MINISTRY OF HEALTH
NATIONAL LEPROSY/TB CONTROL PROGRAMME

NATIONAL GUIDELINES ON THE MANAGEMENT OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

FIRST EDITION
DECEMBER 2023

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and TB Program

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SOURCE DOCUMENTS

Primary resources adapted for use in the writing of these guidelines include:

- WHO Consolidated Guidelines for Tuberculosis, Module 1: Prevention. Tuberculosis Preventive Treatment, 2020.
- WHO Consolidated Guidelines for Tuberculosis, Module 5: Management of Tuberculosis in children and adolescents
- Rapid Communication on Updated Guidance on the Management of Tuberculosis in Children And Adolescents. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.

- *The Gambia, national guidelines for the management of Tuberculosis , Fifth Editiion, June 2022*
- *Diagnostic Atlas of Intrathoracic Tuberculosis in Children: A guide for low income countries, 2003*
- *The Gambia national guidelines for the programmatic management of drug resistant tuberculosis*
- *Tuberculosis Preventive Therapy in the Gambia; the national Leprosy and Tuberculosis control program, Ministry of Health, The Gambia.*

ABBREVIATIONS

ABC	Abacavir
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
AZT	Zidovudine
BCG	Bacille Calmette-Guerin
CBC	Complete Blood Count
CPT	Co-trimoxazole Preventive Therapy
CXR	Chest X-ray
DHIS2	District Health Information Software Version 2
DR-TB	Drug-resistant Tuberculosis
DST	Drug Susceptibility Testing
E	Ethambutol
EST	Erythrocyte Sedimentation Rate
EFV	Efavirenz
EPTB	Extra Pulmonary Tuberculosis
FDC	Fixed-dose Combination
H	Isoniazid
HIV	Human Immune deficiency Virus
ICF	Intensified Case Finding
INH	Isoniazid
TPT	Isoniazid Preventive Therapy
IRIS	Immune Reconstitution Inflammatory Syndrome
LPV	Lopinavir
LPV/r	Lopinavir/ritonavir
MDR TB	Multi Drug Resistant Tuberculosis
Mtb	Mycobateria Tuberculosis
NLTP	National Tuberculosis and Leprosy Program
NVP	Nevirapine
PAS	P-aminosalicyclic Acid
PI	Protease Inhibitor
PLHIV	Person Living with HIV
PMTCT	Prevention of Mother-to-Child Transmission (of HIV)
PTB	Pulmonary Tuberculosis
R	Rifampicin
RTV	Ritonavir
TB	Tuberculosis
TB/HIV	HIV-related Tuberculosis
TDF	Tenofovir Disproxil Furmarate
3TC	Lamivudine
TST	Tuberculin Skin Test
WHO	World Health Organization
Z	Pyrazinamide

DEFINITIONS

TERM	DEFINITION
Adolescent	A person aged between 10 and 19 years.
Child	A person aged less than 15 years (0 – 14 years).
Infant	A child under 1 year of age.
Neonate (or newborn)	An infant under 28 days of age.
Child/adolescent with bacteriologically confirmed TB	A person from whom a biological specimen is positive by smear microscopy, or culture or WHO approved rapid diagnostic (such as GeneXpert® or TrueNat®).
Child/adolescent with clinically diagnosed TB	A person 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. Includes X-ray and histological diagnosis.
Household contact	A person who shared the same enclosed living space as the index case for one or more nights or for frequent or extended daytime periods during the 3 months before the start of the current treatment episode.
Close Contact	Any person who does not live in the same household with but is exposed to the index patient for long periods through shared spaces e.g. workplace, places of workship or places for social gatherings during the 3 months before the start of the current treatment episode.
Contact identification and prioritization	Includes an interview with the index case to obtain the names and ages of contacts and an assessment of contacts' risk for having (generally based on the presence of symptoms compatible with TB) or developing TB, to determine those for whom clinical evaluation is indicated.

TERM	DEFINITION
Contact Screening (Contact Investigation)	A systematic process for the diagnosis or exclusion of active TB among contacts. Clinical evaluation is undertaken if the results of contact identification and prioritization indicate a risk for having or developing TB.
Extra Pulmonary Tuberculosis	Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs.
Lost to Follow-up	A child diagnosed with TB who did not start treatment or whose treatment was interrupted for two or more consecutive months.
Multi-Drug Resistant TB	Resistance to Rifampicin and Isoniazid.
New Patient	A child or adolescent who has never been treated for TB or has taken anti-TB medicines for less than 1 month.
Preventive Therapy	Treatment offered to household or close contacts of an index TB patient to reduce the risk of developing TB.
Child with Presumptive Tuberculosis	A child or adolescent who presents with symptoms and signs suggestive of TB.
Previously Treated Patient	A child or adolescent who has received 1 month or more of anti-TB medicines in the past.
Pulmonary Tuberculosis	Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree.
Relapse Patient	A child or adolescent who has previously been treated for TB, was declared cured or treatment completed at the end of their most recent course of treatment and is now diagnosed with a recurrent episode of TB.
Reverse Contact Investigation (Source case investigation)	Contact investigation undertaken among household members of TB infected children, with the goal of identifying and if necessary, treating the source case and identifying any others they may have infected.

TERM	DEFINITION
Source Case/ Index Case	A child or adolescent with infectious TB (usually bacteriologically confirmed) who transmits infection to one or more other individuals.
TB infection	Infection with mycobacterium tuberculosis may occur following exposure to a patient diagnosed with TB, particularly one with bacteriologically confirmed TB.
TB Disease (Active TB)	Refers to illness that occurs in someone infected with Mycobacterium tuberculosis and is characterized by clinical signs and symptoms, with or without laboratory or radiographic evidence.

RATIONALE

Tuberculosis in children remains under diagnosed and under reported mainly due to lack of clinical guidelines and low confidence among healthcare workers to make a clinical diagnosis of TB in children:

The development of these guidelines was necessary following the recent WHO recommendations on childhood TB diagnosis and treatment and on the increased number of stakeholders involved in Tuberculosis control including clinicians, public health workers, trainers, health planners and civil society organizations.

The guidelines highlight the need to obtain a sample in all children with presumptive TB and introduce the use of alternative samples other than sputum to help clinicians achieve this. The guidelines also emphasize the use of WHO approved molecular tests e.g., the GeneXpert test (Xpert MTB/RIF) as the recommended initial diagnostic test for all children with presumptive TB.

The guidelines further present a clinical algorithm that can be used by clinicians in making a diagnosis of TB in children using symptoms, signs suggestive of TB, and chest radiography (where available). This guidance is intended to enhance the clinician's confi dence in making a clinical diagnosis of TB in children specifically in those children with a negative diagnostic test result (GeneXpert test, smear microscopy or culture) result.

New international recommendations for the TB treatment regimens in children have been adopted. Significant to note is that some children who are newly diagnosed with TB can be treated with a shorter four-month regimen consisting of four drugs in the intensive phase (Rifampicin/ Isoniazid/ Pyrazinamide/ Ethambutol) and two drugs in a shorter two months continuation phase (Rifampicin/ Isoniazid).

These guidelines also emphasize the need for contact investigation of persons in close contact with patients (including children) diagnosed with TB in order to identify those who have undiagnosed TB and those in need of Isoniazid Preventive Therapy.

The guidelines also include new guidance on recording and reporting of data on TB in children in order to adequately track the national response for this group of individuals.

With successful implementation and integration of these guidelines across the different health care points, it is hoped that children with or at risk for TB will promptly be identified, evaluated, treated, recorded, and reported.

SUMMARY OF KEY RECOMMENDATIONS

Chapter 2: Assessment of Children and Adolescents for Tuberculosis

- All children and adolescents presenting at the different health care points should be screened for TB using the TB Intensified Case Finding Guide.
- All children and adolescents with presumptive TB should have a detailed history taken including history of TB contact.
- All children and adolescents with presumptive TB should have a detailed clinical examination conducted for signs suggestive of TB and its complications.
- All children and adolescents with presumptive TB should have the available relevant investigations conducted.

Chapter 3: Diagnosis of Tuberculosis in Children and Adolescents

- The GeneXpert test is the recommended initial TB diagnostic tool for children and adolescents with presumptive TB. (Smear microscopy may be used in health facilities without onsite access to GeneXpert machine and a second sample referred for GeneXpert test).
- The recommended diagnostic algorithm for TB in children and adolescents should be used to guide the clinical diagnosis of TB.

Chapter 4: Management of Tuberculosis in Children and Adolescents

- Children and adolescents aged between 3 months and 15 years with non-severe TB and without suspicion or evidence of rifampicin resistance should be treated with a four month treatment regimen consisting of 4 medicines (Rifampicin, Isoniazid, Pyrazinamide and Ethambutol) in the intensive phase and 2 medicines (Rifampicin and Isoniazid) in a shorter two-month continuation phase according to the recommended dosages.
- The duration of TB treatment in children and adolescents is dependent on the disease classification.
- Children and adolescents who are started on TB treatment should be monitored bi-weekly (every two weeks) during the first month of treatment and thereafter, every month until treatment completion.

Chapter 5: Management of Tuberculosis in HIV Infected Children and Adolescents

In addition to the TB treatment, all children who are co-infected with TB and HIV should receive the comprehensive HIV care package including ART, CPT, nutrition and psychosocial support.

Chapter 6: Management of Drug Resistant Tuberculosis in Children and Adolescents

- Children and adolescents who are retreatment, TB cases and children adolescents who are close contacts of known or suspected MDR TB patients are at risk of MDR TB and should be evaluated for it.
- The sensitivity pattern of the source case should guide the regimen build up for children and adolescents diagnosed with MDR TB except for those who are bacteriologically confirmed.
- Children and adolescents diagnosed with MDR TB will be treated for a total of 20 months.

Chapter 7: Prevention of Tuberculosis in Children and Adolescents

- BCG vaccine should be given to all new born babies.
- All under five contacts of PTB cases without active TB disease should be initiated on TB preventive therapy (EXCEPT contacts of MDR TB cases).
- All children living with HIV without active TB disease are eligible for TPT irrespective of TB exposure. HIV positive children age less than 12 months receive TPT only if there is a history of contact with an active PTB case and active TB has been excluded.
- TB contact screening is indicated for the following categories of index TB cases: Bacteriologically confirmed PTB, MDR-TB or XDR-TB (proven or suspected), Person living with HIV, Child <5 years of age.

Chapter 8: Integration of Tuberculosis Services into Rroutine and Other Healthcare Services

TB services including screening, diagnosis, treatment and prevention should be integrated into the routine and other health care services in order to improve TB care service delivery.

Chapter 9: Recording and Reporting for Childhood and Adolescent Tuberculosis

All children and adolescents initiated on TB treatment and TPT should be recorded and reported through the recommended MoH TB reporting system.

CHAPTER 1:
INTRODUCTION

1.1 The Global Burden of Tuberculosis in Children and Adolescents

It is estimated that there were 1.3 million new cases of Tuberculosis (TB) among children (0 - 14 years) accounting for 12% of the total new TB cases (10.6 million total new TB cases) worldwide in 2022. Of the 1.3 million deaths due to TB in the same year, 214,000 deaths were among children.

1.2 The Burden of TB Among Children and Adolescents in the Gambia

In 2012, The Gambia conducted its first ever nationwide population-based TB prevalence survey which showed a TB prevalence of 128/100,000 populations. This translates into an equivalent of 3900 TB cases each year. Of these, an estimated 585 are children under 15 years. In 2022, the Gambia notified an estimated 180 cases of TB in children under 15 years (7% all notified TB cases) translating into a treatment coverage of only 31% for this age-group. In the same year, only 5.1% of all household contacts were started on TB preventive therapy.

1.3 Transmission of TB

TB is mainly caused by, Mycobacterium tuberculosis (Mtb), a bacteria which is transmitted through the air. TB is spread to children by individuals who have TB of the lungs. When such individuals cough, sneeze, laugh or sing, they release mucous droplets containing the TB bacteria in the air. These droplets may then be breathed in by the children who are in close contact with them. TB transmission is more intense in crowded, poorly ventilated spaces with little anmbient sunglight. Such conditions increase the likelihood of children inhaling the bacilli present in the air.

1.4 Pathogenesis of TB in children and Adolescents

When the TB bacteria are breathed in by the child, they may be deposited in the smallest air sacs of the lungs. In here the bacteria are attacked by the body's immune cells causing a local immune reaction that causes a lesion called the Ghon focus. Some of the bacteria are carried by immune cells called macrophages through the lymphatic vessels to the lung lymph nodes causing them to enlarge. The combination of enlarged lymph nodes and the Ghon fo- cus is referred to as the primary Ghon complex. If the immune system fails to stop the TB bacteria from multiplying, TB disease develops and this is called primary TB disease.

Children who develop TB disease usually do so within two years after exposure and most (90%) within a year. On the other hand, if the immune system manages to stop the bacteria from multiplying, the child does not develop TB disease but rather the bacteria remain dormant within the body. This is called TB infection (also known as Latent TB) and in this case there is no sign of TB disease.

Many factors influence the progression of infection to diseases. Among children, the most important factor is age. Younger children (less than 5 years), particularly those who do not received BCG vaccination are more likely to progress to active TB and have severe forms of TB than older children. Children with immunosuppressive conditions e.g. HIV, diabetes, severe malnutrition and those on cancer chemotherapy are also more likely to progress to active TB disease.

CHAPTER 2:
ASSESSMENT OF CHILDREN AND ADOLESCENTS FOR TUBERCULOSIS

TB commonly affects the lungs but can affect other parts of the body including lymph nodes, brain, abdomen, bone, kidneys, and skin. The presentation of TB in older children is quite classical and consists of the cardinal signs of cough, evening fevers and night sweats. However, the presentation in very young children and those who have HIV may be atypical without the classical signs and symptoms of HIV.

Assessing a child for TB involves the three following steps:

i. Screening the child for TB. Screening for TB in children involves taking a detailed clinical history, particularly a history of TB treatment.
ii. Conducting a detailed clinical examination.
iii. Conducting relevant investigations.

2.1 Screening the Child for TB and Taking a Detailed History

The Intensified TB Case Finding (ICF) Guide is used to screen all children for symptoms suggestive of TB (Figure 1). In primary care settings, the ICF guide should be used as a job aide at all healthcare points such as: general out-patient department, TB clinic, HIV/ART clinic, in-patient ward nutrition unit, immunization clinic, young child clinic, ante-natal clinic (ANC), post-natal clinic (PNC).

Tuberculosis cases are most frequently found among the following:

1. Patients who present themselves on their own initiative at a health facility with symptoms suggesting tuberculosis.
2. Those (especially children and young adults) living in the same household with bacteriologically-positive patients.
3. Those infected with HIV especially those in stage 3 & 4.
4. Those found to have an abnormality that has the appearance of tuberculosis when a chest radiograph has been taken for clinical investigation of a sick patient.

Children and adolescents infected with HIV should be screened for TB at each clinic visit because they have an increased risk of TB exposure, TB infection, TB disease, and TB related deaths.

TB screening should particularly be emphasized for the following categories of children and adolescents because they have an increased risk for TB:

i. Children and adolescents living in crowded settings e.g. urban slums.
ii. Children and adolescents with a history of household or close PTB contact.
iii. Children aged under 5 years of age.
iv. HIV infected children and adolescents.
v. Children and adolescents who have other immunosuppressive conditionse.g. diabetes, cancer and malnutrition.
vi. Children who have recently suffered from measles.
vii. Children and adolescents who did not receive BCG.

Figure 2.1: Intensified TB Case Finding Guide

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INTENSIFIED TB CASE FINDING GUIDE

Use the Guide to Identify Presumptive TB
In HIV Clinic, OPD, IPD and Congregate Settings

This guide should be administered by either a healthcare provider or lay provider at the health facility

STEP 1: The Person Conducting the Assessment Asks the Following Questions

1.	Has the patient been coughing for 2 weeks or more? ***(for known HIV patients, assess cough regardless of duration).***	Yes	No
2.	Has the patient had persistent fevers for 2 weeks or more?	Yes	No
3.	Has the patient had noticeable weight loss? ***(more than 3kgs)***	Yes	No
4.	Has the patient had excessive night sweats for 3 weeks or more? ***(for adults)***	Yes	No
5.	Has the child had poor weight gain in the last one month*? ***(Ask for children <5years)***	Yes	No
6.	Has the child had contact with a person with Pulmonary Tuberculosis or chronic cough? ***(Ask for children <5years)***	Yes	No

** Poor weight gain (weight loss or very low weight (weight-for-age less than -3 z-score), or underweight (weight-for-age less than -2 z-score), or confirmed weight loss (>5%) since the last visit or growth curve flattening.*

STEP 2: Guide for Actions to Take

1. ***If YES to question 1,*** request for sputum test and refer to clinician for further investigations. Direct the patient to a designated area for people with chronic cough.
2. ***If NO to question 1*** and ***YES to any other question***, refer to clinician for further investigations.
3. ***If NO to questions,*** repeat TB Assessment at subsequent visits.

* ***For children who are unable to produce sputum, refer to clinician for further investigations.***

STEP 3: Record of Information at Health Facility Level

1. If you are in a clinic attending to patients enrolled in HIV care record, this information on the comprehensive ART card, this information should be transferred to the Pre ART or ART register.

