

Guidelines for Management of Tuberculosis and Leprosy in Kenya

July 2013

EDITION

FOREWORD

Tuberculosis remains a major cause of morbidity and mortality in Kenya. It affects all age groups, but has its greatest toll in the most productive age group of 15 to 44 years. The major factor responsible for the large TB disease burden in Kenya is the concurrent HIV epidemic. Other factors that have contributed to this large TB disease burden include poverty and social deprivation that have led to mushrooming of peri-urban slums, congestion and limited access to general health services. Recently, there have been increasing concerns about the emergence of drug resistant TB, a threat that would pose major challenges in the fight against TB in resource limited countries like Kenya.

To address challenges posed by the tuberculosis epidemic in the era of HIV, the Ministry of Public Health and Sanitation through the DLTLD has identified areas for increased support namely; Strengthening of human resources capacity at all levels of Division of Leprosy, Tuberculosis and Lung Disease (DLTLD) for effective coordination of control activities, decentralisation of control services to the community, strong collaboration between TB and HIV control programs to promote delivery of integrated TB/HIV services, promotion of private–public partnerships to increase the number of non - public providers integrated into the TB service provider network, sustained public health education campaigns to promote early care seeking and adherence to treatment at community level, and health care worker training and support for better TB case management by health care providers.

This guideline is a revision of earlier versions produced in 1994, 2000, 2003, 2006 and 2009 and marks yet another step forward for the DLTLD. It has been presented in an easy to read form and includes a section on pharmacovigilance and enhancement of the paediatric TB section introduced in the previous edition as a step towards improvement of quality of care. The immediate short-term goal is to sustain 70/85 target that Kenya recently achieved (detect 70 % of infectious TB and cure 85% of the detected cases) and then sustain and improve this effort over a long time to achieve the Millennium Development Goals (MDGs). These guidelines should be used as technical reference material by all health care workers involved in TB and Leprosy care and can also be used for training of health care workers in conjunction with other training materials.

Although Leprosy is no longer a major Public Health problem in Kenya, It is appreciated that there has been a significant loss of skills and knowledge by health care providers to suspect and diagnose leprosy owing to the reduction in number of cases seen over time. This in itself could account for the rapidly falling number of cases notified in the recent years. These guidelines includes an enhance leprosy case management chapter with colour plates and practical approach to case management. It is however recognized that other mechanisms need to be put in place to facilitate active contact tracing to improve case finding.

It is my sincere hope that all healthcare workers will find the revised guidelines useful for successful implementation of tuberculosis and leprosy control activities.



Dr. S. K. Sharif, MBS, MBChB, M.Med, DLSTMH, MSc
Director of Public Health & Sanitation
Ministry of Health

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The following people worked tirelessly towards the review of these guidelines:

Dr. Joseph Sitienei	Head of DLTLDCDC
Dr. Herman Weyenga	Head Care and Treatment, DLTLDCDC
Dr. Benard Langat	Head Policy Planning and Research, DLTLDCDC
Dr. Kamene Kimenye	Drug Resistant TB coordinator DLTLDCDC
Dr. Richard Muthoka	Pharmacist, DLTLDCDC
Dr. Kaseka Kadondi	PTLDC, Nyanza North
Ms Rose Wambu	Nutritionist, DLTLDCDC
Dr. Caroline Olwande	Pharmacist, NASCOP
Ms. Christine Awuor	TBHIV coordinator, NASCOP
Dr Jared Mecha	University of Nairobi
Dr Agnes Langat	CDC
Dr. Fredrick Otieno	Physician Catholic Relief Services
Dr Lameck diero	Moi University (AMPATH)
Dr. Nyukuri	AMPATH
Mr. Samson Kiboi	AMPATH
Late Dr. Joseph Odhiambo	CDC
Dr. Joel Kangangi	WHO
Mr. Hillary Kipruto	WHO
Ms Jane Onteri	ACSM Coordinator DLTLDCDC
Dr. Grace Karanja	KAPTLDCDC
Prof. Elizabeth Obimbo	University of Nairobi
Dr. Abraham Katana	CDC

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Dr. Joseph Sitienei OGW

Head Division of Leprosy Tuberculosis and Lung Disease

PREFACE

Kenya has a large TB disease burden and is ranked 15th among the 22 high burden countries that collectively contribute about 80% of the world's TB cases. The TB case notification rate (CNR) rose from 51 to 338 per 100,000 population between 1987 and 2007 and is currently on a slow decline. As in the rest of Sub-Saharan Africa, the large increase of TB is attributed primarily to the Human Immunodeficiency Virus (HIV).

Other factors that may be contributing to this include the high poverty levels with consequent socio-economic deprivation. This is evident in urban areas where there has been a phenomenal growth of slums and slum population. The increasingly large urban slum population has led to an increase in the proportion of TB cases notified to the DLTLD from urban areas. For example in 2005, over 35% of all notified TB cases in Kenya were from the five largest urban areas of Nairobi, Mombasa, Kisumu, Nakuru and Eldoret, reinforcing the known fact that poverty and TB are closely related. The implication of this observation is that a general improvement in socioeconomic conditions may be the answer to TB control in the long term. However, case finding and specific chemotherapy are the only methods that are known to have an important and immediate impact on the transmission of TB. The finding of TB cases and the provision of efficacious chemotherapy is the mainstay of TB control activities of DLTLD.

The DLTLD adopted the Directly Observed Therapy Short Course (DOTS) strategy for the control of TB in 1993 and achieved countrywide geographic DOTS coverage in 1997. The country achieved the 1993 World Health Assembly global TB control targets of 70% detection of infectious cases and cure 85% of the detected cases by 2005. Further, the country has adopted the TB control Millennium Development Goals of halving and beginning to reverse the mortality and prevalence of TB by 2015.

The DLTLD, in line with international trends, has launched several new approaches to increase access to DOTS and truly expand population DOTS coverage. These approaches include community based TB care DOTS (CB-TBC), Public-Private Mix for DOTS (PPM DOTS), collaboration between TB and HIV control programs and the development of an elaborate advocacy, communication and social mobilization strategy aimed at influencing communities to seek care early when TB symptoms occur and to remain on treatment until this is completed when treatment is initiated.

The Division of Leprosy, Tuberculosis and Lung Disease (DLTLD), previously the National Leprosy and Tuberculosis Programme (NLTP), was launched by the Government of Kenya (GoK) in 1980, combining the hitherto Kenya Tuberculosis Programme which existed since 1956 and several leprosy control projects which were in existence in Western, Coast and Eastern provinces since the early seventies. The DLTLD is mandated to develop policies and guidelines, mobilize political support and resources and carry out activities aimed at controlling both TB and Leprosy so as to eventually remove the threat to public health that these diseases currently pose.

Currently the DLTLD is receiving support from the Government of Kenya, through the Ministry of Public Health and Sanitation and bilateral and multilateral donors and technical agencies such as the Presidential Emergency Plan for AIDS Relief (PEPFAR) through the Centre for Disease Control & Prevention (CDC) and USAID, the WHO, the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) and the Canadian International Development Agency (CIDA) through the Royal Netherlands Tuberculosis Association (KNCV)

LIST OF ABBREVIATIONS

AFB	Acid fast bacilli
ARC	AIDS related complex
BCG	Bacille Calmette Guerin
BCP	Blister cell pack
CDC	Centres for Disease Control
CIDA	Canadian International Development Agency
COLS	Clinical Officer Lung and Skin diseases
DOT	Directly Observed Treatment
DOTS	Directly Observed Therapy Short Course
DST	Drug susceptibility Testing
DTLC	District TB & Leprosy Coordinator
GoK	Government of Kenya
KEPI	Kenya Expanded Programme on ImmunizationKNCV
MOPHS	Ministry of Public Health and Sanitation
MOTT	Mycobacteria Other Than Tuberculosis
NGO	Non-governmental organization
DLTLD	Division of Leprosy Tuberculosis and Lung Disease
PEPFAR	President's Emergency Plan For AIDS Relief
PHC	Primary health care
PLHIV	People Living With HIV/ Aids
PTB	Pulmonary Tuberculosis
PTLC	Provincial TB & Leprosy Coordinator
SCC	Short-Course Chemotherapy
SDP	Service Delivery Point
TB	Tuberculosis
WB	World Bank
WHO	World Health Organisation.
MDR-TB	Multi-Drug Resistant tuberculosis
XDR-TB	Extensively Drug Resistant Tuberculosis
MDGs	Millennium Development Goals
PATH	Program for Appropriate Technology in Health
WRD	WHO-Approved Rapid Diagnostic

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CHAPTER 1 : INTRODUCTION TO TUBERCULOSIS

AETIOLOGY OF TB

Tuberculosis is an infectious disease caused by a bacillus belonging to a group of bacteria grouped in the *Mycobacterium tuberculosis complex*

The most common agent is *Mycobacterium tuberculosis*.

Other agents include;

- *Mycobacterium bovis* (transmitted through contaminated milk and milk products)
- *Mycobacterium africanum*

In rare situations Mycobacteria other than TB (MOTT) may cause a disease similar to typical TB.

TRANSMISSION

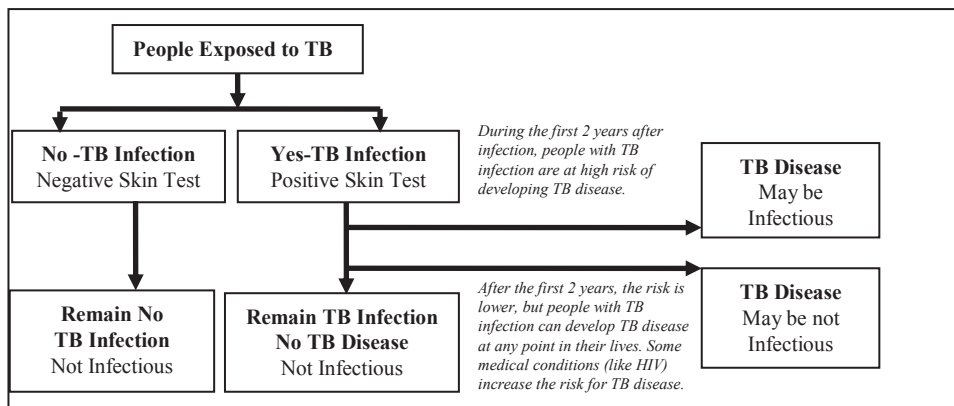
The bacillus is transmitted from person-to-person through aerosolized droplet nuclei.

Aerosols droplets are generated through coughing, laughing, talking, sneezing, singing and spitting from an infectious case of TB. The most infectious patient one with positive sputum smear.


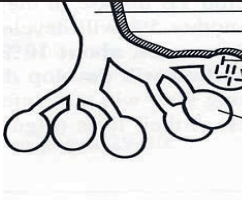
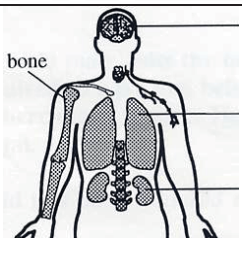
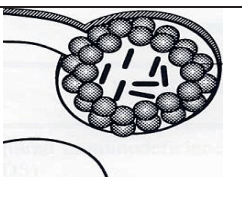
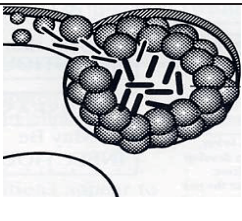
NATURAL HISTORY OF TB INFECTION

Infection refers to a situation in which a person has TB bacilli in the body (Usually lungs-Ghon focus) but does not have signs and symptoms of the disease.

The diagram below shows the path of progression from exposure to an infectious case to various outcomes



PATHOGENESIS OF TUBERCULOSIS

Box 1		Area of detail for boxes 2, 4, and 5 below	<i>Droplet nuclei containing tubercle bacilli are inhaled enter the lungs and travel to the alveoli.</i>
Box 2		Bronchiole Blood vessel Tubercule bacilli Alveoli	<i>Tubercle bacilli multiply in the alveoli.</i>
Box 3		Brain Lung Kidney	<i>A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The bacilli may reach any part of the body, including areas where TB disease is more likely to develop (such as the lungs, kidneys, brain, or bone).</i>
Box 4		Special immune cells form a hard shell (in this example, bacilli are in the lungs)	<i>Within 2-10 weeks the immune system produces special immune cells that surround the tubercle bacilli. The cells form a hard shell that keeps the bacilli contained and under control. (TB infection).</i>
Box 5		The hard shell breaks down and tubercle escape and multiply (in this example, TB disease develops in the lungs)	<i>If the immune system cannot keep the bacilli under control, the bacilli begin to multiply rapidly (TB disease). This process can occur in different places in the body, such as the lungs, kidneys, brain, or bone.</i>

Source: *Self-Study Modules on Tuberculosis*. Centers for Disease Control and Prevention, 1995

To be infected with the tubercle bacillus a person must be exposed to an infectious case of TB

The risk factors for exposure to the TB bacillus include:

- Incidence of infectious TB in the population/community
- Average duration of infectiousness of cases
- Number of cases/contact interactions over time
- Population density
- Family size
- Poverty
- Overcrowding

Following exposure to the bacillus the risk of infection is related to the extent of contact

Risk factors for infection with the TB bacillus following exposure include:

- Bacillary load of infectious cases (smear positivity)
- Extent of contact with infectious cases
 1. Proximity to infectious case
 2. Length of contact with infectious case
- Contact environment
 1. Air clearance (ventilation) – dispersion of bacilli
 2. Sunlight – survival of bacilli

TB DISEASE (ACTIVE TB)

TB disease is a state where a person has signs and symptoms of the disease. In this state, there is active multiplication of the bacilli in the body.

The risk factors for developing disease following infection with the tubercle bacillus include factors that affect body immunity. A significant proportion of cases of TB however does not have any obvious risk factor for disease and unknown biological factors may play a role.

RISK FACTORS FOR TB DISEASE FOLLOWING INFECTION

Major risk factors:

- HIV infection
- Time since infection (Recent infection)
- Poorly treated previous TB

Other factors:

- Age (extremes of age)
- Sex (males more than females)
- Malnutrition
- Diabetes

- Silicosis
- Alcoholism
- Tobacco smoking
- Other conditions e.g. immune suppressing therapy
- Long term treatment with oral corticosteroids
- Treatment with immunosuppressive agents.
- Cancers e.g. Leukemia
- Gender (less in females)

Note: In Kenya the most common risk factor for TB disease is infection with the Human Immunodeficiency Virus (HIV)

Note: Poverty, HIV and Tuberculosis are closely interrelated. Poverty reduction will have a significant impact on Tuberculosis incidence while TB control should be an important component of poverty reduction strategies.

PROGNOSIS OF TB DISEASE (ACTIVE TB)

If left untreated, active pulmonary TB naturally progresses with the following outcomes within 5year:

- 50-60% of the cases die
- 20-25% are Spontaneous cured
- 20-25% remain chronic coughers

Proper treatment with anti-TB medicines reduces mortality to less than 5%

CLINICAL FORMS OF TB

TB occurs in two clinical forms:

1. TB in the lungs-- Pulmonary TB (PTB) and
2. TB outside the lungs – Extra pulmonary TB (EPTB)

PULMONARY TB (PTB)

This is further classified on the basis of smear microscopy into:

- Smear positive PTB
- Smear Negative PTB

CASE DEFINITION

Smear positive PTB

A patient with at least one initial sputum smear examination positive for acid fast bacilli

Smear negative PTB

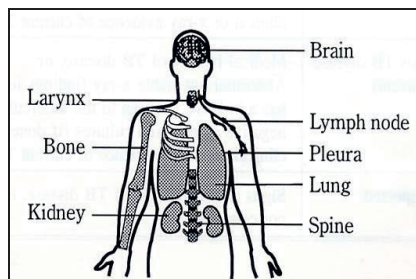
- At least two sputum specimens at the start of treatment are negative for AFB
- Radiologic abnormalities consistent with active pulmonary tuberculosis
- No response to a course of broad spectrum antibiotics (excluding anti-TB drugs and fluoroquinolones and aminoglycosides especially in HIV negative patients)

PTB is the most common form of TB accounting for 80% of the total cases and is of public health concern as it serves as the source of infection.

EXTRA-PULMONARY TB (EPTB)

Extra-pulmonary TB affects other parts of the body outside the lung tissue. Body organs affected by EPTB include: lymph nodes, bones, spine, kidneys, liver, bladder, skin, eyes, and gastro-intestinal system.

EPTB can occur in any organ of the body (except nails, hair and teeth)



CLASSIFICATION OF TUBERCULOSIS

Presumptive TB

Refers to a patient who presents with symptoms or signs suggestive of TB (previously known as a TB suspect)

A bacteriologically confirmed TB case

One from whom a biological specimen is positive by smear microscopy, culture or WRD (such as Xpert MTB/RIF). All such cases should be notified, regardless of whether TB treatment has started.

A clinically diagnosed TB case

One who does not fulfill the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and extrapulmonary cases without laboratory confirmation. Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed. Bacteriologically confirmed or clinically diagnosed cases of TB are also classified according to:

- anatomical site of disease;
- of previous treatment;
- drug resistance;
- HIV status.

Classification based on Anatomical site of disease

Pulmonary tuberculosis (PTB)

This refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Miliary TB is classified as PTB because there are lesions in the lungs. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of PTB.

Extrapulmonary tuberculosis (EPTB)

Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs as described above

Classification based on history of previous TB treatment (patient registration group)

This classification focuses only on history of previous treatment and is independent of bacteriological confirmation or site of disease.

New patients

These patients have never been treated for TB or have taken anti-TB drugs for less than 1 month.

Previously treated patients

This group includes patients who have received 1 month or more of anti-TB drugs in the past. They are further classified by the outcome of their most recent course of treatment (see table in section A.2.1) as follows:

Relapse patients

These are patients who have previously been treated for TB, were declared *cured* or *treatment completed* at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection).

Treatment after failure patients

Are those who have previously been treated for TB and whose *treatment failed* at the end of their most recent course of treatment.

Treatment after loss to follow-up patients

These have previously been treated for TB and were declared *lost to follow-up* at the end of their most recent course of treatment. (These were previously known as *treatment after default* patients.)

Other previously treated patients

These are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

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

Classification based on HIV status

HIV-positive TB patient

This refers to any bacteriologically confirmed or clinically diagnosed case of TB who has a positive result from HIV testing conducted at the time of TB diagnosis or other documented evidence of enrolment in HIV care, such as enrolment in the pre-ART register or in the ART register once ART has been started.

HIV-negative TB patient

This is any bacteriologically confirmed or clinically diagnosed case of TB who has a negative result from HIV testing conducted at the time of TB diagnosis. Any HIV-negative TB patient subsequently found to be HIV-positive should be reclassified accordingly.

HIV status unknown TB patient refers to any bacteriologically confirmed or clinically diagnosed case of TB who has no result of HIV testing and no other documented evidence of

enrolment in HIV care. If the patient's HIV status is subsequently determined, he or she should be reclassified accordingly.

Classification based on drug resistance

Cases are classified in categories based on drug susceptibility testing (DST) of clinical isolates confirmed to be *M. tuberculosis*. This is covered under chapter 6 of this guidelines.

Categorization for treatment purposes

Tuberculosis patients are categorised for treatment purposes as follows:

1. *Category 1&3-New cases* – patients who have never been treated before or used anti-TB drugs for less than one month.
 - a) Sputum smear positive PTB
 - b) Sputum smear negative PTB
 - c) Extra-pulmonary (EP)
2. *Category 2 -Previously treated sputum smear positive PTB*
 - a) Relapses
 - b) First line treatment Failures
 - c) Returnees after default (RAD)
3. *Category 4: Drug resistant TB*
 - a) Multi-Drug Resistant TB
 - b) Extensively Drug Resistant TB
 - c) Poly-drug Resistant TB

Note: All pulmonary TB re-treatment cases should have sputum TB culture and drug susceptibility testing to exclude drug resistance and especially multi-drug resistant TB.

CHAPTER 2 : CONTROL OF TUBERCULOSIS

GLOBAL AND KENYA TUBERCULOSIS BURDEN

Tuberculosis is still a global public-health concern. According to the WHO, 2012 annual TB report, there were 8.7 million range (8.3-9.0 million) incident cases in 2011 including 1.1 cases among PLHIVs. Over the same year 6.2 million notified cases of TB against an estimated 8.7 million cases, representing a case detection rate (CDR) of 66% . There were an estimated 1.4 and 0.43 million TB related deaths among HIV sero negative and positive respectively. Of the new sputum smear positive TB cases registered in 2010, 87% were successfully treated.

Kenya is ranked 15th among the 22 high TB burden countries that account for 80% of the global TB burden and 5th in Africa. In 2012, the country notified a total of 103,159 TB cases (all forms of tuberculosis) of whom 39% were also HIV infected. Tuberculosis treatment results for TB patients started on treatment in 2010 showed a treatment success of 87% for new smear-positive pulmonary TB cases.

TUBERCULOSIS CONTROL STRATEGY

Tuberculosis control in the Kenya is based on the 6 elements of the WHO STOP-TB Strategy namely:

- 1) Pursue high-quality DOTS expansion and enhancement
 - a) Political commitment with increased and sustained financing
 - b) Case detection through quality-assured bacteriology
 - c) Standardized treatment, with supervision and patient support
 - d) An effective drug supply and management system
 - e) Monitoring and evaluation system, and impact measurement
- 2) Address TB/HIV, MDR-TB and other challenges
 - a) Implement collaborative TB/HIV activities
 - b) Prevent and control MDR-TB
 - c) Address prisoners, refugees and other high-risk groups and situations
- 3) Contribute to health system strengthening
 - a) Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery, and information system
 - b) Share innovations that strengthen systems, including the Practical Approach to Lung Health (PAL)
 - c) Adapt innovations from other fields

- 4) Engage all care providers
 - a) Public–Public and Public–Private mix (PPM) approaches
 - b) International Standards for Tuberculosis Care (ISTC)

- 5) Empower people with TB, and communities
 - a) Advocacy, communication and social mobilization
 - b) Community participation in TB care

- 6) Patients’ Charter for Tuberculosis Care Enable and promote research
 - a) Programme-based operational research
 - b) Research to develop new diagnostics, drugs and vaccines

ROLE OF DIVISION OF LEPROSY, TUBERCULOSIS AND LUNG DISEASE (DLTLD)

DLTLD is a Division in the Department of Disease Prevention and Control under the Ministry of Health (MoH). It is charged with the overall coordination of control of TB, Leprosy and Lung Disease. DLTLD mandate is to coordinate the development of policy guidelines, setting of standards, resource mobilization, ensuring an uninterrupted supply of commodities, provision of supportive supervision and coordination, monitoring and evaluation in line with international and local strategies. This mandate is executed in collaboration with partners involve in TB, Leprosy and Lung Disease control.

The control activities are coordinated by Provincial/ County TB and Leprosy Coordinators (P/CTLCS) and District TB and Leprosy Coordinators (DTLCS) at the county and district levels respectively. The TB and Leprosy coordinators are integral members of the Health Management Teams at various levels.

The delivery of DOTS services is integrated into the general health services provided at health care delivery points. By the end of 2011 TB services were available in 2,996 public, NGO and private health care facilities which provide TB treatment services. TB smear microscopy is available in 1,581 laboratories country wide.

CHAPTER 3 : TUBERCULOSIS DISEASE IN ADULTS

PULMONARY TB

PRESENTATION

TB should be suspected in any person presenting with a cough of more than two weeks duration. The cough may be associated with production of blood stained sputum. Other symptoms include:

- Fevers
- Night sweats
- Loss of weight
- Chest pain
- Shortness of breath.

All persons presenting with a cough of a duration longer than two weeks should be screened for TB using sputum smear microscopy unless there is another obvious cause of the cough.

Physical signs may include:

- Bronchial breath sounds
- Tachypnoea
- Wasting
- Haemoptysis

DIFFERENTIAL DIAGNOSIS

- Chronic bronchitis/ COPD
- Bronchiectasis
- Lung abscess,
- Atypical pneumonias e.g. (caused by unusual pathogens such as fungi including *pneumocytis jirovecii*)
- Lung cancer
- Heart failure
- Sarcoidosis

DIAGNOSIS OF TB

The diagnosis of PTB is based on the following:

1. History of presenting complaints (History of cough is a key symptom)
2. Past medical history (Diabetes, HIV)
3. History of Contact with TB
4. Physical examination
5. Sputum AFB microscopy
6. Other supportive investigation
7. Chest x-ray (Supportive for smear negative TB)

8. Specialized bacteriological examination
 - a) Culture
 - b) Molecular tests
 - c) Drug Susceptibility Test (DST) for Anti-TB drugs

Table 3.1: Indication for different TB diagnostic tests

Laboratory Test	Target	Purpose
Smear microscopy (Fluorescent and Light microscopy)	All Pulmonary TB suspects	Detect TB disease Monitoring smear positive patients on treatment at months 2, 3, 5 and 8
Culture techniques	TB patients on retreatment, health care workers, symptomatic contacts of drug resistant TB, smear negative PLHIV	Used for recurrent TB (relapses), treatment failure, returnees , Health care workers to detect drug resistance
Histology	EPTB patients	Detect lymph node disease
Serological tests*		Not widely available

Tuberculin skin test

The tuberculin skin test (Mantoux) should not be used to diagnose TB in adults

This test only indicates that the person has previously been infected with the TB bacillus. Similarly most serological tests are not able to distinguish latent infection from current active disease and therefore should not be used to diagnose PTB.

ESR and other tests

The erythrocyte sedimentation rate (ESR) is usually elevated in active TB, but this test is not sensitive or specific enough to be of value in the diagnosis of PTB.

Sputum smear examination

Patients suspected to have PTB should have two sputum samples collected examined for Acid Fast Bacilli (At least one sample should be collected in the morning)

The recommended sputum collection procedure is the spot – morning.

- The first sputum sample is collected at the time the patient presents to the clinic while
- Second sample an early morning collected the following day

Table 3.2: Spot, Morning sputum collection strategy

Sample		When is it collected?	Where is it collected?
Spot	1 st sample	On the spot	In the health facility
Morning	2 nd sample	Patient collects upon waking up the following morning	At home and brings to health facility (Or in hospital if patient is hospitalized)

Instructing patients to collect sputum specimen

The following should be observed in the process of collecting and submitting sputum samples to the laboratory for TB diagnosis to ensure production of a quality sputum sample and results:-

- Label the sputum containers on the side (**NOT ON THE LID**) before sputum samples are collected
- Fill in the sputum examination forms ensuring that the patient’s contacts are included
- Instruct the patient to collect sputum samples in a well ventilated area preferably outdoors
 - *The patient should **take a deep breath, cough and attempt sputum production.*** This can be repeated several times
 - After collecting the sputum the patient should **close the lid tightly**
 - **All collected sputum samples should be submitted to the laboratory** as soon as feasible together with a correctly filled sputum examination form
- **Give patients clear instructions** on when to return for their results

Results should ideally be available a few hours after the day the last sample is submitted

Sputum induction

- Inhalation of hypertonic saline (greater 0.9%) solution preferably by ultrasonic nebulization
- Bronchial wash or broncho-alveolar lavage sample obtained through fiberoptic bronchoscopy

In general these procedures are available only in tertiary institutions in Kenya and because they may lead to a substantial generation of infectious aerosols, should only be carried out in clinical environments with appropriate infection prevention measures in place.

