	4 tabs	4 tabs	3 tabs
>70	1000	5 tabs	5 tabs	3 tabs

[1] $R_{150}H_{75}Z_{400}$ E_{275} = fixed-dose combination of rifampicin 150mg, isoniazid 75mg, pyrazinamide 400mg and ethambutol 275mg

[2] $R_{150}H_{75}E_{275}$ = fixed-dose combination of rifampicin 150mg, isoniazid 75mg and ethambutol 275mg

Table A8.4: Category II Treatment for Children: 2S(HRZ)/1(HRZ)/5(HR)

Weight (kg)	Intensive Phase for 2 months		Intensive Phase for 1 month	Continuation Phase for 5 months
	Streptomycin[1] (mg)	$R_{60}H_{30}Z_{150}$[2]	$R_{60}H_{30}Z_{150}$	$R_{60}H_{30}$[3]
<7	100	1 tab	1 tab	1 tab
8 – 9	120	1.5 tabs	1.5 tabs	1.5 tabs
10 – 14	150	2 tabs	2 tabs	2 tabs
15 – 19	250	3 tabs	3 tabs	3 tabs
20 – 24	300	4 tabs	4 tabs	4 tabs
25 – 29	400	5 tabs	5 tabs	5 tabs

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

[2]$R_{60}H_{30}Z_{150}$ = fixed-dose combination of rifampicin 60mg, isoniazid 30mg and pyrazinamide 150mg

[3] $R_{60}H_{30}$ = fixed-dose combination of rifampicin 60mg and isoniazid 30mg

Table A8.5: Category III Treatment for Children: 2(HRZ)/4(HR)

Weight (kg)	Intensive Phase for 2 months	Continuation Phase for 4 months
	$R_{60}H_{30}Z_{150}$[1]	$R_{60}H_{30}$[2]
<7	1 tab	1 tab
8 – 9	1.5 tabs	1.5 tabs
10 – 14	2 tabs	2 tabs
15 – 19	3 tabs	3 tabs
20 – 24	4 tabs	4 tabs
25 – 29	5 tabs	5 tabs

[1] $R_{60}H_{30}Z_{150}$ = fixed-dose combination of rifampicin 60mg, isoniazid 30mg and pyrazinamide 150mg

[2] $R_{60}H_{30}$ = fixed-dose combination of rifampicin 60mg and isoniazid 30mg

Annex 9: Category IV Regimens in Botswana

Table A9.1: Weight-based dosing of anti-TB drugs in the treatment of drug-resistant TB, based on available drugs (Drugs which are available through CMS are in bold font)

Medication (Drug, Abbreviation)	Weight			
	<33 kg	33-50 kg	51-70 kg	>70 kg (also max. dose)
GROUP 1: FIRST-LINE ORAL ANTI-TB DRUGS				
Isoniazid (H)	4-6 mg/kg/d	200-300 mg	300 mg	300 mg
Rifampicin (R)	10-20 mg/kg/d	450-600 mg	600 mg	600 mg
Ethambutol	25 mg/kg/d	800-1200 mg	1200-1600 mg	1600-2000 mg
Pyrazinamide	30-40 mg/d	1000-1750 mg	1750-2000 mg	2000-2500 mg
GROUP 2: INJECTABLE ANTI-TB DRUGS				
Streptomycin (S)	15-20 mg/d	500-750 mg	1000 mg	1000 mg
Amikacin (Am)	15-20 mg/d	500-750 mg	1000 mg	1000 mg
Kanamycin (Km)	15-20 mg/d	500-750 mg	1000 mg	1000 mg
Capreomycin (Cm)	15-20 mg/d	500-750 mg	1000 mg	1000 mg
GROUP 3: FLUOROQUINOLONES				
Ciprofloxacin (Cfx)	20 – 30 mg/kg/d	1500 mg	1500 mg	1500 mg
Ofloxacin (Ofx)	800 mg	800 mg	800 mg	800-1000 mg
Levofloxacin (Lfx)	750 mg	750 mg	750 mg	750-1000 mg
Moxifloxacin (Mfx)	400 mg	400 mg	400 mg	400 mg
Gatifloxacin (Gfx)	400 mg	400 mg	400 mg	400 mg
GROUP 4: ORAL BACTERIOSTATIC SECOND-LINE ANTI-TB DRUGS				
Ethionamide (Eto)	15-20 mg/kg/d	500 mg	750 mg	750-1000 mg
Prothionamide (Pto)	15-20 mg/kg/d	500 mg	750 mg	750-1000 mg
Cycloserine (Cs)	15-20 mg/kg/d	500 mg	750 mg	750-1000 mg
Terizidone (Trd)	15–20 mg/kg/d	600 mg	600 mg	900 mg
p-aminosalicylic acid (PAS)	150 mg/kg/d	8g	8g	8g
Sodium PAS	Dosing can vary with manufacture and preparation: check dose recommended by the manufacturer			
Thioacetazone (Th)	150 mg per adult			
GROUP 5: AGENTS WITH UNCLEAR EFFICACY (not recommended by WHO for routine use in MDR-TB patients, and generally not available in Botswana)				
Clofazimine (Cfz) Amoxicillin/Clavulanate (Amx/Clv) Clarithromycin (Clr), Linezolid (Lzd)	Efficacy and dosing in the treatment of drug-resistant TB not fully determined			