2. If you are in a clinic setting (not attending to patients enrolled in HIV care e.g OPD) and a presumptive TB case is found, record the information in a resumptive TB register.

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2.1.1 Presentation of TB in Children

Common presentation of pulmonary TB in adolescents and older children includes presence of any one of the following symptoms:

i. Persistent cough for 2 weeks or more (cough of any duration in HIV infected children).
ii. Persistent fever for 2 weeks or more.
iii. Excessive night sweats.
iv. Haemoptysis (coughing out blood).
v. Chest pain

In children below 5 years, common presentations of TB include:

i. Persistent cough for 2 weeks or more (cough of any duration in HIV infected children).
ii. Persistent fever for 2 weeks or more.
iii. Weight loss or Poor weight gain for 1 month or more.
Poor weight gain is defined as weight loss, or very low weight (weight-for-age less than -3 z- score), or underweight (weight-for age less than -2 z-score), or confirmed weight loss (>5%) since the last visit, or growth curve flattening, or Mid Up- per Arm Circumference (MUAC) measurement in the red colour code. It is important to look at the child's health card with focus on the growth curve for the children under the age of five years.
iv. History of a close or household contact with an individual who has PTB. Infants and young children are more likely to be exposed to TB while at home.
v. Painless large swellings in the neck or armpit
vi. Reduced playfulness or decreased activity in the presence of any of the above symptoms sweats.

In newborns, symptoms of TB are often non-specific and may include:

i. Lethargy
ii. Poor feeding
iii. Low birth weight
iv. Non-resolving pneumonias

In newborns the most important clue for active TB disease is a maternal history of TB or HIV infection. Critical points in the maternal history include non-resolving pneumonias, contact with an index patient with TB or recent initiation of TB treatment.

Extrapulmonary TB (EPTB)

In addition to the symptoms mentioned above, children and adolescents with extrapulmonary TB often present with other symptoms depending on the site of the disease as shown in Table 2.1.3.

2.2 Conducting a Detailed Clinical Examination

All children with presumptive TB should have a detailed clinical examination conducted for signs suggestive of TB and its complications. There are no spe- cific signs that confirm a diagnosis of TB in children however there are certain features that are suggestive of TB. (Table 2.1.1).

Table 2.1: Clinical Features Suggestive of TB in Children

Site of TB	Clinical examination findings (The child can have any of the following)
Pulmonary Tuberculosis (The chest fndings are usually normal and therefore normal chest findings does not exclude TB)	• Clinical evidence of weight loss or poor weight gain as above • High temperature • Increased respiratory rate • Breath sounds and percussion note usually normal • Lymphadenopathy Neonates • Respiratory distress • Non-resolving pneumonia • Hepatosplenomegaly • Lymphadenopathy • Abdominal distension with ascites • Clinical picture of *"neonatal sepsis"*

Children and adolescents may also present with atypical signs of pulmonary TB which are outlined in the table below.

Table 2.1.2: Atypical Presentation of Pulmonary Tuberculosis

Acute severe pneumonia	• Occurs especially in infants and HIV-infected children. • Fast breathing and chest in drawing. • Poor response to antibiotic therapy.
Wheeze	• Asymmetrical and persistent wheeze due to airway compression by enlarged tuberculous hilar lymph nodes. • Not responsive to bronchodilator therapy.

Children and adolescents presenting with extrapulmonary TB will have varying clinical features depending on the site of the disease.

Table 2.2: Presentation of Extrapulmonary Tuberculosis

Site of TB	Clinical Examination Findings (The child can have any of the following)
TB Adenitis	• Asymmetrical non-tender lymph node enlargement • +/- Discharging sinus • Most commonly in neck area
Pleural TB	• Dullness on percussion and reduced breath sounds • Chest pain
TB Meningitis (Usually occurs in children < 5 years of age)	• Irritability/abnormal behaviour • Lethargy • Reduced level of consciousness • Convulsions • Neck stiffness • Bulging fontanelle • Cranial nerve palsies
Miliary TB (Usually occurs in children < 5 years of age)	Non specific clinical examination findings such as: • Lethargy • Severe wasting
Abdominal TB (Usually occurs in children > 5 years of age)	• Abdominal swelling with ascites • Abdominal masses
Spinal TB (Usually occurs in children > 5 years of age)	• Deformity of spine • Lower limb weakness • Paralysis • Inability to walk
TB bone and joint (Usually occurs in children > 5 years of age)	• Swollen end of long bones (usually painless) with limi- tation of movement • Unilateral effusion of usually knee or hip
Pericardial TB (Usually occurs in children > 5 years of age)	• Cardiac failure • Distant heart sounds • Apex beat difficult to palpate

2.3 Conducting Relevant Investigations

Investigations for the diagnosis of TB include laboratory, radiological and blood chemistry investigations.

a. Laboratory investigations e.g., sputum microscopy, GeneXpert testing and culture are able to confirm the presence of mycobacteria and are used as confirmatory tests for TB.
b. Radiological tests e.g. CXR
c. Blood chemistry tests e.g. CRP
d. Test for latent TB e.g. TBSTs and IGRA

   Radiological, and blood chemistry tests and tests for latent TB are used as supportive investigations to aid in the clinical diagnosis of TB. Other supportive tests used to

Investigations for the Diagnosis of PTB in Children

i. Although bacteriological confirmation of TB is not always possible, particularly in children, it should be sought for whenever possible.
ii. Sputum is the main sample used for the laboratory investigation of PTB for the majority of patients.
iii. Due to difficulties obtaining sputum samples, in children and persons living with HIV, the WHO has recommended alternative non-sputum based tests for diagnosis of TB in these populations. Among children, GeneXpert testing on stool is currently recommended by the WHO as an alternative to sputum testing while among persons with advanced HIV disease, testing of urine with LAM is recommended as an alternative route for diagnose TB.

2.3.1 Collection of Specimen for Diagnosing Pulmonary TB

The laboratory diagnosis of TB begins with the collection of a quality clinical specimen. In the majority of older children this is expectorated sputum. For younger children who are unable to expectorate sputum, clinical specimen can be obtained by other means e.g. gastric aspiration, sputum induction and nasopharyngeal aspiration (collection of samples from the upper part of a child's throat). These procedures require specialized training and are described in detail in Appendix A. The methods used to obtain sputum from children include Sputum collection. This applies to older children who are able to cough and produce sputum on their own.

Collection of Specimen for Diagnosing Pulmonary Tuberculosis

The laboratory diagnosis of TB begins with the collection of a quality clinical specimen. In the majority of patients (adults and older children) this is expectorated sputum. For younger children who are unable to expectorate sputum, clinical specimen can be obtained by other means e.g. gastric aspiration, sputum induction and nasopharyngeal aspiration (collection of samples from the upper part of a child's throat). These procedures require specialized training and are described in detail in Appendix A.

Sputum Collection

While collecting sputum by expectoration, patients should be counseled and advised properly on how to produce quality sputum specimens. To minimize the number of patient visits, only two sputum specimens should be collected using the 'spot-morning' approach. The first specimen should be collected at the time when the patient first presents to the clinic (spot sputum collection). During the patient's visit, a second labeled sputum container should be given to the patient so that they collect a second sputum sample early the next morning his or her sputum can be collected the next morning.

Before Collecting Sputum

i. Patients should be well informed about the diagnostic process and the reason for collecting sputum.
ii. Sputum collection should be done in the open air (or ventilated room) away from other people to avoid infecting them.
iii. Patients should clean their mouths if they have been eating.
iv. A health worker should demonstrate how to collect a good quality sputum.
v. Before handing the sputum container to the patient, the healthcare worker should clearly label the sputum container with the patient's name and the date of collection.
vi. The healthcare workers should also fill out the laboratory request form out accurately and completely.
vii. Make sure that the patient's details have been recorded in the TB presumptive register.

How to collect a quality sputum specimen

- Tell the patient that the best specimens come from deep inside the lungs after coughing, not from saliva.
- Demonstrate how to cough deeply.
- Ensure that no one is standing in front of patient producing sputum.
- Instruct the patient to:
  a. Inhale deeply 2 to 3 times and to breathe out hard each time,
  b. Cough deeply from the chest.
  c. Place the open container close to the mouth to collect the sputum, and
  d. Screw the lid tightly.
- Avoid contaminating the outside of the sputum container with sputum. If the outside is contaminated, discard the container and repeat the collection with a fresh container.
- The volume of the sputum should be about 3 to 5 ml.

After Collecting a Sputum Specimen

i. The patient should check that the container is firmly closed, should hand their specimen to the laboratory personnel and should then wash their hands.
ii. The healthcare workers on receiving the sputum samples should ensure that the sputum sample is clearly labelled.

Laboratory personnel should perform sputum smear/Xpert MTB/RIF assay examination the same day samples are submitted, aiming to return a result to the patient within 48 hours.

2.3.2 Transportation of Sputum Specimen

i. Sputum specimens which need to be sent to another laboratory for microscopy of GeneXpert testing should be sent with 24 hours to ensure examination is done within 48 hours of collection.
ii. Sputum specimens for culture, should be stored preferably in a refrigerator or in a cool, safe and dark place and sent to the culture laboratory within 4 days.
iii. Sputum specimen should be packed carefully, preferably in a transport box and accompanied with a laboratory request form.
iv. cold chain should be maintained throughout the transportation process, especially when sending samples for culture.
v. All specimen referred for GeneXpert testing and culture should be send through the national sample transportation network.

2.4 Laboratory Tests for the Diagnosis of PTB in Children

The following tests can therefore be performed on the sputum sample:

i. The GeneXpert (Xpert MTB/RIF) Test

To improve the laboratory confirmation of TB, the NLTP has introduced the new, rapid molecular test (Xpert MTB/RIF), that detects the DNA of the TB bacteria and availas results on the presence of the TB bacteria and rifampicin resistance within 2 hours.

The MOH (NTLP) now recommends the GeneXpert test as the initial TB diagnostic tool for all patients with presumptive TB. The GeneXpert test can be performed on expectorated sputum, induced sputum, nasopharyngeal aspirates and stool. The GeneXpert test is only used for diagnosis and NOT for follow up of patients on TB treatment. Smear microscopy should therefore be used as the follow up test for patients on TB treatment.

In places where the Xpert services is not readily available on the same day, sputum microscopy may be used as a primary diagnostic test for TB in the interim to avoid diagnostic delay.

Where there are limitations, GeneXpert services should be prioritized to the following groups;

- PLHIV presenting with symptoms of TB (only symptom-positive cases after screening is done).
- Children presenting with symptoms of TB (if sputum or any other specimen can be obtained).
- HCWs presenting with symptoms of TB or those newly diagnosed with sputum smear+ TB.
- Patients whose sputa remain + at the end of the intensive phase of Rx (probable Rx failures) or the end of the 5th month of TB treatment (Rx failure).
- Patients previously treated for TB who have a high possibility of drug resistance (return after loss to follow up, relapses).
- Those with a smear negative AFB result who still show symptoms of TB after one week of administration of broad-spectrum antibiotics.
- Contacts of known RR/MDR-TB patients presenting with symptoms of TB.

It is important to note that the absence of bacteriologic confirmation of TB should not delay treatment of a TB presumptive case with a history and clinical findings compatible with TB disease, especially in seriously ill patients, children and People Living with HIV/AIDS.

In some instances, and particularly in children, a culture or molecular test may be negative even though the patient clinically has TB disease (on the basis of clinical, radiographic and histopathology findings or response to anti-TB treatment).

ii. Smear Microscopy

Smear microscopy may be used as the initial diagnostic test in health facilities that do not have onsite access to a GeneXpert machine and a 2nd sample should be referred for a GeneXpert test

Smear microscopy identifies acid fast bacilli (AFB) on microscopic examination of stained sputum smears.. Two staining methods can be used to identify AFB: Ziel-Neelsen staining (ZN) or fluorescent auramine staining (LED FM). Smear microscopy has good specificity but very low sensitivity in detecting TB bacilli in patients with low bacillary load in sputum. It can only allow the detection of TB bacilli when sputa contain 5,000 to 10,000 bacilli per mL of sputum.

The Light-emitting emitting diode (LED) microscopy saves time required to perform a test and has added sensitivity of 10% over ZN technique. To ensure quality of TB diagnostic services, all AFB microscopy diagnostic centers should be quality assured as per the national AFB quality assurance protocol. In the Gambia iLED FM is the tool use for TB smear microscopy in all the diagnostic centers and ZN is only used at the national reference laboratory for AFB confirmation during culture.

iii. TB Culture

Given that TB in children is associated with low bacillary load, sputum culture may be requested for in children with negative GeneXpert or smear micros- copy test results. In addition culture and drug susceptibility testing should be requested/done in children who are at risk for Multi Drug Resistant (MDR) TB. TB culture and drug susceptibility testing is the gold standard test for bacteriologic confirmation of TB diagnosis. TB culture can very low bacilli in sputum and is therefore an important tool in patients with paucibacillary tuberculosis, such as HIV positive patients and children. TB culture can be done on solid or liquid culture.

Solid culture

Löwenstien-Jensen (LJ) media is a culture media with ease of preparation, low cost, and low contamination rate. Solid culture may take several weeks, 21-42 days, to detect growth and produce results. It is the gold standard for diagnosis of MTB.

Liquid culture

The liquid culture technique used in The Gambia is Mycobacterial Growth Indicator Tube (MGIT) 960 system. It is highly enriched media for growing mycobacteria with added 10 % more sensitivity than LJ media, and can produce positive results in about two weeks. However, the method is prone to contamination and is expensive.

2.5 Drug Susceptibility Testing (DST)

Is a technique for screening for susceptibility of the TB bacilli to various Anti-TB drugs using either phenotypic or genotypic techniques:

i. Phenotypic DST diagnostic methods

Phenotypic DST of M. tuberculosis may be determined either by observation of growth or metabolic inhibition in a medium containing anti-tuberculosis drug. Phenotypic DSTs require a positive culture (pure MTB isolate) before testing for drug susceptibility can be performed.

Phenotypic DSTs can be performed for the following drugs: Rifampicin, Isoniazid (high and low), Ethambutol, Pyrazinamide, and Streptomycin for 1st line of anti-TB drug and Amikacin, Kanamycin, Capreomycin, Ethionamide, Ofloxacin, Moxifloxacin for 2nd line anti- TB drugs

ii. Line Probe Assay (LPA):

Line Probe Assay is a rapid DST technique using molecular technology that shortens the time required to get result to within two days. It detects specific mutations on the resistance determining genes of the two most potent first line anti-TB drug (Isoniazid and Rifampicin) as well as fluoroquinolones and injectable core second line TB drugs. LPA can be performed directly from sputum specimen(if the patient has sputum positive TB) or from culture isolates. Firstline and second line LPA services in the The Gambia are available at national reference laboratory

Indications for sputum culture and drug susceptibility testing include:

- To diagnose paucibacillary disease in patients with presumptive TB (e.g. HIV positive patients) who have two negative smears or a negative GeneXpert test.
- To test for drug resistance in patients with presumptive TB and a history of previous TB treatment (interruption, failure, relapse) OR patients who remain smear positive at the end of the intensive/ continuation phase of treatment OR those who fail to improve clinically during treatment.
- To test for drug resistance in people at high-risk of DR-TB such as MDR and XDR-TB contacts, health care personnel and prisoners.
- To establish susceptibility or resistance to other drugs in patients with rifampicin resistance on GeneXpert testing cases diagnosed as rifampicin resistant on GeneXpert for susceptibility testing of other drugs
- In unusual cases where Rifampicin is susceptible using Xpert and the patient is still failing treatment and treatment adherence is good and thus resistance to drugs other than Rifampicin is presumptive.
- To monitor treatment response in DR-TB patients and to assign treatment outcomes in these patients.

Children with unexplained finding on CXR should submit sputum for confirmatory test preferably by X-pert MTB/RIF test. All children diagnosed with TB should undergo drug resistance screening test at least for rifampicin at baseline using rapid DST technique preferably by Xpert or FL-LPA. For all patients with confirmed RR/MDRTB, send sputum for SL-DST using LPA for core second line drugs before or within one week of treatment initiation with DRTB regimen. Patients with rifampicin resistance on Genexpert testing should be confirmed started on second line TB treatment while their results are being confirmed using culture and phenotypic DST. Children with presumptive or confirmed TB should be an HIV test.

2.6 Radiologic Investigations for the Diagnosis of PTB

➲ Chest X-rays

Chest X-ray remains an important tool for diagnosis of PTB in children especially younger children who cannot produce sputum. However, CXR changes are often non-specific and may be completely normal in the HIV-infected patients or malnourished children. Therefore, chest x-ray findings especially in patients with a negative sputum smear should be correlated with clinical findings, history and physical examination.

The following abnormalities on Chest X-ray are suggestive of TB:

i. Enlarged hilar lymph nodes and opacification in the lung tissue.
ii. Widened mediastinum due to enlarged lymph nodes (this is the most common x-ray abnormality in children with TB).
iii. Following dissemination, miliary disease may present as scattered markings across the lung fields on x-ray.
iv. In older children (>5 years), upper lobe cavitation and / or pleural or pericardial effusion may be seen on CXR.

The finding of any of these abnormalities on CXR in a child with no signs of respiratory distress (no fast breathing or chest in-drawing) is supportive of TB.