Sputum culture examination

In general the indications for sputum TB culture and DST are:

- Failure of first line treatment (Smears still remains positive at month 5)
- Lack of smear conversion at end of month 2 while on first line treatment
- Returning after default (RAD)
- Symptomatic contacts of drug resistant TB cases
- Health care workers
- Relapse

Sample from invasive procedures

TB can be diagnosed through the examination of lung biopsy specimens obtained through:

- Fibre-optic bronchoscopy
- Open lung biopsy or the trans-thoracic route.
- Peritoneal biopsy

Obtaining lung biopsy specimens demands the availability of a technically qualified person and equipment, and therefore these diagnostic techniques are rarely done

Chest X-ray

The chest x-ray may aid the diagnosis of PTB but it should not be used as the sole means of establishing a TB diagnosis.

All patients with chest x-ray features suggestive of TB should have sputum specimens submitted for microbiological examination. It is a major omission to diagnose TB on the basis of a chest x-ray ONLY

The radiographic features that usually suggestive PTB include:

- Upper zone of lung showing patchy shadows (May have evidence of cavitations and scarring (fibrosis))
- In HIV infected persons the radiological picture is more often atypical with the lower or mid-zone shadows and the presence of hilar or mediastinal lymph node enlargement being relatively common.
- Miliary mottling, Pleural and/or pericardial effusion (Case of EPTB)

COMPLICATIONS OF PTB

Haemoptysis

Presentation

- Usually a symptom of post TB bronchiectasis
- Precipitated by an infection in the bronchiectatic cavities
- Recurrent haemoptysis in a patient previously treated for TB may also be a symptom of an aspergilloma (fungal ball) in a bronchiectatic lesion or post TB cavitory lesion

Management

- Reassure the patient
- Sedate with a low dose of chlorpromazine at 25mg twice daily
- A course of broad spectrum antibiotics is indicated in those patients with post TB bronchiectasis
- If the bleeding is severe and life threatening, patients should be admitted to hospital for more specialized treatment

Spontaneous Pneumothorax

This is usually a result of rupture of a pleural based TB cavity. It is often associated with formation of pus in the pleural space (empyema) leading to a pyopneumothorax.

Presentation

- Shortness of breath
- Chest pain.

Management

- The patient should be admitted to hospital for appropriate management.
- Underwater seal drainage

Bronchiectasis

Presentation

- Cough
- Copious amounts of sputum which is mainly greenish, blood stained and foul smelling

Management

- The hallmark of management of productive bronchiectasis is chest physiotherapy. This

include postural drainage and other manoeuvres aimed at improving drainage of respiratory secretions

- Infective exacerbations will require antibiotics. Broad spectrum antibiotics like amoxicillin-clavulanate, Metronidazole or clindamycin for anaerobic infection. Anti-pseudomonal antibiotic like ciprofloxacin, 3rd generation cephalosporin (Ceftazidime) should be used when colonization with *Pseudomonas* is suspected.

Fibrosis of the lungs

- This is sequelae of extensive tuberculous disease
- In severe terminal cases, long term oxygen therapy may be required
- These patients should be referred to a hospital for review

Lung abscess

- Seen in a patient with extensive damage to the lungs after tuberculosis
- Antibiotic treatment is given. The choice of antibiotic is aided by the results of a sputum culture-sensitivity test.
- Surgical intervention may also be necessary

Aspergilloma

Result of colonization of tuberculous cavities or bronchiectatic lesions with the fungus, *Aspergillus fumigatus*

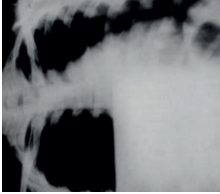
Presentation


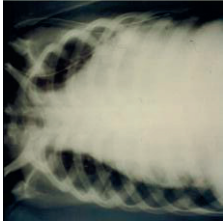
- Recurrent or persistent haemoptysis
- Malaise
- Fever
- Chest x-ray shows shadow with an air crescent (halo) around it
- High levels of specific immunoglobulin G against *Aspergillus* in blood (Confirmatory test)



The only effective treatment is surgical removal of the aspergilloma.

COMMON FORMS OF EXTRA-PULMONARY TB AND DIAGNOSTIC APPROACHES

Table 3.3: EPTB signs symptoms and diagnostic approaches

Form of Extra-Pulmonary TB	Signs and Symptoms	Diagnosis
Pleural TB with Pleural Effusion 	Tuberculous pleural effusion usually presents with: Local chest symptoms that include chest pain Shortness of breathlessness whose degree depend on amount of effusion Many patients also have a cough and systemic symptoms including fever and night sweats. When examined the trachea and the point of maximum cardiac impulse (apex beat) may be found to have shifted away from the side of the effusion. Percussion of the chest reveals “stony” dullness and breath sounds are reduced on the side of the effusion.	Chest x-ray is often required to confirm the presence of the effusion especially when effusion is small. It is also advisable, if the expertise exists, to always perform a diagnostic pleural aspiration at the minimum to distinguish pus (empysema) from “usual” effusion. Where facilities exist aspirated fluid should be sent to the laboratory for biochemical tests (sugar, protein, and lactic dehydrogenase), cell count, cytology and microbiological tests including smears for tubercle bacilli. A pleural biopsy is rarely required in young patients below the age of 40 years. Older patients and especially those with a significant smoking history may have other diagnoses and in these patients it is advisable to perform a pleural biopsy using an Abraham’s needle. An ultrasonography usually shows matted loops of bowel with free fluid. Peritoneal biopsy rarely done: many of these end up with a laparotomy.
Tuberculous Peritonitis and Ascites	Tuberculous Peritonitis and Ascites usually presents with: Abnormal pain and swelling. Disturbance of bowel motion i.e., constipation or diarrhea. A general constitutional disturbance. Fever.	The diagnosis of tuberculous meningitis rests on: Examination of cerebrospinal fluid (CSF) obtained following a lumbar puncture: CSF stain positive for mycobacterium.
Tuberculous Meningitis	This disease is increasingly frequent with HIV. It is often very difficult to diagnose and requires a very high index of clinical suspicion. This disease presents with: Chronic headache	The diagnosis of tuberculous meningitis rests on: Examination of cerebrospinal fluid (CSF) obtained following a lumbar puncture: CSF stain positive for mycobacterium.

Form of Extra-Pulmonary TB	Signs and Symptoms	Diagnosis
<p>Miliary TB</p> 	<p>Miliary TB is a result of haematogenous spread. It presents as pyrexia of uncertain cause. Large liver and spleen are common. Choroid tubercles on fundoscopic examination. Miliary lesions on chest X-ray. Night sweats, wasting and other so called constitutional symptoms with very little respiratory symptoms</p>	<p>Whenever miliary TB is suspected; The eyes should be examined, where feasible, for choroidal tubercles The chest x-ray shows multiple small millet sized nodular shadows The diagnosis is rarely confirmed but where facilities are available culture of blood, CSF, liver and blood may be positive for the tubercle bacilli</p>
<p>Tuberculous Pericarditis</p> 	<p>Tuberculous pericarditis is increasingly becoming common in the HIV era and it may present with a variety of symptoms including: Shortness of breath is the most common symptom Chest pain Cough Leg swelling and Fever. Usually has a high pulse rate (tachycardia) May have a low blood pressure, impalpable apex beat, quiet heart sounds and signs of heart failure like a large liver, ascites and leg edema.</p>	<p>A chest x-ray is always required and usually shows a large globular heart. Where feasible patients suspected to have a pericardial effusion should be referred to a heart specialist for confirmation of the diagnosis using echocardiography. A pericardial tap for diagnostic purpose is rarely required but may be life saving if there are signs of cardiac compression (tamponade). This procedure must be done by experienced health care workers (cardiologists) only.</p>
<p>Tuberculous Meningitis</p>	<p>This disease is increasingly frequent with HIV. It is often very difficult to diagnose and requires a very high index of clinical suspicion. This disease presents with: Chronic headache</p>	<p>The diagnosis of tuberculous meningitis rests on: Examination of cerebrospinal fluid (CSF) obtained following a lumbar puncture: CSF stain positive for mycobacterium</p>

Form of Extra-Pulmonary TB	Signs and Symptoms	Diagnosis
<p>TB adenitis</p> 	<p>Tuberculous adenitis is one of the common types of extra-pulmonary TB</p> <p>Usually unilateral</p> <p>Most common site is the cervical area</p> <p>Painless swelling—initially discrete then matted</p> <p>Fistula and sinus formation</p>	<p>Node aspirate</p> <p>Node biopsy for both histology and culture</p>
<p>TB encephalitis including Tuberculoma</p>	<p>The clinical presentation is similar to that of other space occupying brain lesions and includes</p> <p>Headaches</p> <p>Vomiting</p> <p>Convulsions</p> <p>Limb weakness</p> <p>Cranial nerve palsies.</p>	<p>Brain CT scans are useful in demonstrating lesions.</p> <p>Often it is difficult to confirm the diagnosis of brain TB and most patients are treated on an empiric basis.</p>
<p>TB of the skin</p>  <p>Response to chemotherapy of tuberculous verrucous ulcer</p>	<p><i>Lupus vulgaris</i>: Persistent and progressive form of cutaneous TB. It occurs as small sharply defined reddish-brown lesions with a gelatinous consistency (called apple-jelly nodules)</p> <p>Untreated, lesions persist for years, leading to disfigurement</p> <p><i>Scrofuloderma</i>: Skin lesions result from direct extension of underlying TB infection of lymph nodes, bone or joints</p> <p>Often associated with TB of the lungs. Firm, painless lesions that eventually ulcerate with a granular base. May heal even without treatment but this takes years and leaves unsightly scars</p>	<p>The diagnosis is usually made or confirmed by a skin biopsy. Typical tubercles are caseating epithelioid granulomas that contain acid-fast bacilli. These are detected by tissue staining, culture and polymerase chain reaction (PCR)</p>
<p>NOTE: When patients present with symptoms of TB disease and the health care worker is not able to quickly make a diagnosis or there are signs of severe disease, a rapid referral to the next appropriate level is highly recommended. When health care workers do not know what they are dealing with or do not have the facilities to make a definitive diagnosis or to adequately manage the disease or its complications the patient should immediately be referred to the next appropriate level.</p>		

TREATMENT OF NEW CASES OF TB (PTB & EPTB) IN ADULTS

THE AIMS OF TREATMENT

The following are aims of treatment of tuberculosis

- Cure patients and therefore prevent suffering and death from TB
- Prevent long term complications or sequel of TB
- Prevent relapse of the disease
- Prevent transmission of the infection
- Prevent the development of drug resistant TB

It is important to remember that, treatment of tuberculosis benefits both the individual patient and the community as a whole and; thus, any public health program or private provider undertaking to treat a patient with tuberculosis is assuming a public health function that includes not only prescribing an appropriate regimen but also ensuring adherence to the regimen until treatment is completed.

Basic Principles of TB treatment

- Never use single drugs
- Always use drugs in combinations –using Fixed Dose Combinations (FDCs)
- Drug dosage based on weight
- Drug intake should be directly observed
- ***Ensure the entire 6-8 months treatment is taken***

First line ant-drugs TB

- Isoniazid (H)
- Rifampicin (R)
- Pyrazinamide (Z)
- Ethambutol (E)
- Streptomycin (S)

Tuberculosis treatment involves the use of multiple drugs taken in combination. This is done to prevent the emergence of drug resistance to any of the drugs.

Fixed Dose Combinations (FDC): Contain two or more medicines within the same tablet or capsule.

Advantages of FDCs include:

- Reduced risk of resistance developing to the drugs in the event of missed doses
- Fewer medication errors
- Fewer prescription errors

Disadvantages of FDCs include:

- Reduced bioavailability of some drugs particularly Rifampicin
- Flexibility in obtaining an optimal dose of some agents such as pyrazinamide may be lost

NB: Only those FDC's that have been proven to provide unaltered bioavailability of the component drugs should be used.

In the first two months of treatment four drugs are used to rapidly reduce the number of tubercle bacilli (bacillary load) in the body. This phase is called the Intensive phase of anti-TB treatment. After two months two drugs are used for 4-6 months and this phase is called the Continuation Phase of treatment.

Table 3.4: Treatment regimen for new adult TB patients

Abbreviation of the regimen	2RHZE/4RH	
Phase	Intensive Phase	Continuation Phase
Duration	Directly Observed Treatment (DOT), for two months	Directly Observed Treatment (DOT), for four months
Drugs used	Rifampicin (R) Isoniazid (H) Pyrazinamide (Z) Ethambutol (E)	Rifampicin (R) and Isoniazid (H), 4months.

Anti-TB drugs should be taken in the right combinations and doses, and the correct schedules for the appropriate duration. To promote total adherence to treatment an individualized patient centered approach should be developed.

A patient centered approach to facilitate adherence to treatment including Direct Observation of Treatment (DOT) should be promoted. DOT should be provided using a treatment supporter who is acceptable and accountable to the patient and to the health system

This treatment supporter could be a health care worker, a family member or a community volunteer and the DOT may take place at home, workplace, health facility or other convenient place agreeable to the patient, the treatment supporter and the health care system.

TREATMENT REGIMEN FOR NEW ADULT TB PATIENTS

All patients who have not been on TB therapy previously should have a two month initial phase of treatment consisting of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol followed by a continuation phase of Ethambutol and isoniazid for six months or Isoniazid and Rifampicin for four months.

The treatment regimen for new adult category 1 and 3 TB patients is: 2RHZE/4RH which is offered through weekly drug collection during the intensive phase and 2 weekly (RH) during the continuation phase

TREATMENT REGIMEN FOR TB PATIENTS WHO RELAPSED, FAILED OR RETURNED AFTER DEFAULT FROM INITIAL TREATMENT

For patients who have previously been treated for TB for more than one month including those who have relapsed after successful previous treatment, or those who defaulted from previous treatment or failed previous treatment, with sputum smears remaining positive at 4/5, 6/8 months (Category 2 patients) the regimen used is two months of SRHZE followed by one month of RHZE and then five months of RHE. This regimen is abbreviated 2SRHZE/1RHZE/5RHE. Patients in this category should have their sputum submitted for culture and DST.

Table 3.5: Treatment regimen for retreatment patients

Abbreviation of the regimen	2SRHZE / 1RHZE / 5RHE		
Phase	Intensive Phase		Continuation Phase
Duration	Daily treatment with appropriate patient support for two months	Daily treatment with appropriate patient support for one month	Daily treatment with appropriate patient support for five months
Drugs used	Streptomycin (S) + Ethambutol (E) + Rifampicin (R) + Isoniazid (H)+ Pyrazinamide (Z)	Ethambutol (E) + Rifampicin (R) +Isoniazid (H)+ Pyrazinamide (Z)	Ethambutol (E) +Rifampicin (R)+Isoniazid (H)

TREATMENT DOSAGES FOR ADULTS

Table 3.6: Treatment dosages for adults

Drug Dosages	Formulation	Pre-treatment weight		
Drug	Formulation	Over 55 kg	40-54 kg	30-39 kg
Streptomycin	im injection	1 g	0.75 g	0.50 g
Rifampicin 150 mg + Isoniazid 75 mg + Pyrazinamide 400 mg + Ethambutol 275 mg	4-FDC tablet RHZE	4	3	2
Rifampicin 150 mg + Isoniazid 75 mg +Pyrazinamide 400 mg	3-FDC tablet RHZ	4	3	2
Rifampicin 150 mg + Isoniazid 75mg	2-FDC tablet RH	4	3	2
Rifampicin 150, Isoniazid 75 and Ethambutol 275 (RHE)	Tablet RHE	4	3	2
Isoniazid 150 mg and Ethambutol 400 mg	Tablet EH	2	2	2

Patients over 64 years of age also should not be given more than 0.75mg of Streptomycin

The re-treatment drugs are provided in 4 FDC (RHZE) to be taken with Streptomycin in the first two months and alone in the third month followed by a 3 FDC combination of RHE for the five months continuation phase.

Patients on TB treatment should be monitored for:

1. Clinical response - weight gain, resolution of symptoms, and signs
2. Bacteriologic response - follow-up sputum for all SM+ patients as follows
 - Patient treatment on EH – at 2, 5 and 8 months
 - Patient treatment on RH – at 2, 4 and 6 months
 - Patient on retreatment – at 3, 5 and 8 months

Patients who still have a positive smear at the end of the intensive phase should have the intensive phase extended for not more than one month and sputum smears done again at the end of the third month at which point they should be switched to the continuation phase.

Patients who still have a positive smear at month 4 when on RH or month 5 when on EH should be considered to have failed initial treatment and switched to the re-treatment regimen (2SRHZE/1RHZE/5RHE) and sputum collected for culture and DST. The medications given, the bacteriologic and clinical response should be all recorded in the patient record card and the TB treatment register.

TB PATIENT TREATMENT PACKS

TB treatment is now provided in individualized patient packs. Patient packs are also available to private health care providers irrespective of the source of drugs (GoK or otherwise). Before allocating a pack to a patient determine where the patient will actually receive his or her treatment. Patients being transferred out to another health facility should not be given their pack to move with; instead the patient should be given a one week supply of medicines for use while on transit. The patient packs should remain in the health facility and appropriate doses taken out or added to the pack for the recommended duration of treatment. Adjustment in doses should be made at the beginning of treatment according to the instructions in the patient packs.

All patients started on treatment in the health facility should be entered in the treatment register with all entries filled in. The same information together with the clinical notes should be entered into the patient's TB treatment record card (and the patient appointment card).

TB TREATMENT IN MOBILE POPULATIONS

In Kenya, about 10% of all registered tuberculosis patients live in the arid and semi-arid areas. Patient support and follow-up of treatment is difficult due to the sparse distribution of health

facilities and the patient mobile life styles. DLTLD has now standardized treatment all over the country and the same regimens are now used in patients treated in the TB Manyattas.

The re-treatment regimen for this population with relapse (R), treatment failure (F), or treatment resumed (TR), with active tuberculosis disease and who have a positive sputum smear or culture result however remains the same ie: 2SRHZE/4RHZE.

TREATMENT OF TB IN PREGNANCY

In general, pregnancy should be avoided during anti-TB treatment. ***However when it occurs, termination of pregnancy is not be recommended.*** Like most drugs anti-TB drugs have not been specifically studied in pregnancy. There is always some risk of teratogenicity with any drugs especially when the drug is given in the first trimester. There have been no significant reports that anti-TB drugs pose a greater than usual risk of teratogenicity and therefore all pregnant women with active TB should be treated with a full complement of anti-TB drugs. It is useful to give Pyridoxine with Isoniazid to avoid the small risk of damaging the infant's nervous system. In addition, Streptomycin should not be used in pregnancy because it may cause deafness in the infant. When treating drug resistant TB the amino glycosides (Kanamycin, Amikacin and Capreomycin) and the thioamides (Ethionamide and Prothionamide) should not be used in pregnancy because of associated ototoxicity.

ADJUNCTS TO ANTI-TB DRUG TREATMENT

Health education

It is the responsibility of the health staff to continuously educate patients with TB, their relatives and treatment supporters about the disease.

Health education is essential to obtain the patient's co-operation during the whole treatment period.

An understanding, sympathetic and concerned attitude on the part of the health staff is essential for getting the message across.

To attain a high cure rate and to prevent default, health education should be provided every time the patient receives care from the health care provider

Infection prevention measures like hand capping; opening windows at home should be addressed

What the Patient Should Know

At diagnosis the patient needs to know:

- Tuberculosis is an infectious disease that is transmitted from one person to another through coughing, sneezing etc.

- The patient may have infected other people who may also develop tuberculosis. He/she should therefore, be asked to encourage other people with whom he/ she has been in close contact to undergo screening for TB.
- Infection prevention measures like hand capping, opening windows at home, proper lighting, and benefits of spending most of their time in open air.
- Tuberculosis drugs are available and free of charge at any government health facility, most mission hospitals and some private health facilities.
- Once treatment with these drugs is initiated the symptoms of tuberculosis disease will disappear quickly, but the drugs still need to be continued daily until the end of the prescribed treatment period. Failure to comply with treatment requirement may cause the disease to start again, with the possibility that drug resistance may have developed which would make treatment with the same drugs inadequate. This could also cause a greater risk for the health of the patient and that of his or her close contacts.
- Side effects may include urine discoloration by Rifampicin, skin reactions by Isoniazid, blurring of vision etc.
- The type of regimen, the exact number and type of tablets that the patients will take.
- How long the intensive phase and the continuation phase will take, where and when the drugs will be administered.
- A sputum-smear examination is required at certain intervals to monitor the progress towards cure. Explain to the patient when the examination will be required.
- HIV testing offers an opportunity for further treatment, care and support especially to those who are HIV positive. For those who are HIV negative it offers them an opportunity to know their HIV status and how to prevent HIV infection.

After initiation of treatment:

- Encourage contacts (e.g. household members especially children under 5 years of age, PLHIV and persons above 65 years) to come for TB screening.
- Patients are requested to inform the staff at the clinic when they intend to travel. An adequate supply of drugs can then be given to cater for the period they are away from their local area.
- Patients are requested to inform the staff at the clinic when they intend to move to another area. The clinic staff will then write a transfer letter and give advice as to where they can continue treatment.

At the end of treatment:

- Tuberculosis disease may occur again. The patient should therefore report immediately to the health care provider when similar symptoms recur.

NUTRITIONAL SUPPORT FOR TB PATIENTS

NUTRITIONAL NEEDS IN TUBERCULOSIS:

Energy

There is increased energy need because of the disease (approximately 35 – 40 kcal per kg of ideal body weight) and some of the energy giving foods should eat include:

- Ripe banana.
- Sweet potatoes
- Irish potatoes
- Maize
- Arrow roots
- Yams
- Millet
- Sorghum
- Bread
- Fat and oils

To meet the above energy requirements, one needs to consume snacks in between the main meals made out of some of the mentioned foods e.g. half cup of chopped potatoes will give 70kcal or 1 mug of 300ml porridge made of maize flour will give 210 Kcal.

Protein

Dietary protein intake is important to prevent the wasting of the body stores (lean body mass).

A protein intake of about 1.2 – 1.5 g per kg body weight or 12%- 15% of total daily energy intake or approximately 70- 100g per day is needed. Example of some protein giving foods includes:

- All kinds legumes e.g. beans and peas; green, black, yellow or brown grams; and
- Animal sources including fish meat eggs milk and milk products etc.

To meet the above requirements one needs to consume both plants and animal proteins e.g. half cup of dried beans will provide 17g of proteins or 1 serving of 50g of fillet meat will give 15g of proteins.

Micronutrients

A good multivitamin and mineral supplement or combined formula providing 50% - 150% of daily recommended allowance is advisable since it is most unlikely that a TB patient will be able to meet the increased requirements for vitamins and minerals from dietary sources alone due to poor appetite (TB treatment regimens increase appetite, while presence of opportunistic infections may interfere with food intake).

DRUG - NUTRIENT INTERACTIONS

Isoniazid is one of the most frequently used anti- TB drugs. The drug is antagonistic to vitamin B₆. It is therefore standard procedure to supplement adults with 25mg of the vitamin per day. Children are

not routinely given vitamin B₆, but if their blood levels are low or if they get high dosages of Isoniazid (more than 10mg/ day) they will also need 25 mg of vitamin B₆ in the form of supplementation.

NUTRITIONAL RECOMMENDATIONS FOR TB PATIENTS

- Pulmonary disease often adversely affects nutritional intake, due to poor appetites, making patients at risk of malnutrition. Small frequent meals are recommended (6 meals in a day instead of 30)
- The meals should be appetizing in appearance, taste and provide enough energy and proteins
- Ready to use therapeutic foods or supplementary foods made from locally available foods are recommended.
- Nutrient rich/dense foods should be offered to the client.
- At least 500ml – 750ml of milk or yoghurt should be offered daily (where milk is not available, other sources of vitamin D should be offered e.g. fish, or fish oils, sunlight).
- 5-6 portions of fruits and vegetables (plenty of fresh fruits) should be eaten.
- The best dietary sources of vitamin B₆ (pyridoxine) is yeast, wheat germ (from wheat products), pork liver, whole grains, legumes, potatoes, bananas, millet and sorghum. Patients should be encouraged to take adequate portions.
- Alcohol should be avoided
- Adequate fluid intake, 8 glasses of 250ml/ day should be consumed.
- A good multivitamin and minerals supplement should be taken as needed.

Note: A nutritional assessment, education and counseling should be done at every visit, then make individual nutritional care plans for the TB patients.

Patients on anti-TB treatment usually experience an increase in appetite. This is a good sign and indicates a good clinical response. However in some situations the increased appetite may pose challenges for the patients when access to adequate amounts of food is a problem. Food may be used as an incentive to keep patients on treatment. Patients on anti-TB treatment should be encouraged to eat a well balanced diet but should not be made to incur more than the usual cost for food in the name of finding special nutritious foods.

USE OF ALCOHOL AND TOBACCO DURING TREATMENT FOR TB

Alcohol is injurious to the liver. Anti-TB drugs also may be toxic to the liver. Therefore the combination of alcohol and anti-TB drugs may lead to a greater risk of hepatic reactions. It is advisable therefore to encourage patients on anti-TB treatment to reduce the amount of alcohol taken if it cannot be entirely avoided. Tobacco smoking is injurious to body organs too and should be strongly discouraged in patients receiving TB treatment. There is however no known contraindication to sexual intercourse during treatment with anti-TB drugs.

TREATMENT OUTCOMES FOR TB PATIENTS (EXCLUDING PATIENTS TREATED FOR RR-TB OR MDR-TB)

All bacteriologically confirmed and clinically diagnosed TB cases should be assigned an outcome from this list **except** those with RR-TB or MDR-TB, who are placed on a second-line drug regimen.

Outcome	Definition
Cured	A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.
Treatment completed	A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.
Treatment failed	A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
Died	A TB patient who dies for any reason before starting or during the course of treatment.
Loss to follow up	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A TB patient for whom no treatment outcome is assigned. This includes cases “transferred out” to another treatment unit as well as cases for which the treatment outcome is unknown to the reporting unit.
Treatment success	The sum of <i>cured</i> and <i>treatment completed</i>

Patients found to have an RR-TB or MDR-TB TB strain at any point in time should be started on an adequate second-line drug regimen. These cases are **excluded** from the main TB cohort when calculating treatment outcomes and included only in the second-line TB treatment cohort analysis.

CHAPTER 4: CHILDHOOD TUBERCULOSIS

THE BURDEN OF CHILDHOOD TB

Of the 9 million new cases of TB that occur in the world every year, it is estimated that 15% occur in children less than 15 years of age. Seventy-five percent of these childhood cases occur in the 22 high TB-burdened countries, of which Kenya is one. In Kenya, TB in children below the age of 15 years accounts for about 11% all cases. Children are defined as those below the age of 15 years.