Note:

- Pyrazinamide is always included in the intensive phase
- Ethambutol is included throughout intensive and continuation phase **if** DST showed sensitivity

Table A9.2: Summary of the basic principles of designing a Category IV regimen

Basic Principle	Comments
1. Use at least 4 drugs certain or highly likely to be effective	Effectiveness is supported by a number of factors (the more present the more likely the drug will be effective in the patient): **A.** DST results show susceptibility **B.** No previous history of treatment failure with the drug. **C.** No known close contacts with resistance to the drug. **D.** Drug resistance survey indicates resistance is rare in similar patients. **E.** The drug is not commonly used in the area. If at least 4 drugs are not certain to be effective, use 5–7 drugs depending on the specific drugs and level of uncertainty.
2. Do not use drugs for which resistance crosses over	**A.** All rifamycins (rifampicin, rifabutin, rifapentene, rifalazil) have high levels of cross-resistance. **B.** Fluoroquinolones are believed to have variable cross-resistance, with in vitro data showing that some higher-generation fluoroquinolones remain susceptible when lower-generation fluoroquinolones are resistant. In these cases, it is unknown whether the higher-generation fluoroquinolones remain clinically effective. **C.** Not all aminoglycosides and polypeptides cross-resist; in general, only kanamycin and amikacin fully cross-resist.
3. Eliminate drugs that are not safe in the patient	**A.** Known severe allergy or unmanageable intolerance. **B.** High risk of severe adverse effects including renal failure, deafness, hepatitis, depression and/or psychosis. **C.** Quality of the drug is unknown or questionable.
4. Include drugs from Groups 1 – 4 in a hierarchical order based on potency	**A.** Use any Group 1 (oral first-line) drugs that are likely to be effective and preferably based on DST results (see section 1 of this table). **B.** Use an effective aminoglycoside or polypeptide by injection (Group 2 drugs). **C.** Use a fluoroquinolone (Group 3) **D.** Use the remaining Group 4 drugs to make a regimen of at least 4 effective drugs. For regimens with ≤4 effective drugs, add second-line drugs most likely to be effective, to give up to 5–7 drugs in total, on the basis that at least 4 are highly likely to be effective. The number of drugs will depend on the degree of uncertainty.
5. Be prepared to prevent, monitor and manage adverse effects for each of the drugs selected	**A.** Ensure laboratory services for haematology, biochemistry, serology and audiometry are available. **B.** Establish a clinical and laboratory baseline before starting the regimen. **C.** Initiate treatment gradually for a difficult-to-tolerate drug, split daily doses of Eto and Cs. **D.** Ensure ancillary drugs are available to manage adverse effects. **E.** Implement DOT for all doses.

Annex 10: Adverse effects of anti-tuberculosis drugs

Table A10.1: Summary of side effects of first-line anti-TB drugs

Drug	Common side effect	Rare side effect
Isoniazid	Peripheral neuropathy Elevated liver enzymes Sleepiness, lethargy	Skin rash (rarely Stevens-Johnson syndrome) Pellagra Hepatitis Convulsions Hallucinations, psychosis Agranulocytosis
Rifampicin	Elevated liver enzymes Itchiness (Orange/red urine and tears)	« Flu syndrome » Skin rash (rarely Stevens-Johnson syndrome) Hepatitis Acute renal failure Thrombocytopenia, haemolytic anaemia Anaphylaxis
Pyrazinamide	Joint pains (hyperuricaemia) Nausea	Vomiting, loss of appetite, abdominal pains Skin rash (rarely Stevens-Johnson syndrome) Hepatitis Photodermatitis Anaemia
Ethambutol		Retrobulbar neuritis Hyperuricaemia Haematological disturbances
Streptomycin	Auditory and vestibular nerve damage (also to foetus)	Skin rash (rarely Stevens-Johnson syndrome) Renal damage