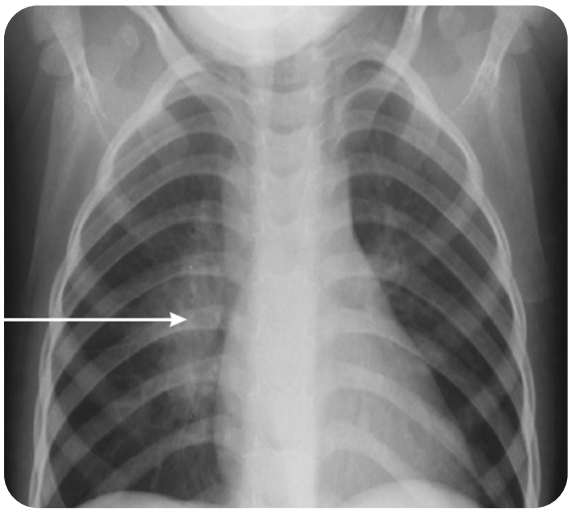
Recently, the increased availability of digital Xrays and computer aided diagnosis (CAD) makes the use of chest Xrays in the diagnosis of TB easier. Although Computer aided diagnosis (CAD) systems detect abnormalities consist with TB and compute an abnormality score ranging from 0-100. Higher abnormality scores indicate greater likelihood of PTB. For programmatic use, often a binary classification or threshold score is used. Scores less than the threshold are interpreted as indicating that PTB has been ruled out, while scores greater than or equal to the threshold indicate a possible diagnosis of PTB. CAD system are currently calibrated to aid the diagnosis of TB in children starting at 4 years. Studies are ongoing to calibrate the software for younger children.

All persons with chest radiographic findings suggestive of TB should submit sputum specimens for microbiological examination.

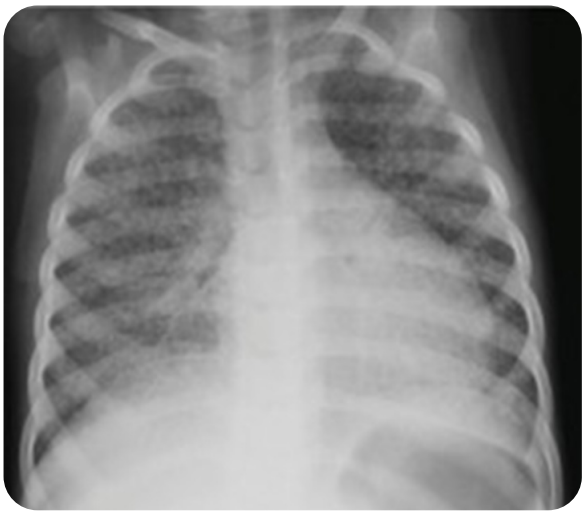
A normal normal x-ray does not rule out TB in a patient with compatible symptoms and clinical findings. Patients with a normal x-ray who remain symptomatic should be referred to a clinician for further investigations.

Examples of Chest X-ray pictures for PTB in children

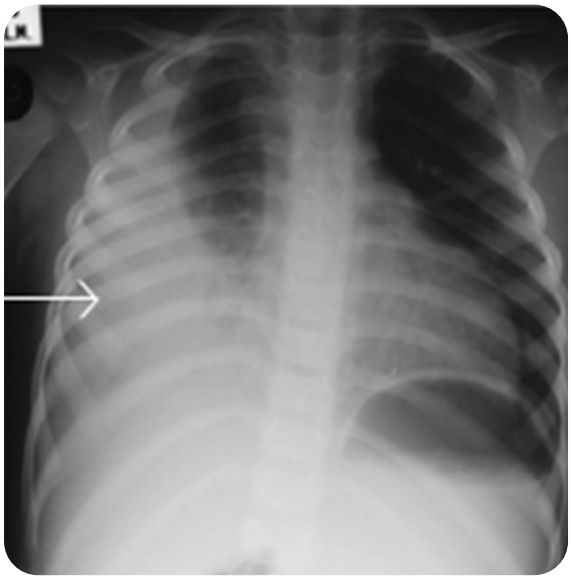
a) Hilar lymph node enlargement



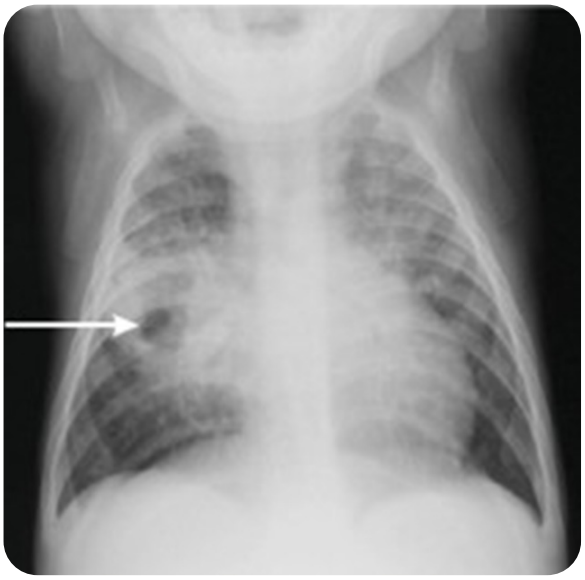
b) Miliary TB Disease



c) PTB with right sided pleural effusion



d) PTB with cavity in the right middle lobe



Additional Supportive Methods for the Diagnosis of TB

➲ HIV test

HIV testing SHOULD be performed for all children with presumptive or diagnosed TB as part of their routine management according to the national guidelines on HIV counselling and testing. This facilitates diagnosis and initiation of appropriate care.

➲ C-reactive protein

C-reactive protein (CRP) is a non-specific acute phase serum protein that is elevated in patients with tuberculosis. Among HIV+ve patients, an elevated sensitivity of 98% and a specificity of 59% for culture positive TB. Therefore among adolescents living with HIV, C-reactive protein using a cut-off of >5 mg/L may be used to screen for TB disease.

➲ TB Specific Skin Test (TBST)

Newer Tuberculosis antigen-based skin tests (TBST) have been developed to measure the cell-mediated immunological response to Mtb specific antigens. These tests are therefore less likely to cross react with BCG making them suitable alternatives in populations with prior BCG vaccination. In addition, the sensitivity and specificity of the new TBST tests is similar to IGRA making them a suitable alternative in low and middle income countries where laboratory infrastructure to support widespread use of IGRA testing is lacking.

Just like the old Mantoux test, the TBST is injected just under the skin. (Appendix B) A positive TST indicates that a person is infected with the TB bacteria but does not necessarily indicate TB disease. If available, the TBST can be used to support diagnosis of TB in children in combination with other diagnostic tools. The TBST is therefore NOT a requirement for the diagnosis of TB. The TBST results are interpreted as follows:

Table 2.3: Interpretation of the TBST

Positive TBST	Patient Characteristic
≥5 mm	HIV infected children and severely malnourished children.
≥10 mm	All other children (regardless of whether they have received a BCG Vaccination or not).

➲ IGRA test

White blood cells from most persons that have been infected with M. tuberculosis will release interferon-gamma (IFN-g). Interferon-Gamma Release Assays (IGRAs) are whole-blood tests that measure a person's immune reactivity to M. tuberculosis by measuring the amount of IFN-g in a person's blood and can aid in diagnosing Mycobacterium tuberculosis infection. IGRAs are advantageous because they require a single patient visit to conduct the test and do not cross react with prior BCG vaccination. However, they require extensive laboratory infrastructure to set up.

2.7 Investigations for the Diagnosis of EPTB in Children

- Since Extra-pulmonary tuberculosis (EPTB) refers to a case of TB (defined above) involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. Diagnosis is based on at least one specimen with confirmed M. tuberculosis or histological or strong clinical evidence consistent with active EPTB, followed by a decision by a clinician to treat with a full course of tuberculosis chemotherapy.

- Patients presumptive to have extra-pulmonary TB should have specimens obtained from the affected site and conduct Xpert MTB/RIF assay and culture. This is important for the early diagnosis of TB and detection of drug resistant TB particularly among high-risk groups. Xpert MTB/RIF test may be conducted on cerebrospinal fluid, pleural biopsies, gastric washings/ lavages and lymph node fine needle aspirates.

- All patients presumptive of EPTB should be offered HIV counseling and testing. If HIV positive, they should start co-trimoxazole preventive therapy (CPT) and antiretroviral therapy (ART) immediately.

- The laboratory and radiologic investigations for EPTB are dependent on the site of the TB and are summarized in the table 3. As mentioned above, all patients with presumptive or diagnosed TB should have HIV testing performed.

- As with pulmonary TB, where available, the GeneXpert test is the initial diagnostic tool for the examination of specimen derived from sites with extrapulmonary TB. When GeneXpert testing is not available, smear microscopy may be used. The table below shows the recommended samples for a GeneXpert test in patients with presumptive EPTB:

Table 2.4: Investigations for the Diagnosis of EPTB in Children

Site of EPTB	Type of Investigation		
	Laboratory Investigations		Radiological Investigations
	Specimen	Tests	
TB adenitis	Lymph node needle aspirate	ZN or FM Microscopy or GeneXpert on fine needle aspiration Histology on lymph node biopsy	N/A
Miliary TB	N/A	N/A	CXR
TB Meningitis	Ce rebrospinal fluid (CSF)	CSF analysis# GeneXpert on CSF	Cranial ultra sound for younger children
Pleural	Pleural	Pleural analysis#	CXR
Abdominal TB	Ascitic Fluid	Ascitic fluid analysis#	Abdominal ultrasound
TB spine	N/A	N/A	Spinal X-ray
Bone and Joint TB (excludes TB spine)	Joint tap	Joint fluid analysis#	X-ray of affected bone and/or joint
TB pericardtis	Pericardial fluid	Pericardial fluid analysis#	CXR Cardiac echo

 # Typical findings: straw coloured fluid, exudates with high protein, white blood cells pre-dominantly lymphocycles on microscopy. Pleural, Ascitic and Pericardial fluid is however not recommended for GeneXpert testbecause of very low yield for bacteriological confirmation of TB using any diagnostic method.

** Referral may be necessary for investigation and laboratory support as well as clinical care.*

If all options for referral have been explored and referral is not possible, start anti-TB treat-ment. Start anti-TB treatment immediately if TBM is suspected.

Key Message

- Clinical assessment for TB in a child includes:
  i. Screening for TB using the ICF guide.
  ii. Detailed history taking including history of TB contact.
  iii. Conducting a detailed clinical examination.
  iv. Conducting relevant laboratory investigations.

- The GeneXpert is the initial diagnostic tool for all children with presumptive TB. However microscopy may be used as the initial diagnostic for facilities that do not have onsite access to a GeneXpert machine and a 2nd sample referred for a GeneXpert test.

- Every child with presumptive or diagnosed TB must have an HIV test performed according to the national guidelines on HIV counselling and testing.

CHAPTER 3:
DIAGNOSIS OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

As seen in Chapter 2, the diagnosis of TB in children is dependent on conducting a wholistic assessment of the child which includes the following steps:

i. Screening the child for TB-including taking a detailed history
ii. Conducting clinical examination and performing relevant investigations.

After these three steps are completed, the healthcare worker must then make a diagnosis of TB either based on the results of laboratory investigations or based on a clinical decision to treat TB. The approach to diagnose TB in HIV infected children is similar to that in HIV negative children.

3.1 Laboratory Diagnosis of TB in Children and Adolescents

As mentioned above, the NLTP recommends the GeneXpert test as the initial TB diagnostic tool for all children with presumptive TB aged 0 – 14 years. All children with a positive laboratory test for TB (smear microscopy or GeneXpert or TB culture) are classified as having bacteriologically confirmed TB and should be started on TB treatment. Children with rifampicin resistance on GeneXpert are considered to have Multi Drug Resistant TB (MDR TB) and should be referred to a health facility with MDR TB treatment site for further management.

3.2 Clinical Diagnosis of TB in Children and Adolescents

A clinical diagnosis of TB in children is dependent on the findings from TB screening, clinical examination, radiology investigations and other tests (HIV test, TST, histology). Once a decision has been made to start TB treatment, such children are classified as having clinically diagnosed TB. The following are scenarios where a clinical diagnosis applies:

i. Children with a negative laboratory test for TB such as negative smear microscopy, negative GeneXpert or negative culture. Majority of the children, especially those under the age of 5 years, will have a negative laboratory test for TB.
ii. Children in whom a sample for TB testing has not been obtained.

Key Message

A diagnosis of TB in children can be made with confidence even when a laboratory test for TB is negative or a sample has not been obtained.

3.2.1 Clinical Diagnosis of TB in HIV Negative Children

Initiate TB treatment for any HIV negative child with presumptive TB who has **TWO or MORE** of the following:

1. **Two or more symptoms suggestive of TB:**
   a. Persistent cough for 2 weeks or more.
   b. Persistent fever for 2 weeks or more.
   c. Poor weight gain for one month or more.

2. **Positive history of contact with a PTB case** (A child with a history of MDR TB contact must be referred to MDR TB treatment site for further evaluation and management)

3. **Any physical signs suggestive of TB such as:**
   a. Severe malnutrition.
   b. Enlarged lymph nodes around the neck or the armpit.
   c. Presence of a swelling on the back bone (Gibbus).
   d. Acute pneumonia not responding to a complete course of appropriate broad spectrum antibiotics.
   e. Persistent wheeze not responding to bronchodilators (usually asymmetrical).
   f. Signs of meningitis in child with symptoms suggestive of TB.

4. **CXR suggestive of PTB such as:**
   a. Miliary picture
   b. Hilar adenopathy
   c. Cavitation

5. **Manotoux ≥ 10mm** in a well nourished child OR ≥ 5mm in a severely malnourished child.

3.2.2 Clinical Diagnosis of TB in HIV Positive Children

Initiate TB treatment for any HIV positive child with presumptive TB who has **ONE or MORE** of the following:

1. **Two or more symptoms suggestive of TB:**
   a. Persistent cough for 2 weeks or more.
   b. Persistent fever for 2 weeks or more.
   c. Poor weight gain for one month or more.

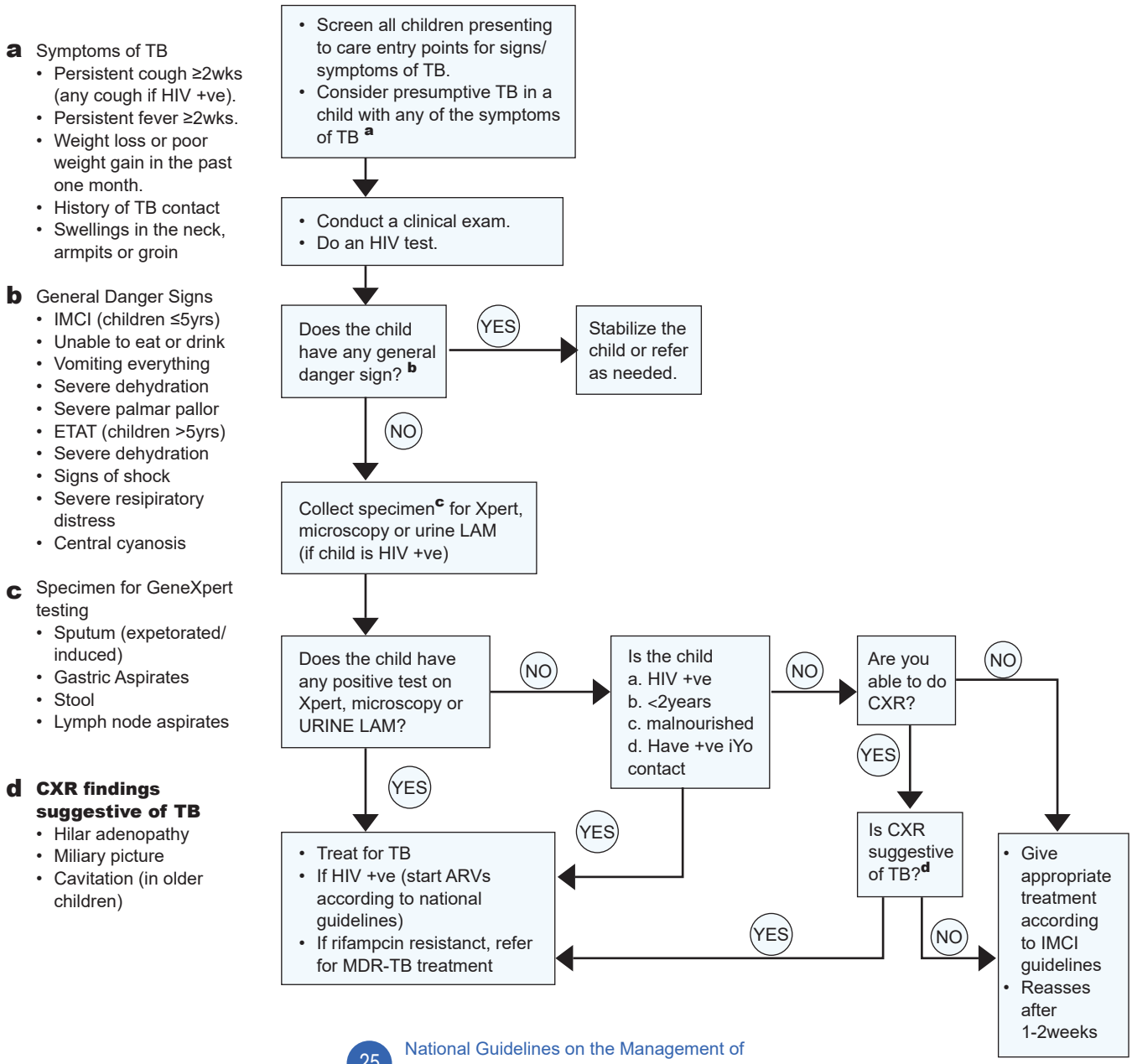
2. **Positive history of contact with a PTB case** (A child with a history of MDR TB contact must be referred to MDR TB treatment site for further evaluation and management).