Suspect a child has TB he/she has the following:

- Cough over 2 weeks
- Fever (please rule out common childhood illness ie malaria)
- Weight loss /poor weight gain/ clothes not fitting (check growth chart)
- Lethargy, playing less

DIAGNOSIS OF TUBERCULOSIS IN CHILDREN

The diagnosis of TB in children relies on a careful and thorough history and physical examination as well as any relevant investigations e.g. sputum smear microscopy, CXR, and TST

PULMONARY TB

The key elements to a successful diagnosis of PTB in children include:

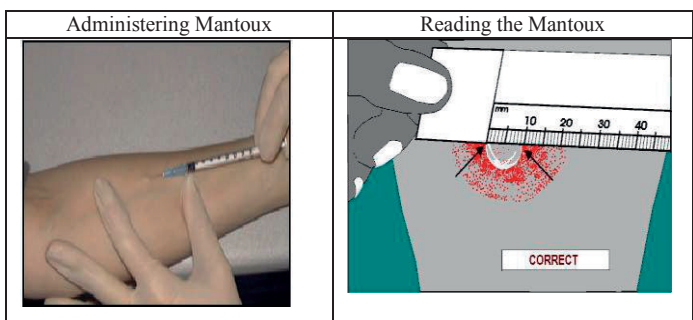
1. Careful history taking (including TB contact and symptoms consistent with TB)
2. Clinical examination (especially growth monitoring)
3. Bacteriological diagnosis
 - a. Microscopy for acid fast bacilli
 - b. TB culture and drug susceptibility testing where possible
 - c. Histopathology depending on specimen
 - d. Xpert MTB/RIF (to be used only with sputum and sputum sediments)
 - e. Line Probe Assays (LIPA)
4. Chest radiography: This is particularly important in children with suspected PTB. Radiological features suggestive of PTB will include:
 - a. Persistent lung opacification especially if focALLY enlarged hillar or subcarinal lymph nodes

- b. Diffuse micronodular infiltrates (miliary pattern)
 - c. Pleural effusions with apical infiltrates and cavities especially in adolescents.
 - d. The finding of marked abnormality on CXR in a child with no signs of respiratory distress (no fast breathing or chest in-drawing) highly supportive of TB
5. HIV testing
All children with suspected TB should be tested for HIV
 6. Tuberculin skin testing (TST)
A positive TST is evidence that one is infected with MTB, but does not necessarily indicate disease.

Performing and Interpretation of Tuberculin Skin Test

Giving tuberculin skin test (mantoux) in children

- Locate and clean injection site 5-10cm below right elbow joint
- Fill 27-gauge syringe with 0.1 ml tuberculin
- Inject subcutaneously (should create a wheal)



Interpretation:

- After 72 hours check site for induration, measure the widest diameter in mm
- TST is regarded as positive if the induration is:

- More than 10mm in all other children, whether they received BCG vaccine or not
- More than 10mm in all other children, whether they received BCG vaccine or not
- More than 5mm in, HIV infected, immune compromised, or severely malnourished.

A negative mantoux does not rule out TB (especially in the HIV or malnourished child)

Score Charts/ Diagnostic Criteria

Clinical diagnosis of PTB in children shall be based on the following.

The approach to a child with suspected PTB is shown in the algorithm/ flow chart below

Presence of 2 or more of the following symptoms

Cough > 2weeks

Weight loss or poor weight gain

Persistent fever and/or night sweats > 2 weeks

Fatigue, reduced playfulness, less active

PLUS

Presence of 2 or more of the following:

Positive contact history

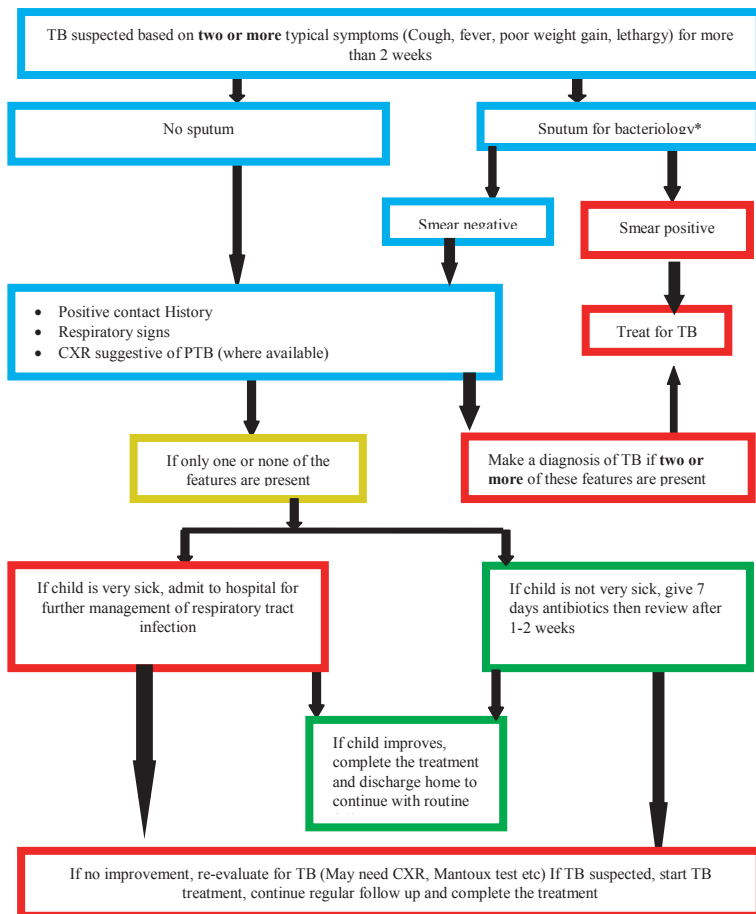
Respiratory signs

CXR suggestive of PTB (where available)

Positive Mantoux test (where available)

Then PTB is likely, and treatment is justified

APPROACH TO DIAGNOSIS OF PULMONARY TB DIAGNOSIS IN CHILDREN



Notes:

1. All children should be tested for HIV
2. Mantoux test should be interpreted as follows
 - >5mm diameter of induration in high risk children (includes HIV-infected children and severely malnourished children)
 - >10 mm diameter of induration in other children (whether they have received vaccination or not)
3. Please note that a mantoux may be negative despite the child having TB especially in severe disseminated TB, malnutrition and HIV disease.

EXTRA PULMONARY TUBERCULOSIS (EPTB) IN CHILDREN

Extra pulmonary TB is common in children and presentation varies with age. Table lists typical clinical features for various forms of EPTB and suggested investigations for each category. Symptoms are usually persistent and progressive. The most common form of EPTB is TB lymphadenitis

Table 4.1: EPTB Presentation and Diagnosis In Children

Site of EPTB	Typical clinical presentation	Investigation	Comment
TB lymphadenitis	- Asymmetrical, painless, non-tender lymph node enlargement for more than one month +/- discharging sinus - Most commonly in neck area	Fine needle aspiration when possible Mantoux	Treat if axillary node enlargement on same side as BCG in HIV-positive infant, consider BCG disease and refer
Pleural TB	Dullness on percussion and reduced breath sounds +/- chest pain	CXR Pleural tap	Treat if pus in pleural tap, consider empyema and refer
TB meningitis	Headache, irritability/abnormal behaviour, lethargic/reduced level of consciousness, convulsions, neck stiffness, bulging fontanelle, cranial nerve palsies	Lumbar puncture obtain CSF CXR CT scan	Hospitalise for TB treatment ²
Miliary TB	Non-specific, lethargic, fever, wasted	CXR	Treat and refer where appropriate
Abdominal TB	Painless abdominal swelling with ascites	Ascitic tap Ultra-sound Mantoux test	Refer where appropriate
Spinal TB	Painless deformity of spine May have lower limb weakness/paralysis	X-ray spine	Refer where appropriate ²
Pericardial TB	Cardiac failure Distant heart sounds Apex beat difficult to palpate	CXR Cardiac ultrasound Pericardial tap	Refer where appropriate
TB bone and joint	Painless, non-tender swelling end of long bones with limitation of movement Painless, non-tender unilateral effusion of usually knee or hip	X-ray of affected bone and/or joint Joint tap	Refer where appropriate

Require 5ml of CSF.

Typical findings: straw coloured fluid, exudates with high protein, white blood cells especially lymphocytes

Referral may be necessary for investigation procedure and laboratory support as well as clinical care. If referral is difficult or not readily available, start anti-TB treatment.

The above table highlights the more common forms of EPTB; however TB may infect other organs.

Abdominal ultra-sound shows complex ascites +/- septation

All specimens (FNA, CSF, aspirates etc) should be sent for AFB microscopy and TB culture where visible

TREATMENT OF TB IN CHILDREN

Some of the important points to note about TB treatment in children are.

- Children usually have pauci-bacillary (low organism numbers) pulmonary disease, cavitating disease is rare and EPTB is common.
- Severe and disseminated TB occurs especially in young children (less than 4years) and in HIV the infected.
- Both the bacillary load and type of disease may influence the treatment regimens.
- Treatment outcomes in children are generally good even in the HIV infected provided treatment is started promptly.
- Children generally tolerate the anti- TB drugs better than adults.

CLASSIFICATION OF TB IN CHILDREN

TB is classified as pulmonary (PTB) or extra-pulmonary tuberculosis (EPTB) based on disease site. It is also classified according to severity, treatment history, and drug resistance

Table 4.2: Classification of tuberculosis

1. Non Severe TB
<ul style="list-style-type: none">• Pulmonary TB without extensive parenchymal lung disease• TB lymphadenitis• TB pleural effusion
2. Severe TB
<ul style="list-style-type: none">• PTB with extensive parenchymal lung disease• Miliary TB• All other forms of extra-pulmonary TB including:<ul style="list-style-type: none">○ TB bone or joint○ TB meningitis○ Pericardial TB○ Abdominal TB etc.
3. Retreatment
4. Multi-drug resistant TB

Standard Operating Procedures for Treatment

- Classify the case of TB before starting treatment into non-severe or severe, pulmonary or extra-pulmonary, or retreatment. For extra-pulmonary forms, specify the site.
- Treatment regimens by disease category are listed in treatment table below
- Record the TB diagnostic category, treatment regimen and date anti-TB treatment was started on road-to-health book as well as on TB treatment card
- A caregiver should be identified as the DOT provider for all ages including older children – educate them on anti-TB regimen and adherence
- Record weight at each visit
- Calculate drug dosages at every visit according to the child’s current weight (note that children gain weight while receiving anti-TB treatment)
- Once treatment is started it must be completed; “trial of TB treatment” should never be used as a diagnostic tool

RECOMMENDED TREATMENT REGIMENS

Table 4.3 below shows the new WHO recommended TB treatment regimens with the new four drug pediatric formulations of RHZE. The following changes are recommended:

- Use of four drugs during intensive phase for all children living in HIV endemic areas such as Kenya, adding ethambutol as a fourth drug for children of all ages.
- Treatment of TB meningitis and TB bone to be extended to a total of 12 months (2 months intensive phase, and 10 months continuation phase)
- In TB meningitis, ethambutol to replace streptomycin during intensive phase (RHZE) due to poor penetration of streptomycin across the blood brain barrier as well as toxicity

Table 4.3: New WHO recommended treatment regimen

Form of TB	Recommended regimen*	
	Intensive phase	Continuation phase
All forms of PTB and EPTB except TB meningitis and osteoarticular TB	2 HRZE	4 HR
TB meningitis and Osteoarticular TB	2 HRZE	10 HR
**Retreatment	3 RHZE	5 HRE
Drug resistant TB	Refer to a DRTB specialist	
*Numerical refers to number of months of the regimen. H= Isoniazid R= Rifampicin Z= Pyrazinamide E= ethambutol 2 HRZE refers to two months of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol		

Ethambutol is safe and can be used in children in doses not exceeding 20mg/kg/day

** For children on retreatment, assess for clinical improvement after one month of treatment

Dosages for Paediatric TB treatment using dispersible FDC tablets of RHZ, RH and single Ethambutol tablets for *new cases*

Table 4.4: Dosage of dispersible FDC tablets in a new case between 5 - 22 Kg

Weight band (kg)	Intensive phase , 2 months (RHZE)			Continuation phase , 4 months (RH)	
	No. of tablets of RHZ (60/30/150mg)	No. of tablets of RH (60/60mg)	Ethambutol (100mg)	No. of tablets of RH (60/30mg)	No. of tablets of RH (60/60mg)
5 - 7	1	1	1	2	0
8- 14	2	1	2	2	1
15 -22	3	2	3	3	2

Table 4.5: Dosage of dispersible FDC tablets for a new case between 23 -30 kg

Weight band (kg)	Intensive phase , 2 months(RHZE)		Continuation phase , 4 months (RH)	
	No. of tablets of RHZE (150/75/400/275mg)	No. of tablets of RH (60/60mg)	No. of tablets of RH (150/75mg)	No. of tablets of RH (60/60mg)
23-30	2	2	2	2

*For children above 30kg, do not give RH 60/60 but treat as adults
All children must be on pyridoxine 1-2mg/kg/day*

Dosages for Paediatric TB treatment using dispersible FDC tablets of RHZ, RH and single Ethambutol tablets for *retreatment cases*

Table 4.6: Dosage of dispersible FDC tablets in a retreatment case between 5 - 22 kg

Weight band (kg)	Intensive phase , 3 months (RHZE)			Continuation phase , 5 months (RHE)		
	No. of tablets of RHZ (60/30/150mg)	No. of tablets of RH (60/60mg)	No. of tablets of Ethambutol (100mg)	No. of tablets of RH (60/30mg)	No. of tablets of RH (60/60mg)	No. of tablets of Ethambutol (400mg)
5 - 7	1	1	1	2	0	1
8- 14	2	1	2	2	1	2
15 -22	3	2	3	3	2	3

Table 4.7: Dosage of dispersible FDC tablets in a retreatment case between 23 - 30 kg

Weight band (kg)	Intensive phase , 3 months (RHZE)		Continuation phase , 5 months(RHE)		
	No. of tablets of RHZE (150/75/400/275mg)	No. of tablets of RH (60/60mg)	No. of tablets of RH (150/75mg)	No. of tablets of RH (60/60mg)	No. of tablets of Ethambutol (400mg)
23-30	2	2	2	2	1

For children above 30kg, do not give RH 60/60 but treat as adults

All children must be on pyridoxine 1-2mg/kg/day

Do not use Streptomycin for TB retreatment in children. If a child on retreatment is not improving at one month of treatment assess for adherence and rule out drug resistant TB

Table 4.8: Dosages for pyridoxine supplementation of children on treatment for TB

Weight (kg)	Number of tablets of pyridoxine (50mg)
5-7	¼
8-14	½
15 and above	1

Other important observations to note include

- Treatment regimens are the same for HIV-infected and HIV-uninfected children
- Response to treatment in HIV infected may be slower.
- Register all children receiving anti-TB treatment with the National TB Program
- TB drugs are very well tolerated in almost all children.
- Side-effects are unusual and the most important is hepatotoxicity.
- Ethambutol can be safely used in all ages of children at recommended dosages of **20 mg/kg** or as per the drug dosage chart.

ADDITIONAL MANAGEMENT DECISIONS

- Hospitalization: The following categories of children with TB should be treated as in-patients
 - Severe forms of PTB and EPTB (e.g. Spinal TB) for further investigation and initial management.
 - TB meningitis
 - Severe malnutrition for nutritional rehabilitation
 - Signs of severe pneumonia (i.e. chest in-drawing)
 - Other co-morbidities e.g. severe anaemia
 - Social or logistic reasons to ensure adherence
 - Severe adverse reactions such as hepatotoxicity
- Steroid therapy: This should be given in the following situations:
 - TB meningitis,
 - PTB with respiratory distress,
 - PTB with airway obstruction by hilar lymph nodes.

- Severe Miliary TB,
- pericardial effusion,

Give prednisone at 2mg/kg once daily for 4 weeks, and then taper down over 2 weeks (1mg/kg for 7 days, then 0.5mg/kg for 7 days)

- For all HIV-infected children
 - Commence Cotrimoxazole prophylaxis (25 – 30mg/kg of CTX once daily, or see table 5.3 for dose in weight bands)
 - Commence antiretroviral therapy within 2 – 8 weeks of starting anti-TB therapy
 - Conduct family-based care/screening

- Immune re-constitution inflammatory syndrome (IRIS) - This is a paradoxical deterioration after initial improvement following treatment initiation.
 - Seen during the initial weeks of TB treatment with initial worsening of symptoms due to immune re-constitution.
 - IRIS is commonly seen in the severely immuno-compromised TB/HIV co-infected child after initiating ARV treatment
 - Management: Continue anti-TB therapy; give non steroidal anti-inflammatory drugs or/and prednisone until severe symptoms subside.

- Referral of children with TB should be considered if
 - Diagnosis is uncertain
 - Necessity for HIV-related care e.g. to commence ART
 - Failure to respond to treatment despite good adherence
 - Pyridoxine 5 – 10 mg once daily should be given to.
 - All malnourished children throughout the anti-TB therapy.
 - HIV infected children
 - Breast feeding infants.
 - Pregnant Adolescents

HIV IN CHILDHOOD TB

Children who are HIV infected may be at increased risk of developing TB just like adults. The diagnosis of TB in HIV-infected children is more complex, as many HIV-related lung diseases can easily be confused with TB. It is possible that a significant proportion of HIV infected children with pulmonary disease and treated as TB do not in fact have TB.

As in adults, all children with TB should be offered HIV testing and counselling in accordance with the published guidelines for HIV testing in children.

Refer to the Paediatric TB guidelines for a detailed management of TB/HIV co-infection.

FOLLOW-UP OF A CHILD ON ANTI-TB THERAPY

Patients visit the health facility 2 weekly during intensive phase and monthly during continuation phase and should be assessed for.

- Drug adherence.
- Drug toxicity.
- Weight gain.
- Symptom assessment.
- Sputum for AFBs at month 2,5, 6/8 for those who were smear positive at the beginning of treatment.

This is a critical part of effective TB treatment requiring a clear management plan.

The following should be done at each visit

Weigh the child at each visit, document and adjust dosage if necessary

Address Adherence issues

Explain and emphasize to care-giver and child why they must take the full course of treatment even if they are feeling better

Note risk factors for poor adherence such as distance/transport; orphan (especially if mother has died) or primary care-giver unwell; adolescents

Education and adherence support especially TB/HIV

Explain that anti-TB drugs in children are well tolerated and safe.

Assess the child to check for any improvement or worsening of the signs and symptoms, general well being of the child

CXR is not required in follow-up if the child is responding well to anti-TB treatment

At the end of treatment, all children who had abnormal x-rays at base line should have a repeat x-ray

PARADOXICAL REACTIONS IN CHILDHOOD TB

A temporary exacerbation of symptoms, signs or radiographic manifestations sometimes may occur after beginning anti-tuberculosis therapy. This can simulate worsening disease, with fever,

increased size of lymph nodes or tuberculoma, but is usually the result of immune reconstitution brought about by improved nutritional status or the anti-tuberculosis treatment itself. Anti-tuberculosis treatment should be continued and in the majority of cases oral corticosteroids should be added

TB PREVENTION IN CHILDREN

SCREENING FOR CHILD CONTACTS OF KNOWN TB CASES

Young children living in close contact with a source case of smear positive pulmonary TB are at a high risk of TB infection and disease. The risk of infection is greatest if the contact is close and prolonged. The risk of developing disease after infection is much greater for malnourished children, children under 5 years and HIV infected children than it is for HIV un-infected children and those over 5 years. If the disease develops it usually does so within 2 years of infection, but in infants the time lag can be as short as a few weeks.

Isoniazid preventive therapy (IPT) for young children with infection who have not yet developed disease will greatly reduce the likelihood of developing TB during childhood.

Contact screening refers to the screening or evaluation for TB infection or disease of all close contacts of smear positive source PTB case

The main purposes of child contact screening are to:

1. Identify symptomatic children (i.e. children of any age with undiagnosed TB disease), and treat them for TB.
2. Provide Isoniazid preventive therapy (IPT) for the high risk children who have no signs or symptoms of TB disease i.e.
 - All children aged under 5 years
 - All HIV infected children

The best way to detect TB infection is the TST, and CXR is the best method to screen for TB disease in symptomatic children contacts. Where these two tests are unavailable contact screening and management can be conducted on the basis of simple clinical assessment.

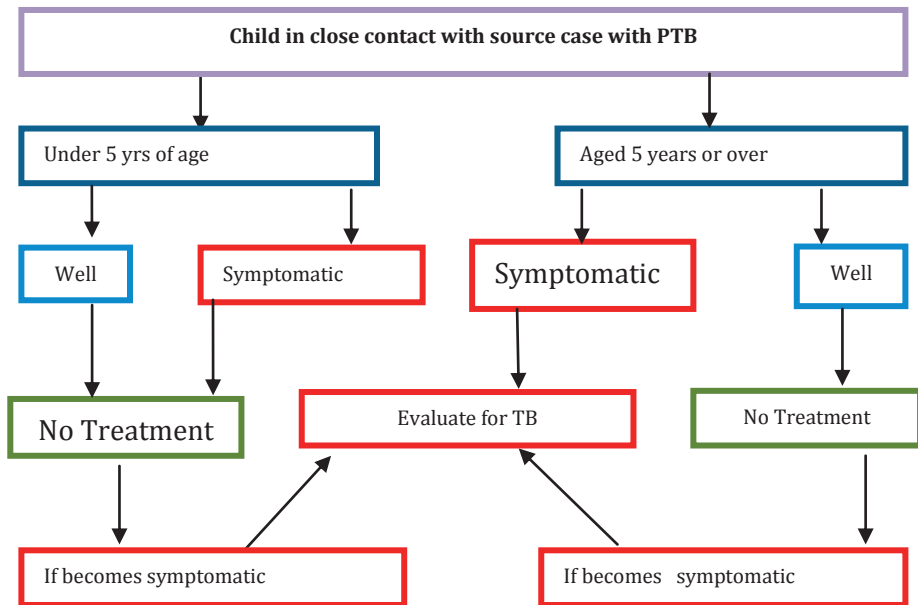
Generally clinical assessment is sufficient to decide whether the contact is well or symptomatic

Symptoms for Child Contact Screening

1. Non remitting cough of more than 2 weeks
2. Persistent fever of more than 2 weeks
3. Loss of weight/poor weight gain
4. Lethargy/malaise/reduced play
5. Enlarged cervical LN

EVALUATION OF A CHILD EXPOSED TO PTB

The algorithm below outlines the approach to management of a child contact



The symptomatic contacts should be evaluated for TB disease and managed in the usual manner once found to have TB.

Child contact known to be HIV-infected

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

Suspected HIV infection of contact

If the source case is a parent and is HIV infected, their children may be at risk of both TB and HIV infection. It is important to counsel and test for HIV as we screen for TB infection in all the contacts. (Consider joint TB/HIV contact investigations)

Child contacts of infectious MDR-TB cases

By definition MDR-TB is resistant to both Isoniazid and Rifampicin, it is unlikely that use of these drugs to treat latent infection caused by an MDR-*M. Tuberculosis* strain will prevent the development of active TB disease. Close contacts of MDR-TB patients should receive careful clinical follow-up for a period of at least 2 years. *If active disease develops, prompt initiation of treatment of the child with a regimen designed to treat MDR-TB is recommended.* The use of second-line drugs for chemoprophylaxis in MDR-TB contacts is currently not recommended.

Note: The source case may have transmitted TB to the child several months earlier, and may not currently be living in the household.

ISONIAZID PROPHYLACTIC THERAPY (IPT) IN CHILDREN

Isoniazid preventive therapy (IPT) for young children with infection who have not yet developed disease will greatly reduce the likelihood of developing TB during childhood

Which child should receive IPT?

- All children below 5 years who have had recent (past 12 months) exposure to an adult or adolescent with PTB or suspected PTB, provided they have no evidence of active TB disease
- All HIV infected children above one year of age provided they have no evidence of active TB disease.
- All HIV infected children below one year – give IPT only to those with recent (past 12 months) contact with a TB case, provided they have no evidence of active TB disease.
- Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening, and have no contact with a TB case should receive six months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care services.
- In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive six months of IPT if the evaluation shows no TB disease

These children should receive six months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care services

Dose and duration of INH for IPT in children

IPT should be given at a dose of 10mg/kg for duration of 6 months.

Table 4.9: Dose of Isoniazid for prophylaxis (IPT) in children

Weight	Dose in mg/day	Number of 100 mg, INH tablets	Number of 300 mg (Adult) tablets
<5	50	½	-
5.1 – 9.9	100	1	-
10-13.9	150	1½	½
14-19.9	200	2	-
20-24.9	250	2½	-
>25 and adults	300	3	1

IPT Follow-up:

All children should be registered in the IPT register

- Review monthly and continuously reinforce message of adherence
- Screen for TB disease i.e. persistent cough, fever, fatigue, poor weight gain
- Monitor INH adverse effects.
- Maintain a contact register

MANAGING THE PTB EXPOSED CHILD

At diagnosis

The mother is started on anti-TB treatment; the child is started on isoniazid chemoprophylaxis for three months.

At 2 months

The sputum of the mother is checked. If still smear positive, sputum for AFB microscopy is tested at 3 months. In most of the cases it should be negative by this time.

At 3 months

A tuberculin skin test (TST) should be carried out on the child and if there is a reaction of more than 5 mm diameter, Isoniazid chemoprophylaxis should be continued for another three months. If TST is not available Isoniazid should be given for 6 months. If a tuberculin test is negative at 3 months, Isoniazid should be stopped. In case the child is not vaccinated with BCG, vaccination should be given after Isoniazid has been stopped for three days (after three days without isoniazid, the child is given BCG vaccination). If active TB disease develops during the 6 month period, prophylaxis should be stopped, and switched to full anti-TB treatment with 3-4 drugs as appropriate.

BCG VACCINATION IN CHILDREN

BCG is a live attenuated vaccine derived from *M. bovis*, the vaccine offers protection against the more severe types of TB such as Miliary TB and TB meningitis, which are common in young children.

All children should be vaccinated against BCG vaccine as soon as possible after birth EXCEPT those with suspected TB infection at birth. The BCG vaccination should then be deferred till 2 weeks after IPT/ TB treatment.

A child who has not had routine neonatal BCG immunization and has symptoms of HIV disease/ congenital immunodeficiency syndrome should also not be given BCG because of the risk of disseminated BCG disease.

A small number of children (1–2%) may develop complications following BCG vaccination. These commonly include:

- Local abscesses at the injection site
- Secondary bacterial infections
- Suppurative adenitis in the regional axillary lymph node
- Local keloid formation.
- Disseminated BCG disease

Most reactions will resolve spontaneously over a few months and do not require specific treatment. Children who develop disseminated BCG disease should be investigated for immunodeficiencies and treated for TB using a 4-drug first-line regimen: 2RHZE then 4RH (The BCG bacillus has poor susceptibility to Pyrazinamide)

NUTRITIONAL NEEDS OF CHILDREN WITH TUBERCULOSIS

All children presenting with malnutrition or failure to gain adequate weight must be evaluated for possible TB. Studies of children presenting with different forms of malnutrition indicate that TB is present in 12- 30% of the cases. When weight gain patterns of children with TB are studied, it is evident that 66% of them fail to gain weight or show loss of weight prior to diagnosis. (children require proteins 2.5 – 3 g/kg body weight, and the malnourished may need 50% - 100% more energy and micronutrients).

CHAPTER 5: TUBERCULOSIS AND HIV

INTRODUCTION AND RATIONALE

The HIV infection exponentially increases the risk of TB in co-infected individuals. TB on the other hand is a leading cause of morbidity and mortality among PLHIVs. HIV infected individuals are more likely to suffer acute opportunistic infections and develop drug reactions and therefore call for close attention. Thus all patients presenting with signs and symptoms of any of the two diseases should be actively screened for the other and managed appropriately.

Ways in which the two diseases interact with each other are listed below

Interaction of HIV with TB

1. Increased lifetime risk of TB from 5-10% to 50%
2. Increased rate of progression of new TB infections to disease
3. Increased risk of recurrence of previously treated TB
4. Increased risk of death from TB
5. Increased risk of adverse reactions to anti-TB drugs
6. Increased stigma to the two diseases

Interaction of TB with HIV

1. Rapid progression of HIV disease
2. TB is the leading cause of HIV-related morbidity
3. TB is a leading cause of mortality among PLHIV (*one-third of all AIDS related deaths are due to TB*)
4. Increasing TB cases among PLHIV enhances the risk of TB transmission in the community regardless of their HIV status

TB/HIV COLLABORATIVE ACTIVITIES:

The close association between TB and HIV makes it imperative to develop strategies for the delivery of combined TB and HIV services in what is commonly referred to as TB/HIV collaborative activities. These activities are aimed at coordination of TB and HIV programs at all levels, reducing the burden of TB among PLHIV and reducing the burden of HIV in TB patients.