Table A10.2: Symptom-based approach to management of common side effects

Degree and type of side effect	Drug(s) most likely to be the cause	Management
Minor 1. Symptomatic treatment 2. Continue anti-TB-drugs		
Nausea, vomiting, abdominal pain	Pyrazinamide, rifampicin	Take drugs with non-fatty foods (or just before going to bed)
Skin rash with mild itching, no blisters or mucous membrane involvement	Most anti-TB drugs	Consider other causes scabies etc) Aqueous cream, Calamine skin lotion Chlorpheniramine 4 mg tds or Promethazine 25-50 mg nocté
Numbness, tingling, burning sensation in hands and/or feet (Peripheral neuropathy)	Isoniazid	Pyridoxine 25 mg daily can be given as prevention Pyridoxine 50 mg daily for treatment, may add Amitriptyline 25-75 mg nocté or Carbamazepine
Major 1. Rule out other possible causes of presenting symptom 2. Patient may need admission 3. Anti-TB-treatment (or other offending drug) may need to be stopped and reintroduced carefully		
Skin rash with persistent itchiness, mucous membrane involvement and/or blistering	Most anti-TB-drugs (except ethambutol)	Stop TB drugs Refer to hospital and admit
Jaundice	Isoniazid, rifampicin, pyrazinamide	Stop TB drugs Refer to hospital and admit
Confusion	Most anti-TB drugs	Stop anti-TB drugs
Colour blindness, visual impairment	Ethambutol	Stop ethambutol
Anaphylactic shock, purpura, acute renal failure	Rifampicin	Stop rifampicin
Difficulty in hearing, deafness	Streptomycin	Stop streptomycin, use ethambutol
Dizziness	Streptomycin	Stop streptomycin, use ethambutol

Annex 11: Recording and Reporting Forms

Form 1: Suspect and Sputum Dispatch Register (MH 2028)

Date Registration (Suspects Only)	Patient Number		Name (in full)	Sex	Age	Address	Sputum Specimen			
								Date		
	Suspect Serial Number	Case Unit TB No.						Collection	Dispatch	Result Rec.
							1			
							2			
							3			
							1			
							2			
							3			
							1			
							2			
							3			
							1			
							2			
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Form 2: Mycobacteriology Request and Report Form (MH 2011)

Form 3: Tuberculosis Laboratory Register: MH 1041

WHERE IS TH IS FORM?

Form 4: Facility/District Tuberculosis Register (MH 2003)

Form 5: Tuberculosis Treatment Card (MH 1050)

Form 6: Patient's Tuberculosis Card (Appointment and DOT Card) (MH 1022/1)

Form 7: Tuberculosis Contact Examination Form (MH 2035)

Form 8: Notice of Transfer of a Patient (MH 1024)

Annex 12: Reporting Process for IPT

Table 12.1: Manual reporting process

FREQUENCY	WHEN ACTION IS TAKEN	RESPONSIBLE PERSON	ACTION
Monthly	By the 2nd week of the month	District TB Coordinators	• Generate the following reports for the previous month: > Missing Data Report > Data Errors Report > Client Status Report • Write a brief analysis of the 2 data quality reports explaining what problems are causing the data errors and what action(s) will be taken to improve data quality. • Send the 3 reports to the regional coordinator.
	Upon receipt of the reports	Regional Coordinators	• Review the reports and the analysis of data quality. • Provide feedback to the district coordinators within 5 working days if there are any questions concerning data quality or client status.
	By the 3rd week of the month	Regional Coordinators	• Send all district reports, including the data quality analyses, to the national programme.
	Upon receipt of the reports	National Programme	• Review the reports and provide feedback to the regional coordinators within 5 working days if there are any questions concerning content.
Quarterly	By the 2nd week of the month following the end of a quarter	District TB Coordinators	• Generate the Client Status Report for the previous quarter. • Run the dispatch function starting from the last dispatch to the end of the previous quarter. • Send the dispatch file and report to the regional coordinator.
	Upon receipt of the dispatch file and Client Status Report	Regional Coordinators	• Review the report and provide feedback to the district coordinators within 5 working days if there are any questions concerning content. • Load the dispatch file into the IPT system.
	By the 3rd week of the month	Regional Coordinators	• Send all district reports and dispatch files to the national programme.
	Upon receipt of the dispatch files and reports	National Programme	• Review the reports and provide feedback to the regional coordinators within 5 working days if there are any questions concerning content. • Load the dispatch file into the IPT system.

Note: The quarterly reporting period requires the following deliverables to be sent from the districts to the regional coordinators and then to the national programme:

- Missing Data Report for the previous month, including analysis of data quality
- Data Errors Report for the previous month, including analysis of data quality
- Client Status Report for the previous month
- Client Status Report for the previous quarter
- Quarterly dispatch file

Table 12.2: Electronics reporting process:

FREQUENCY	WHEN ACTION IS TAKEN	RESPONSIBLE PERSON	ACTION
Quarterly	By the 3rd week of the month following the end of a quarter	District TB Coordinators	• Run the dispatch function starting from the last dispatch to the end of the previous quarter. • Send the dispatch file to the national programme.
	Upon receipt of dispatch files	National Programme	• Load the dispatch file into ETR.