3. **Any physical signs suggestive of TB such as:**
   a. Severe malnutrition.
   b. Enlarged lymph nodes around the neck or the armpit.
   c. Presence of a swelling on the back bone (Gibbus).
   d. Acute pneumonia not responding to a complete course of appropriate broad spectrum antibiotics.
   e. Persistent wheeze not responding to bronchodilators (usually asymmetrical).
   f. Signs of meningitis in chid with symptoms suggestive of TB.

4. **CXR suggestive of PTB such as:-**
   a. Miliary picture
   b. Hilar adenopathy
   c. Cavitation

5. **Mantoux ≥ 5 mm**

Figure 3.1: Algorithm for the Diagnosis of TB In Children



3.3 Differential Diagnosis of TB in Children

There are other disease conditions that may present like TB in children and are summarized in the table 4.

Table 3.1: Differential Diagnosis of TB in children

Differential Diagnosis for PTB	
Cause	**Clinical Features**
Lymphocytic Interstitial Pneumonitis (LIP)	• Unusual before 1 year of age and mainly in the HIV infected. • Associated with generalized symmetrical lymph adenopathy, clubbing, and parotid enlargement. • CXR: diffuse reticulonodular pattern and bilateral perihilar adenopathy. • No compression of airways
Bronchiectasis	• Productive cough with purulent sputum. • Finger clubbing. • On CXR, there is honeycombing usually of lower lobes. • Usually complicates recurrent bacterial pneumonia, LIP or TB.
Pneumocystis Jiroveci Pneumonia (PJP)	• Common in HIV infected children • Common cause of severe, fatal pneumonia especially in infants. • Persistent hypoxia is common. Unusual after one year of age.
Mixed infection	• Common problem: LIP, bacterial pneumonia, TB • Consider when poor response to first line empiric management.
Kaposi Sarcoma	Uncommon characteristic lesions on skin or palate.
Cardiac failure	Recurrent episodes of cough, difficulty in breathing, fast breathing, edema, failure to thrive.

Differential Diagnosis for Extra-pulmonary Tuberculosis (EPTB) (This varies with the site of TB)	
Cause	**Clinical Features**
Persistent Generalized Lymphadenopathy	Persistent swollen or enlarged lymph nodes >1cm at two or more non-contiguous sites, excluding inguinal, without known cause.
Bacterial or Viral Meningitis	**Signs of meningitis including:** • Irritability/abnormal behaviour • Lethargy, reduced level of consciousness • Convulsions • Neck stiffness • Bulging fontanelle • Cranial nerve palsies
Malignancies	• These may present as lymphomas, Kaposi sarcoma. • Symptoms may include persistent fevers, weight loss, enlarged lymph nodes, masses.

Differential Diagnosis for Neonatal TB	
Cause	**Clinical Features**
Atypical pneumonia	Increased respiratory rate, +/- abnormal breath sounds/ added sounds.
Bacterial or Viral Meningitis	**Signs of meningitis including:** • Irritability/abnormal behaviour • Lethargy, reduced level of consciousness • Convulsions • Neck stiffness • Bulging fontanelle • Cranial nerve palsies

CHAPTER 4:
MANAGEMENT OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

The decision to treat a child should be carefully considered while utilizing the TB diagnosis algorithm for children and once such a decision is made, the child should be treated with a full course of therapy. A trial of treatment with anti-TB medications should not be used as a method to diagnose TB in children.

4.1 Case Definitions and Category for Treatment of Tuberculosis

It is crucial to define TB cases properly for accurate patient registration and selection of treatment regimens. This will in turn aid standardization of data collection and cohort analysis for treatment outcomes. The TB case definitions below are based on the level of certainty of the diagnosis and on whether or not laboratory confirmation is available.

4.1.1 A Case of TB

A case of TB is:

- A patient with pulmonary symptoms having at least one sputum-smear examination positive for acid-fast bacilli (AFB) by either conventional or fluorescent microscopy.
- A patient with M. tuberculosis complex identified from a clinical specimen, either by culture or by a molecular diagnostic method such as Xpert MTB/RIF or
- A patient in whom a health worker or a clinician has diagnosed TB and has decided to treat with a full course of TB treatment.

Cases of TB are also classified according to the:

- Anatomical site of disease,
- Bacteriological results (including drug resistance),
- History of previous treatment, and HIV status.

4.1.2 Anatomical Site of Disease

In general, recommended treatment regimens are similar, irrespective of the anatomical site of disease. Defining the site is important for recording and reporting purposes and to identify the more infectious patients—those with pulmonary involvement (who will be further subdivided by smear status).

➲ Pulmonary Tuberculosis (PTB)

This is a form of tuberculosis that involves the lung tissues. Miliary tuberculosis is classified as pulmonary TB because there are lesions in the lungs as well. A patient with both pulmonary and extra-pulmonary TB should be classified as a case of pulmonary TB.

➲ Extra-pulmonary Tuberculosis (EPTB)

This type of TB involves one or more organs other than the lungs, for example, the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones and/ or meninges.

Both intra-thoracic tuberculous lymphadenopathy (e.g. involving the mediastinal and/or hilar lymph nodes) and tuberculous pleural effusion, when radiographic abnormalities in the lungs are absent, constitute cases of extra-pulmonary TB.

4.1.3 Bacteriological Results (Including Drug Resistance)

Bacteriological status refers to the detection of M. tuberculosis by smear, culture or molecular methods, and to the detection of drug sensitive and drug resistant cases. Any case with a positive bacteriological result (microscopy, culture or molecular method) is defined as a "bacteriological positive TB case". If the bacteriological tests are all negative or not done the case is defined as a "bacteriological negative TB case". TB cases are sub-classified as "smear-positive" or "smear-negative", which is useful because it best correlates with infectiousness.

- **Smear-positive pulmonary TB:** Patient with at least one sputum smear-positive sample (at least one AFB is found in at least one sputum sample: scanty results are considered as positive).
- **Smear-negative pulmonary TB:** Pulmonary TB that are negative for AFB and for whom a clinician prescribes anti-TB treatment.

4.1.4 History of Previous Treatment and HIV Status

TB cases can also be defined according to whether or not a patient has a new infection or has previously received TB treatment. It is important to identify previously treated patients because they are at increased risk of having drug-resistant TB. At the start of treatment specimens for culture and DST should be obtained from all previously treated patients.

Table 4.1: Category of patients based on history of previous treatment

Terminology	Definition
New patient	A patient who have never been treated for TB or have taken anti-TB drugs for less than 1 month.
Transfer-in	A patient who has been transferred from another TB clinic to continue treatment.
Previously treated patients	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 as follows.
Relapse patients	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	Patients who 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	Are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.
TB Patients with unknown previous treatment history	Are patients who do not fit into any other categories listed above.

NOTE

Any person given treatment for TB should be recorded as a case. Incomplete "trial" TB treatment should not be given as a method for diagnosis.

4.2 Treatment of TB in Children

Children should start treatment as soon as a diagnosis of TB is made and treatment given according to the MOH (NLTP) recommended regimens under Directly Observed Therapy (DOT).

4.2.1 Aims of TB Treatment

The aims of treatment of tuberculosis are:

a. Cure the child
b. Prevent complications and TB related deaths
c. Prevent relapse
d. Reduce transmission of TB
e. Prevent the development and transmission of drug resistant TB
f. Promote growth and development

4.2.2 First Line anti-TB Medicines Used for the Treatment of TB in Children

The following first line anti-TB medicines are used for the treatment of TB in children including neonates.

i. Rifampicin (R)
ii. Isoniazid (H or INH)
iii. Pyrazinamide (Z)
iv. Ethambutol (E)

TB that responds to the first line anti-TB medicines is also referred to as drug susceptible TB.

4.2.3 Recommended First Line TB Treatment Regimen for Children With Newly Diagnosed TB

Young children with TB usually have paucibacillary TB disease (TB disease forms with a lower burden of M. tuberculosis than is typical in adult-type cavitary TB disease) and are at lower risk for transmitting TB to other children or adults. School-aged children and adolescents, however, may have bacteriologically confirmed TB, sometimes with cavities on CXR. All children diagnosed with TB disease (irrespective of bacteriological confirmation) should complete treatment with a full course of the appropriate TB regimen. Trials of TB treatment (using response to TB treatment as a diagnostic tool) are discouraged. Once initiated, the TB treatment regimen should be continued until completion, unless an alternative diagnosis has been established. High rates of cure and treatment completion can be achieved in children with TB (85).

4.2.4 Recommended Regimens for Treatment of Drug Susceptible Pulmonary TB in Children

- As in adults, TB treatment in children and adolescents includes a 2-month intensive phase followed by a continuation phase of 2–4 months.
- Infants aged 0–3 months with suspected or confirmed pulmonary TB or tuberculous peripheral lymphadenitis should be promptly treated with the 6-month treatment regimen (2HRZ(E)/4HR). Treatment may require dose adjustment to reconcile the effect of age and possible toxicity in young infants.
- Children and adolescents aged between 3 months and 16 years with non-severe TB (without suspicion or evidence of MDR/RR-TB), should be treated with 4-month treatment regimen (2HRZE/2HR).
- Children and adolescents who do not meet the criteria for non-severe TB should receive the standard 6-month treatment regimen (2HRZE/4HR) or recommended treatment regimens for severe forms of extrapulmonary TB.

Non-severe TB:
Is defined as peripheral lymph node TB; intrathoracic lymph node TB without airway obstruction; uncomplicated TB pleural effusion or paucibacillary, non-cavitary disease confined to one lobe of the lungs and without a miliary pattern.

In adolescents aged 12 years and over, the 4-month isoniazid, rifapentine, pyrazinamide and moxifloxacin (HPZM) regimen may be used in all settings. Table 4.2 shows Pulmonary TB treatment regimens by age group and disease severity.

Table 4.2: Treatment Regimens for Extrapulmonary TB

Age and Type of EPTB	Treatment Regimen	
	Intensive Phase	Continuation Phase
Infants aged <3 months or weighing <3kg		
Peripheral lymph node TB	2HRZE[a]	4HR
Children and adolescents aged 3 months to <16 years		
Peripheral lymph node TB	2HRZE[a]	2HR
Adolescents aged >16 years		
Peripheral lymph node TB	2HRZE[a]	4HR
Children and adolescents aged 0 – 19 years		
EPTB[b]	2HRZE	4HR
TBM (strong recommendation)	2HRZE	10HR
Osteoarticular TB[c]	2HRZE	10HR

a *Ethambutol has been included in the first two months of treatment, because the prevalence of HIV among patients diagnosed with TB in The Gambia is >5%*

b *This involves all other forms of EPTB except per lymph node TB e.g. pleural TB, pericardial TB, abdominal TB.*

c *This involves all forms of bone and joint TB including spinal TB.*

4.3 Implementation Considerations for the 4months Regimen

4.3.1 Assessing eligibility for the 4-month regimen

A **In children and adolescents who have undergone bacteriological testing and CXR, a 4-month treatment regimen should be started in children and adolescents meeting all of the following three criteria:**

i. CXR findings consistent with non-severe TB (CXR should ideally be done at baseline) which include:
   - Intrathoracic lymph node TB without significant airway obstruction, or
   - PTB confined to one lobe with no cavities and no miliary pattern, or
   - Uncomplicated pleural effusion (without pneumothorax or empyema)

ii. TB that is negative, trace, very low or low using Xpert MTB/RIF or Ultra, or smear negative (if Xpert MTB/RIF or Ultra not available).

iii. The child or adolescent has mild symptoms that do not require hospitalization.

B **In settings without access to CXR, a 4-month treatment regimen may be implemented in children and adolescents meeting the following criteria:**

i. TB that is negative, trace, very low or low using Xpert MTB/RIF or Ultra, or smear-negative (if Xpert MTB/RIF or Ultra not available) and the child or adolescent has mild symptoms that do not require hospitalization

ii. Isolated extrathoracic (peripheral) lymph node TB, without confirmed or suspected involvement of other extrapulmonary sites of disease; and the child or adolescent has mild symptoms that do not require hospitalizationa.

C **In the absence of both bacteriological testing and CXR, a 4-month treatment regimen may also be started in children meeting either of the following criteria:**

i. Isolated extrathoracic (peripheral) lymph node TB, without confirmed or suspected involvement of other extrapulmonary sites of disease and the child has mild symptoms that do not require hospitalization.

ii. The child has a clinical diagnosis of pulmonary TB and the child has mild symptoms that do not require hospitalizationa.

Mild symptoms that do not require hospitalization means:

- None of the danger or high-priority signs (according to IMCI)
- No asymmetrical and persistent wheezing.
- No signs of EPTB other than peripheral lymph node TB.
- None of the following: SAM, respiratory distress, high fever (over 39°C), severe pallor, restlessness, irritability or lethargy.

4.3.2 Recommended Daily Dosages for First Line anti-TB Medicines in Children

The TB treatment dosage for children is determined by the weight of the child. Therefore all children must have weight measured before treatment is initiated and re-weighed at every visit.

i. Recommended dosages for individual TB medicines by weight

Table 4.3: Recommended Dose of anti-TB Medicines in Children TB Medicine

TB Medicine	Mg/kg/Body Weight (Range)	Maximum Daily Doses
Rifampicin (R)	15 (10-20)	600mg
Isoniazid (H)	10 (7-15)	300mg
Pyrazinamide (Z)	35 (30-40)	
Ethambutol (E)	20 (15-25)	

ii. Recommended dose of anti-TB medicines in children by weight bands

Medicines used for the treatment of TB usually come in combinations referred to as Fixed Dose Com-binations (FDCs). The Gambia currently dispersable fruit flavoured FDC formulations (RHZ 70/50/50 and RH 70/50).

Table 4.4: Recommended dose of anti-TB Medicines by Weight and Using Expected New FDCs

Weight Bands	Intensive Phase		Continuation Phase
	RHZ	E	RH
	75/50/150	100	75/ 50
4-7 kg	1	1	1
8-11 kg	2	2	2
12-15 kg	3	3	3
16-24 kg	4	4	4
25kg and above	Use adult dosages and formulations		

4.4 Adjunct Therapy in TB Treatment

Non anti-TB medicines are usually given as adjunct therapy to the anti-TB medicines mainly to counteract the side effects of anti-TB medicines or TB associated complications. The 2 commonly used medicines are: pyridoxine (Vitamin B6) and prednisolone.

a. Pyridoxine (Vitamin B6):

Isoniazid interferes with the metabolism of pyridoxine leading to its deficiency. Pyridoxine deficiency presents as neuropathy and mainly occurs in HIV positive children and severely malnourished children who should be priotized for it. The recommended dose for pyridoxine is 12.5mg/day for children <5 years and 25mg for children >5 years.

b. Use of Corticosteriods:

Use of corticosteroids e.g. prednisolone is indicated when the TB disease is associated with severe inflammation such as: TB meningitis, TB pericaridits or airway obstruction by enlarged lymph nodes. The dose is 2mg/kg/ day as a single dose for 4 weeks, and then reduced over a period of 2-4 weeks.

c. Use of Nutritional Supplemnts:

Malnutrition results in the reduction of cell-mediated immunity, thereby increasing the risk of diseases such as TB. The catabolic effect of TB disease results in weight loss and wasting, which in turn worsens the malnutrition. Children and adolescents with TB disease frequently present with failure to thrive or weight loss. Severe malnutrition is associated with increased mortality in children and adolescents with TB. Provision of nutritional support to children and adolescents with TB is therefore an integral part of TB treatment, Malnutrition should therefore be managed according to the national guidelines for the management of moderate and severe malnutrition.

4.5 Management of a Child with TB and other Co-Morbidities

i. Liver Disease

Suspect liver disease in a child who has yellow coloration of eyes, abdominal pain, hepatomegaly, vomiting. Refer such a child for further evaluation and management. If the child is already on treatment, stop the treatment and refer.

ii. Renal Disease

Suspect renal disease in a child who has reduced amount of urine, reduced frequency of passing urine, body swelling, and oedema. Refer such a child for further evaluation and management.

4.5.1 Treatment of Children and Adolescents who Have Previously Been Treated for TB (Retreatment cases)

The following are the steps taken when a child presents with a history of previous TB treatment

Table 4.5: Management of Children with Previously Treated TB

A child or adolescent who was previously treated for TB	What to do	Comments
(Relapse, Treatment Failure, Lost to Follow-up)	• Check adherence to previous treatment. • Assess for history of contact with a person who has MDR - TB. • Obtain a sample • Do GeneXpert test to screen for rifampicin resistance.	• If the GeneXpert test is positive and rifampicin sensitive, treat the child with a six month course regimen. • If the GeneXpert test is positive and rifampicin resistant, refer the child to an MDR treatment site for further management. • If the GeneXpert test is negative OR the child is unable to provide a sample and the health worker is unable to obtain sample refer to a higher level facility for further evaluation and management.