The key TB/HIV collaborative activities are shown in Table 5.1 below

Table 5.1: Collaborative TB/HIV activities implemented in various settings

Objective/ Activity	Implementer
A. Establish the mechanism for collaboration <ol style="list-style-type: none"> 1. TB/HIV coordinating bodies 2. HIV surveillance among TB patient 3. TB/HIV planning 4. TB/HIV monitoring and evaluation 	TB and HIV Programmes
B. To decrease the burden of TB in PLHIV- Three Is <ol style="list-style-type: none"> 1. Intensified TB case finding 2. Isoniazid preventive therapy 3. TB infection control in health care and other settings 	HIV programme
C. To decrease the burden of HIV in TB patients <ol style="list-style-type: none"> 1. HIV testing and counselling 2. HIV prevention 3. Cotrimoxazole preventive therapy 4. HIV/AIDS care and support 5. Antiretroviral therapy to TB/HIV co-infected patients 	TB programme

INTENSIFIED TB CASE FINDING AMONG PLHIVS

The prevalence of TB is higher among PLHIV than in the general population as is morbidity and mortality. Diagnosis of TB among PLHIVs is more challenging than in HIV negative persons and therefore calls for a high index of suspicion and active case search to identify and treat cases early. Best practice requires that all persons found to be HIV positive at HIV testing sites including VCT centres, STI clinics, MCH sites etc be screened for TB and referred to the nearest TB diagnostic centres. PLHIV enrolled in chronic HIV care should also be screened for TB on every visit using the ICF tools.

Benefits of intensified TB case finding

Intensified TB case finding promotes early TB case detection reducing the duration of disease which effectively reduces transmission, morbidity and mortality.

TB ICF should be implemented in all HTC and treatment sites in Health care and community settings. TB-ICF is critical for entry into Isoniazid Preventive Therapy (IPT) by identifying HIV infected persons who are suitable candidates for this intervention

ICF beyond PLHIVs

TB intensified case finding should be implemented in other high risk populations to reduce diagnostic delays. These include:

- All person presenting with cough
- Diabetics and patients with other immune-suppressive illnesses
- Prisoners/ remandees
- Other institutionalised individuals
- TB / X/MDRTB contacts
- Health care workers
- In Patients

Table 5.2: Recommendations for TB ICF beyond health care settings

<p>TB-ICF in Prisons</p> <p>The prevalence and incidence of TB is higher among prisoners than the general population.</p> <p>Recommendations</p> <ul style="list-style-type: none"> • All new inmates should be screened for TB at entry • Quarterly rescreening of all inmates and remandees • All TB suspects should be offered HTC
<p>TB-ICF in Community Pharmacy</p> <p>A significant proportion of TB patients self-medicate before TB diagnosis</p> <p>Recommendations</p> <ul style="list-style-type: none"> • The standard TB screening tool should be administered to All patients presenting with cough at community pharmacies
<p>TB-ICF at Community Level</p> <p>TB transmission mostly occurs at the community level.</p> <p>Recommendations</p> <ul style="list-style-type: none"> • The community ICF tool should be administered by community health workers to all patient presenting with cough • Referral of all TB suspects from the community to health facility.

HIV TESTING AND COUNSELLING (HTC)

All patients with confirmed or suggestive symptoms of active tuberculosis should be offered HIV counseling and testing as standard of care

In many patients, a diagnosis of tuberculosis is often the first indication of underlying HIV infection. HIV counseling and testing should be carried out in all TB suspects as part of the investigations for TB. A diagnosis of HIV infection at the earliest opportunity possible has several benefits including:

- Enrolling the patient into HIV care and treatment (including cotrimoxazole preventive therapy and ART); both of which will greatly improve TB treatment outcomes.
- Accessing HIV prevention services: HIV positive TB patients may have household members with undiagnosed HIV infection. Using a family-centered approach or couple HIV counseling and testing, these infected family members can be identified and referred for care and treatment as well. All patients undergoing HTC should receive a full package of Prevention with Positive services and reviewed in accordance with the national PwP guidelines.
- Using the family-centered approach; household contacts of sputum positive TB patients are screened for TB, and those with active TB offered prompt treatment. This will also provide the opportunity to provide isoniazid preventive therapy to eligible household contacts with no active disease.

Note: It is considered substandard care not to offer HIV testing and counseling to patients presenting with an illness that may be HIV related including TB.

When carrying out HTC the health care worker should ensure that the patient fully understands the purpose and benefits of testing during the pre-test counseling. The patient should also be informed of the disadvantages of declining the HIV test including the missed opportunities for treatment and prevention of opportunistic infections. The health care worker should be able to respond to the patient's questions and concerns; and very importantly, the patient should know that he or she has a right to decline the test (opt-out). For those who decline the test the health care worker should try to identify

the barriers to testing and solve them. All patients who decline testing should be offered the test during their subsequent visits.

Before giving the results the health care worker should provide post-test counseling with emphasis on interventions that can be provided. Post test counseling should include the following:

Those who test HIV negative:

- Should be informed about couple discordance and be encouraged to refer their partners for testing.
- Should be motivated to maintain non-risky behavior so as to avoid acquisition of HIV infection.
- Should be informed that the negative test does not rule out HIV infection and should be encouraged to visit a VCT centre for retesting after 3 months.

Those who test HIV positive:

This group of patients may require intensive counseling and support to cope with the positive result and may benefit from referral to a formal counselor. The basic post counseling session should include:

An empathic disclosure of the positive result and:

- A discussion with the patient about the care available and referral to a Comprehensive Care Clinic as soon as possible.
- A discussion on disclosure of result to the partner and partner referral for a HIV test and provision of other PwP messages and interventions including referral to post-test clubs or any other support groups for psychosocial support
- Nutritional advice

Note:

Always be on the lookout for other Opportunistic Infections (OIs) and treat or refer the patient accordingly.

Ensure that the patient accesses a full package of PwP services

MANAGEMENT OF TUBERCULOSIS AND HIV CO-INFECTED PATIENTS

PROVISION OF COTRIMOXAZOLE PREVENTIVE THERAPY

Cotrimoxazole Preventive Therapy (CPT) reduces mortality among TB patients with HIV infection irrespective of CD4 count. CPT should therefore be provided to all TB/HIV co-infected individuals (unless contraindicated) at the time of anti TB initiation and continued throughout treatment. Patients given cotrimoxazole should be monitored for side effects including rash and gastrointestinal disturbances. Cotrimoxazole should be withdrawn whenever moderate to severe reactions occur.

Table 5.3: Dose of Cotrimoxazole for CPT

Weight (Kg)*	Suspension 240mg per 5ml	Single strength tablet 480mg (SS)	Single strength tablet 480mg (SS)
1-4	2.5ml	¼ SS tab	-----
5-8	5ml	½ SS tab	¼ DS tab
9-16	10ml	1SS tab	½ DS tab
17-30	15ml	2 SS tab	1 DS tab
>30(Adults and adolescents)		2 SS tab	1 DS tab

MANAGEMENT OF PATIENTS WITH COTRIMOXAZOLE ALLERGY

Patients with mild to moderately severe rash should stop CTX and once recovered should undergo desensitization as shown in table 5.4 below.

Patients with severe rash (oedema, vesiculation of the skin, mucosal involvement) should NOT be desensitized; CTX should be stopped and never re-used.

Desensitization is effective in the majority of patients. The rapid regimen can be used in situations where treatment for PCP is needed.

Dapsone is recommended in patients allergic to CTX. Dapsone is not as effective as CTX for chemo-prophylaxis but only provides protection against PCP (To provide effective prevention against toxoplasmosis, pyrimethamine should be added)

Dose of dapsone

Dapsone is available as 25mg and 100mg tablets

Children: **4 mg /kg per week** OR 2 mg/kg once daily (maximum dose 100 mg)

Adults: 100 mg once daily.

Dapsone should be commenced in patients with WHO stage 4 disease and/or those with a CD4 <200 cells/mm³

Dapsone should be discontinued once the CD4 has been greater than the following values for at least 6 months.

- 200 cells/mm³ for adults and children >5 years
- the age specific threshold for severe immunodeficiency for younger children

COTRIMOXAZOLE DESENSITIZATION

Table 5.4: Standard and rapid desensitization regimen for patients on CTX

Standard desensitization regimen days		Rapid desensitization regimen (Hours)	
day	Dose of TMP/SMX suspension 40/200 per 5ml	Hour	Dose of TMP/SMX suspension 40/200 per 5ml
1	0.5 ml	0	0.5 ml
2	1 ml	1	1 ml
3	2 ml	2	2 ml
4	3 ml	3	3 ml
5	4 ml	4	4 ml
6	5 ml	5	5 ml
7	1SS tablet	6	1SS tablet
8	2SS tablets/ 1DS tablet per day		

or ALL ART- naïve patients with TB/HIV co-infection, after starting TB therapy; ART should be started irrespective of CD4 cell count and as soon as TB treatment is tolerated (**Within the first two to eight weeks of initiation of TB treatment**)

PROVISION OF ANTI-RETROVIRAL THERAPY (ART)

All TB /HIV coinfected patients should be started on ART irrespective of CD4 count. Recent evidence shows that early initiation of ART reduces mortality and improves TB outcomes.

CHOICE OF ARV DRUGS IN TB/HIV CO-INFECTED ARV-NAÏVE PATIENTS

Table 5.5: TB/HIV co infected patients, ART naïve or on first line ART

Patient Category	TB treatment	ART treatment
Adults and Adolescents	2RHZE/4RH	TDF/AZT+3TC+EFV
Pregnant women	RHZE	AZT+3TC+ABC/TDF (in first trimester- change to below regime as soon as patient enters 2 nd trimester) TDF/AZT+3TC+EFV(in 2 nd and 3 rd trimesters)
Children age below 3 years or weight < 10 kg	2RHZ/4RH	Preferred option: ABC/AZT + 3TC + LPV/r + RTV (add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV). If not NVP exposed change to ABC/AZT + 3TC + NVP Alternative option (If nevirapine exposed): ABC+3TC+AZT Change ART to AZT +3TC+ LPV/ r after completion of TB treatment
Children age above 3 years or weight > 10kg	2RHZ/4RH	ABC/AZT+3TC+EFV If NVP exposed: ABC/AZT +3TC +LPV/r +RTV (add extra dose of RTV to make the LPV/ RTV RATIO 1:1-super boosted LPV)

HIV/TB co-infected patients on 2nd line ART (PI based regimes)

Rifabutin is available as a substitute for rifampicin in adult TB patients on second-line antiretroviral drugs containing protease inhibitors. Currently rifabutin is given at a dose of 150mg on alternate days while the rest of the drugs are given on daily basis. There is no adequate safety data for use of rifabutin in children.

Table 5.6 Treatment of TB in patients on second-line ART (PI based)

Patient Category	TB treatment	ART treatment
Adults and Adolescents	2 RFB ₃ ZHE/ 4RFB ₃ H	TDF/AZT + 3TC + LPV/r
Pregnant women	2RZHE/4RH	Consult an Expert
Children age below 3 years or weight < 10 kg	2RHZ/4RH	ABC/AZT + 3TC + LPV/r + RTV(add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)
Children age above 3 years or weight > 10kg	2RHZ/RH	ABC/AZT + 3TC + LPV/r + RTV(add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)
<i>ART management of TB patients should be in accordance with the current National ART Guidelines</i>		

For women planning a pregnancy or not using contraception, EFV should be avoided if alternatives are available. There are still safety concerns about EFV use in the first trimester. However, EFV can be used from the second trimester.

Patients who are started on triple nucleoside regimen should be changed to a standard regimen once the TB treatment is complete.

Dual treatment of TB/HIV co-infection is complicated by:

Drug interactions involving rifampicin with NNRTIs and PIs

- Overlapping toxicities e.g. INH and NVP that both cause hepatotoxicity
- High pill burden of combined ARV and anti-TB drugs.

Therefore, close monitoring and psychosocial support are advised.

ISONIAZID PREVENTIVE THERAPY (IPT)

Recent data indicates that Isoniazid preventive therapy is effective in protecting people living with HIV from developing tuberculosis. A six month course of INH at 5 mg/kg bodyweight isoniazid daily prevents the development of active TB in HIV infected persons with the benefit lasting up to two years. It is critical to ensure that active TB is confidently ruled out to avoid inadvertent mono-therapy with Isoniazid in patients with undiagnosed TB, potentially leading to drug resistance.

Table 5.7: Indications for IPT

Indication for IPT
<ol style="list-style-type: none">1. All asymptomatic PLHIV – including:<ul style="list-style-type: none">• Children > 12 months• Pregnant women2. Children under 5 years who are contacts of infectious TB3. Prisoners <p>Note: There is little benefit in administering IPT to children aged 12 month and below unless they have been exposed to a suspected or confirmed case of TB</p>

Isoniazid preventive therapy is implemented sites offering HIV care and treatment as well as TB clinics.

These sites should be evaluated for suitability to offer IPT on the basis of TB and HIV indicators listed below

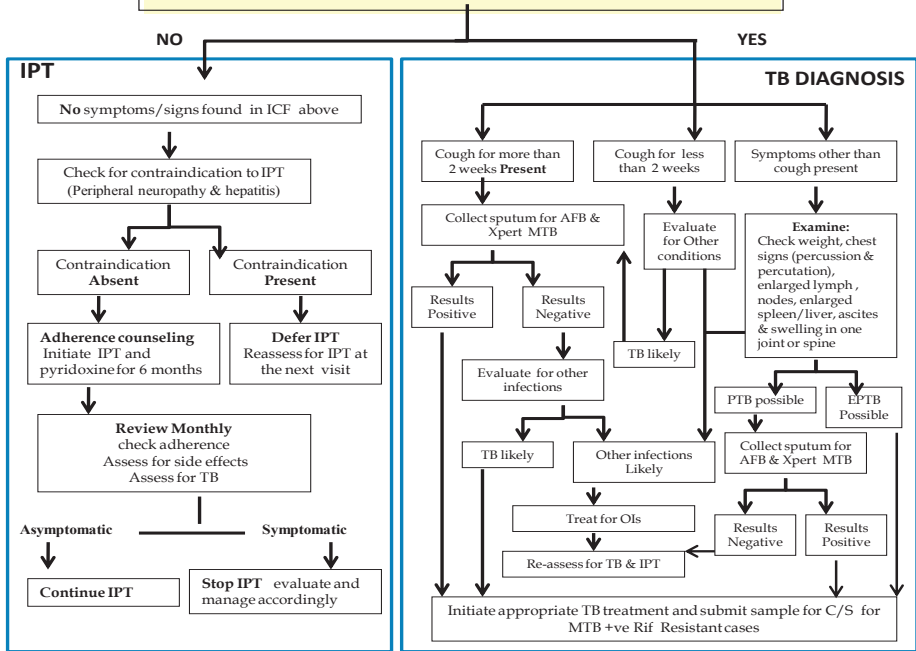
- Site should meet the minimal package for TB infection prevention
- TB cure rate of > 90%
- Defaulter tracing mechanism in place
- HIV client retention rate >90%
- Reporting mechanism in place
- Presence of an implementing partner support

Eligible clients should be subjected to the four question symptom screening questionnaire on every visit to the health facility and those screening negative to all the questions and meet additional eligibility criteria initiated on IPT.

TB SCREENING, DIAGNOSIS AND ISONIAZID PREVENTIVE THERAPY

On every clinic visit ask for the following

- Cough of any duration
- Fever
- Night sweats (adults and adolescents)
- Noticeable weight loss (adults & adolescents)



INITIATION OF IPT

Before initiating IPT, the following should be ensured:

- Negative TB screening based on the symptom questionnaire
- Rule out:
 - Hepatitis: Clinical evaluation for asymptomatic and investigations for symptomatic patients
 - Peripheral Neuropathy: Clinical evaluation
- Patient should be potentially adherent based on counseling and assessment

CONTRAINDICATIONS OF IPT

- Active tuberculosis disease
- Active hepatitis
- Signs and symptoms of peripheral neuropathy
- Active substance abuse by patient or self
- Abnormal chest X ray
- Poor adherence to Cotrimoxazole Preventive Therapy or poor understanding of IPT by guardian
- Infant < 1 year unlikely to have active TB and not exposed to smear positive TB

DOSAGE OF IPT

Administration is based on the weight as shown in table 5.8 below

Table 5.8: Dosage of IPT

Weight range (kg)	No. of 100mg INH tablets per dose per dose	Dose given (mg)
<5	½ tablet	50
5.1-9.9	1 tablet	100
10-13.9	1 ½ tablet	150
14-19.9	2 tablets	200
20-24.9	2 ½ tablets	250
>25	3 tablets or one adult tablet	300

IPT PATIENT MONITORING

Harmonize clinic appointments for INH review and routine HIV care. Patients on IPT are reviewed every 28 days.

During the visit the patients should be screened for TB using the standard ICF tool, be evaluated clinically to rule out hepatitis and peripheral neuropathy and any other illness and be assessed for adherence to isoniazid prophylaxis

MANAGEMENT OF COMPLICATIONS OF IPT

Table 5.9 below summarizes the management of IPT complications

Table 5.9: Management of IPT complications

Complication	Management
Development of active TB	<ul style="list-style-type: none">• Classify and manage as any other TB patient• Obtain sputum or any relevant specimen for:<ul style="list-style-type: none">• AFB microscopy• Culture and DST (To rule out DR TB)• Follow up in TB clinic
Hepatitis	<ul style="list-style-type: none">• Stop INH• Rule out other causes of hepatitis• Manage appropriately

CHAPTER 6 : DRUG RESISTANT TB

MAGNITUDE OF DRUG RESISTANT TB IN KENYA

The emergence of drug resistant TB is a major threat to the control of tuberculosis. Treatment of drug resistant TB is expensive prolonged and associated with poor treatment outcomes compared with drug susceptible TB. Since 2002 Drug resistant TB surveillance has been conducted among patients at high risk particularly retreatment TB cases. Currently 90% of this population is covered by the surveillance system. It is important to note that the best opportunity that we have to treat TB is the first one. All efforts should therefore be applied to prevent the development of TB.

DEVELOPMENT OF DRUG RESISTANCE

Drug resistant TB is a man made problem that may arise from one or more of the factors tabulated below:

Table 6.1: Causes of drug resistant tuberculosis

Health care worker (inadequate regimen)	
<ul style="list-style-type: none">• Inappropriate guidelines• Non compliance with guidelines• Absence of guidelines• Poor training	<ul style="list-style-type: none">• No monitoring of treatment• Poorly organized or funded TB control programs
Drugs: Inadequate supply or quality	
<ul style="list-style-type: none">• Poor quality• Unavailability of certain drugs (stock outs or delivery disruptions)	<ul style="list-style-type: none">• Poor storage conditions• Wrong dose or combinations
Patients: Inadequate drug intake	
<ul style="list-style-type: none">• Poor adherence (or poor DOT)• Lack of information• Lack of money (no treatment available free of charge)• Lack of transportation	<ul style="list-style-type: none">• Adverse effects• Social barriers• Malabsorption• Substance dependency disorder

CLASSIFICATION OF DRUG RESISTANCE

Drug resistance may be classified based on exposure, resistance pattern or treatment history as shown in table 6.2 below

Table 6.2: Classification of drug resistant TB

Classification based on exposure
<ul style="list-style-type: none"> • Primary resistance: If there was definitely no previous treatment. • Acquired resistance: If there is a definite history of previous treatment.
Classification based on the type of resistance expressed by the TB bacilli
<ul style="list-style-type: none"> • Mono resistance: Documented resistance to only one drug • Poly resistance (PDR): Documented resistance to at least 2 drugs but not to both Isoniazid and Rifampicin • Multidrug resistant (MDR): Documented resistance to at least INH and RIF • Extensively Drug Resistant TB (XDR TB): Documented MDR TB and resistance to a Quinolone and at least one injectable second line drug
Based on treatment history
<p>Category IV patient: This is any form of TB requiring 2nd line drugs i.e PDR, and MDR, XDR & TDR.</p> <ul style="list-style-type: none"> • New Category IV patient (primary resistance): A DRTB patient who has never received anti-tuberculosis treatment or one that has received anti-tuberculosis treatment for less than one month, or one who had DST at the start of a WHO category I regimen and then switched to a Category IV regimen because of evidence of drug resistance • Category IV patients previously treated with first-line drugs (acquired or secondary) A DRTB patient who has been treated for one month or more with first-line drugs only • Category IV previously treated with second-line drugs A DRTB patient who has been treated for one month or more with second-line drugs, with or without first-line drugs. They could be: <ul style="list-style-type: none"> • Return after default DRTB patient who was on second line treatment, who interrupted treatment but has been found and returned to treatment • Transfer in This is a DRTB patient who has been transferred from one district register of drug resistant TB patients to another • Others These are DRTB patients who do not fit any of the above definitions

MANAGEMENT OF DRUG RESISTANT TB

The management of drug resistant TB through the principles of DOTS has been mainstreamed into routine TB control activities. The objective is to strengthen anti-TB drug surveillance system for early detection of drug resistant TB and to provide drug treatment to those detected to have drug resistant TB.

DLTLD is encouraging the routine collection of sputum specimens from all TB re-treatment cases and submission of these to the Central Reference TB Laboratory to carry out TB cultures and DST. The DLTLD has established quality assurance and quality control systems for all laboratories offering sputum smear microscopy, culture and DST for *Mycobacteria TB*.

DIAGNOSIS

The diagnostic tool for MDRTB is DST. DST can be done by rapid molecular testing using XPERT MTB/RIF or LPA or by culture using the solid or liquid medium. The gene Xpert algorithm is as outlined below in the chart.

Samples for DST include:

Pulmonary TB

- Sputum
- Bronchoalveolar Lavage Fluids
- Bronchial Washings & Brushe

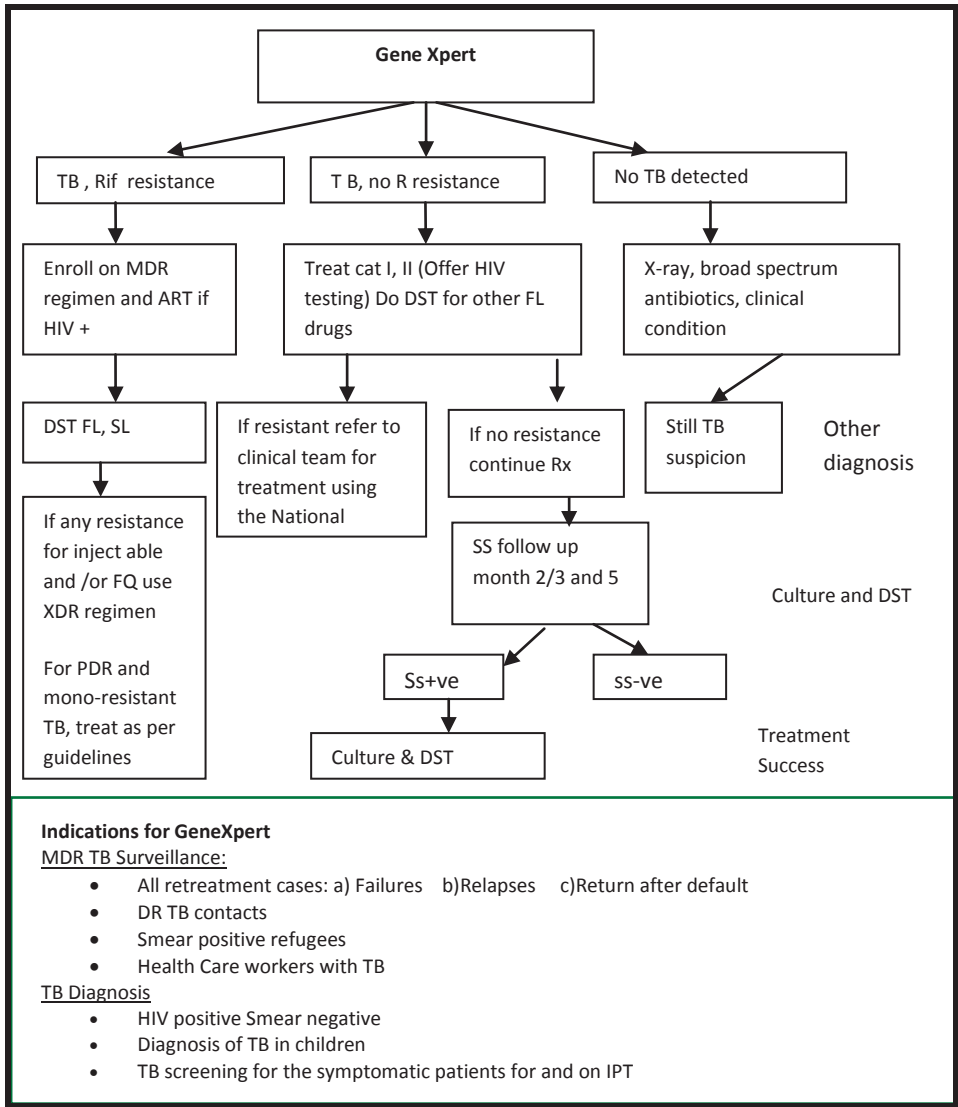
Extra-Pulmonary

- Tissue fluids (Synovial, Pleural, Peritoneal, Paracentesis, Pericardial, Ascites, dialysis fluid,
- Laryngeal Swabs & Aspirates,
- Stool
- Urine
- Tissue
- Lymph Nodes, bone, and other biopsies, etc.

The genexpert test is a new molecular diagnostic test based on the principal of molecular hybridization. Test can amplify low concentrations of MTB DNA and at the same time detect the gene that codes for rifampicin resistance which is an important marker of MDRTB. It is however limited by the fact that it cannot differentiate dead from living bacteria and therefore not recommended as a test to followup the response to therapy. The test is further limited by the high cost and its ability to test for resistance to only one drug.

The application of the genexpert test is shown in the algorithm below.

THE GENEXPERT ALGORITHM



CASE FINDING STRATEGIES FOR DRTB

DRTB surveillance is conducted among the high risk group including:

- Patients who remain or turn positive after 3 months of TB treatment.
- Patients previously treated for TB (relapses, return after default, failures)
- Patients who have a contact with known MDR TB.
- Patients who have a contact who died while on directly observed therapy for TB.
- Hospital and health care workers.
- Patients with HIV
- Smear positive refugees
- Treatment in programs that operate poorly or no program
- Residents of high resistance areas
- Failure of treatment

Diagnosis of DRTB in children

Clinical features and chest radiography do not distinguish drug sensitive from DRTB. DRTB diagnosis is made based on microbiological isolation of drug resistant TB strains from a specimen collected from a DRTB suspect. This is often difficult in children owing to challenges surrounding specimen collection. The following should be considered in the diagnostic work up of a child suspected to have DRTB:

- Obtain specimens from all possible sources for culture and susceptibility testing.
- The child should be considered a probable case of DRTB if
 - The child is a contact of an adult with infectious DR tuberculosis; or a source patient who is a retreatment case (especially treatment after failure) with unknown drug susceptibility, or who is a contact of DR-TB
 - the child, while adhering to treatment responds unsatisfactorily or deteriorates, or relapses shortly after completing
 - the *community* in which the child resides (or had resided) has a high prevalence of drug-resistant tuberculosis

TREATMENT AND FOLLOW UP OF DRUG RESISTANT TB.