4.6 Indications for Referral or Hospitalization of Children with TB

i. Severe forms of TB such as miliary TB with respiratory distress, TB men- ingitis, TB meningitis, TB pericarditis, and TB spine with neurological complications.
ii. Severe malnutrition for nutritional rehabilitation.
iii. Signs of severe pneumonia (i.e. chest in-drawing).
iv. Other co-morbidities e.g. severe anaemia.
v. Severe adverse reactions such as hepatotoxicity.

4.7 Follow-up and Monitoring Children on TB Treatment

It is recommended that all children initiated on TB treatment are reviewed bi-weekly (every two weeks) during the first month of treatment and thereafter, every month until treatment completion. The following are monitored during the follow up period:

i. Clinical Monitoring

a. Nutritional Status

i. **Weight:** Measure the weight of the child on every clinic visit in order to adjust for any change in weight or weight band.

ii. **MUAC:** MUAC is another parameter that can be used to track change in nutritional status while on treatment

b. Symptoms

Ask about presence of TB symptoms at every clinic visit. Most children will start to show improvement within the first 2 – 4 weeks after starting treatment. If a child shows no symptom improvement or worsening symptoms despite adherence to treatment, consider TB treatment failure and also assess for other lung conditions that may present like TB.

c. Adherence

Assess for adherence at each clinic visit by reviewing the TB treatment card. Adolescents are at particular risk for poor adherence and should be helped to adhere to treatment through strategies including their involvement in the treatment plan, identification of a treatment supporter.

d. Side Effects

Assess the child for any side effects at each clinic visit. The side effects of anti TB medicines are similar for adults and children. Once identified, these should be managed appropriately as shown in the table 10.

Table 4.6: Common Side Effects of First Line anti-TB Medicines and Management

Side Effects	Likely Drug(s)	Management
Low appetite nausea, abdominal pain	• Pyrazinamide • Rifampicin	Give drugs with a small meal or just before going to bed.
Joint pains	Pyrazinamide	Give analgesic e.g Paracetamol.
Burning sensation in the feet	Isoniazid	Give Pyridoxine at a dose of 25 - 30 mg/day
Orange/red urine	Rifampicin	Reassure the care giver (and/or older child.
Skin rash	Any first line anti-TB drug	Stop anti-TB drugs, wait for the child to recover, then introduce one drug a time. OR Refer the child

Side Effects	Likely Drug(s)	Management
Jaundice, liver tenderness, hepatomegaly (other causes exclused	Pyrazinamide, Rifampicin, Isoniazid	Stop all drugs once resolved restart the anti-TB drugs OR Refer the child
Mental confusion	Isoniazid, Refampicin and Pyrazinamide	• If the child has jaundice, suspect liver failure, and manage as above OR Refer the child. • If the child has no jaundice, suspect isoniazid and increase dose of pyridoxine or Refer the child.
Visual impairement	Ethambutol	Stop Ethambutol and refer the child.

ii. Laboratory Monitoring

Sputum Follow-up: All children who were bacteriologically confirmed at the start of treatment should have sputum smear follow up at 2 months, beginning of 5 months, and beginning of 6 months. GeneXpert SHOULD NOT be used to follow up patients (including children) on TB treatment. Children who are clinically diagnosed at the start of treatment will be monitored clinically.

iii. Radiologic Monitoring

Chest X-rays (CXRs): Follow up CXRs are not routinely recommended when children are improving on treatment because the response is slower on the CXR. Follow up CXR is indicated if a child has poor clinical response to treatment or is on treatment for MDR TB.

Table 4.7: Summary of Routine Monitoring for Children on TB Treatment

Monitoring	What to monitor	Week/Month on Treatment													
		Intensive Phase					Continuation Phase*								
		0	2 Wks	4 Wks	8 Wks	3 Months	4 Months	5 Months	6 Months	7 Months	8 Months	9 Months	10 Months	11 Months	12 Months
Clinical Monitoring †	Symptoms	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Signs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Side effects	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Adherence	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Laboratory Monitoring †	GeneXpert [a]	✓													
	Smear Microscopy [b]	✓			✓			✓	✓						
	HIV [c]	✓													
Radiology Monitoring	CXR [d]	✓													

* *Continuation phase is for: 4 months for all forms of TB (excluding TB Meningitis and bone TB); and 10 months for Bone TB and TB Meningitis.*

† *Refer to the national HIV care monitoring schedule for a child with TB/HIV co-infection.*

a *GeneXpert is the preferred initial diagnostic test for children aged 0 – 14 years and should not be used as a follow up test.*

b *Smear microscopy may be used as the initial diagnostic test in health facilities that do not have access to GeneXpert test. Smear microscopy is the recommended test for sputum follow up.*

c *HIV test should be conducted for all children presumptive and diagnosed TB*

d *CXR can be used as a diagnostic tool where it is available. If it is not available, it should not hinder diagnosis of TB children. A repeat CXR may be conducted for children who do not improve on treatment.*

4.8 How to Handle TB Treatment Interruption in Children

It is recommended that health facilities have mechanisms in place to trace children who are on TB treatment and have missed their clinic appointments. children who have interrupted TB treatment are managed as follows:

4.8.1 Management of Treatment Interruption

Interruption in the treatment of drug-susceptible TB should be managed carefully. The duration, time on treatment at which the interruption occurs, and bacteriological status of the child or adolescent before and after the interruption should be considered. Table 4.8 shows the management of treatment interruption (109).

Table 4.8: Management of Treatment Interruption in Children and Adolescents on on Drug-Susceptible TB Treatment

Treatment Phase of Interruption	Details of Interruption	Management
Intensive Phase		
Intensive phase: Applies to 4-month and 6-month regimens	Interruption <14 days	Continue treatment and complete all intensive phase does
	Interruption <14 days	Restart intensive phase
Continuation Phase (4-month 2HRZ(E)/2HR regimen)		
Continuation Phase (4-month regimen)	Completed ≥80% of doses within 8 weeks	Further treatment not necessary
Continuation Phase (4-month regimen)	Completed <80% of doses and cumulative interruption <1 month	Complete remaining doses of treatment
Continuation Phase (4-month regimen)	Completed <80% of doses and cumulative interruption <1 month	Restart treatment from beginning of intensive phase
Continuation Phase (6-month 2HRZE/4HR regimen)		
Continuation Phase (6-month regimen) and bacteriologically negative at initiation	Completed ≥80% of doses within 16 weeks	Further treatment not necessary
Continuation Phase (6-month regimen) and bacteriologically negative at initiation	Completed ≥80% of doses within 16 weeks	• Complete remaining doses of treatment • If consecutive lapse is >2 months, use clinical judgement
Continuation Phase (6-month regimen)	Completed <80% of doses and cumulative interruption <2 month	Complete remaining doses of treatment

In all circumstances, if TB symptoms recur during the interruption, reassess the child or adolescent with a rapid molecular test and culture/ DST to assess for drug resistance

4.8.2 Management of Treatment Failure

A person with treatment failure is defined as one whose treatment regimen needed to be terminated or permanently changed to a new regimen or treatment strategy. Consider the possibility of TB treatment failure for a child who is receiving TB treatment and has any of the following:

a. No symptom resolution or has worsening symptoms at 2 months.
b. Continued weight loss.
c. Positive sputum smear at 2 months' follow-up.
d. Emergence of drug resistance after 2 or more months of TB treatment.

The box below summarizes important questions to ask if a child or adolescent is not responding to or is deteriorating on TB treatment.

Questions to Ask in Children and Adolescents Not Responsing to or Deteriorating on TB Treatment

1. Is the dosage correct?
2. Is the child or adolescent taking the medicines as prescribed (good adherence)?
3. Is it possible that the child or adolescent has poor gastrointestinal absorption of the medicine?
4. Does the child or adolescent have medicine toxicity?
5. Is the child or adolescent living with HIV? If so, has the child or adolescent developed IRIS or other opportunistic infections?
6. Is the child or adolescent severely malnousished and is SAM managed appropriately?
7. Is there a reason to suspect DR-TB (index patient has DR-TB or is not responding to treatment)?
8. Is there a reason for the illness other than or in addition to TB?

Management

a. Children and adolescents in whom treatment failure is suspected should be referred for a rapid molecular test to determine rifampicin resistance, and where possible isoniazid resistance, especially if this is within 6–12 months of treatment completion.
b. Based on the drug susceptibility profile, a treatment regimen can be repeated if no resistance is documented. If rifampicin resistance is present, a second line regimen should be prescribed according to WHO recommendations.
c. In children and adolescents who have had treatment interruption, the reason for the interruption should be addressed, such as medicine stockouts, adverse effects from medicines, or need for additional patient or provider education.
d. Children and adolescents with previous treatment for unconfirmed TB should not be retreated for unconfirmed TB without referral to a centre with expertise in child TB management and paediatric care.

Key Message

- All children diagnosed with TB will be treated with four medicines in the intensive phase (RHZE) and two medicines in the continuation phase (RH).
- Ethambutol is safe for use in children when provided in the recommended dose.
- The doses of the medicines should be determined by the weight of the child.
- Streptomycin is no longer recommended for use in the treatment of TB in children.

CHAPTER 5:
MANAGEMENT OF TUBERCULOSIS IN HIV INFECTED CHILDREN AND ADOLESCENTS

Once a diagnosis of TB is made, TB treatment should be initiated irrespective of Anti-retroviral Therapy (ART) status. In addition to TB treatment, all chil-dren who are co-infected with TB and HIV should receive the comprehensive HIV care package including ART, Co-trimoxazole Preventive Therapy (CPT), nutritional and psychosocial support. The principles of TB treatment in HIV infected children and HIV negative children are the same.

5.1 TB-ART Co-Treatment

As mentioned above, all children with TB/HIV co-infection should be initiated on ART irrespective of CD4 counts. HIV-infected children are treated with the same TB treatment regimens and for the same duration as HIV negative children. (Table 5) However caution should be taken to avoid drug-drug interactions. TB/HIV co-treatment significantly increases pill burden for the child and therefore calls for strict adherence under DOT.

➲ TB-ART Co-Treatment in HIV Infected Children Who are NOT on ART at the Time of TB Diagnosis

If the child is not on ART, initiate TB treatment immediately and ART within 2-8 weeks after TB treatment initiation (aim at earlier initiation of ART).

Table 5.1: First Line ART Regimens for TBHIV Co-infected Children and Adolescents Initiating ART

Age Group	Recommended Regimen
Adults, pregnant and breastfeeding women and adolescents	TDF + 3TC + EFV
Children aged 3 to ≤12 years	ABC + 3TC + EFV
Children aged 0 to ≤3 years	ABC + 3TC + AZT

➲ TB-ART Co-Treatment in HIV Infected Children on ART

If the child is already on ART, initiate TB treatment immediately and make nec-essary adjustments to the ART regimen as shown in table below.

Table 5.2: Recommended ART Regimen for TB/HIV co-infected patients on ART

Age Group	Regimen when Diagnosed with TB	Recommended Action/Substitution
Children and adolescents older than 12 years.	If on EFV-based regimen	Continue with the same regimen and dose.
	If on DTG-based regimen	Continue the same regimen but increase but increase the dose of DTG 50mg twice daily instead of one daily).
	If on NFV-based regimen	Substitute NVP with EFV. If EFV is contradicted, give a triple NRTI regimen (ABC+3TC+AZT)
	If on LVP/r or ATV/r-based regimen	Continue the same regimen and substitute rifampicin with rifabutin for TB treatment.
Children aged 3 to ≤12 years	If on EFV-based regimen	Continue the same regimen.
	If on NVP or LVP/r-based regimen	Substitute NVP or LVP/r with EFV. If EFV is contrandicated, give a triple NRTI regimen (ABC+3TC+AZT).
Children aged 0 to ≤3 years	If on LVP/r or NVP-based regimen	Give triple NRTI regimen (ABC+3TC+AZT).

NOTE: *Patients who have been substituted should revert to their to their original regimen once TB treatment is completed.*

5.2 Follow-up of children with TB/HIV co-infection

The general follow up of an HIV infected child on TB treatment is similar to that of an HIV negative child. (Section 4.5) It is important to schedule the TB and HIV clinic appointments on the same day to enhance adherence and minimize loss to follow up. A child on TB-ART co- treatment requires close monitoring for side effects of both TB treatment and ART.

5.3 Drug - Drug interactions

Rifampicin is a potent CYP450 enzyme inducer, an enzyme which reduces the concentration of Nevirapine (NVP) and protease inhibitors (PIs) in the body. This results in sub-optimal drug concentrations which may not effectively suppress HIV replication and predispose to ART resistance. It is therefore critical to adjust the ART regimen/ dose of NVP and boosted PIs. If available, rifampicin may be replaced by rifabutin, another first line anti- TB medicine, with less effect on the ART. In that case, there is no need for ART regimen/ dose adjustments. The table below summarizes the overlapping side effects of anti-TB medicines and antiretroviral drugs.

Table 5.3: Side Effects of anti-TB Medicines and Antiretroviral Drugs

Side effects	Clinical presentation	Main ARV involved	Main Anti-TB medicine involved	Management
Peripheral neuropathy (early or late side effects)	Burning sensa - tion; pins and needles mainly in hands and feet.		Isoniazid	Give Pyridoxine at a dose of 25 – 50 mg/day
Liver toxicity	Nausea, vomiting, yellow coloration of eyes, right sided abdominal pain right hypochondriac tenderness, hepatomegaly	Nevirapine Protease Inhibitors	Pyrazinamide Rifampicin Isoniazid	Stop all drugs, once resolved. Restart with anti-TB medicines.
Gastrointestinal dysfunction	Nausea, vomiting, abdominal discomfort	All	All	Manage the symptoms as they come and counsel the patient.
Hypersensitivity (usually early side effect)	Skin rash	Nevirapine Efavirenz Abacavir	Rifampicin Isoniazid Pyrazinamide	Anti-histamine if mild. if severe STOP all drugs and REFER the child.
Central nervous system dysfunction	Irritability, psychosis, drowsiness, seizures	Efavirenz	Isoniazid	Pyridoxine given as preventive therapy and treatment for INH toxicity. STOP INH in case of seizures and refer.
Anaemia	Palor of mucus membranes, Signs of heart failure in severe cases.	Zidovudine	Rifampicin	Change from Zidovudine to ABC (for children <10 years) or TDF (for children >10 years and ≥35 kg). Manage the anaemia using IMCI guidelines.

5.4 TB Immune Reconstitution Inflammatory Syndrome

Immune Reconstitution Inflammatory Syndrome (IRIS) is an inflammatory process characterized by transient worsening of clinical disease following ini- tiation of treatment due to restoration of the body's immunity. Onset is usually within the first 3 months after starting ART most commonly within the first month. Risk factors for TB IRIS include; low baseline CD4 count, extensive TB disease, early initiation of ART, and rapid immunological and virologic responses to ART. Symptoms of TB IRIS include worsening TB symptoms and CXR features, new and persistent fevers after starting ART, and evidence of local and/ or systemic infection or inflammation (e.g enlarging lymph nodes and the development of firstulae and cold abscesses).

The following are actions to be taken when TB IRIS is detected:

i. Rule out TB/HIV treatment failure, side effects of TB and HIV treatment, and pre-existing untreated opportunistic infections.
ii. Continue both ART and anti-TB treatment unless severe toxicity is suspect- ed or confirmed (e.g. elevated LFTs).
iii. In severe cases, give prednisolone at a dose of 1-2mg/kg for 1 to 2 weeks; and thereafter, gradually decrease the dose.
iv. Provide other supportive measures as needed.

Key Message

- All children with HIV infection should be screened for TB, and all children with TB should be tested for HIV.
- All children living with HIV should receive the comprehensive HIV care package including ART, CPT, nutrition support and psychosocial support.
- All HIV infected children diagnosed with TB and are not on ART should be started on TB treatment immediately and ART initiated within 2-8 weeks after starting TB treatment.
- All HIV infected children diagnosed with TB and are on ART should be started on TB treatment immediately and their ART regimens modified appropriately.

CHAPTER 6:
MANAGEMENT OF DRUG RESISTANT TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

6.1 Definition of Drug-Resistant TB (DR-TB)

Drug resistance is said to occur when TB organisms continue to grow in the presence of one or more anti-TB drugs.

Forms of Drug-resistant Tuberculosis

- **Mono-resistance:** Resistance to one first line anti-tuberculosis drug.
- **Poly-resistance:** Resistance to more than one first line anti-tuberculosis drug, other than both Isoniazid and Rifampicin.
- **Isoniazid-resistant TB (Hr-TB)** is caused by Mycobacterium tuberculosis strains resistant to isoniazid and susceptible to rifampicin.
- **Rifampicin-resistant TB (RR-TB)** is caused by M. tuberculosis strains that are resistant to rifampicin. RR-TB strains may be susceptible to isoniazid or resistant to it (i.e., MDR-TB), or resistant to other first- line or second-line TB medicines.
- **Multidrug-resistant TB (MDR-TB)** is caused by M. tuberculosis strains that are resistant to at least both isoniazid and rifampicin.
- **Pre-XDR TB** is TB caused by Mycobacterium tuberculosis strains that fulfil the definition of multidrug resistant and rifampicin resistant TB (MDR/RR-TB) and which are also resistant to any fluoroquinolone.
- **Extensively drug-resistant TB (XDR-TB)** is TB caused by Mycobacterium tuberculosis (M. tuberculosis) strains that fulfill the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone and at least one additional Group A drug.