The treatment of patients with drug resistant TB is complex and requires trained TB clinicians. Treatment should be offered in settings where infection control measures are in place. Drug resistant TB is treated using a combination of drugs. These drugs are classified into five groups for therapeutic purposes as shown in table 7.3 below

Table 6.3: Classification of antiTB medicines

Group I (Oral First line drugs)	
Isoniazid	Ethambutol
Rifampicin	Pyrazinamide
Group II (Injectable agents)	
Streptomycin	Amikacin
Kanamycin	Capreomycin
Group III (Quinolones)	
Ofloxacin	Levofloxacin
Ciprofloxacin	Moxifloxacin
Group IV	
Ethionamide	Para amino salicylic acid (PAS)
Cycloserine	
Group V (other Agents)	
AMX/CLV	Clarithromycin
Clofazimine	Linezolid

MDR-TB TREATMENT

Treatment of MDR TB consists of two phases: an intensive phase of 8 months and a continuation phase of 12 months.

Intensive Phase – 8 Km-Pto-Lfx-Cs-Z

This lasts for a minimum of 8 months and the following drugs are used

- | | |
|-----------------------------|--------------------------|
| a) Inj. Kanamycin [Km] | d) Tabs Cycloserine [Cs] |
| b) Tabs Prothionamide [Pto] | e) Tabs Pyrazinamide [Z] |
| c) Tabs Levofloxacin [Lfx] | |

Continuation Phase– 12Pto- Lfx -Cs-Z

This lasts for 12 months and uses the following drugs

- a) Tabs Prothionamide [Pto]
- b) Tabs Levofloxacin [Lfx]

- c) Tabs Cycloserine [Cs]
- d) Tabs Pyrazinamide [Z]

EXTRA-PULMONARY MDR-TB TREATMENT

The treatment strategy is the same as in patients with pulmonary MDR-TB

MONO AND POLY DRUG RESISTANT TB TREATMENT

Mono and poly drug resistant TB is treated based on the drug resistance pattern. Table 6.4 below shows the recommended regimen for treatment of various form of mono and poly-drug resistant TB

Table 6.4: Regimen for mono and polydrug resistant TB treatment

Pattern of drug resistance	Regimen	Duration of treatment
H (± S)	R/Z/E/LFX	9 months
H and Z	3KN/R/PTO/LFX 15/R/PTO/LFX	18months
H and E	3KN/R/PTO/LFX 15/R/PTO/LFX	18months
H, E, Z (± S)	3KN/R/PTO/LFX 15/R/PTO/LFX	18months
R	Treat as MDRTB	20 months
R and E (± S)	Treat as MDRTB	20months
R and Z (± S)	Treat as MDRTB	20 months
H, E, Z (± S)	3KN/R/PTO/LFX 15/R/PTO/LFX	18months

TREATMENT DELIVERY AND ADHERENCE

Management of drug resistant TB requires a multi-displinary team. These teams will be formed in the counties and sub-county levels will be responsible for managing DR TB in those regions. They will consist of:

- RTLC
- Clinician (physician/M.O)
- DTLC
- Pharmacist
- DOTs Nurse
- Social worker
- Public health officer
- Lab technologist
- Nutritionist
- Partners supporting TB control

The team will identify one member to be the focal person.

Partners managing DR TB should send a representative to the clinical team meetings

Roles of the team

- The overall responsibility of managing DR TB in their regions
- Reviewing DST and culture results of DR TB suspects and patients on treatment.
- Recommend initiation of DR TB treatment
- Schedule follow up of DR TB patients on treatment
- Reviewing complex cases as the need arises e.g. adverse drug effects, co-morbidities and recommending appropriate interventions
- Co-ordinate referrals of DR TB patients to and from their counties
- Ensuring adequate and consistent commodity supply in their regions

PATIENT CARE

The package drug resistant TB care should include the following:

- All the doses for second line should be observed by the health care worker and confirmed as swallowed by asking the patient a question.
- DRTB patients should be monitored closely for adverse drug effects and appropriate actions taken.
- All drug resistant TB cases should be evaluated for patient and family support which includes; accommodation, food, transport, non-TB drugs, and other extra investigations if required.
- All DRTB patients, their families and communities should receive health education, including stigma reduction

TREATMENT ADHERENCE

Treatment of DRTB should aim to ensure maximum adherence. To prevent non-adherence and default from treatment the following measures are essential:

- Education of patients
- Assessment for risk factors for non-adherence
- Appropriate treatment delivery settings
- Defaulter prevention and retrieval

PATIENT MONITORING

Initial evaluation monitoring of treatment

Pre-treatment screening and evaluation is done to establish a baseline for this treatment and to identify patients who are at risk of increased incidence of side effects . Table 6.5 below summarizes what is recommended for the DRTB patient initial evaluation and treatment monitoring.

Table 6.5: DRTB patient initial evaluation and monitoring of treatment

Monitoring Evaluation	Recommended frequency
Evaluation by Clinical team	At baseline, monthly until conversion, then every 2-3 months
Screening for side effects by DOT worker	At every DOT encounter
Weight	At baseline and monthly
Sputum smear and cultures	Baseline, monthly till conversion, then monthly smears and quarterly cultures every 3 months
DST 1 st and 2 nd line	Baseline and anytime there is a positive culture 2 nd line DST should be done for all MDR TB patients
CXR	At baseline then 6 monthly
Heamogram	At baseline then at month 3 and 6, then 6 monthly (or when necessary)
Serum Creatinine	At baseline then monthly while on injectable drug (or when necessary)
Serum potassium	At baseline, then one week, then monthly while on the injectable agent (or when necessary)
Serum calcium and magnesium	At baseline then monthly while on the injectable agent (or when necessary)
TSH	At baseline then 3 and 6 months, then 6 monthly if on ethionamide/ prothionamide / PAS
	Monitor clinically monthly for hypothyroidism
ALT	At baseline then 1-3 monthly if on pyrazinamide
HIV screening	At baseline and if clinically indicated
Pregnancy test	At baseline for women of childbearing age; repeat if indicated. Family planning methods should be offered to all women of reproductive age undergoing DR-TB treatment.
Audiometry	At baseline then monthly while on injectables

SPUTUM CONVERSION WHILE ON SECOND LINE TREATMENT

A patient is considered to have sputum conversion after two sets of consecutive negative smears and cultures taken 30 days apart. The date of the first set of negative cultures and smears is used as the date of conversion.

Intensive phase in MDRTB treatment will last a minimum of 8 months. Change from intensive to continuation phase should only be done after sputum conversion as defined above.

WHEN TO SUSPECT TREATMENT FAILURE

Treatment failure should be suspected if:

- The patient has persistent growth on cultures and positive smears past 6 months of treatment
- There is progressive extensive and bilateral lung damage confirmed on X-Ray for patients with no option for surgery
- There is worsening of patient's condition usually characterized by weight loss and respiratory insufficiency

MANAGEMENT OF PATIENTS AFTER MDR-TB/DR TB TREATMENT FAILURE

- Review the treatment records and assess adherence to determine if the patient is receiving all the right drugs and doses
- Review the treatment regimen in relation to medical history to determine if the patient may have been re-infected during the course of treatment
- Review all DST reports to determine the adequacy of the regimen and consider an alternative regimen where possible
- Do second line DST

TREATMENT OF XDRTB

- XDR TB should be managed by using an individualized regimen based on the DST results and patient drug history

- The patient should use at least an injectable, high generation quinolone, Cycloserine, Proethionamide, Pyrazinamide and add at least two drugs from group 5
- The injectable should be given for at least 12 months
- For every culture positive after month 3 of treatment, add 3 months of injectable after the 12th month of injectable
- If the patient becomes culture positive after a period of negative cultures, repeat the culture and DST
- If still culture positive, count the first culture positive as the first month of treatment and restart treatment

SUSPENDING THERAPY

Treatment should be suspended when it is confirmed that all the drugs have been administered and there is no possibility of adding other drugs or carrying out any surgical intervention. At this point, supportive care regimen is considered. The 2 most important considerations to suspend therapy and consider supportive care are:

- **Patient's quality of life:** continued use of the failing regimen can cause additional suffering without any benefits
- **Public health concern:** Continuing with the failing regimen can amplify resistance in the patient's strain and subsequent infection to the public with strains that have higher resistance

The decision to suspend treatment should be made by the DRTB management team and should include proper preparation of the supportive care plan for the patient after consensus with the patient and the family members.

The plan should include but not limited to:

- pain relief
- management of respiratory insufficiency
- nutritional support
- regular medical visits-particularly psychosocial support
- home nursing care and
- prevention and infection control measures as these patients normally remain infectious for a long period of time

TREATMENT OUTCOMES

Cured

This is a DRTB patient who has completed treatment according to the protocol and has at least five consecutive negative cultures from samples collected at least 30 days apart in the final 12 months of treatment, or

A patient with only one culture positive and no concomitant clinical evidence of deterioration, provided that this positive is followed by a minimum of three consecutive negative cultures taken at least 30 days apart.

Treatment completed

This is a DRTB patient who has completed treatment according to protocol but lacks bacteriological results.

Died

This is a DRTB patient who dies from any reason during the course of MDR-TB treatment.

Failed

This is a DRTB patient whose two or more of the five cultures recorded in the final 12 months of therapy are positive or one of the final three cultures is positive or a clinical decision has been made to terminate treatment early because of poor response or adverse events.

Defaulter

This is a MDRTB patient whose treatment was interrupted for two or more consecutive months for any reason without medical approval.

Transferred out

This is a MDRTB patient who has been transferred to another district and for whom the treatment outcome is unknown.

TREATMENT UNDER SPECIAL CONDITIONS

Drug resistance may coexist with any number of medical problems and thereby present clinical challenges in the management of both diseases. These challenges include increased risk of drug toxicity, alterations in drug metabolism or pharmacokinetics that

requires dose adjustment, multiple drug therapies leading to drug-drug interactions etc. These co-morbid conditions often require a high level of clinical expertise and therefore early cross referrals with relevant clinicians with this expertise where feasible is highly recommended. Some common clinical conditions that may co-exist with TB include pregnancy, breastfeeding, contraceptives, drug resistant TB in Children, diabetes mellitus, renal insufficiency, liver disorders, seizure disorders, psychiatric disorders, drug and other substance abuse and HIV infection and use of anti-retroviral drugs.

SIDE EFFECTS AND THEIR MANAGEMENT

The appearance of adverse events should be recorded and categorized as follows:

- Mild: Awareness of sign or symptom but easily tolerated
- Moderate: Discomfort sufficient to cause interference with normal activity
- Severe: Incapacitating or life threatening

Note: All adverse events irrespective of the severity must be recorded in the patient record card.

BASIC APPROACHES TO AVOID TB DRUG RESISTANCE IN THE COMMUNITY

The main task of a TB control program is to reduce transmission of TB through early detection and effective treatment of infectious patients without creating drug resistance. Treatment for MDR-TB is complex, expensive, takes long with severe side effects and poor treatment outcomes.

The basic approaches for prevention include:

1. Implementation of good DOTS program
2. Good history taking to choose a proper regimen (Cat I or Cat II)
3. Use of recommended standard treatment regimens
4. Use of Fixed Dose Combinations (FDC) and avoid adding a single drug to a failing regimen
5. Advocate for free treatment of all TB cases
6. Strict Supervision of treatment (DOT) for rifampicin based regimens
7. Improve TB care in the private sector.

CHAPTER 7 : TB INFECTION CONTROL IN HEALTH CARE SETTINGS, CONGREGATE SETTINGS AND WITHIN THE COMMUNITY

INTRODUCTION

All healthcare settings need an infection control program designed to ensure the following:

- Prompt detection of infectious patients
- Airborne precautions
- Prompt treatment/ management of people who have suspected or confirmed tuberculosis (TB) disease

In all healthcare settings, particularly those in which persons who are at high risk for exposure to *Mycobacterium tuberculosis* work or receive care, policies and procedures for TB control should be developed, reviewed periodically, and evaluated for effectiveness to determine the actions necessary to minimize the risk for transmission of *M. tuberculosis*. TB IC activities should be well coordinated with other infection control activities in clinical settings e.g. blood safety, injection safety practices, and respiratory infection control.

Awareness on reduction of TB transmission in the community should be enhanced through early identification of TB suspects and referral for follow-up in the health care settings and advice given on basic infection control measures in households and other areas where people congregate.

WHAT NEEDS TO BE DONE

- Avail official national TB IC policy guidelines
- Appointment of an infection control committee and an infection control officer/ coordinator
- Formulation of an infection control plan which should be made known to all health care providers in the facility
- For each health facility, do a baseline risk/needs assessment
- For each health facility, institute, regularly monitor and evaluate IC control

OVERVIEW OF TB INFECTION-CONTROL MEASURES

The TB infection-control program should be based on a three-level hierarchy of control measures and include:

1. Administrative controls
2. Environmental controls
3. Respiratory protective equipment

Administrative (managerial and policy) Control measures

These are the most effective and least expensive measures and thus are highest priority in resource limited settings. They comprise policies and procedures intended to promptly identify infectious TB patients (smear positive) by same day sputum examination and initiation of treatment of infectious cases to reduce exposure to close contacts.

TB infection control policies and procedures include:

- The establishment of an infection control committee
- Appointment of an infection control officer
- Formulation of an infection control plan which should be made known to all health care providers in the facility
- Physical separation of patients suspected or known to have TB including those with DRTB from other patients especially those patients who are immune-compromised. (Isolation wards / rooms / one section of the waiting bay or ward) and
- The triaging of patients with chronic cough (two or more weeks) in the outpatient department to hasten TB screening. In-patients with cough should be screened for TB.
- Diagnostic tools for TB (request forms, sputum mugs) should be freely available in all departments

Environmental /Engineering controls

These measures reduce transmission of TB in the hospital by reducing the concentration of infectious droplet nuclei in the air. They include natural and or mechanical ventilation, use of and high efficiency particulate air filtration but **should not replace administrative controls.**

Environmental control measures include:

- Natural and or mechanical ventilation
- Use of and high efficiency particulate air filtration.
- Upper room Ultraviolet Germicidal Irradiation (UVGI)

Natural ventilation is the least expensive environmental measure. Transmission is less outdoors and therefore TB suspects and patients should be encouraged to spend most of the day time outdoors. Special comfortable sheds which maximize on natural ventilation and sunlight should be promoted for outpatient departments with a high burden of TB suspects and patients.

Adequate ventilation inside health facilities should be a priority. The use of extraction fans, which work properly, to improve ventilation, may be used in facilities where a large number of DRTB patients are cared for.

Ventilation may be supplemented by upper room Ultraviolet Germicidal Irradiation (UVGI) which may also be used in ventilation ducts or in fan driven air sterilizing devices mounted on ceilings, walls or portable units that can be moved from room to room. These measures are however expensive and are not be routinely available in Kenya.

Personal protective equipment (respiratory protection)

Respiratory protection should be used only when all other administrative and/or environmental control measures are fully implemented to limit HCW and patient exposures to infectious TB droplet nuclei.

In specialized settings and referral hospitals, HCWs may be exposed to infectious droplet nuclei during sputum induction procedures, while providing patient care in TB isolation rooms or in poorly ventilated ambulatory rooms, and while performing autopsies, bronchoscopy or other cough-inducing or aerosol generating procedures. In addition to administrative and environmental control measure in these circumstances, the recommended control measure is the protection of the health care workers from inhaling infectious droplets through the use of respiratory protective devices, (e.g. the N-95 mask) which are designed to fit over the mouth and nose and filter out infectious TB particles. Respiratory protective devices for HCWs that are capable of adequately filtering out infectious particles are more expensive than surgical or procedure masks. Nevertheless, their use in high-risk MDR/XDR-TB settings is recommended, particularly in high burden HIV settings where many health care workers may be HIV infected.

It should be noted that ordinary surgical masks do not protect the wearer from inhaling infectious materials but they reduce the amount of infectious droplets released from an infectious case.

The development of an infection control plan that specifies the activities to be implemented from the three levels of control measures is a crucial first step towards putting infection control in place at a health facility or congregate setting.

SPECIAL CONDITIONS, AREAS AND CONSIDERATIONS

Condition	Consideration
MDRTB	Patients with known or suspected (treatment failure, chronic TB) MDR TB and/or XDR TB should be identified and efforts made to separate them from patients who have HIV infection both in the outpatient and inpatient settings.
Health care workers	It is advised that health care workers who are HIV positive or who suspect they may be HIV positive should not work in high risk TB areas. All health care workers should be encouraged to know their HIV status. HCWs need to be educated on DRTB and TB IPC. All staff working in TB clinics should be provided with respirators i.e. N95 masks. Staff in health facilities are encouraged to go for periodic TB screening and HIV tests. TB should be strongly considered as part of the differential diagnosis for immuno-compromized HCWs with respiratory complaints. Immuno-compromized HCWs suspected of having TB should be promptly evaluated, and those diagnosed with TB treated, preferably on an outpatient basis.
Radiology (x-ray)	Schedule inpatient chest radiographs on infectious and suspect TB patients for non- busy times, such as the end of the afternoon Provide coughing patients with a surgical or procedure mask to wear; alternatively Provide tissues or cloth Provide expedited priority service to potentially infectious TB patients to minimize the length of time spent in the department Restrict access to the radiology suite during operating hours to patients and essential personnel only (e.g., post signs, enforce the policy). Use the room with the best ventilation for taking images of potentially infectious TB patients
Laboratory	The laboratory should process sputum samples as quickly as possible. It is preferable that a same day sputum smear microscopy service is established in every hospital to allow for a rapid turnaround of sputum smear results. Results of smear positive cases must be communicated as quickly as possible to the clinicians managing the patient. In particular, staff must ensure that smear positive results from “in patients” are forwarded to the wards as soon as the results are known.
Surgical and Autopsy suites	Personal protective equipment (respiratory protection) should be used by all personnel working in the operating room or autopsy suite when procedures are performed on suspected or known TB patients. All TB patients who come for chest drains, biopsies and other TB related procedures should wear surgical masks while in the minor theatre.
Sputum induction and cough-inducing procedures	Cough-inducing procedures (e.g., sputum induction or bronchoscopy) should be done only when absolutely necessary on patients who may have TB e.g. if the patient is unable to produce an adequate specimen without induction. Bronchoscopy should be used as a last resort and should be avoided in patients with established TB diagnosis should be avoided. Personal protective equipment (respiratory protection) should be used in addition to other measures.
Intensive care areas	To decrease the risk of nosocomial TB transmission: Avoid intubation on potentially infectious TB patients “think TB” in intensive care patients improve ventilation in intensive care areas use respiratory protection for procedures that are likely to create aerosols in potentially infectious TB patients

ROLE OF THE (TB) INFECTION CONTROL OFFICER

Health facilities should appoint one or more health care workers as the infection control coordinating officer. This officer(s) should coordinate infection control measures (including those for TB control) in the health facility including triage, diagnosis, treatment, separation/ isolation, case recording and reporting, recommending and installation of environmental measures and to ensure that the logistics, required for infection control in the health facility are working optimally.

DRTB PATIENTS CARE

During the initial phase of DRTB treatment, therapy will mostly be delivered in a hospital/clinic setting (the DRTB treatment centre) because of the need for daily injections. However it is possible to deliver the same treatment at home through community nurses, a treatment delivery mechanism that may reduce the risk of hospital transmission of DRTB and which may be inexpensive for the health care system and the patients.

In ideal setting patients who are smear or culture positive MDR-TB should be treated in isolation facility. An isolation facility should meet all infection control measures as per WHO and national guidelines. Patients who have converted can be treated on an ambulatory basis or through home based care and observing infection control measures.

In case there are not enough isolation beds, the isolation facility should prioritize patients who need admission due to side effects to the DRTB drugs.

PDR patients should be hospitalized separate from the MDR-patients. XDR patients SHOULD NOT be mixed with MDR, PDR, or other TB patients.

PREVENTION AND CONTROL OF TB TRANSMISSION IN THE COMMUNITY

Awareness on reduction of TB transmission in the community should be enhanced through early identification of TB suspects and referral for follow-up in the health care setting. Health education should be given to patients, family and community on the signs and symptoms of TB disease and the need to support patients on treatment so that they complete their regimens effectively to avoid drug resistance. The DRTB patients should be advised to spend as much time as possible outdoors, sleep in a separate bedroom at home, to wear the ordinary masks when receiving visitors, to practice cough etiquette (to cover their mouth when they cough), use sputum mug and dispose of the mugs in pit

latrines. Where sputum mugs are not available, locally available containers with fitting lids should be used. Due to HIV TB co infection the community should be encouraged to go for HIV Testing and Counseling. Contacts of DRTB patients should be screened for TB and HIV.

INFECTION CONTROL MEASURES IN SPECIAL SETTINGS

There are special settings in the community that are of high risk and call for special attention as far as TB infection, prevention and control is concerned. Structures and buildings in congregate settings should comply with national norms and regulations for public buildings, and should meet the design criteria for sufficient ventilation. These places include;

- Prisons and remand cells
- Informal settlements (slums)
- Refugee and internally displaced persons (IDP) camps
- Learning institutions (schools, colleges)
- Security forces camps (military, GSU, police national youth service etc) Public transportation: Matatus, buses, trains and Air transport

TB is spread more readily in congregate settings such as prisons, remands, informal settlement and public transport. This is because of the long duration of potential exposure, crowded environment, poor ventilation, and limited access to health care services.

Prisons and remand cells

All inmates and remandees on admission should be screened for TB using the PF 10 form. The prison and remand cell should follow and implement TB infection control guidelines. There is need for active advocacy and sensitization of the relevant ministry and departments for the implementation of TB infection control guidelines in prisons.

Informal settlements (slums and refugee camps)

To reduce TB transmission in the informal settlement, there is need to have adequate sensitization and advocacy on proper ventilation on the existing structures/ housing and practice of cough etiquette. The implementation of community TB infection control guidelines should be emphasized. Screening, contact tracing and defaulter tracking should be highly emphasized in such settings.

Learning institutions and security forces training camps

Learning institutions and training camps should embrace TB infection control guidelines. TB infection control should be incorporated in the school health program. Learning institutions and training camps should adopt and own TB environmental measure and UVGI.

Public transportation

TB infection control guidelines should be implemented in public transport sectors. There should be adequate ventilation by opening windows on both sides of the vehicles or applying mechanized ventilation. Advocacy and sensitization with different ministries and the community is required for this to succeed. Airline services should implement TB Infection control guidelines. Transportation of suspected MDR-TB Patients from one facility to another should be by well ventilated means of transport with personal respiratory protective devices.

CHAPTER 8: LEPROSY

DEFINITION OF LEPROSY

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. It mainly affects the skin, peripheral nerves and mucous membrane. Leprosy has an incubation period of 3-20 years but the average incubation period is 5 years.

EPIDEMIOLOGY AND HISTORY OF LEPROSY

Leprosy is one of the oldest documented diseases in the world. It is mentioned in the Bible, Koran and other religious book. However the description in these books may include other dermatological conditions with similar manifestations.

Leprosy is a droplet infection transmitted from a source patient through, coughing and sneezing. *Mycobacterium leprae* can be found in breast milk but there is no documented evidence of leprosy being transmitted through this route.

Globally over 200,000 leprosy cases are reported annually with majority of leprosy patients being found in South Asia and Africa. In Kenya leprosy endemic areas include Western, Nyanza, Eastern, Coast and Nairobi provinces although sporadic cases are still reported in other parts of the country.

Despite the apparent low number of cases reported annually in Kenya, the number of children under the age of 15 years diagnosed with leprosy every year suggests stable active transmission of leprosy in the community.

PATHOPHYSIOLOGY

Leprosy is a droplet infection that follows prolonged contact with an infectious leprosy patient although other routes, particularly entry through broken skin, cannot be ruled out. Closeness of contact is related to the dose of infection, which in turn is related to the occurrence of disease.

The mode of onset is highly variable. An early lesion may occur as a vague, ill-defined, hypopigmented or erythematous patch with anaesthesia. The disease can also occur with multiple infiltrated patches or just diffuse skin infiltration. In certain instances, leprosy can manifest itself as areas of anaesthesia in the skin with no skin patches (neural leprosy).

The chronic onset of leprosy is so gradual and insidious that the disease advances to a considerable extent before any abnormality is evident. There may be tenderness, tingling, or thickening of a nerve; an area of anaesthesia, with some change in the appearance of the skin; loss of sensitivity to burning; or tingling or numbness of extremities. Discoloured skin patches may be mistaken for eczema or ringworm; these may at first be small, gradually increasing in size. In acute onset, which is much less common, there are occasionally multiple lesions with less diffuse margins, which tend to spread rapidly and which contain numerous bacilli. The first noticeable sign may be an evanescent rash. The onset may be determined by occurrence of some other acute disease or physiological change or stress: for example, extra strain imposed on the body during puberty, parturition, and menopause.

Damage to nerves occurs due to inflammatory reaction of the body to the bacilli, hence damage to one or more of the three components of the nerve with different sequelae:

- Sensory fibres: loss of sensation
- Motor fibres: weakness or paralysis in innervated muscles
- Autonomic fibres: dryness and hypo-pigmentation of the innervated skin

CLINICAL PRESENTATION OF DISEASE

Patients with leprosy may present with any of the following signs and symptoms

- Burning sensation in the skin
- Pale patches on the skin with loss of sensation to cotton wool touch
- Numbness and tingling sensation in the feet and/or hands
- Weakness of the eyelids, hands or feet
- Tender nerves
- Painless swelling or lumps, especially in the face and ear lobes
- Painless wounds and unnoticed injuries and burns on the hands feet and eyes
- Joint pains

The following are considered to be Cardinal signs of Leprosy and the diagnosis of leprosy may be made if any one of them is present:

- Skin patch with loss of sensation
- One or more enlarge peripheral nerves
- The presence of leprosy bacilli

DIFFERENTIAL DIAGNOSIS

Leprosy is primarily a disease of the nerves, particularly the cooler, peripheral nerves. It secondarily affects the skin.

Differential diagnosis related to the skin

Some of the skin manifestations that may be confused with leprosy include hypopigmented non-raised (macules) and raised lesion (plaques)

Nonraised hypopigmented lesions (macules)

1. Nutritional dischromia
This is commonly seen in malnourished children with worm infestation and vitamin deficiency in the diet.



2. Vitiligo or Leukoderma
While in true leprosy there is only a partial loss of pigment of the skin, in this condition, there is a total loss of pigment (skin is white), although in the early stages of leukoderma, the patches are hypopigmented and can be confused with indeterminate leprosy. There is no sensory deficit in the patches.



3. Tinea Versicolor

The neck and trunk are the prime sites. Generally the lesions are multiple and have no loss of sensation. Fungi can be seen under the microscope.



4. Pityriasis Rosea

Lesions manifest as small oval patches on the trunk. The scaly lesions can be confused with leprosy but there is no loss of sensation.



5. *Scleroderma (Morphea)*

The hypopigmented patches of Scleroderma may be confused with leprosy macules. Usually there is no loss of sensation in these patches which feel tough to the touch.



6. *Reaction to Injury*

When the scar patches are hypopigmented they can resemble leprosy but often they are hyperpigmented. There is no loss of sensation.