6.2 Risk Factors for Drug-Resistant Tuberculosis

Although several factors can contribute to the development of drug-resistant TB, inadequate anti- TB treatment is probably the most important. Inadequate anti-TB treatment leads to overgrowth of initially drug-resistant bacilli or mutations in drug-susceptibility bacilli making them drug resistant.. Below are situations of inadequate anti-TB treatment:

i. Inadequate drug regimen.
ii. Inadequate duration of treatment.
iii. Drugs not taken regularly by the patient.
iv. Use of poor-quality drugs.

Risk Factors for DR TB in Children

Children with any of the following are at risk of DR TB (suspected DR TB) and should therefore be evaluated for DR TB:

i. A child who is a close contact of a known MDR TB patient.
ii. A child who is a close contact of a suspected MDR TB patient such as a case of treatment failure, retreatment (relapse, loss to follow up) or recent death from TB.
iii. A child with confirmed TB who is still bacteriologically positive after five months of treatment (Treatment failure).
iv. A child who is not responding to first-line anti-TB drugs at 2 months despite adherence (e.g failure to gain weight, persistent fevers, failure to regain activity, CXR with radiological worsening).
v. A child previously treated for TB presents with recurrence of TB disease.

6.3 Diagnosis of Drug-Resistant Tuberculosis

Drug susceptibility testing (DST) is central to the diagnosis of DR-TB. The current guidelines for drug-resistant TB treatment stress the need for access to reliable, quality-assured DST, to be provided so as to inform the use of the WHO-recommended treatment regimens. Rapid molecular testing is making it increasingly feasible to detect MDR/RR-TB and other types of resistance, and to use the results to guide treatment decisions.
This has been made possible with screening using a nucleic acid amplification test (NAAT) such as GeneXpert, Truenat or the Line Probe Assay (LPA) which detects genetic determinants of resistance. Definitive diagnosis of drug resistance is made using phenotypic DST. All patients who are presumed to have drug- resistant TB should therefore have sputum/other specimens taken for culture and DST in vivo. The DST results are generally used to guide the choice of chemotherapy in MDR-TB regimens.

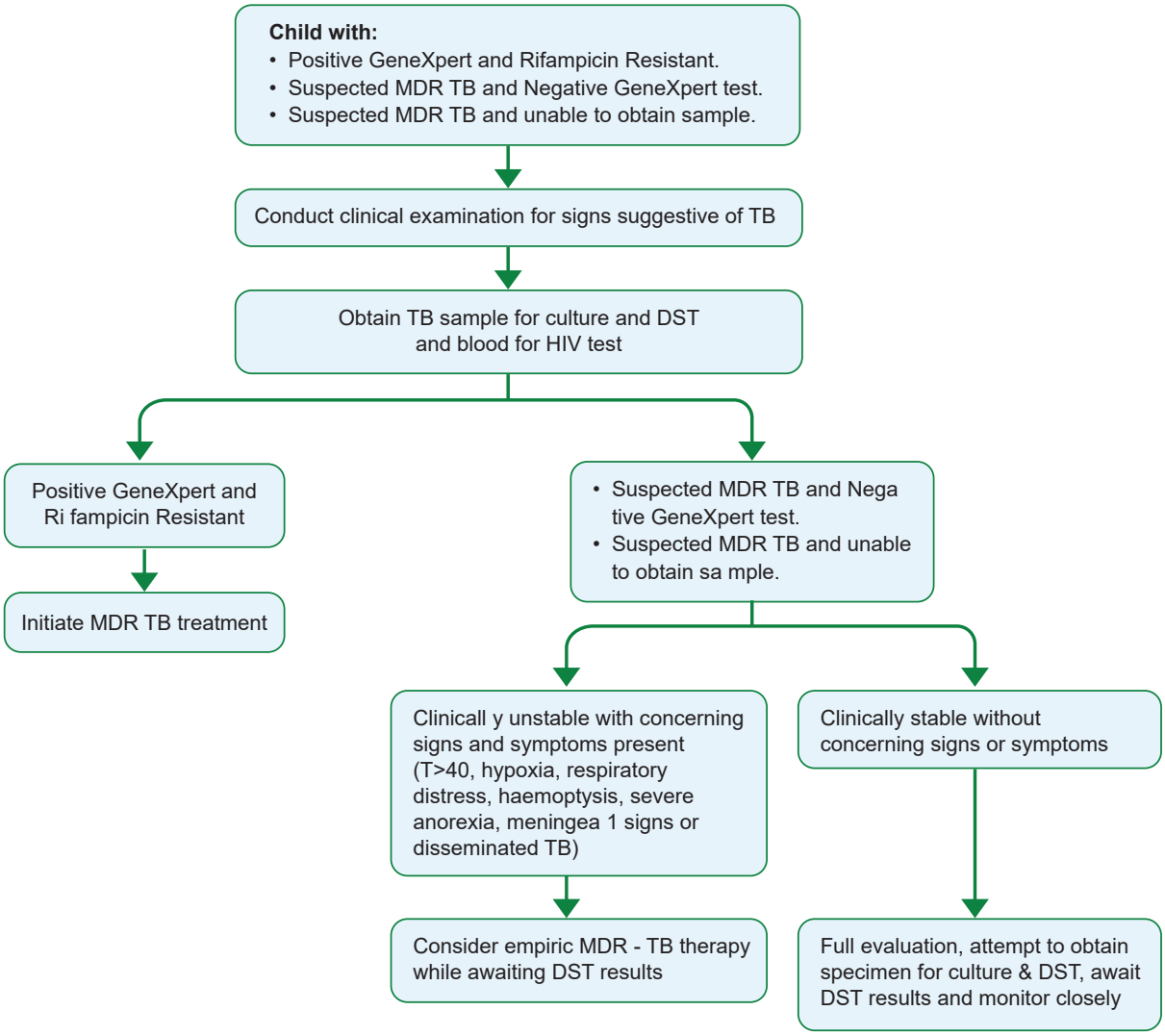
6.4 Management of MDR TB in Children

The following are the scenarios in the management of MDR TB in children (figure 4):

i. Positive GeneXpert and Rifampicin Resistant.
ii. Suspected MDR TB and Negative GeneXpert test.
iii. Suspected MDR TB and unable to obtain sample.

The management of MDR TB in children is guided by the same principles used for adults. Individuals, including children, who are diagnosed with MDR TB are treated using another group group of medicines referred to as second line anti-TB medicines. The medicines used to treat MDR TB in children are similar to those used in adults. The use of these medicines is also guided by the weight of the child.

Figure 6.1: Algorithm for Management of MDR-TB in Children



6.5 Treatment of Multidrug-Resistant and Rifampicin-Resistant TB in Children and Adolescents

It is estimated that between 25,000 and 32,000 children and young adolescents aged under 15 years develop MDR-TB disease annually. Contact investigation and screening of child and adolescent contacts of infectious MDR/RR-TB source cases are essential for the rapid diagnosis of children with MDR/RR-TB disease and for prompt initiation of treatment. Children with clinically diagnosed or bacteriologically confirmed MDR/RR-TB should be treated with a WHO-recommended treatment regimen.

A clinical diagnosis of MDR/RR-TB can be made based on a clinical diagnosis of TB and either exposure to a known case of MDR/RR-TB or presence of other risk factors for MDR/RR-TB (e.g. child treated previously for TB or exposed to a source case who died from TB or failed TB treatment). Up to 83% of the time, children are very likely to have TB with the same resistance pattern as their most likely source case. Therefore, the sensitivity pattern of the source case should guide the regimen build up in children with MDR TB except in those children that are bacteriologically confirmed.

DR TB requires longer treatment periods than susceptible TB. The treatment duration depends on regimen used, drug resistant type and response to treatment. Newer drugs have been developed and these have helped improve treatment of drug resistance by ensuring treatment is for shorter periods and that treatment is all oral instead of having injectable drugs added. This is also associated with less side effects and together with shortened treatment periods is anticipated to improve adherence to treatment and ultimately improve patient outcomes. Based on the drug resistance identified and duration, the following are the current treatment regimens available.

6.5.1 Multidrug-Resistant and Rifampicin-Resistant TB Treatment Regimens

The risks and benefits of each medicine should be considered carefully while designing a regimen. Generally, none of the available TB medicines is contraindicated in children. When a decision has been made to treat a child for MDR/RR-TB, two main regimens are available. Current guidelines recommend prioritizing the standardized shorter all-oral bedaquiline-containing regimen for people with MDR/RR-TB. For people not eligible for this regimen, an individualized longer regimen should be constructed.

The following are the treatment regimens available for MDR TB treatment in children:

i. Regimen for Rifampicin-Susceptible and Isoniazid-Resistant TB (Hr-TB)

Hr-TB Regimen: 6REZ-Lfx

This regimen is used once isoniazid resistance has been confirmed and rifampicin resistance excluded. In these patients, treatment with rifampicin, ethambutol, pyrazinamide and levofloxacin is recommended for a duration of 6 months.

As there is no FDC for this regimen, the available FDCs can be used to constitute the regimen. For example, pediatric formulations of RHZ + E + Lfx for children < 25 kg and adult formulations of RHZE + Lfx for children and adolescents > 25kg could be used. In instances where fixed-dose combination formulations are used, isoniazid is included but is not a must for the regimen.

It is not advisable to give a regimen for Hr-TB unless isoniazid resistance is confirmed.

> The regimen recommended for treatment of Hr-TB does not have an intensive and a continuation phase.

The clinical monitoring of patients on Hr-TB treatment follows similar principles to those that apply to other first-line TB regimens. Bacteriological monitoring of sputum generally follows the same schedule as DS TB, with direct microscopy at months 2, 5 and 6. It is desirable, however, to perform a culture together with smear microscopy (at least in the last month of treatment) to check for any emergent resistance, especially to rifampicin.

ii. Shorter all-Oral Bedaquiline-Containing Regimen for MDR/RR-TB

The standardized shorter all-oral bedaquiline-containing regimen can now be used in children of all ages under programmatic conditions. This is an all-oral bedaquiline-containing treatment regimen for MDR/RR- TB that has a duration of 9–12 months. This regimen can be used in both people who have HIV and those without HIV.

The eligibility criteria for this regimen for children with confirmed MDR/RR-TB are the same as for adolescents and adults i.e.

- No resistance to fluoroquinolones.
- No previous exposure for more than 1 month to second-line medicines used in this regimen (unless susceptibility to these second-line medicines has been confirmed).
- No severe forms of EPTB (other than peripheral lymphadenopathy).
- No extensive TB disease (presence of cavities or bilateral disease on CXR).

Please Note

There are two standardized shorter all-oral bedaquiline-containing regimens that could be used i.e.

i. 4–6 Bdq(6 m)-Lfx/Mfx-Cfz-Z-E-Hh-Eto / 5 Lfx/Mfx-Cfz-Z-E

Which is divide into:
Initial Phase : 4-6 Bdq(6m)-Lfx-Cfz-Z-E-Hh-Eto
Continuation phase : 5 Lfx-Cfz-Z-E

OR

ii. The BPaLM regimen

BPaLM regimen

This regimen comprises Bedaquiline, Pretomanid, Linezolid and Moxifloxacin and may be used in place of 9 months or longer (>18 months) regimens in patients with MDR/RR TB who have not had previous exposure to Bedaquiline, Pretomanid and Linezolid. If there has been previous exposure, this should not have lasted > 1 month. It is possible to omit moxifloxacin and continue with the BPaL regimen for MDR/RR- TB patients with confirmed fluoroquinolone resistance. In this case the regimen becomes BPaL.

Response to treatment for patient on a shorter all oral regimen is monitored on the basis of monthly sputum smear microscopy, as well as culture, ideally at the same frequency. This is similar to the schedule used in patients on the longer all- oral MDR-TB regimen.

Table 6.1: TB Medicine and Duration of Treatment for the Standardized all-oral Bedaquiline-Containing Shorter Regimen

Month	1	2	3	4	5	6	7	8	9
Bedaquiline									
High-dose isoniazid									
Ethionamide/Prothionamide									
Levofloxacin									
Clofazimine									
Pyrazinamide									
Ethambutol									

iii. Longer Regimens for MDR/RR-TB

This consists of 18-month treatment regimen composed of bedaquiline for the first 6 months and levofloxacin or moxifloxacin, linezolid, clofazimine for 18 months (18 Bdq (6 m)-Lfx/Mfx-Lzd-Cfz) and should be used in children not eligible for the standardized all-oral bedaquiline-containing regimen.

Children who are not eligible for the standardized all-oral bedaquiline-containing regimen include:

- Those without bacteriological confirmation (e.g. with a clinical diagnosis) **OR**
- Without fluoroquinolone resistance ruled out (in their own specimens) **OR**
- With drug-resistant EPTB other than peripheral lymphadenopathy **OR**
- With extensive pulmonary disease **OR**
- With prior exposure for more than 1 month to the medicines in the shorter regimen.

These children should be treated with the longer individualised treatment regimens. In general, the treatment principles for MDR/RR-TB in children follow those recommended for adolescents and adults.

Table 6.2: Weight-based Dosing Chart for MDR-TB Medicines in Children

Drug	Daily Dose Mg/Kg	Frequency	Maximum Daily Dose	Dosing or different weight bands		
Levofloxacin (Lfx 250mg tablet [tab])	Patients < 30kg: <5y/o:15-20 >5y/o:10	See Note for dosing by age	750 mg	**NOTE:** 5 years and under → 15-20 mg/kg split into 2 doses (morning and evening) > 5 years of age → 10 mg/kg once daily. Child > 30 kg → Use adult dosing.		
				Weight → 5-10kg <5yrs → 1/2 tab bd	**Weight → 16-23kg** <5yrs → 3/4 bd >5yrs → 1 tab bd	**Weight → 24-29.9kg** <5yrs → 1 tab bd >5yrs → 1 1/2 tab od
Moxifloxacin (Mfx, 400mg tab)	Patients <30kg:7.5-10	Once daily	400 mg	**Weight** → 10-17kg Dose → 1/4 tab	**Weight → 18-29.9kg** Dose → 1/2 tab	**Weight → 30kg** Use adult dosing table
Ethionamide (Eto, 250mg tab)	Patients <30kg:15-20	In 2 divided doses or once daily if toler - ated	1 g	**Weight:** 5-10kg **Dose:** 1/2 tab	**Weight and Dose** 11-18kg → 1 tab 19-24kg → 1 1/2 tabs	**Weight and Dose** 25-29.9kg → 2 tabs >30kg → use adult dosing
Cycloserine (Cs, 250mg) capsule [cap])	Patients <30kg:10-20	In 2 divided doses or once daily	1 g	NOTE: Dissolve one 250mg capsule in 10ml of water. Doses reflect total daily dose.		
				Weight and Dose 5kg → 50mg (2.0ml) 6-12kg → 125mg (5.0ml)	**Weight and Dose** 13-25kg → 250mg (10ml/1cap)	**Weight and Dose** 26-29.9kg → 500mg (20ml/2cap) > 30kg → use adult dosing
Paminosalicylic acid(PASER®) (PAS, 4g sachets)	Patients <30kg:200-300	Once or daily dose divided into 2 and given twice	12 g	NOTE: Use PASER® dosage scoop with mg demarcations to ensure proper dose		
				Weight and Dose 5kg → 500 mg bd 6-7kg → 750 mg bd 8-10kg → 1000 mg bd	**Weight and Dose** 11-14kg → 1500 mg bd 15-18kg → 2000 mg bd 19-22kg → 2500 mg bd	**Weight and Dose** 23-26kg → 3000 mgbd 27-29.9kg → 3500 mg bd >30kg → use adult dosing
Pyrazinamide (Z, 500mg tab)	Patients <30kg:30-40	Once daily	2 g	**Weight and Dose** 5-6kg → 125mg (1/4 tab) 7-9kg → 250 mg (1/2 tab) 10-11kg → 375mg (3/4 tab)	**Weight and Dose** 12-18kg → 500mg (1 tab) 19-25kg → 750mg (1 1/2 tabs)	**Weight and Dose** 26-29.9kg → 1000mg (2 tab) >30kg → use adult dosing
Pyrazinamide (Z, 400mg tab)	Patients <30kg:30-40	Once daily	2 g	**Weight and Dose** 5-7kg → 200mg (1/2 tab) 8-9kg → 300 mg (3/4 tab) 10-14kg → 400mg (1 tab)	**Weight and Dose** 15-20kg → 600mg (1 1/2 tabs) 21-27kg → 800mg (2 tabs)	**Weight and Dose** 28-29.9kg → 1g (21/2 tabs) >30kg → use adult dosing

6.5.2 Adjuvant Therapy in MDR TB Treatment

The principles guiding the use of adjuvant therapy in MDR TB are similar to those in drug susceptible TB mentioned above.

a. Pyridoxine is recommended for all patients on Cycloserine, Ethionamide/ Prothionamide and Terizidone to prevent neurological side effects.
b. Prednisolone is used in cases where the MDR TB disease is associated with severe inflammation such as MDR TB meningitis and complications of airway obstruction by TB lymph nodes.

6.6 Follow-up and Monitoring Children on MDR TB Treatment

The main objective of monitoring is to:

i. Ascertain response to treatment
ii. Ensure timely adjustment of doses
iii. Ensure early detection and limitation of adverse events

In children, laboratory monitoring of treatment is often challenging. This particularly hinders the diagnosis of treatment failure in children. In children, weight loss or, more commonly, failure to gain weight adequately in the presence of proper nutritional intake, is of particular concern and often one of the first (or only) signs of treatment failure. Persistent abnormalities on chest radiographs do not necessarily signify a lack of improvement.

6.6.1 Clinical Monitoring

a. Nutritional status

i. Weight: Weight should be taken at each visit and used to track gain in nutritional status. Medicine doses should be adjusted for any change in weight bands. Evaluate for treatment failure in a child with failure to gain weight or weight loss while on treatment and adequate nutritional intake.
ii. Mid Upper Arm Circumference (MUAC): Measure MUAC at each visit to track gains in nutritional status.
iii. Height

b. Symptoms

Resolution of symptoms including cough, fevers, and change in weight should be evaluated for and documented at each visit in the Second-line TB Treatment Card.

c. Adherence

Adherence is often a challenge, particularly in adolescents and especially during the continuation phase. Counselling of child and family about the importance of completing the full course of anti-TB treatment is important and requires regular reinforcement.

d. Adverse effects

Adverse effects are common in patients taking second- line anti-TB regimens. Record adverse effects in the Second-line TB Treatment Card and the Suspected Adverse Drug Reaction Reporting Form.

6.6.2 Laboratory Monitoring

See monitoring schedule in the table 16 children on MDR TB treatment. Ar- range for sputum sample collection especially in younger children who are unable to produce sputum on their own. (Appendix A)

6.6.3 Supportive Management

i. Nutrition

A child with MDR-TB requires more calories than a healthy child ofthe same age given the wasting that occurs with TB and extra energy expended ighting the disease. Educate the caregiver on the need to provide a balanced diet using affordable locally available foods. Failure to improve nutritional status in a child with MDR- TB is an early indicator that the MDR-TB may not be under control.

ii. Family support

The family members need to be counselled and support- ed psychologically given the long duration of treatment and unfavour- able treatment outcomes associated with non-adherence to treatment.

Table 6.3: Monitoring Schedule for Children on MDR TB Treatment

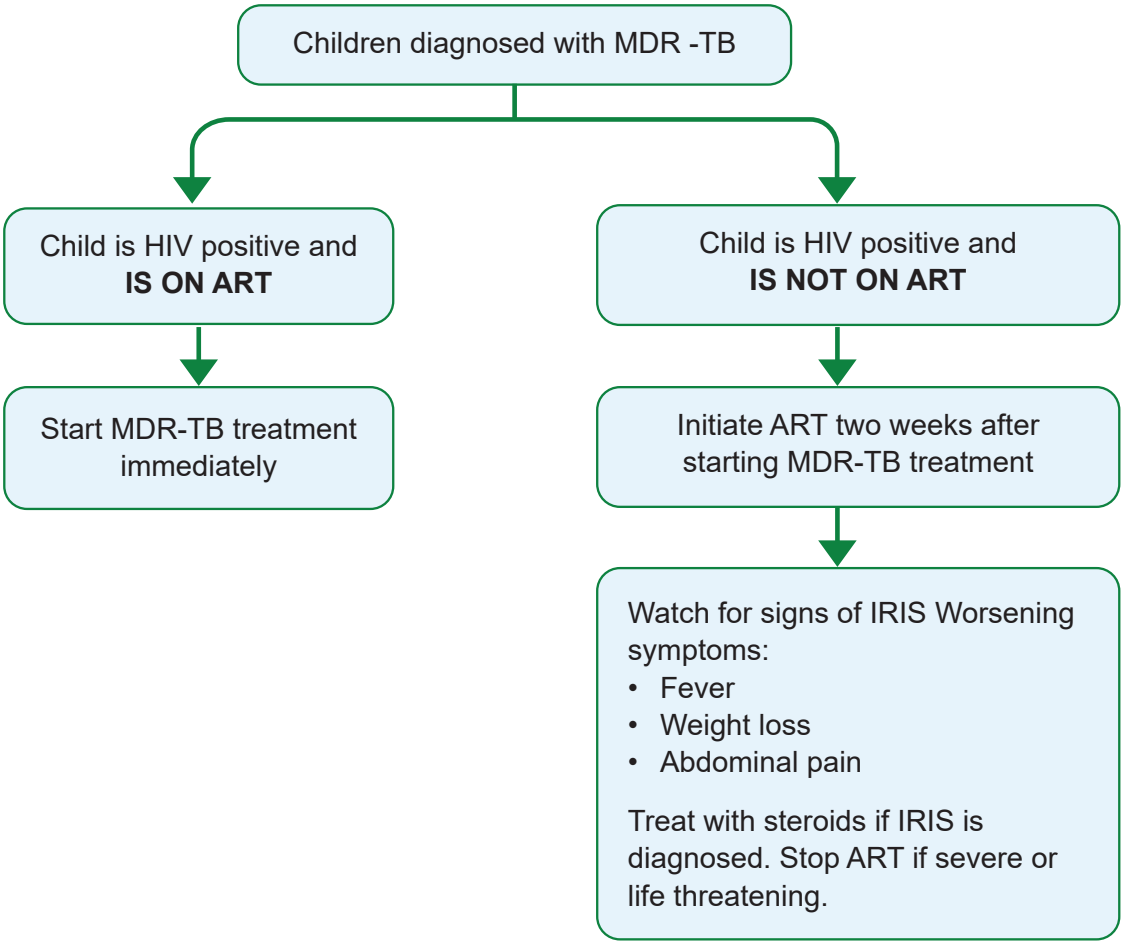
Monitoring	Recommended Frequency Month of treatment																				
Clinical evaluation (+ weight MUAC, height) monthly	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
DOT, symptoms, and SEs	Each encounter →																				
Sputum AFB smear (monthly)																					
Sputum TB culture [1]																					At end
DST[2]																					
Chest X-ray																					At end
Liver function[3]																					
Serum creatinine; hearing																					
Electrolytes (Na, K,Cl,Mg)																					
Complete blood count																					
TSH																					
HIV and Pregnancy tests																					
If HIV+; CD4, cholesterol, VL[4]																					
Social evaluation (and Contact evaluation)				HIV & <5																	At M24

1 *Monthly culture until conversion then bimonthly during continuation phase (and 6&12mo after completion)*
2 *Repeat when indicated*
3 *LFTs monthly for HIV on ARV, patients on BDQ, or underlying liver disease when PZA is in the regimen*
4 *HIV testing as per HTC guidelines*
5 *Contacts with HIV or children < 5 years add month 3 evaluation.*

6.7 Management of MDR TB/HIV Co-Infection in Children

All children with suspected or confirmed DR-TB must be screened for HIV infection as part of their routine investigations. All patients diagnosed with TB and HIV are initiated on ART irrespective of CD4 counts. ART is started within 2-8 weeks of initiation of anti-TB treatment in HIV-infected children. Children who are on MDR-TB treatment and ART need to be monitored for drug – drug interactions and signs of IRIS. In addition to early ART initiation, all TB/HIV cases should receive the comprehensive HIV are package including CPT, nutrition and psychosocial support.

Figure 6.2: Algorithm for management of children on treatment for MDR-TB and HIV



CHAPTER 7:
PREVENTION OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

The approaches for preventing TB in children include:

7.1 Bacille Calmette Guerin vaccination

The Bacille Calmette Guerin (BCG) vaccine is a live attenuated vaccine and is administered to all new born babies according to the Expanded Programme of Immunizations (EPI) guidelines. The vaccine is only effective in protecting against severe forms of TB. Therefore TB must still be considered in BCG vaccinated children with symptoms suggestive of TB. An infant born to a mother with active TB disease should not receive the BCG vaccine until the infant has been evaluated for TB disease. An infant who did not receive BCG at birth and is confirmed to have HIV, should not be given BCG. This is because children with HIV are at risk of developing severe and often fatal BCG disease.

Side effects to BCG vaccination include local effects (local redness, swelling, pain, abscesses, keloids) and regional or disseminated lymphadenitis. Infants who initiate ART early may develop BCG IRIS with regional or disseminated lymphadenitis as the commonest. Any child with suspected BCG disease or IRIS should be referred for further management.

7.2 TB Preventive Therapy

TB Preventive Therapy (TPT) refers to the administration of Isoniazid to prevent latent TB infection from progressing into active TB disease. It is important to screen and exclude active TB before any child who is a contact of a bacteriologically confirmed PTB is started on TPT to avoid monotherapy in a child who actually has active TB disease. In addition, TST is not a requirement for TPT initiation.

7.3 Eligibility for TPT

7.3.1 TPT in Children

Providing treatment for TB infection to prevent TB disease is a critical aspect of TB control. Several regimens are currently available with their efficacy ranging from 60% to 90%.
TPT is recommended for the following categories:

➲ Infants, Children and Adolescents with HIV

i. Infants aged under 12 months living with HIV who are in contact with a person with TB and who are unlikely to have TB disease on an appropriate clinical evaluation or according to The Gambia national guidelines should receive TPT.

ii. Adolescents and children aged 12 months and over living with HIV who are considered unlikely to have TB disease on an appropriate clinical evaluation or according to The Gambia national guidelines should be offered TPT as part of a comprehensive package of HIV prevention regardless of contact with TB.

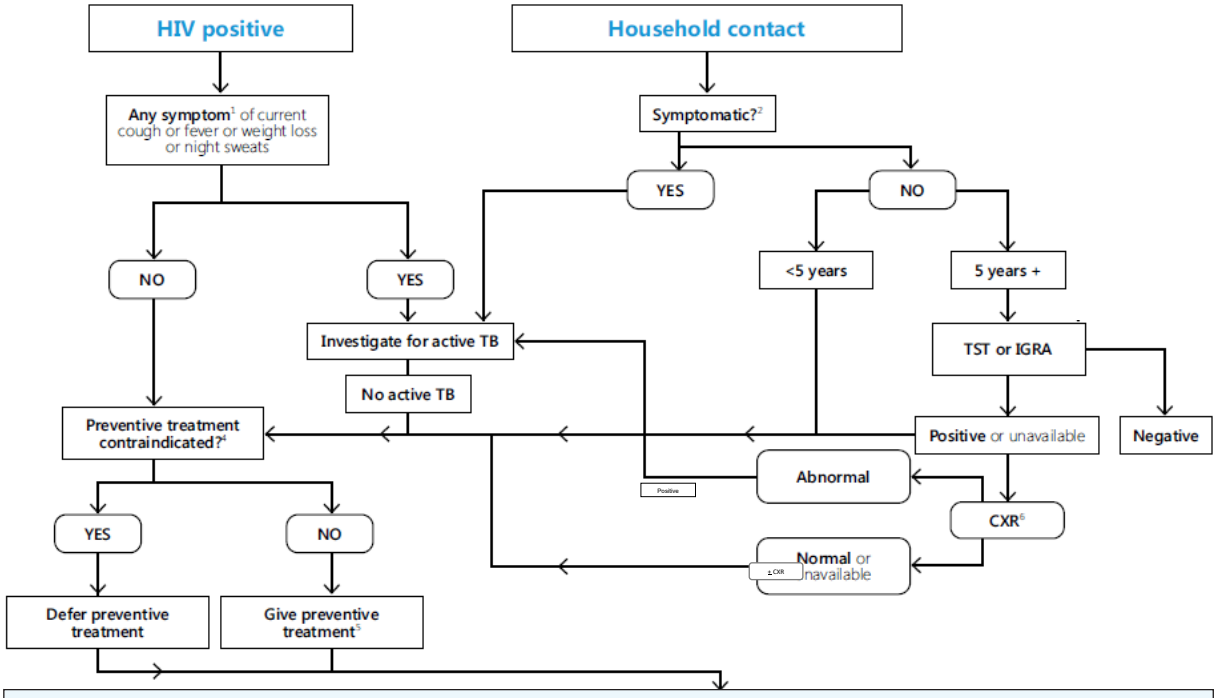
Household/Close Contacts (Regardless of HIV)

i. Children aged under 5 years who are household/close contacts of people with bacteriologically confirmed PTB and who are found not to have TB disease on an appropriate clinical evaluation or according to The Gambia national guidelines should be given TPT.

ii. Children aged 5 years and over and adolescents who are household/close contacts of people with bacteriologically confirmed PTB who are found not to have TB disease by an appropriate clinical evaluation or according to The Gambia national guidelines may be given TPT.

It is important to exclude TB disease before initiating TPT.

Figure 7.1:



Follow-up for active TB as necessary, even for patients who have completed preventive treatments.

1. If <10 years, any one of current cough or fever or history of contact with TB or reported weight loss or >5% since last visit or growth curve flattening or weight for age <-2 z-scores. Asymptomatic infants <1 year with HIV are only treated for LTBI if they are household contacts of TB, TST or IGRA may identify PLHIV who will benefit most from preventive treatment. Chest radiography (CXR) may be used in PLHIV on ART, before starting LTBI treatment.
2. Any one of cough or fever or night sweats or haemoptysis or weight loss or chest pain or shortness of breath or fatigue. In children <5 years, they should also be free of anorexia, failure to thrive, not eating well, decreased activity or playfulness to be considered asymptomatic.
3. Including silicosis, dialysis, anti-TNF agent treatment, preparation for transplantation or other risks in national guidelines.
4. Including acute or chronic hepatitis; peripheral neuropathy (if isoniazid is used); regular and heavy alcohol consumption. Pregnancy or a previous history of TB are not contraindications.
5. Regimen chosen based on considerations of age, strain (drug susceptible or otherwise), risk of toxicity, availability and preferences.
6. CXR may have been carried out earlier on as part intensified case finding.

7.4 Contraindications to TPT

TPT should not be given in the following circumstances:

i. Children with active TB.
ii. Children on TB treatment.
iii. Children who are contacts of MDR TB cases.
iv. PLHV previously treated for MDR TB.
v. Children with known or suspected hypersensitivity to Isoniazid.
vi. Children with chronic liver disease or symptoms suggesting active hepa- titis (jaundice, right upper quadrant pain, dark urine, pale stools).
vii. Children with history of afebrile convulsions (This includes children with epilepsy).
viii. Children with history of mental illness.
ix. Children with moderate to severe peripheral neuropathy (burning sensa- tions of the limbs).
x. Children on concomitant medication: phenytoin, carbamazepine, warfarin, theophylline, disulfiram, selective serotonin re-uptake inhibitors, anti-depressants (e.g. citalopram, fluoxetine, paroxetine, sertraline), oral ketoconazole or itraconazole.

7.5 Tuberculosis Preventive Treatment Options

TB preventive treatment for drug-susceptible TB can be broadly categorized into two types: monotherapy with isoniazid for at least 6 months (or isoniazid preventive therapy,) and treatment with regimens containing a rifamycin (rifampicin or rifapentine).

The following options are recommended for the treatment of LTBI regardless of HIV status:

- 6 months of daily isoniazid (6H) or
- 3-month regimen of weekly rifapentine plus isoniazid (3HP)
- 1- month regimen of daily rifapentine plus isoniazid (1HP)
- 3-month regimen of daily isoniazid plus rifampicin

Until recently, 6H has been the only available regimen for TPT among eligible HIV positive persons and under 5 child contacts of pulmonary bacteriologically confirmed TB patients. However, shorter treatment regimens with less pill burden are now available. These regimens improve uptake and promote treatment adherence. It is important that before TPT is initiated, active TB is excluded. This is done to avoid monotherapy for active TB, because TB should always be treated with combination therapy. The choice of TPT option to use is determined by many factors such as: age, risk of toxicity or interaction, co-morbidity, drug susceptibility of the strain of the most likely source case, availability and the individual's preferences.

The following 3 TPT regimens are recommended for use in children and adolescents by the WHO:

➲ HIV Positive Contacts of Patients Diagnosed with Drug Susceptible TB

i. 3HP for adolescents and children older than 2 years living with HIV.
ii. 6H for children below 2 years and PLHIV on protease inhibitors.

HIV Negative Contacts of Patients Diagnosed with Drug Susceptible TB

i. Preferred option: 3HR

> 3HR is a preferred TPT option among HIV-negative children since child-friendly dispersible FDCs are widely available and already used for TB treatment, while awaiting data on dosages across all age groups and child-friendly formulations for rifapentine-based regimens. For children living with HIV, 6H remains the preferred option until further data are available.

Child Contacts of Patients Diagnosed with Multidrug Resistant TB

i. There is currently no recommended preventive therapy for contacts of patients diagnosed with MDR-TB. Therefore, none of the regimens mentioned above should not be used as preventive therapy for MDR-TB contacts.

ii. Asymptomatic children who are contacts of MDR TB patients should be evaluated for signs and symptoms of TB at three months following the index patient's diagnosis of DR-TB, then at 6, 12, 18 and 24 months. If a child develops signs and symptoms of TB during the follow up period, s(h)e should be referred to a health facility for further evaluation.