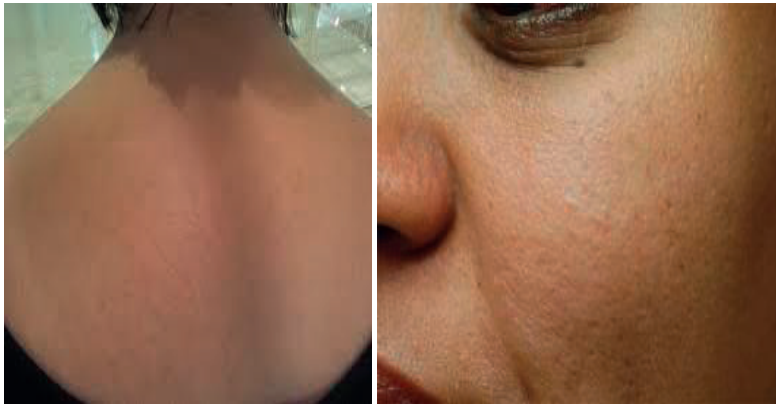
7. *Naevus Anaemicus*

The lesions usually present as hypopigmented patches anywhere on the body, and present from birth. Careful questioning when taking case history is essential. There is no anaesthesia in the lesions. These non-raised skin lesions can be confused with leprosy.



8. *Polymorphous Light Eruption*

Usually occur on parts of the body that are exposed for example the face flexor aspects of the upper limbs but there is no sensory loss or *M.Leprae* in the lesions.

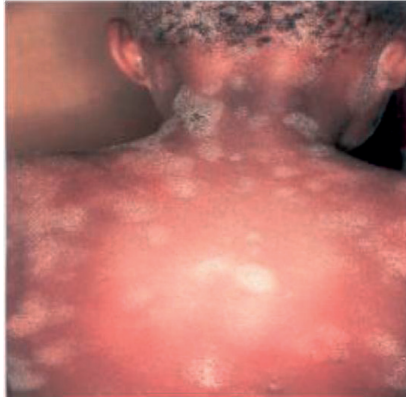


Raised hypopigmented lesions: (Papules / Plaques/ Nodules)

1. *Seborrhoeic Dermatitis*

This condition generally occurs on the flexor aspect of the elbow and knee. When in the scalp, dandruff is a common finding and the oily or greasy yellowish scales

sometime resemble lesions of leprosy. However severe itching in the patches and lack of sensory loss differentiates this condition from leprosy.



2. *Granuloma Annulare*

The small ring-like patches are mostly seen on the dorsum of the hand. Sensation is normal.



3. *Tinea Corporis*

These lesions, generally known as “Ringworm”, usually present in the groin and waist area. Unlike a leprosy patch, they are always itchy and fungal elements can be seen under the microscope. There is no loss of sensation.



4. *Syphilis*

Skin manifestation of leprosy can mimic lepromatous leprosy, especially in the late, secondary stage but there is no sensory loss.



5. *Post Kalaazar Dermal Leishmaniasis*

Nodular lesions resembling lepromatous leprosy; Lesions are usually circumoral. Leishmania donovani (L.D) bodies are seen in Leishman-stained slides. Sensation are preserved.



6. *Psoriasis*

Silvery white patches of psoriasis have no sensory loss.



7. *Kaposi's sarcoma*

Kaposi's sarcoma lesions are often found on the foot or leg. The lesions are shiny, violaceous and nodular. Sensation is preserved.



8. Discoid Lupus Erythematosis
Usually butterfly shaped and symmetrically distributed over the face with no loss of sensation.



9. *Lupus Vulgaris (T.B. of skin)*
Common in the tropics and can resemble the Tuberculoid and Borderline types of leprosy. Sensation is well preserved.



10. *Multiple Neurofibromatosis*

There are two type of neurofibromatosis, type I and II.

Type I is characterized by changes in skin coloring (pigmentation) and the growth of tumors along nerves in the skin brain and other parts of the body. In early childhood the spots or patches are flat on the skin and darker than the surrounding areas. The spots increase in size and number as the individual grows. Additional signs include high blood pressure short stature and unusually large head (macrocephally) No *M. leprae* are seen in nodules biopsy.

Type II is characterized by growth of non cancerous tumors in the nerous system. The commonest tumors are acoustic neuromas. The most Common signs include hearing loss,

ringing in the ears (tinnitus) and problems with balancing. Some people may develop cataract.



11. *Multiple Lipomatosis*

This condition can be confused with nodular lepromatous leprosy but no *M. leprae* are seen under the microscope.



12. *Allergic dermatitis, hypothyroidism and shiny, oily skin* can be differentiated from lepromatous leprosy because skin smears are negative for *M. leprae*.

13. *Diabetic ulcers* can often be confused with ulcers following neglected leprosy.



14. *Burgers Disease*

Often results in gangrenous feet, can be confused with leprosy, particularly among early smokers.



Differential diagnoses relating to nerves

1. *Vitamin B deficiency*
This may be seen in undernourished children and alcoholics. Loss of sensation in the lower limbs can sometimes be experienced by those suffering from Vitamin B12, resulting in lesions in the posterior column of the spinal cord.
2. *Hypertrophic Interstitial Neuritis*
This condition is very rare it results in a thickening of the peripheral nerves requiring a biopsy of the nerve to properly diagnose.
3. *Toxic Neuritis*
Patients working in paint factories or other heavy metal industries dealing with lead, arsenic etc. may develop a leprosy-like anesthesia and paralysis. Careful recording of case histories is essential.
4. *Syphilitic Neuritis*
This is another disease affecting the posterior column of the spinal cord, resulting in lesions that lead to sensory loss. A careful case history needs to be taken a V.D.R.L. test made.
5. *Primary Amyloidosis of the Nerves*
This condition is very rare requiring a nerve biopsy to differentiate.
6. *Traumatic Neuritis*
A careful recording of case history may reveal physical injury to the nerve, perhaps through an accident.
7. *Diabetes Mellitus*
Many patients with ulcerated feet have been wrongly diagnosed as having leprosy because peripheral neuritis in diabetes can result in loss of sensation, particularly in the lower extremities which often produces trophic or plantar ulcers. A careful physical examination will reveal glycosuria and hyperglycemia.
8. *Cervical Rib*
This is another rare condition which is caused by pressure on the brachial plexus due to the presence of an accessory rib. Patients may be seen with leprosy-like hands with the small muscles atrophied and with sensory deficit at the ulnar border of the hand. In order to correctly diagnose this condition, an X-Ray needs to be taken of the cervical spine.
9. *Over-Riding of the Ulnar Nerve*

This rare abnormality can result in loss of sensation in the ulnar aspect of the hand due to the ulnar nerve tripping over the medial epicondyle when the forearm is flexed, causing physical trauma to the nerve. This condition can even result in atrophy of the small muscles of the hand if allowed to persist for too long. It is important to be careful in making clinical examinations. This condition is corrected by surgery.

10. *Congenital Absence of Pain*

This is an extremely rare condition characterized by lack of pain sensation.

11. *Progressive Muscular Atrophy*

In this case, there is bilateral wasting of the small muscles of the hands and feet as in tuberculoid leprosy. There is no loss of sensation.

12. *Syringomyelia*

Mainly confined to the tropical areas of the world, there is a leprosy-like atrophy of the muscles and a loss of pain and temperature sensation in the hand and forearm, although the feeling of touch remains.

13. *Carpal Tunnel Syndrome*

This condition gives all the impression of tuberculoid leprosy hand deformity affecting the median nerve at the wrist.

14. *Bell's Palsy*

This condition results from Facial Nerve involvement causing facial paralysis and lagophthalmos.

IMMUNOLOGY OF LEPROSY

TYPES OF IMMUNITY

- (1) “Humoral Immunity” or Antibody Mediated Immunity and
- (2) “Cell-Mediated Immunity” (CMI).

Humoral immunity

In humoral Immunity, certain chemicals (antibodies) are generated by the body when it is invaded by antigens. In certain types of infection, antibodies are effective in cleansing the system of the toxins liberated by the invading organism. However, while humoral Immunity is very effective in fighting many forms of infection, it has little ineffective against *M.leprae* and can in fact cause much suffering through mediation of type 2 leprosy reaction.

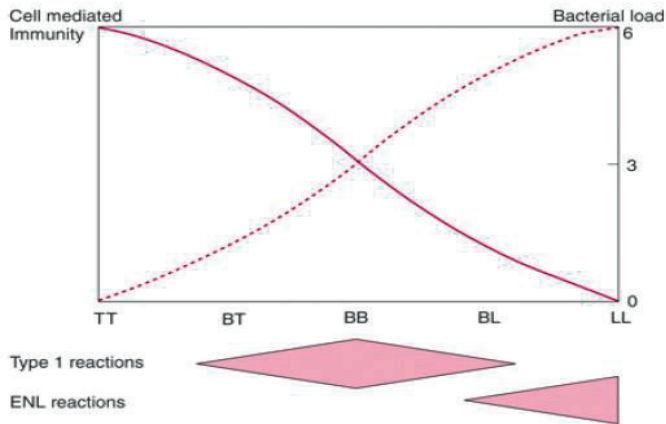
Cell-Mediated Immunity (CMI)

Some of the invading foreign bodies and their antigens stimulate the production of certain special defense cells, at the same time establishing an inflammatory reaction. Cell-mediated immunity is essential for the body’s defense against such diseases as tuberculosis, and leprosy. Where the antigens accumulate, immune cells mainly lymphocytes collect at the site. In the case of leprosy, these are mainly the peripheral (cooler) nerves and, more particularly, the nerve’s Schwann cell. *M.leprae* has an affinity for the cooler areas of the body and this characteristic has a bearing on the types of deformities that result from the invasion of *M.leprae*.

The smaller lymphocytes, have no phagocytic property therefore cannot ingest/digest the *M.leprae*, like the macrophages. The role of the lymphocytes is to secrete certain chemicals which attract the larger macrophages to the site of antigen build-up and assist the macrophages to engulf and digest the *M.leprae*. Cell-Mediated-Immunity (CMI) is the protective immunity that the body needs against leprosy. Majority of the humans have this type of immunity however in varying degrees.

At one end of the “Immunological Spectrum” leprosy patients with a well established CMI have the form of the disease known as “Tuberculoid” leprosy, but they may have little Humoral immunity. At the other end of the Immunological Spectrum, Lepromatous leprosy is a complete opposite with a well established Humoral Immunity but no CMI. The latter is the infectious form of leprosy the multibacillary leprosy.

Figure 8.1: Immunological spectrum and classification of leprosy



Although immunity, in most cases, helps the body’s defenses against the invasion of bacteria and their antigens, there are occasions when the body reacts violently to the *M. leprae* antigens. This is called the “Lepra Reaction”. Reactions in leprosy are of several types: “Type 1” and “Type 2”

IMMUNOLOGICAL RESPONSE AND DEFORMITY

Although tuberculoid leprosy patients, with strong CMI, may have few bacilli in their bodies that they cannot be detected by ordinary microscopy, they may suffer severe nerve damage due to the massive lymphocytic response, causing the nerves to swell 5 or more times the normal size.

On the other hand, lepromatous, infectious patients, whose bodies may be teeming with millions of *M.leprae*, may suffer relatively little nerve damage (in the early stages), because the lack of CMI means that there is no strong build-up of defense cells around the nerves.

Leprosy is a very enigmatic disease. Although it can look to be a highly contagious disease, in actual fact, of all the communicable diseases, Leprosy (the tuberculoid type) is the least contagious.

DIAGNOSIS OF LEPROSY

Diagnosis of leprosy requires a high index of suspicion. A proper clinical history and physical examination are critical in making a diagnosis of leprosy.

CLINICAL DIAGNOSIS

Clinical entails taking a detailed history and proper physical examination in a room with good lighting.

Clinical History

History of presenting illness

Ask for the duration and progress of symptoms, history of leprosy in the family or prolonged contact with a leprosy patient and treatment history.

Systemic Review

A thorough review of the systems should be done however the following systems should specifically be reviewed

1. Skin
Ask the patient about skin discoloration and duration of its presence, Presence and duration of nodules and itchiness in the skin
2. Nervous system
Specifically ask about weakness of muscles of hands, feet and eyes as well as loss of sensation in these parts.
3. Musculoskeletal
Ask for history of unnoticed injuries in the hands feet and eyes

Physical examination

Examine the patient in good lighting focusing mainly focus on the skin and the nervous system. Specifically look for hypopigmented skin lesions, weakness of muscles and ulcers

Skin

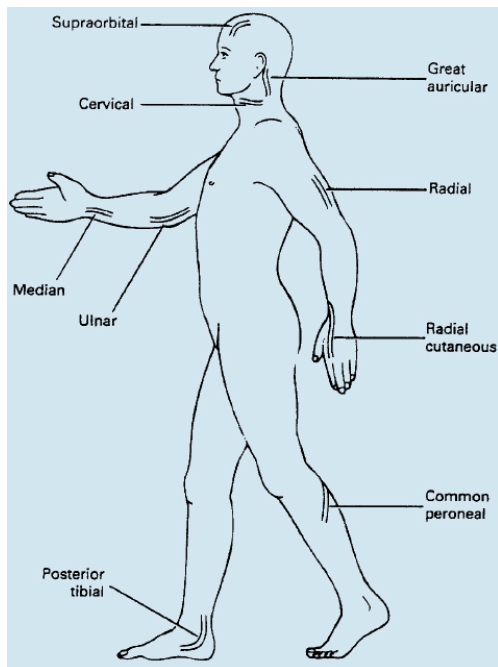
Look for hypopigmented skin patches with loss of sensation use cotton wool to examine for light touch). Examine for nodules. Look for dryness cracks and hair loss on the patches and the eye brows lashes. Examine for muscle wasting.

Nervous

Systematically examine the peripheral nerves for nerve enlargement tenderness and loss of function (autonomic, sensory and motor)

The following peripheral nerves are usually affected with different consequences and must be examined.

Figure 8.2: sites where peripheral nerves can be palpated



- *Facial Nerve*

Facial nerve damage leads to facial palsy (weakness in the muscles of the face).

When the orbital branch is affected the patient will present with difficulty in closing the eyes (**lagophthalmos** (rabbit-like eyes)).

- *Trigeminal nerve*

Damage to the trigeminal nerve leads to loss of the blink reflex resulting dryness and exposure keratitis. While examining the patient, observe for blinking.

The damage causes loss of sensation of the cornea leading to frequent injuries of the cornea by foreign objects. This may result to infection, healing with fibrosis, opacity formation and blindness. The eyes should always be examined for injuries.

- *Great auricular nerve*

The nerve usually runs across the neck. In leprosy the nerve enlarges and a firm rod-like structure may be seen and felt under the skin. There is usually no obvious loss of function. The enlargement of this nerve is almost confirmatory of the presence of leprosy.

- *Radial nerve (high radial)*

When damaged it leads to a wrist drop

- *Ulna nerve*

The nerve runs in the olecranon groove in the medial aspect of the elbow joint. When damaged it leads to dryness in the hypothenar eminence, the fifth finger and the medial aspect of the fourth (ring finger), it also leads to loss of sensation in the same area. There is also wasting of the hypothenar eminence and clawing of the fourth and the fifth fingers. The ulna nerve also supplies the intrinsic muscles of the hand. Therefore damage results in ridging of the hand due to muscle wasting.

- *Median nerve*

This nerve runs deep under the flexor retinaculum sheath in the wrist and therefore difficult to palpate. When inflamed it is possible to elicit tenderness when one presses over the anterior aspect of the wrist joint. Damage of the median nerve manifests as dryness, cracking and loss of sensation in the thenar eminence, the thumb, the 2nd, 3rd and the lateral aspect of the 4th finger. There is also wasting of the thenar eminence and ridging of the dorsum of hand as seen in ulna nerve damage. Wasting of the thenar eminence leads to loss abduction resulting ape thumb and clawing of the thumb 2nd and 3rd fingers.

- *Radial cutaneous nerve*

There is no obvious loss of function but the nerve is useful in confirming the diagnosis of leprosy when enlarged. This nerve can be palpated on the lateral aspect of the distal end of the radius proximal to the wrist.

- *Common peroneal nerve (lateral popliteal)*

The common peroneal nerve can be felt just below the head of fibula below the knee arising from the popliteal fossa. This nerve is responsible for dorsiflexion and eversion of the foot. When damaged it leads to plantar flexion and inversion of the foot (foot drop). Observe the patients for evidence of foot drop while walking.

- *Posterior tibial nerve*

Posterior tibial nerve is palpated below the medial malleolus. It is responsible for autonomic sensory and motor functions of the foot.

Damage leads to dryness and cracks in the sole of the foot, loss of sensation wasting of the sole foot pad leading to the loss of the foot arch (flat foot) resulting in plantar ulcers (mechanical ulcers).

LABORATORY DIAGNOSIS

Where available, laboratory tests may be used to confirm the diagnosis of leprosy. These include:

- Bacteriological
- Histological
- Molecular methods

Bacteriological

Slit skin smears

Smears can be taken from any area of the body that manifest leprosy like a patch a nodule area of anesthesia or infiltration. In practice smears are commonly taken from ear lobes, one elbow, and a contra lateral knee.

Nasal swabs

A special forcep is inserted into the nose to open it up and cotton swab used to scrap materials from the nasal wall. The smears are then prepared on a microscope slide for staining. This is not recommended due to the presence of normal mycobacterial flora in the nose.

Histology

Skin or nerve biopsies can be taken for histological examination using various histological techniques like, ZN, FITES, etc.

Molecular techniques

Molecular techniques can be used to detect genetic materials of *M.leprae* for example PCR.

The diagnosis of leprosy is based on any one of the three cardinal signs

Hypopigmented skin patch with loss of sensation
One or more enlarged peripheral nerves
The presence of leprosy bacilli

CLASSIFICATION OF LEPROSY

There are two main classifications of leprosy disease based on two criteria;

1. The number of lesions as recommended by WHO and
2. Immunological and clinical features as per the Ridley Joplin classification

WHO

WHO classifies leprosy into two groups for epidemiological and treatment reasons.

Pauci-bacillary leprosy:

- Patients with 1 to 5 hypopigmented patches
- Skin smears negative

Multi-bacillary leprosy (MB)

- Have more than 6 patches
- Skin smear often positive
- Patients with MB leprosy may present with plaques, macules, papules and or nodules with skin infiltration

Patients with neural leprosy are classified and treated as MB leprosy

RIDLEY AND JOPLIN CLASSIFICATION

Leprosy is classified into six types based on the clinical features (Ridley & Joplin classification). The type of the disease is a reflection of the immune status of the host.

Indeterminate leprosy:

A single symptomless lesion characterized by hypo-pigmented spots. The lesion undergoes spontaneously healing.

Tuberculoid leprosy (TT):

Usually a single patch with well-defined raised borders or a large hypo pigmented

asymmetrical lesion. Lesion is dry and hairless, infectivity is minimal at this stage loss of sensation is seen. Few nerves become thick followed by loss of function. Skin smears are negative and may spontaneously get cured.

Borderline Tuberculoid leprosy (BT):

BT leprosy is characterized by numerous skin lesions with less well defined margins and satellite lesions. The disease goes back to the tuberculoid stage or without treatment may progress to BB. There is usually early nerve damage. Skin smears are negative.

Borderline Borderline leprosy (BB):

Several small and irregular punched out lesions are seen moderate sensory loss is seen. This is a very unstable form of leprosy with a high likelihood of either going back to the previous stage or progressing to the next stage. Nerve damage and deformities are very common and skin smears are positive.

Borderline Lepromatous leprosy (BL):

Several lesions such as, ill defined macules, plaques, papules, and nodules are seen. The nodules tend to affect the lower parts of the ear lobes. Patients present with lateral madarosis. There is early nerve involvement.

Lepromatous leprosy (LL):

Early symptoms include several lesions such as plaques, macules, papules, and nodules. Nasal congestion, discharge and bleeding is seen. Inflammation of the leg and ankles.

Progressive symptoms include thickening of the skin (skin infiltration) in the forehead and ear lobes loss of eyebrows and eyelashes. Nodules in the legs break and form ulcers. Skin lesion begin as vaguely erythematous or hypopigmented macules often on the lower back without itch or pain. The skin smears is always positive with late nerve damage.

CHEMOTHERAPY

Multiple drugs (Multiple Drug Therapy –MDT) are used in treatment of leprosy. Treatment of leprosy is based on the WHO classification.

TREATMENT OF P.B. (PAUCI-BACILLARY) LEPROSY

This is treated with (two drugs) dapson and rifampicin for a duration of six months see table 8.1 below for dosages.

TREATMENT OF M.B (MULTIBACILLARY) LEPROSY

This is treated with (three drugs) rifampicin, clofazimine and dapsone for a period of 12 months. Rifampicin is given every 28 days under supervision by health care worker when the patient comes for a prescription refill. Clofazimine is given at a higher dose every 28 days supervised by the health care worker on the day the patient visits the clinic and a maintenance self administered daily dose Dapsone is self administered daily. Dosages for these are shown in table 9.4 below

Table 8.1:WHO recommended MDT regimen for PB leprosy

AGE	0 – 5 yrs	6 – 14 yrs	>14yrs
<i>Dapson – daily</i>	25 mg	50 mg	100 mg
<i>Rifampicin - 4 weekly supervised</i>	150 mg	300 mg	600 mg

Table 8.2:WHO recommended MDT regimen for MB and neural leprosy

AGE	0 – 5 yrs	6 – 14 yrs	>14yrs
<i>Dapsone – daily</i>	25 mg	50 mg	100 mg
<i>Clofazimine (laprene) given 4 weekly under supervision</i>	100 mg	200 mg	300 mg
<i>Clofazimine (laprene) given daily unsupervised</i>	50 mg	50 mg	50 mg
<i>Rifampicine given 4 weekly supervised</i>	150 mg	300 mg	600 mg

COMMON DRUG SIDE EFFECTS AND MANAGEMENT

Dapsone

Slighting itching

Reassure patient and treat symptomatically with an anti-histamine.

Anaemia

Investigate for other causes of anemia, and manage appropriately/ refer to medical officer or DTLC for further management.

Exfoliative dermatitis

The skin is itchy, and later peels off. The patient is usually very ill. Stop drugs immediately and refer the patient to medical officer or DTLC or nearest hospital.

Fixed drug reaction

Stop drugs the eruption will slowly clear after stopping.

Clofazimine (Laprene)

Gastro intestinal disturbances nausea, vomiting, abdominal pains.

Give drugs after meal.

Red skin/eyes

The patient has no complaints at all apart from the cosmetic effect. This is a harmless condition, reassure the patient and continue treatment

Rifampicin

Red urine

Harmless, no action needed. Reassure the patient and continue treatment.

Symptoms as for severe flu

Treat symptomatically and reduce the dosage to half until the symptoms have disappeared

Jaundice

Stop all drugs immediately and refer patient to a medical officer or DTLC

Anaemia

Investigate for other causes of anemia, manage appropriately/ refer to medical officer or DTLC for further management.

LEPROSY REACTIONS

Manifestation of leprosy disease is mainly due to the immune response to the invasion of the *M.leprae* into the body tissues.

A leprosy reaction is an acute inflammatory episode that occurs in a leprosy patient in the course of disease but does not necessarily indicate deterioration of the disease process. This results from of exaggerated immune response to body tissues due to the invasion by

M. leprae. Reaction can occur at any time before, during and even after completion of treatment.

Almost any person with leprosy is at risk of getting a reaction, although, those with only one or two skin patches and no nerve enlargement have the lowest risk.

Reactions are mediated through an inflammatory process that may affect any organ. Inflammation is the body's usual response to infection, and its typical features are:

- Swelling
- Redness
- Heat
- Pain
- Loss of function

Reaction in a skin patch can be uncomfortable, but it is rarely very serious. However there may be evidence of acute inflammation in form of local swelling, redness, tenderness on tapping, increased local temperature and loss of function manifesting as dryness and scaling.

Inflammation in a nerve, on the other hand, can cause serious damage, with loss of function caused by swelling and pressure in the nerve. Some people with inflamed nerves have severe symptoms, while others have no obvious signs. Patients must be examined carefully to detect reactions before they cause damage.

Early detection of leprosy and treatment with MDT remains the best way to prevent disability. Unfortunately many patients are diagnosed late and are at greater risk of developing reactions and neuritis. If these reactions are treated effectively, early nerve damage can be reversed and disability can still be prevented.

Types of Leprosy Reactions

Leprosy reactions are classified into two categories:

- Type 1 leprosy reaction
- Type 2 leprosy reaction

TYPE 1 REACTION

Type 1 reaction is elicited through cell mediated immunity. The cell mediated immunity is responsible for the nerve damage observed in these patients initially through the acute inflammatory process where there is swelling and enlargement of the nerve with pain and tenderness and loss of function whose severity varies with the extent of nerve damage.

This type of reaction commonly occurs in patients with TT, BT, BB and BL, (See figure 8.1)

It is important to note that type 1 reaction occurs both in patients with PB and MB leprosy. Approximately 25% of all patients with leprosy will develop type 1 reaction. Most of the patients will develop the reaction within 6 months of initiation of treatment and thus the need to predict reaction and adequately prepare the patient. Some patients may come with nerve damage without having experienced the acute episode of inflammation and this is what is referred to as the silent reaction (silent neuritis).

Reaction occurring after completion, of treatment as sometimes confused with a leprosy relapse. It should however be noted that in a relapse there is usually evidence of new lesions and the old lesions are active with clearly demarcated borders. It is therefore important at all times to document the sites of lesions in leprosy patients.

Signs and symptom of type 1 reaction

Skin

The most common clinical feature of a Type 1 reaction is inflammation in the skin patches, with swelling, redness and warmth. The patches are not usually painful, but there may be some discomfort. Some patches may not have been very visible before, so you may think that the inflammation has brought out new patches. There may be swelling of the limbs or face.

Usually some or all the original leprosy skin patches are involved.

Nerves

As already mentioned, tenderness of nerves and loss of function are important features. Most Type 1 reactions settle down within six months, but without treatment, any effects on the nerves would lead to permanent loss of function. The muscles involved in closing the eyelid may be affected, but the eye itself is not affected by a Type 1 reaction.

General Systemic Involvement

Because the inflammation is localized in the skin and the nerves, the person does not feel too ill and there is usually no fever.

TYPE 2 REACTION

Type 2 reaction is elicited through humoral immunity. This occurs due a large number of bacilli or breakdown byproducts of the bacilli stimulating the formation of antibodies which in turn lead to the formation of antigen antibody complexes. These complexes are

distributed by the circulatory system causing generalized symptoms. The antigen antibody complexes get deposited in organs with microcirculation for example the eye, lymphnodes, testes, kidneys, small bones of the hand and feet, small joints, liver and spleen and provoke an acute inflammation and sequel.

Type 2 reaction commonly occurs in patients with, BB, BL and LL (see figure 10.3) and is usually a late reaction occurring after initiation of treatment or even years after completion of treatment.

Symptoms and Signs of type two reaction

Skin

There is sudden appearance of new painful subcutaneous nodules in the face the upper and lower extremities and the trunk. There is inflammation with all the features present. The lesions are painful and erythematous and thus called Erythema Nodosum Leprosum (ENL). These nodules should be differentiated from the leprosy nodules which are normally superficial on the skin and not painful. A biopsy from a leprosy nodule shows presence of bacilli while ENL nodules shows evidence of inflammatory response. ENL nodules can be mild and transient or severe. If very severe they can break and form ulcers with secondary bacterial infection (Lucio phenomenon) a life threatening condition.

General systemic involvement

Patients with type 2 reaction usually have systemic involvement. The patient is usually very sick, with general malaise and high fever with temperatures of 38-40° C Patients may present with edema of the hands the feet legs and face due to infiltration of the skin.

Deposition of antigen antibody complexes in organs with microcirculation may result in symptoms and signs specific to the involved organ.

- Eye involvement results in iridocyclitis that can lead to blindness
- When the testes are involved, there is epididymorchitis leading to damage of testicular cells that produce testosterone causing a hormonal imbalance and consequent gynaecomastia, loss of libido, impotence and infertility
- Lymph node involvement will lead to tender lymphadenopathy
- Small bones of hand and feet involvement results in dactylitis, ischemic necrosis of the bone absorption and deformity in the long run
- Kidneys involvement may manifest with features of nephritis
- Involvement of liver and spleen presents with tender hepatosplenomegally

DIFFERENTIAL DIAGNOSIS OF LEPROSY REACTIONS

Other conditions that may be confused with a leprosy reaction include:

- *Drug reactions*
Drug reactions are not common, they are usually accompanied by itching, which is not a typical feature of leprosy reactions
- *Other causes of inflammation, such as local sepsis or infection*
The signs on the skin will not correspond with the leprosy patches and are more likely to be flat lesions (not the raised lumps of ENL), possibly with hyperpigmentation.
Local sepsis may not involve the leprosy patches. It will generally be localized to just one part of the body and the cause may be more obvious, such as a wound or an insect bite.

FACTORS PREDISPOSING TO LEPROSY REACTION

Occurrence of leprosy reaction is influenced by the following factors.

Antileprosy treatment

Once a patient is started on treatment and the immunity improves they are more likely to suffer from type 1 reaction upgrading.

The breakdown byproducts of the bacilli as a result of treatment in patients with MB act as antigens which stimulate production of antibodies that lead to formation of antigen antibody complexes that cause type 2 reaction.

Intercurrent infection

Any infection that interferes with the immunological balance between the bacilli and the host will provoke both type 1 and type 2 reaction e.g HIV, Malaria, TB, Pneumonia etc.

Physiological factors

Pregnancy: A pregnant woman can suffer type 1 reaction downgrading and after child birth during the puerparium can suffer type 1 reaction upgrading.

Puberty in males: When they develop secondary sexual characteristics, due to hormonal changes tend to suffer type 2 reactions.

Psychological factors

Psychological factors such as stressful conditions as a result of stigma in the community lead to type 2 reactions.

MANAGEMENT OF REACTIONS

Whenever patients have leprosy reactions, treatment should not be stopped. A proper clinical examination of the patient should be carried out and relevant laboratory test done.

The following drugs are used in management of leprosy reactions

1. Antileprosy drugs to continue uninterrupted
2. Corticosteroids e.g. prednisolone
3. Anti-inflammatories e.g. Clofazimine, Chloroquine and Thallidomide
4. Analgesics e.g. Paracetamol
5. Ansulitics e.g. Diazepam, and low dose Largactyl 25mg

Management of type 1 reaction

For the purpose of drug management, type 1 reaction is divided into three categories

- Mild
- Moderate
- Severe

Mild type 1 reaction

A mild reaction is one that occurs in the skin only (as long as it does not occur over a major nerve or in the face)

He patient may have mild fever and slight swelling of the limbs

Treatment

Do baseline VMT/ST, paracetamol 1g eight hourly for 1 week and review after 1 week. If there is deterioration to moderate or severe, treat as recommended.

Moderate type 1 reaction

A number of skin patches are involved, some of the nerves are enlarged and tender but no evidence of loss of function.

Treatment

Paracetamol 1g eight hourly for 2 weeks combined with Chloroquine 500mg eight hourly for the same period. Clinically review the patient, do VMT/ST if there is

deterioration, treat as recommended

Severe type 1 reaction

Most or all the skin patches are affected. A number of nerves are enlarged, tender, with evidence of loss of nerve function.

Treatment

Admit the patient and start on long course prednisolone, do 2 weekly VMT/ST as you monitor the treatment. Prednisolone is given using the regimen below:

- Start with 40mg OD for 2 weeks, followed by
- 30mg OD for 2 weeks then
- 20mg OD for 6 weeks

After 6 weeks of prednisolone therapy, patients may fall into any of the two categories below be based on the response:

Patient A:

There is no response or no changes in the VMT/ST. The treatment has failed, probably the patient presented with late nerve damage possibly having been present for more than six months.

Wean the patient off prednisolone by reducing to 15mg OD for 2 weeks then, 10mg OD for 2 weeks and finally 5mg OD for 2 weeks.

Assess the patient for reconstructive surgery, rehabilitation and health education on the care of the eyes, hands and feet.

Patient B:

This is a patient who at a prednisolone dose of 20mg OD for 6 weeks, and after the 6 weeks of therapy still shows improvement in nerve function based on the VMT/ST.

Extend the 20mg of Prednisolone daily conduct 2 weekly VMT/ST until you get 3 similar VMT/ST readings. This patient has now stabilized on prednisolone. Gradually wean the patient off the steroids.

Note

1. If the VMT/ST deteriorates after reducing from high dose to low dose, resume the higher dose for 2 weeks and then step down the dosage.
2. Administration of steroids suppresses the adrenal gland and therefore it is important to gradually wean off the patient from steroids.
3. A patient that has been on long course steroids needs to carry a steroid card to alert other medical practitioners of the therapy for appropriate management

Management of type 2 reaction

Type 2 reaction is divided into 4 categories for purposes of drug management.

- Mild type 2 reaction
- Moderate type 2 reaction
- Severe type 2 reaction
- Chronic (recurrent) type 2 reaction

Mild type 2 reaction

This is a patient with transient ENL nodules and no nerve or systemic involvement.

Treatment

Treated on outpatient basis with paracetamol 1 gram 8 hourly for 7 days, review and act appropriately

Moderate type 2 reaction

These patients have generalized ENL and may have mild fever.

Treatment

Treat with paracetamol at 1g eight hourly for 2 weeks as an outpatient, review every week and act appropriately.

Severe type 2 reaction

There is a generalized ENL. The patient has high a fever of 38-40°C most of the time the bed reddens and there is evidence of involvement of other organs like eyes testis lymph nodes, spleen liver hand feet etc. Some nerves may be enlarged and tender.

<p><i>This is a medical emergency and requires admission</i></p>

Treatment

The patient should be put on short course prednisolone as follows:

- Start at 60mg OD for 3 days then
- 40mg OD for 3 days then
- 30mg OD for 3 days then
- 20 mg OD for 3 days then
- 15 mg OD for 3 days then
- 10 mg OD for 3 days then
- 5 mg OD for 3 days

In addition give paracetamol 1g 8 hourly for 1 week.

If patient is anxious give diazepam 5mg 8 hourly or 25mg BD or chlopromazine 100 mg nocte for 1 week.

Chronic (recurrent) type 2 reaction

This is a patient with severe type 2 reaction but is steroid dependent. (Relapses as soon as the dose of steroids are reduced to lower levels or weaned off steroids)

Treatment requires reinitiation of the short course steroids together with clofazimine at a dose of 100mg eight hourly for 1 month then 100mg twice a day for a month then 100mg once a day for 1 month.

Thalidomide may be given instead of clofazimine for duration of 4 months.

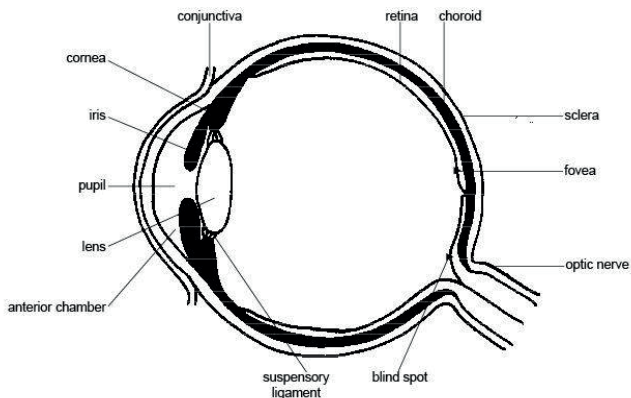
Please note that thalidomide should not be used in women of child bearing age.

THE EYE IN LEPROSY

PATHOPYSIOLOGY OF LEPROSY IN THE EYE

The eye is affected in leprosy in two main ways.

1. Direct bacillary invasion and
2. Leprosy reactions involving the eye



Direct Bacillary Invasion of the Eye

M.leprae can invade the eye forming a leprosy nodule (leproma) this may lead to interference with the closure of the eye causing exposure keratitis.

This was commonly seen in patients with dapsone resistance during dapsone monotherapy. Management was mainly surgical excision of the nodule if too big. Alternatively the patient could be started on MDT and the nodule would resolve.

Bacillary invasion of the cornea usually leads to vascularization of the cornea resulting in opacities and blindness. This is managed by initiating MDT.

LEPROSY REACTIONS IN THE EYE

Type 1 reaction

Type 1 leprosy reaction affects the eye through damage to the facial nerve leading to inability of the patient to close the eye (lagophthalmos).

This results in exposure keratitis which can lead to opacities and blindness. It also exposes the eye to injuries by foreign objects that get into the eye at night or windy day. Consequently the eye gets infected, heals with fibrosis and blindness. If the eyes are not active the obicularis oculi muscle atrophy leading to entropion.

Entropion the inward turning of the eyelashes leads to irritation of the cornea. This can also introduce infection which can further damage the cornea. Loss of sensation to the eye leads to use of excessive force while trying to clean the eye causing damage healing with fibrosis and ultimately impaired vision.

Ectropion the outward turning of the eyelid leaves a space between the eye ball and the eyelid causing accumulation of tears in the space that in turn cause continues tearing. The patient in an attempt to clear the tears from the eye, causes mechanical injury, and introduces infection into the eye leading to healing with fibrosis and blindness.

Damage to the trigeminal nerve is associated with loss of blink reflex leading to exposure keratitis and blindness as described above. There is also loss of corneal sensation which leads to unnoticed injury of the cornea, secondary bacterial infection and blindness.

Type 2 reaction

The deposition of antigen antibody complexes into the ciliary body leads to acute inflammation (iridocyclitis). Iridocyclitis leads to increased intraocular pressure

(Glucoma) which blocks the circulation of blood resulting in ischemic necrosis of the retina and blindness. Glucoma results from anterior and posterior synechiae.

Signs and symptoms of iridocyclitis

Iridocyclitis presents with:

- Perilimbal redness of the cornea
- Pain in the eye
- Blurred vision
- Photophobia
- Constricted pupil with poor reaction to light

In recurrent attacks of type 2 reaction the patient may develop premature cataract

MANAGEMENT OF THE EYE IN LEPROSY

The approach to management of the eye complication entails prevention through prediction of reaction in a leprosy patient on treatment.

- If the patch is on the face treat as MB even if the patient is PB
- Treat the patient adequately
- If the patient has lagophthalmos do:

- i) Tarsorrhaphy- both median or laterally
- ii) Temporalis Muscle Tendon (TMT) transfer muscle for chewing

Management of iridocyclitis

Iridocyclitis in leprosy is a medical emergency and should be treated as outlined below:

Initial care at the peripheral health facility

1. Instill atropine eye drops into the eye
2. Pad the eye
3. Refer a patient for admission and further management

Inpatient care

The patient should receive an ophthalmologist or physician review where available

Atropine sulphate drops relaxes the iris muscle relaxing them shorter thus reducing the risk of attachment

DEFORMITIES AND CONSEQUENCES

There are several causes of deformities in leprosy these include:

- Bacterial invasion causing poor transmission of nerve impulses
- Loss of sensation that leads to unnoticed injuries
- Dryness of the skin leading to cracking, open wounds and infection
- Paralysis leading to wasting, disuse, poor posture or improper handling of objects
- Mechanical injury involving working tools, wrong footwear and general injuries

Common deformities and disabilities in leprosy:

- Madarosis: Loss of eyebrows and eye lashes
- Lagophthalmos: Leads to inability to close and open the eye voluntarily
- Collapsed nose (saddle nose): Associated with difficulty in breathing
- Wrist drop: Inability to extend the wrist
- Ape thumb: Associated with loss of thumb apposition and abduction and consequently loss of fine skills
- Claw hand: Inability to flex the proximal metacarpophalengial joint of the fourth and fifth fingers and inability to extend the distal metacarpophalengial joints of the fourth and fifth fingers.
- Foot drop: Inability to dorsiflex and evert the foot
- Claw toes: leads to injuries to the metatarsal heads and toes
- Plantar ulcers

DISABILITY GRADING

WHO recommends the use a simplified diassability grading criteria for epidemiological purposed.

Grading

Grade 0: Normal or no damage

Grade 1: Loss of sensation

Grade 2: Obvious deformities visible e.g. clawing

VOLUNTARY MUSCLE TESTING & SENSORY TESTING (VMT/ST)

Monitoring for deformities and disabilities in leprosy patients is a critical component of case management. This can be achieved through proper voluntary muscle testing and sensory testing (VMT/ST). VMTST requires skills in clinical examination and recording. The indicators for VMT/ST procedure form part of the initial patient assessment tools.

REHABILITATION IN LEPROSY

Leprosy affects the patient in the physical , social, psychological and economic perspectives. The plan of management of this patient should include interventions that are aimed as returning the patient to as near normal life as possible.

Interventions geared towards restoring the patient's condition include:

- Physical rehabilitation
- Socio-economic rehabilitation
- Surgical intervention (reconstruction surgery)
- Orthopedic appliances

PHYSICAL REHABILITATION

This involves physical exercises, sometimes in line with pre and post operation management of leprosy. It also includes vocational training and fabrication of adaptive aids. Patients are encouraged to participate in recreational activities such as reading and indoor games.

SOCIO-ECONOMIC REHABILITATION

Patients are encouraged to form groups and start income generating activities. Those with vocational skills can start trades that will make them self reliant

SURGICAL INTERVENTION

This involves surgical procedures to correct deformities:

- Madarosis: Hair grafting
- Lagophthalmos: Tarsorrhaphy, Temporalis muscle tendon transfer (TMT)
- Nasal collapse: Postnasal inlay graft
- Wrist drop: Wrist arthrodesis
- Ape thumb: Opponens plasty
- Claw hand: Extensor to flexor 4 tail graft and sublimis muscle transfer
- Foot drop: Tibialis posterior muscle transfer (TPT)
- Plantar ulcers: Trans-metatarsal head resection , skin grafting, sequestrectomy and amputation as indicated

ORTHOPEDIC APPLIANCES

These include appliances include: Foot ware: normal tyre sandal with micro-cellular rubber (MCR), plasterzote sandal , plasterzote boot, elephant boot, Peg leg, below-knee prosthesis and above-knee prosthesis

DISABILITY PREVENTION

This is a critical component of care for the leprosy patient. It includes:

- Sensitization / creation of awareness in the community about leprosy for early case detection and stigma reduction
- Anti leprosy treatment
- Leprosy reaction anticipation and management as well as health education of the patient's relatives
- Physiotherapy in an attempt to restore function and prevent further damage

A home program is a critical component of physiotherapy

- Reconstructive surgery
- Provision appropriate foot wear

HEALTH EDUCATION

Health education is usually directed to the public, patients, family and friends.

In disease control at least the following information should be provided components of health education include information on : disease cause, treatment and curability, stigma reduction in the community.

The family friends and relatives should be informed about what causes the disease: Leprosy is not a curse, is not caused by an evil spirits neither is it a taboo. They should be informed that leprosy is not transmitted through food or, sharing common items. They should be infirmed about symptoms and signs of leprosy and that it is curable following a complete course of proper treatment.

The patient should receive the above information and in addition be educated about reactions the course of disease and be provided with self care information below.

Self care education

Care for the eyes:

- A regular examination of the eyes in a mirror to check for redness and tearing
- Patient should be told to think-blink (actively remember to blink regularly),
- Use protective eye care equipment e.g. goggles,
- Wear a wide hat,
- Use a pipe when blowing fire
- Cover face with clean cloth at night to prevent foreign objects from entering the eye

Hands:

The patient should be taught to regularly inspect the hands for dryness, blisters, wounds, and clawing

- Daily hand care involves soaking in cold soapy water, applying oil regularly and doing exercises
- Use of a protective cloth or gloves when performing any activity

Feet:

Like the hands the feet should be regularly inspected for cracks, dryness, and wounds

- Daily care involves soaking in cold soapy water, applying oil regularly and exercising
- Resting
- Putting on proper foot ware

General body hygiene

- The patient should clean his residential area to keep away cockroaches, jiggers, rats, and other pests
- Regular cleaning of the body

CHAPTER 9 : MONITORING AND EVALUATION OF TB CONTROL ACTIVITIES

Monitoring is the routine tracking of service and programme performance. It is a continuous process intended to provide information on the extent to which a programme is achieving its intended targets within specified timeframes.

Evaluation is a time specific assessment of results that can be attributed to programme activities. It uses routine monitoring data and, often, indicators that are not collected through routine information systems. A well designed evaluation should allow for the causes of failure to achieve intended results to be identified. This can be achieved by all health workers at all levels utilizing the information collected routinely to improve service delivery with the aim of achieving the set targets.

Tuberculosis case recording and reporting is an important tool for monitoring and evaluating TB control activities at the health facility, region and nationally. The importance of completing correctly the data collection tools at every TB treatment facility cannot be overemphasized.

Every health care provider who treats TB has a professional responsibility to record and report all cases he or she treats

Accurate keeping of records of all individual patients and maintenance of registers are minimum requirements that need to be met by all health care workers involved with the diagnosis and treatment of tuberculosis patients. It is the responsibility of the facility In-charge (I/C) with training and technical support (supervision) from the DTLC to ensure that recording of details about patients is done properly and correctly. The number and design of cards, forms and registers has been limited and kept as simple as possible to enable the DLTLD to have good patient care and monitoring of performance at all levels.

All patients diagnosed in health care facilities supervised by the DLTLD must be registered at the start of treatment.

Note: TB is a notifiable disease under the Public Health Act Cap 242, and therefore all TB Cases (diagnosed by the public or private sector) must be notified to the MOPHS.

REGISTERS, CARDS AND FORMS

The following registers, cards and forms are used for the management of TB at health care facilities supported by the DLTLD:

1. Tuberculosis Patient Management tools:

- TB Patient Record Card
- TB Patient Appointment Card
- TB Treatment Facility Register
- TB Treatment District Register
- TB Patient Pack Control Card (currently in-printed on the Packs)
- Referral Form to TB clinic
- Referral Form from TB Clinic to other care providers

2. Laboratory:

- TB Sputum-smear Examination Request Form
- Laboratory Register for Sputum-smear Examination (AFB Register)
- TB Culture and sensitivity Request Form

3. Drugs and other supplies:

- Daily Activity Drug Register (DADR)
- Facility CDRR (Consumption Drug Report & Request)Form
- District CDRR
- Bin Card
- S11.

4. Others

- TB/leprosy Patient Defaulter Tracing Chart
- TB/leprosy Patient Transfer Form
- Facility Supervision Tool
- Patient Interview Schedule
- Quarterly Case Finding Report Form
- Cohort Report Forms
- Quarterly AFB Report Form

INSTRUCTIONS FOR RECORDING

TB APPOINTMENT CARD

This card has to be filled by the health worker when the patient is started on treatment. The card remains with the patient during and after the full period of treatment. This will enable the patient to collect drugs and to continue treatment at another TB clinic other than the one he/she is registered when in transit or moving residence. In case of a more or less permanent transfer, a transfer form must be filled and given to the patient.

The appointment card holds the following information:

District: - Write the name of the District

District registration number -This is the number under which the patient is registered in the district register and can only be given by the DTLC when he/she visits the clinic during supervision rounds and fills the district registration number in the treatment unit register. When the patient comes to collect drugs, the number should be written on the card. *It is not necessary that a patient should have a district registration number before treatment can be started.* Take note, that in case a patient has to continue treatment in another unit other than the one where he/she was diagnosed and started on treatment, the registration number should be given at the health unit where the patient will continue treatment.

Name of the facility: Write the name of the *facility* where the patient is/will be registered.

Full name of the patient: Write the three names of the patient.

Address: Write the location where patient can be traced (residence or work spot) and note down his/her phone number, or the number of a relative, friend or treatment supporter, if the patient does not have a phone, or any other useful detail.

Age: Write the age (in years) of the patient

Sex: Write the sex of the patient (“M” for Male and “F” for Female)

Pulmonary Tuberculosis: Tick as appropriate in the provided box if Smear Positive, Smear Negative, or Extra-pulmonary

The regimen: Tick in the appropriate box the regimen patient is started on.

Date Started Treatment: Write the date when treatment started.

Date Cured or TC: Write the date when the patient is declared cured or has completed treatment.

- Note: The latter is important in case the patient gets tuberculosis again after finalizing treatment. For this reason it is also important that the patient keeps the card even after the end of treatment.

Monthly body weight (in kg): Weigh the patient (in Kg) at the start of treatment and every 28 days when the patient comes to collect drugs and write the respective weight in the provided boxes

Intensive phase of treatment: Tick the card after observing the patient swallowing the daily dose.

Note: When Rifampicin is among the drugs the patient is taking, it is critical to ensure that a patient support system is available to ensure adherence to treatment. This must include DOT by a treatment supporter. The first day TB drugs are collected; the health care worker will demonstrate how to observe TB patients swallowing their medicines and how to tick the appointment card. The observation by the DOT supporter will be done for the whole duration of treatment in case of the 6-month regimen and during the intensive phase only in case of the 8-month regimen. This means that although the drugs are dispensed for seven days, the very first dose should be taken at the health facility.

The patients should be encouraged to bring back with them to the facility the empty blister packs as evidence of treatment compliance. The empty blister packs should be put back in the patient pack.

The first two months of treatment: Write the dosage of the drugs the patient should take during the different phases of treatment expressed in tablets per day.

Continuation Phase New (months 3-8): Write Dates of four-weekly drug collection in the continuation phase.

Sputum-smear examination: Write the result at start of treatment. Thereafter, for new smear-positive PTB patients, enter the follow-up results at 2, 5, 8 months (2, 5 and 6 for Rifampicin throughout regimen). For smear positive re-treatment patients, this will be at 3, 5, 8 (6) months. The last sputum smear examination should be done when the patient comes to collect the last 4-weekly (or 2-weekly for Rifampicin throughout regimen) supply of drugs.

Weekly Drug Collection: Write the dates of the weekly drug collection and the due date for the next collection for the intensive phase.

TB PATIENT RECORD CARD

Although, seemingly, containing more or less the same information as the Appointment Card, the Patient Record Card is focussed more on the clinical aspects of patient management. It also contains information, which cannot be put on the Appointment Card, and as such cannot be replaced by it. The Patient Record Card is a very valuable source of information for operational/clinical research on TB management. It contains data, which often cannot be found in the TB Registers. The card should be filled as completely as possible, during every visit of the patient by the health worker who manages their treatment. It must be left at the unit where the patient receives treatment.

Note: The TB Patient Record Card contains medical information, which is strictly confidential, and must be handled accordingly.

The Patient Record Card holds the following information:

- **District registration number.** (See TB appointment card)
- **Name of the clinic** where the patient is/will be registered.
- **Name of the district**
- **Dates when treatment started** and when the **patient is declared cured or has completed treatment.** The latter is important in case the patient gets tuberculosis again after finalizing treatment.
- **Full name** of the patient
- **Address** of the location where patient can be traced (residence or work spot), but also the name of the primary school nearest to the patient's residence.

- **Name & address of the patient's treatment supporter** (if applicable) and the relationship of the treatment supporter to the patient. The latter can be a household member/friend, a health care worker (including CHW) or a community volunteer.
- **Age (in years) and sex** of the patient
- **Disease classification:** Pulmonary or extra-pulmonary TB

Children (<15 years) who are diagnosed as a PTB case, but have no smear result, will be classified as smear negative. A patient older than 15 years, who has been diagnosed as a PTB case based on a chest X-ray or on clinical grounds, but without sputum smear results, must be classified as having PTB but smear not done. This latter way of diagnosing PTB patients should however be limited as much as possible.

If a patient has extra-pulmonary TB (EPTB) the location (or locations) must be ticked on the card.

- **Patient classification:** Patients are categorized for epidemiological and operational reasons. The following categories are used in the DLTLDD. To produce reliable and comparable data, health staff should strictly adhere to the definitions given below:

New

This is a tuberculosis patient who has never received anti-tuberculosis treatment before, or has been treated for less than 4 weeks

Smear positive relapse

A smear-positive PTB patient is one who has been treated before and was declared *cured (sputum-smear negative)*, or *treatment was completed (no sputum-smear result done)* after which the patient presents again with active disease.

Smear negative/extra pulmonary relapse

A smear-negative PTB or extra-pulmonary TB patient is one who has been treated before and was declared *cured (sputum-smear negative)*, or *treatment was completed (no sputum-smear result done)* after which he/she presents again with active disease.

Failure

This is a smear-positive PTB patient who, while on treatment, remained or became smear positive again at 5 months, or later during the course of treatment.

Return after Default (RAD)

This is a TB patient who returned to the health service after having interrupted previous treatment for 2 months which they had received for longer than 4 weeks.

Transfer in

A patient who has been transferred into a district from another where he/she has been registered for treatment. Preferably the treatment outcomes of such patients should be reported to the district in which they were initially registered.

Note: If it is already known at the start of treatment that a patient will transfer to another district after a short period of treatment it is not advisable to register them in the district where they were diagnosed and/or started on treatment. It is better to register the patient as a new patient in the district they are transferring to. On the Transfer Form it must be mentioned that they have not been registered in the district they have transferred "from".

Such a patient should be given one week supply of drugs to take until he reports to the new facility where he/she wishes to continue treatment. It should be ensured that this patient has actually arrived at this facility.

- ***The regimen:*** The TB treatment the patient is started on.
- ***Sputum-smear examination:*** Is done for all PTB suspects (new and re-treatment) and thereafter, for follow-up of PTB+ patients.
- ***Intensive Phase (daily) - 2 months:*** This is the first two months of treatment and number of tablets the patient has to take every day, or the daily dosage of Streptomycin to be injected.
- ***Continuation Phase (daily) – 4 to 6 months:*** This is the number of tablets the patient has to take daily during the continuation phase of treatment.
- ***Monthly body weight (in kg):*** The patient's body weight must be filled every month when they come to collect drugs. It is an indicator for improvement of the patient's condition. *It should not be used to adjust the dosage of drugs during treatment however.*
- ***Culture and Drug Sensitivity Testing results:*** If a sputum sample (or another clinical sample) was sent for culture and DST (all re-treatment cases), the

results must be filled in the relevant chart. An ‘**S**’ should be filled if the TB bacilli are *sensitive* to the listed drug; an ‘**R**’ should be filled if the TB bacilli are *resistant* to the drug. Also the *date of collection of the sample* from the patient must be filled.

- **Treatment outcome:** The eventual outcome of treatment, and the date this occurred, must be recorded in the relevant chart. This information is very important for the health services because it monitors how effective the programme is in curing and controlling TB. This information is used to facilitate planning for programme improvement. The following outcomes of treatment are used (inter)-nationally

Cured: This refers to a TB patient who was initially sputum-smear positive and completed his or her treatment ending with a negative sputum-smear examination result.

Treatment completed: This refers to a TB patient who completed treatment but without a sputum-smear examination at the end of treatment.

Died: This is the results recorded if a tuberculosis patient dies during treatment irrespective of the cause of the death. However, the cause of death should be recorded if known.

Out of Control: This refers to a TB patient who fails to attend three consecutive four-weekly clinics during the continuation phase (Note: A defaulter is a patient who fails to collect drugs at the due date).

Transferred out: This is a patient who changes treatment point from one district to another. The patient will be recorded as “Transferred in (TI)” in the receiving district.

- Patient referred by/Patient referred to:

a) Patient referred by

The following units should refer every person who tests positive for HIV or any person with signs/symptoms suggestive of tuberculosis to a TB diagnostic centre for screening and, if indicated, TB treatment, by means of the recently introduced *Referral Form for*

TB screening and/or treatment

- VCT centre
- HIV (comprehensive) care clinic
- STI clinic
- Home based care (programme)
- Antenatal/PMTCT clinic

- Private sector; private practitioner or private institution referring TB suspects or patients for screening or (further) treatment at the DLTLD clinics.
- Chemists/Pharmacists are encouraged to refer patients coughing longer than 2 weeks when they present themselves to the chemist/pharmacy to procure cough medications or other medicines. Therefore attendants at the chemists/pharmacies should ask all patients who make enquiries about drugs for cough “how long they had have the cough”. And all those who have had a cough for longer than two weeks directed to the nearest TB diagnostic facility for sputum smear microscopy. DTLCs are encouraged to disseminate lists of TB diagnostic facilities to all chemists/pharmacists in their areas.
- It should also be marked in the relevant chart if a TB suspect presented themselves at the TB diagnostic centre by:
 - *Self-referral*: (directly at the TB clinic or through the OPD)
 - *Contact-invitation*: a close contact of a TB patient with signs/symptoms that are suspect for tuberculosis (invited directly by the healthcare worker treating the TB patient or by the TB patient him/herself)

b) Patient referred to

Every TB clinic should refer a diagnosed TB case for HIV testing (if the service is not available at the health unit) or, in case the TB patient tests HIV positive, for additional care including counselling (if not available at the health unit), psycho-social support, ART and/or Cotrimoxazole prophylactic therapy (if not available at the TB clinic or after finalizing TB treatment), STI treatment etc. Any patient who wants to continue treatment under supervision of a private health care provider too should be referred as needed. The patient can be referred using the *Referral Form for TB patients* to other care services to the following units:

- VCT centre
- HIV (comprehensive) care clinic
- STI clinic
- Antenatal/PMTCT clinic
- Private sector
- Home based care programme

- ***HIV status/Regular sexual partner(s) tested for HIV:*** HIV infection is the single highest risk factor for a person to develop tuberculosis disease. An estimated 39% of TB cases in Kenya are HIV positive. Death rates amongst HIV infected patients with active TB are high, even when they receive appropriate TB treatment. Because of the increasing availability of ART and Co-trimoxazole prophylactic therapy, survival rates and life expectancy are increasing significantly for these patients. It has been shown that 14% of couples are discordant with regard to HIV. It is therefore of utmost importance that HIV high risk groups, like TB patients/suspects and their partners, are tested for HIV to enable them access additional care and prevent further transmission of HIV to their negative partner(s) or others. The DLTLTD's policy, in accordance with the *GoK/MOPHS Policy on HIV testing in clinical settings*, is, that *every TB patient must be counselled and tested for HIV*, as part of the diagnostic routine (DTC), *unless the patient refuses* this (opt-out). HIV testing and counselling should be done as soon as the TB diagnosis is made, preferably at the health unit where the patient is first seen. Postponing testing might give the health worker temporary reprieve of telling the bad or good news to the patient, but it won't benefit the latter.

For more elaborate information on HIV testing and counselling of TB cases and their partner(s) see the relevant chapter in these guidelines or consult the stand alone guidelines on TB/HIV collaborative activities.

An appropriate entry should be made in the relevant chart and space provided for HIV status of patient to indicate if the patient was tested and if so, what the HIV test result was. The date the HIV testing was done should be written in the space provided

An appropriate entry should be made in the space provided for HIV status of the sexual partner of the patient to indicate if an HIV test was carried out on the partner too. The date when the sexual partner underwent the HIV test should be written in the space provided. The test result of the partner should not be entered into the medical file of the patient, but into their own medical file.

- ***Prophylaxis for opportunistic infections:*** The treatment provided to a HIV infected TB patient to prevent opportunistic infections (Co-trimoxazole) should be indicated (ticked) in the space provided and the dates when this treatment is initiated or stopped.

- **CD 4 counts.** Although it is not mandatory for all HIV positive TB patients to have their CD 4+ counts done, the ART programme requires these patients undergo several tests including CD4 counts prior to initiation of ARVs. When the CD4 count of a HIV infected TB patient is known, it should be entered in the space provided. Monitoring the CD4+ count is an important tool for assessing the efficacy of ART.
- **Anti Retroviral Therapy (ART):** Most HIV positive TB patients in Kenya are eligible for ART during their TB treatment and all of them should be referred, as soon as feasible, to a Comprehensive Care Clinic (CCC) for further evaluation and start of ART. The ART regimen used will depend on the phase of TB treatment the patient is in, and especially if the TB patient is taking Rifampicin at the time. The HIV positive TB suspects, who are already on an ART regimen, should be referred from the CCCs for diagnosis and treatment of their TB. This might result in a change of the ART regimen they are on. The details of the ART provided to the patient should be entered in the appropriate space provided (ticked) and the date when this treatment was started or stopped. In case a patient is being shifted to another ART regimen, the new regimen should be indicated (ticked) and the also the date when the new treatment was initiated or stopped.
- **Initial phase of treatment (8 weeks):** This table is for ticking and /or writing down the date of daily drug intake during the initial phase of treatment (8 weeks) as observed by a health worker or another treatment supporter.
- **Continuation phase of treatment (6 x 4 weekly periods):** This section of the chart allows the date of the next 4 weekly drug collections during the continuation phase to be written down. In case of a smear-positive PTB case, a reminder for follow-up sputum collection is printed under the 5-th and 8-th 4 weekly periods.

Remarks: The full third page and part of the fourth page of the Patient Record Card is reserved for additional information not covered by the different tables

TUBERCULOSIS FACILITY TREATMENT REGISTER

The TB Treatment Register must be maintained at each health facility where tuberculosis treatment is supported by the DLTLTD. It should not be carried by the DTLC or kept in his/her office. The Tuberculosis Treatment Unit/facility Register is one of the most important monitoring & evaluation tools of the DLTLTD. Based on the information in this register all reports on TB/HIV case finding and treatment outcome related data are analysed and translated into activities essential for TB control in the country. Maintenance of this register is the task of the health worker(s) who are responsible for the TB clinic, and because of its contents this register should be handled as any other medical document containing confidential information. It must be kept in a lockable place where unauthorized persons don't have access to it. However, it should be accessible to visiting DLTLTD technical staff.

It is the responsibility of the DTLC to train and supervise the health worker(s) involved in the proper keeping of this register.

Every patient receiving tuberculosis treatment at the health facility must be recorded in this register. The register contains most of the information also found in the TB Patient Record Card and therefore should be consistent with the latter. It must be updated immediately after a patient attends the clinic for drug collection or when additional information becomes available like sputum examination results, HIV test results etcetera.

To facilitate filling of proper information in the Register's columns, links guide you to the items as mentioned under the TB Patient Record Card and the legends at the bottom of the pages in the register.

REFERRAL FORM TO TB CLINIC

This Patient Referral Form was recently introduced for use by different types of health units or services, and it is intended to facilitate the referral of TB suspects or PLHIVs to a TB clinic for TB screening and subsequent treatment.

The forms are provided in a booklet in duplicate. One copy is filled and goes with the patient to the unit he/she is referred to and the other copy remains in the booklet at the

referring unit. Since these forms contain confidential medical information, the booklet must be kept in a secure, lockable place.

Name, age and sex should be filled.

Reason for referral: Tick one or more of the listed reasons for referral. In case “other” is ticked, it should be specified on the line underneath the table.

Name of referring unit should be filled.

Type of referring unit: Tick one of the listed types. In case of “others”, specify the type on the line underneath the table.

Name of TB diagnostic facility the client/patient is referred to should be filled.

Date of referral must be filled.

THE REFERRAL FORM MUST BE SIGNED

REFERRAL FORM FROM TB CLINIC TO OTHER CARE PROVIDERS

This recently introduced form is used by the TB clinics to refer TB patients to other care providers for additional or continuing care

The forms are provided in a booklet in duplicate. One copy is filled and goes with the patient to the unit he/she is referred to and the other copy remains in the booklet at the referring unit. Since these forms contain confidential medical information, the booklet must be kept in a secure, lockable place.

Name, age and sex should be filled

Type of tuberculosis: Tick one of the given options

Treatment regimen used: Tick the regimen the patient is on

TB drugs used at present: Tick the anti -TB drugs the patient is taking at the time of referral

Patient referred to: Tick one of the options given. In case of “other”, specify

Reason for referral: Tick one of the options on the list. In case of “other”, specify

Name of the facility the patient is referred to and the name of the referring facility should be filled

Name/ signature of person referring and **date of referral** must be present on the form

LABORATORY REQUEST FORM FOR SPUTUM EXAMINATION

This form should be used by health care workers who are examining patients at the outpatient departments, chest clinics, and wards of health facilities. The following must be filled:

Name: All three names of the patient must appear in the Request Form.

Age: The actual age of the patients must be written (not adult or child), estimate age when not known.

Address: Care should be taken that the address is properly filled so that the patient can be traced in case if necessary.

Reason: The reason for the request must be clearly written irrespective if it is a new or follow-up patient. For follow-up patients, indicate the month i.e. 2, 5, 8 (8) months

Name requesting: Health workers making the request and their signature should also be written too.

AFB LABORATORY REGISTER

This register is kept and maintained by the laboratory staff. The following entries must be done:

Serial number: The laboratory serial number should start at 1 with the first patient examined in the year and end with the serial number of the last patient examined at the end of the year.

The date stands for the 1st date of registration of the request

The column for **Registration number** is for follow-up patients who already have their DLTLD TB district registration numbers

Name: All three names of the patient should be entered in this column

OPD/WD/clinic: It is important to fill column to facilitate the delivery of lab report to the right place in a timely manner

Age: The actual age should be entered in this column

Sex: The correct sex (M/F) should be entered into this column

Results column: The results for the same patient should be indicated in the same row. Positive results should be quantified and written with a red pen, Negative results should be indicated with a '0' sign.

Examined by -This column should have the **name**, not the signature of the laboratory technician who examined the smear. Absence of the lab tech's name makes the entry into the register incomplete

CULTURE REQUEST FORM

Culture and sensitivity examination must be done for every pulmonary tuberculosis re-treatment case. The Culture Request Form must be filled by the Clinician handling the patient.

In the first paragraph the following information should be clearly written:

- Name (all three names)
- District registration number
- OP/IP number
- Address
- Actual age of patient
- Sex of patient
- Referring clinic or ward,
- Facility name
- Type of specimen
- Date of collection,
- Clinician's name and signature.
- Examination required: Specify whether for smear, culture or sensitivity
- Type of patient: Tick the correct type of patient.
- Previous treatment: Indicate the duration of treatment and drugs used.

On the opposite side of the same form there is room for the laboratory report for direct smear, culture report, and sensitivity testing. The report should also have the *name, signature and designation* of the laboratory officer and the *date* the report was finalized.

CHAPTER 10: ENGAGING ALL CARE PROVIDERS IN TB CARE AND CONTROL

INTRODUCTION

The non state or private health care sector is an important player in the delivery of health services in Kenya. Collectively this sector provides nearly 50% of all health care provided to Kenyans. The range of providers in this sector is wide, from large health institutions that offer state of the art health care services to informal providers who have to play cat and mouse games with regulatory authorities to remain in business. The Kenyan population utilizes, in a very pluralistic way, all these providers in addition to public health care services. Except for small segments of the population, patients with TB symptoms will very commonly and with ease move between these two sectors (public and private).

A key element of the Stop TB Strategy is the engagement of all care providers in what is called Public – Private Mix (PPM) DOTS.

The PPM initiative is aimed at linking private health care providers to the national TB control program to help

- find all TB cases
- promote early TB case finding,
- reduce errors in TB case management and thus reduce the risk of generation and dissemination of DRTB
- to promote the implementation by private health care providers of essential public health related activities such as case recording and reporting and contact investigation.

RATIONALE FOR PPM

Private health care providers pose both threats and opportunities for TB care and control. Unengaged private health care providers often manage TB cases in a manner that deviate from set international and national standards which can promote the development and spread of drug resistance. A structured engagement of private health care providers can on the other hand lead to earlier and more complete TB case detection and proper management of TB cases which would improve the chances of a successful outcome of the TB episode and reduce the risk of acquired drug resistance. The PPM approach is considered essential for “turning off the tap” of MDRTB and XDRTB.

The private health sector may be more conveniently located near the homes or workplaces of TB suspects and patients and may also have more flexible operating times which could enhance access to TB services if this segment of health care providers is engaged. This is particularly relevant in urban slums where the incidence of TB is high and the rigors of “surviving” may make it inconvenient and even costly for TB suspects to access TB care services located elsewhere from where patients live or work and which may have inconveniencing service hours. Potentially, PPM can save poor patients money when free TB services, combining both public and private provision are located within easy reach.

COMPONENTS OF PPM

- a) Involving all public, voluntary, corporate and private providers through public-private mix approaches
- b) Promote use of the International Standards for Tuberculosis Care

WHO NEEDS TO BE ENGAGED?

- The Military Health Service
- The Prison Health Service
- Faith and NGO based Health Services
- Private for profit (or self financing) hospitals
- Corporate Health Services
- Individual private for profit health care providers
- Retail pharmacies, chemists and drug shops
- Informal Care Providers

For the purpose of these guidelines informal care providers comprise:

- Traditional healers, Herbalists and faith healers
- Grocers and Shopkeepers
- Home based care groups providing care to HIV positive patients and other volunteers
- Community units – Lay Community Health Care Workers (CHWS) , Community Health Extension Workers

OBJECTIVES OF PPM

The main objectives of the PPM approach in Kenya have been and remain:

1. To improve and standardize TB case management by all providers, public and private, and align TB case management with the International Standards for Tuberculosis Care (ISTC) and national TB control guidelines.
2. To improve TB case finding (early and complete TB case finding), including DRTB case finding and treatment outcomes for all forms of TB by offering accessible, acceptable and affordable quality TB services for all patients.
3. To ensure private health care providers, like their public sector counterparts carry out essential public health responsibilities such as case recording and reporting and contact investigation.

IMPLEMENTING PPM FOR TB CARE AND CONTROL AT THE DIFFERENT TB CONTROL LEVELS: THE ESSENTIAL STEPS

DLTLD and Other GoK Staff Sensitization and preparedness.

It is critical to ensure that DLTLD staff at all levels (National, county level, Health Facility) and other relevant GOK health staffs are fully sensitized about PPM and have internalized the goal, the mission and objectives of PPM for their own level. The local capacity for effective implementation of PPM must be defined and roles of various players identified and documented to avoid role conflicts when implementation of PPM activities begins effort at the various levels.

Provider mapping and selection

All health care providers in the local setting must be mapped and if the number is too large as to overwhelm the capacity to engage them a priority list of providers to be engaged should be made. The priority list of providers may include those that see a high number of TB suspects and patients, those with a capacity of to enhance the local TB service, those that are already engaged in TB care and control or those that are located in strategic places within a specific geographic area and whose engagement may enhance the reach of the TB service. The tasks that selected providers will be requested to perform should be listed against each provider to form the basis of dialogue with the provider as engagement begins.

Provider Sensitization and or Training

Prioritized and selected providers should be sensitized. dialogue should focus on informing the provider the rationale of the initiative, the role the provider is expected to

perform, the time and other commitments that the provider is expected to make, the benefits that may accrue to the provider for participating in the initiative, the harm that may be associated with participating in the initiative, and the incentive and enablers if any that will be used in the initiative. Any further training provided by the initiative must be task oriented and should use training materials developed to deliver effective training for the tasks that the provider is expected to carry out in the initiative.

Provision of implementation and monitoring tools

Providers who have been prioritized, selected and sensitized /trained should then be provided with the relevant tools to allow implementation and monitoring of the initiative

TASKS IN PPM IMPLEMENTATION

Identification of TB symptomatics and other persons who need TB screening:

- Referral of TB suspects
- Collect specimens for TB diagnosis
- Notify & Record TB and DRTB Cases
- Carry out TB bacteriology
- Carry out laboratory diagnosis of DRTB
- Carry out HIV testing and counselling
- Prescribe TB treatment
- Prescribe DR TB treatment

Requirements for a MDRTB treatment centre in the private sector

- Human Resources : Trained Clinician (s), Nurses, Pharmacists, nutritionist and social worker(s)
- Availability of or easy access to an infection (MDRTB) isolation ward with all the requisite infrastructure
- Presence of an infection transmission prevention plan
- Availability of drugs to treat MDRTB and to manage adverse effects of second line drugs
- Availability of laboratory services to monitor drug side effects (thyroid function tests, kidney function tests, blood count)
- Availability of recording and reporting tools
- Education to Patients
- Provide Treatment supporters (DOT)
- *Tracing defaulters*

- Training of Providers
- Supportive supervision and clinical mentorship
- Quality Assurance of laboratories
- Monitoring and evaluation
- Drug and other commodities supply management
- Enforcement of policies by professional and regulatory bodies including sale and registration of medicines and laboratory commodities.

ANNEXES

ANNEX 1: HEALTH CARE PROVIDER TASK MIX IN TB/DRTB CONTROL IN KENYA

Any facility offering TB treatment must commit to offer the minimum package of care
An accreditation criteria will be developed and used to identify private facilities to offer MDRTB treatment

Task	Government including military and prison health services				Faith based Organizations/NGO			Private providers Including corporate				Informal Sector	Professional/Regulatory Bodies
	NTP/DOTS Agency	Hospitals	Health Centres	Dispensary	Hospital	Health centre	Dispensary	Hospital	Clinic	Retail pharmacy	Stand alone laboratory		
Identify TB Suspects and other persons who need TB screening		X	X	X	X	X	X	X	X	X	X	X	
Collect Specimens		X	X	X	X	X	X	X	X	X	X		
Refer & record suspects		X	X	X	X	X	X	X	X	X	X	X	
Notify/Record Cases		X	X	X	X	X	X	X	X	X	X		
Carry out Smear microscopy		X	X	X	X	X	X	X	X		X		
Gene-Xpert (where available)		X	X		X	X		X			X		
Line Probe Assay(where available)		X			X			X			X		
Liquid Culture (where available)		X			X			X			X		
Solid Culture (where available)		X									X		
Carry out HIV testing and Counselling		X	X	X	X	X	X	X	X	X	X		
Carry out Culture and DST		X			X			X					
Prescribe TB Treatment		X	X	X	X	X	X	X	X				
Prescribe DRTB** treatment		X			X			X					
Education of Patients	X	X	X	X	X	X	X	X	X	X		X (HBC)	
Provide treatment supporters (DOT)		X	X	X	X	X	X	X	X	X		X	
Trace defaulters		X	X	X	X	X	X	X	X	X		X	
Training of providers	X	X			X								X
Supervision	X				X								
QA of Laboratories*	X	X	X	X	X	X	X	X	X		X		
M&E	X	X	X	X	X	X	X	X	X	X	X		X
Drug and other commodities supply management	X	X	X	X	X	X	X	X		X			X
Enforcement of policies	X												X
Provide Stewardship (regulation and financing)	X												X

ANNEX2: TB INFECTION CONTROL MONITORING AND EVALUATION TOOL FOR CLINICAL SITES

Date _____ Health Facility _____ Level 6, 5, 4, 3, 2, 1

District / County _____ Auditor _____

Patient Population: HIV , TB , MCH , Peds , General OPD

Site Type: In-patient , Out- patient

Managerial	Scoring
An IC Committee or Person is designated in this site	Y or N
A written IC plan or check list is available for this site	Y or N
Staff TBIC training has been done	Y or N
Facility design and patient flow have been assessed	Y or N
M&E of TBIC data forms are routinely reviewed	Y or N
A tracking system for all TB suspects, referrals, sputum smear results is in place	Y or N
A register is kept for all patients reported to NTP	Y or N
All TB patients are managed on DOT as per NTP guidelines	Y or N
Patient and visitor TBIC information is available for all and offered by staff	Y or N
Operation research to improve TBIC measures is conducted at this site	Y or N
Administrative	
Patients are routinely asked about cough upon entering facility	Y or N
Coughers are separated and "fast racked" to caregiver	Y or N
A "Cough Monitor" assists with triage and cough etiquette	Y or N
Signage for cough etiquette present in the clinic	Y or N
Sputum is collected in a designated area away from others	Y or N
HCWs who assist sputum collection take precautions	Y or N
Sputum processing is expedited – there is a tracking mechanism for TAT	Y or N
There is a tracking mechanism to monitor TAT of patient within health facility	Y or N
There is a log for all staff diagnosed with TB	Y or N
Staff receive TB evaluation at least annually	Y or N
Staff are offered HIV test annually and placed on ART if positive	Y or N
HIV+ staff are reassigned if requested	Y or N
IPT is offered to HIV+ staff	Y or N
Environmental Controls	
Natural and/or mechanical airflow is monitored by staff daily –especially in waiting rooms, sputum collection point (if available) and at least one examination room	Y or N
Regular maintenance for directional and extractor fans is conducted	Y or N
Signage in place to keep doors and windows open when feasible	Y or N
If UV lighting is used, routine maintenance is scheduled	Y or N
Patients are not crowded in hallways or waiting areas	Y or N
PPE	
N-95 or FFP2 respirators are readily available for staff	Y or N
Staff trained on proper fit of respirators	Y or N
Supplies (tissues, cloths, masks, trash bins etc) are available for coughers	Y or N
Staff are provided CME opportunities and annual exams on TBIC	Y or N
Additional comments, room design, patient flow etc	
Strengths / Weaknesses of this health facility:	
Solutions / Recommendations	

ANNEX 3 : DOSAGE OF INDIVIDUAL FIRST LINE ANTI-TB DRUGS IN CHILDREN ACCORDING TO BODY WEIGHT

Drug	Recommendations Average dose in mg/kg	Range in mg/kg	Maximum Dose
Isoniazid	10	10 – 15	300 mg
Rifampicin	15	10 – 20	600 mg
Pyrazinamide	35	30 – 40	1.5 g
Ethambutol	20	15 – 25	1.6 g

ANNEX 4: COMMON SECONDLINE DRUGS ADVERSE DRUG REACTIONS

Drug	Daily dose	Side effects	Side effects control test	interaction
Capreomycin (Cm)	15-30mg/Kg	VIII cranial nerve lesion Nephrotoxicity	Vestibular function Audiometry BUN	Neuromuscular blockers
Kanamycin (Km)	15-30mg/Kg	VIII cranial nerve lesion Nephrotoxicity	Vestibular function Audiometry BUN	Neuromuscular blockers
Ethionamide (Eth)	15-30mg/Kg	GIT disturbances Hepatotoxicity	SGOT SGPT	nil
PAS	150mg/Kg	GIT disturbances Hepatotoxicity	SGOT SGPT	Not reported
Cycloserine (Cs)	10-20mg/Kg	Psychosis Seizures Rash	Psychological test	Alcohol
Ofloxacin (Ofx)	800mg daily	Hepatotoxicity		

ANNEX 5: PRACTICAL APPROACH TO MANAGEMENT OF SIDE EFFECTS OF SECONDLINE ANTITB DRUGS

Side Effect	Suspected Agent			Management
	Frequent	Common	Rare	
Hepatitis	H		R, Z	Elevation of liver enzymes universal in the first weeks of treatment Overt liver disease (5 times over the normal range) – temporarily withdraw drugs until overt disease clears Reintroduce drugs sequentially or all, once overt disease clears Exclude other causes of hepatitis where possible (viral hepatitis A,B,C)
Peripheral neuropathy			H	Preventable with low dose pyridoxine (12.5-25mg daily) Treated with high dose pyridoxine (100-150mg daily) Reassure patient
Orange discoloration of body fluids	R			If severe use NSAIDs to manage.
Arthralgia	Z			Reassure patient
Nausea		Z		
Rash			Z	
Retrobulbar neuritis			E	Confirm with ophthalmic review where possible. Warn all patients who will receive ethambutol Never give ethambutol again if this adverse effect is suspected or confirmed
Vestibular toxicity	S			It is often, though not always, dose dependent. When the symptoms of vestibulo-cochlear toxicity occur, the dose of Streptomycin should be checked and reduced if possible. If the dose cannot be reduced or the symptoms do not improve with dose reduction, Streptomycin should be stopped and not be given again.
Cochlear toxicity		S		Monitor renal functions
Renal damage			S	

ANNEX 6: PRACTICAL APPROACH TO MANAGEMENT OF SIDE EFFECTS OF SECONDLINE ANTITB DRUGS

Side effects	Suspected agent	Management
Hepatitis	Z, H, R, Th, Ofx, Lfx, Cs, PAS	Stop therapy Rule out other causes Re-introduce drugs serially while monitoring for liver function, with most likely agent introduced last
Renal failure	S, Km, Am, Cm	Discontinue suspected agent Consider using Cm if an aminoglycoside had been prior parenteral regimen
Arthralgia	Z, Ofx, L, Cs	Therapy with NSAIDs Initiate exercise regimen Lower dose of suspected agent, if can be done without compromising regimen Discontinue suspected agent if can be done without compromising regimen
Gastritis (severe form is rarely observed) Nausea and Vomiting	PAS, Tha, H, E, Clz, Z PAS, Tha, H, E, Clz, Z	Give antacids, this should timed so as not to interfere with absorption of anti-TB drugs Rehydration Anti-emesis Lower doses of suspected agent, if can be done without compromising regimen Discontinue suspected agent if can be done without compromising regimen
Seizures (History of prior convulsion is not CI for therapy)	Cs, H, Ofx, L, Cs	Anti-convulsive therapy (Phenytoin, Valproic acid), continued until MDR-TB treatment is completed Increase Pyridoxine to 300mg daily Lower doses of suspected agent, if can be done without compromising regimen Discontinue suspected agent if can be done without compromising regimen
Psychosis	Cs, Ofx, Lfx, Cx, H, Tha	Initiate anti-psychotic drugs Hold suspected for short period of time (1-4 wks) while symptoms are brought under control Lower doses of suspected agent, if can be done without compromising regimen Discontinue suspected agent if can be done without compromising regimen
Hearing loss	S, Km, Am, Cm, Clr	Change parenteral to Cm Lower doses of suspected agent, if can be done without compromising regimen Discontinue suspected agent if can be done without compromising regimen
Peripheral neuropathy	Nearly all	Increase Pyridoxine to 300mg daily Change parenteral to Cm Begin exercise regimen focusing on affected region Initiate therapy with tricyclic anti-depressants
Hypothyroidism	PAS, Tha	Initiate thyroxine therapy Substitute the two drugs

ANNEX 7 : ANTI-TB DRUG INTERACTION

ISONIAZID INTERACTIONS

Effects of isoniazid potentiated	Effects of isoniazid opposed	Effect of drug potentiated by isoniazid	Effect of drug opposed by isoniazid
PAS Insulin Carbamazepine Theophylline	Prednisolone Ketoconazole	Anti-coagulants Anti-epileptics Benzodiazepines Haloperidol Tricyclic anti-depressants Theophylline	Enflurane

PYRAZINAMIDE INTERACTIONS

Effects of pyrazinamide potentiated	Effects of pyrazinamide opposed	Effect of drug potentiated by pyrazinamide	Effect of drug opposed by pyrazinamide
Allopurinol	Zidovudin (?)		Uricosuric drugs

ETHAMBUTOL INTERACTIONS

Effects of ethambutol potentiated	Effects of ethambutol opposed	Effect of drug potentiated by ethambutol	Effect of drug opposed by ethambutol
	Aluminum-magnesium antacids		

RIFAMPICIN INTERACTIONS

Effects of rifampicin potentiated	Effects of rifampicin opposed	Effect of drug potentiated by rifampicin	Effect of drug opposed by rifampicin
Co-trimoxazole		Acetaminophen	Anti-arrhythmics Anti-asthmatics Wafarin Anti-fungals Anti-malarials NVP, LPV/r Barbiturates Benzodiazepins Beta blockers Hormones Immunosuppressants Cardiac glycosides Opioids Vitamin K and D Trimethoprim

SUGGESTED FURTHER READING

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