Table 7.1: Recommended Regimens and Dosages of Medicines for TB Preventive Treatment

Medicine frequency & duration	Formulation	Dose of TPT medicine (mgs)	Dose/ weight	Recommended number of tablets per body weight in kilograms								
3HP (once weekly rifapentine plus isoniazid for 3 months)	Fixed Doze Combination (FDC) Tablet	Rifapentine 300mg/ Isoniazid 300mg		**3–5.9 kgs**	**6–9.9 Kgs**	**10–15 kgs**	**16–23 kgs**	**24–30 kgs**	**31-34 kgs**	**35-45 kgs**	**>45 kgs**	
	Single medicine tablet	Pyridoxine 25mg/day				1	1.5	2	2.5	3	3	
						1	1	1	1	1	1	
6H (daily isoniazid for 6 months)				**3–5.9 kgs**	**6–9.9 Kgs**	**10–13.9 kgs**	**14–19.9 kgs**	**20–24.9 kgs**	**25-34.5 kgs**	**35-44.5 kgs**	**45-49.9 kgs**	**≥50 kgs**
	Single medicine tablet	Isoniazid 100 mg	<10 years 10mg/kg	0.5	1	1.5	2	2.5				
			> 10 years 5mg/kg						1.5	2	2.5	
		Isoniazid 300 mg	≥ 10 years 5mg/kg									1
	Single medicine tablet	Pyridoxine 25 mg		0.5	0.5	1	1	1	1	1	1	1
3RH (daily Rifampicin Isoniazid for 3 months)				**< 4 kgs**	**4-7 Kgs**	**8-11 kgs**	**12-15 kgs**	**16–24 kgs**	**25-32 kgs**	**33-39 kgs**	**40-54 kgs**	
	Fixed Doze Combination (FDC) Tablet	RH 75mg/50mg	< 10 years R - 15mg/kg H - 10mg/kg	0.5	1	2	3	4	4			
		RH 150mg/75mg	≥ 10 years R - 10mg/kg H - 5 mg/kg							2	3	
	Single medicine tablet	Pyridoxine 25mg/day		0.5	1	1	1	1	1	1	1	
1HP (once daily rifapentine plus isoniazid for 1 month - 28 days) for adolescents >13 years & adults				**3–5.9 kgs**	**6–9.9 Kgs**	**10–15 kgs**	**16–23 kgs**	**24–30 kgs**	**31-34 kgs**	**35-45 kgs**	**>45 kgs**	
	Single medicine tablets	One Isoniazid (H) 300mg tablet 4 Rifapentine (P) 150mg tablets / day	Regardless of weight band			1	1.5	2	2.5	1	1	
						1	1	1	1	4	4	
		Pyridoxine 25mg/day				1	1	1	1	1	1	
Medicine frequency & duration	**Formulation**	**Dose of TPT medicine (mgs)**	**Dose/ weight**	**Recommended number of tablets per body weight in kilograms**								
1HP (once daily rifapentine plus isoniazid for 1 month - 28 days) for adolescents >13 years & adults										**35-45 kgs**	**>45 kgs**	
	Single medicine tablets	One Isoniazid (H) 300mg tablet	Regardless of weight band							1	1	
		4 Rifapentine (P) 150mg tablets / day								4	4	
		Pyridoxine 25mg/day								1	1	

7.6 TPT Initiation and Follow-up

7.6.1 When and How to Start TB Preventive Treatment

Start TB Preventive Treatment	• When a client has been screened and active TB excluded. • When contraindications to TB preventive treatment have been excluded. • When the client is well counseled and willing to start TB preventive treatment.

The health workers should use the 5 A's to prepare eligible people for TB preventive treatment.

Assess for	• Signs and symptoms of active TB. • Use of other medications. • Signs and symptoms of liver disease, peripheral neuropathy & mental illness. • Heavy alcohol consumption.
Advise	Give information about benefits of TB preventive treatment, side effects, regimen and duration of TB preventive treatment, in preparation for self-management. This includes treatment advice and counseling.
Agree	Ensure recipient of care understands, wants and agrees to the TB preventive treatment plan. This is the basis for forming a partnership with the recipient of care & supporting good self-management while on TB preventive treatment.
Assist	Provide help to the recipient of care in terms of skills to adhere to TB preventive treatment & overcome barriers. Treatment buddies offer added benefit for adherence.
Arrange	• Prepare follow up visits according to the schedule in table 1 & 2 below. • Record initiation date in the TPT client held card, TPT care card, TPT register, HIV care/ ART card, and ART registers. • Record appointments in the TPT register & appointment book • Make linkages and referrals for necessary care & support.

All children initiated on TPT should be reviewed every 2 weeks in the first month after initiating therapy and thereafter every month until treatment is completed. Follow up visits for the HIV positive children should be synchronized with the ART clinic visits. Children on TPT should be evaluated for the following on each visit until the treatment is completed.

i. Symptoms and signs of TB
ii. Side effects due to TPT
iii. Adherence to TPT

7.6.2 How to Handle TPT Interruptions

Table 7.2: Managing TB Preventive Treatment Interruptions

6H	3HP	3RH	1HP
If interruption **<1 month**, counsel reassure and client to continue TB preventive treatment. Compensate for lost days.	If interruption is within **3 days** stick to same day of the week e.g. Sunday. If you missed Sunday take the medication within 3 days and go back to your normal Sunday routine.	If interruption is **≤1 month**, counsel and reassure client to continue TB preventive treatment. Compensate for lost days	If interruption **≤1-23 days**, counsel and reassure client to continue TB preventive treatment. Compensate for lost days.
If interruption **>1 month** reassess, rule out active TB, seek client's consent and cooperation for resuming TB preventive treatment. Resume TPT and compensate for lost days.	If interruption **>3 days**; Take your next doze on your usual day. This means you have skipped a week and you will need to continue the medication for an additional week.	If interruption **>1 month**, reassess, rule out active TB, seek client's consent and cooperation to resume preventive TB treatment. Restart 3-months of TPT.	If interruption **>23 days** reassess, rule out active TB, seek client's consent and cooperation to restart TPT all over again.
6H should be **completed within 9 months** or else TPT should restarted all over again.	3HP should **completed within 4 months** or else TPT should restarted all over again.	3RH should be **completed within 4 months** or else TPT should restarted all over again.	

7.6.3 When to Stop TPT

TPT should be discontinued when:

i. Symptoms of TB are present. In such a situation, investigate to rule out active TB.
ii. Child develops active TB.
iii. Severe adverse events occur: Yellow eyes, fever, severe tingling & burning sensation, blurred vision, loss of vision, convulsions, unusual bleeding.

7.6.4 Documentation of TPT

All patients (including children) who are initiated on TPT should be recorded in the TPT register and this register updated on each clinic visit. Information on contacts of bacteriologically confirmed index TB cases who are initiated on TPT should be updated in the unit TB register.

7.7 Contact Screening (Contact Tracing) and Management

Contact Screening

Contact screening (contact tracing) is a systematic process for identifying TB contacts who have TB or are at risk of developing TB. Contact screening comprises of contact identification and prioritization which is a process that includes:

i. Interviewing the index TB case to obtain contact information (e.g. name, age)
ii. Assessment of contacts' risk of having TB or developing TB.

Children less than 5 years and children living with HIV who are in contact with a person with active PTB are at particular risk of TB infection and disease. All household and close contacts of active TB cases should therefore be screened for signs and symptoms of TB. This enables the identification of children who require TPT and TB treatment.

Reverse Contact Investigation (Source Case investigation)

Reverse contact investigation involves the screening of adults who have been in contact with a child diagnosed with TB in order to identify the source case. This has benefits of treating the source case and reducing the transmission of the disease in the household.

Categories of TB Cases who Should have TB Contact Screening Conducted

The following categories of index TB cases should have contact screening conducted:

i. Bacteriologically confirmed PTB
ii. MDR-TB or XDR-TB (confirmed or suspected)
iii. Person living with HIV
iv. Child <5 years of age

7.7.1 How to Conduct TB Contact Screening

Symptom based screening approach is used to identify contacts at risk for TB and contacts with TB. The following are the steps to conduct contact screening:-

Step 1: Identify the index TB cases that should be prioritized for contact screening

Step 2: Initiate the process of TB contact screening by educating the index TB case on contact screening; inquiring about contacts; using health facility and community structures to conduct home visits or inviting the index TB case to bring his or her contacts to the health facility for screening and further management.

Step 3: Contact Identification which involves interviewing the index TB case for information about contacts (e.g. name, age).

Step 4: Assess contacts and assign priorities

The following are at greatest risk of developing TB infection:

i. Close contacts of Bacteriologically confirmed index TB cases.
ii. Persons with HIV infection.
iii. Highly exposed persons e.g. a breastfeeding infant.

The following are at greatest risk of active TB disease

i. Children < 2 years of age
ii. Persons with HIV infection
iii. Persons with other immune compromising conditions or therapies

Step 5: Evaluate contacts

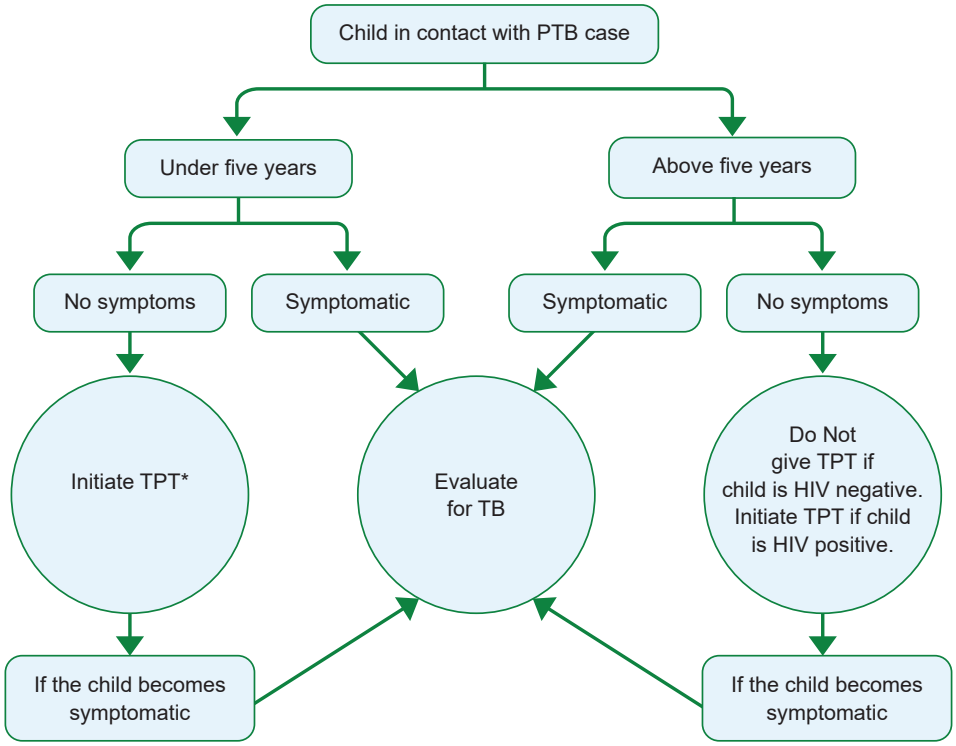
7.7.2 How to Handle Children Exposed to a Case of PTB

Patients with bacteriologically confirmed PTB are more infectious than those who are clinically diagnosed. The following are action points on how to handle children exposed to a case of PTB.

i. All contacts of patients with diagnosed PTB (especially bacteriologically confirmed TB) including MDR TB should be screened for symptoms and signs of TB.
ii. All symptomatic children should be referred to a health facility for further evaluation including history taking, clinical examination, and investigations.
iii. All asymptomatic children under the age of 5 years should be referred to a health facility for TPT initiation. Contacts of MDR TB cases should not receive TPT.

The flow chart summarises the follow up of children who are contacts of TB cases.

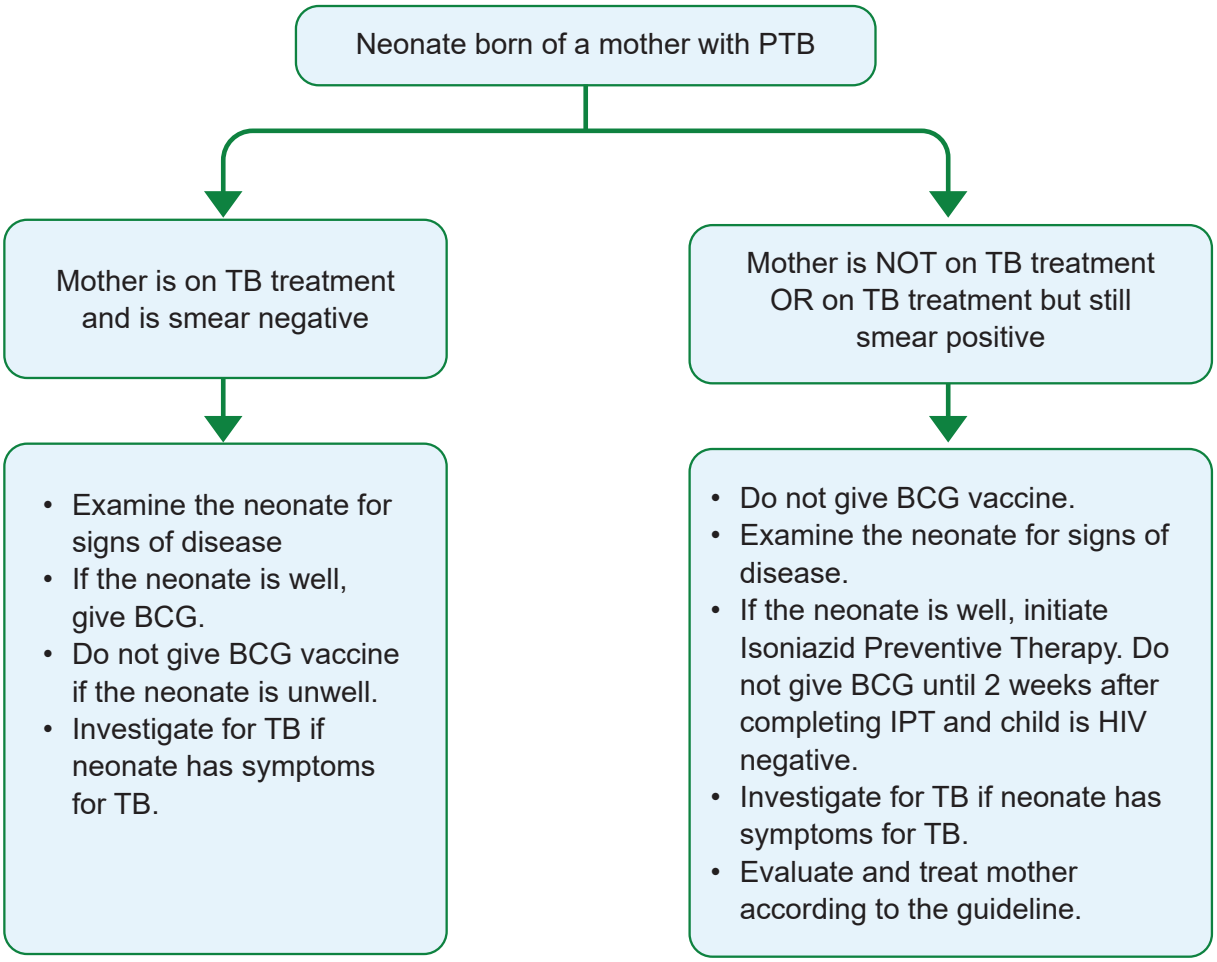
Figure 7.2: Follow-up of a Child Exposed to PTB Case



7.7.3 How to Handle Neonates (Newborns) Exposed to a Mother with PTB

i. A neonate exposed to a mother with PTB (especially bacteriologically confirmed TB) should be screened for TB disease.
ii. Limit contact between the mother and her newborn to breastfeeding periods only until the mother starts on treatment. Advise the mother to continue breastfeeding.
iii. Complete separation of the mother and neonate is only necessary if the mother has possible or confirmed MDR TB. A newborn of a mother with MDR TB should be separated from a mother with untreated MDR TB or who is still smear/culture positive despite treatment. Once a mother is no longer infectious (smears/ culture negative the infant may be cared for by the mother (separation is no longer needed). Once the mother is no longer infectious but still in the intensive phase of treatment at the MDR TB centre, family members may bring the infant for visits, which should occur outdoors.
iv. The infant should not be given BCG until evaluation for TB disease is completed.

Figure 7.3: Follow up of a neonate (new born) of a mother with PTB



7.8 Tuberculosis Infection Control

The goal of infection control is to detect TB disease early and provide prompt treatment to children in order to prevent transmission of the disease in the general community. Older children with TB may transmit TB (those who are bacteriologically confirmed) and therefore infection control is important even in health facilities or areas dedicated only to the management of children. Every health care facility should have a TB infection control plan which ensures that patients presumed to have TB are rapidly investigated, appropriately isolated and rapidly treated to prevent TB transmission.

Key Message

- All newborns should receive BCG vaccination at birth.
- The following categories of children should receive IPT upon exclusion of active TB disease:
  - i. Children under the age of 5 years with a positive history of contact with an active PTB case. This includes both HIV negative and HIV positive children.
  - ii. HIV positive children and adolescents irrespective of TB exposure status and ART status. HIV positive children aged less than 12 months receive IPT ONLY if there is a history of contact with an active PTB case.
- Contacts of MDR TB patients should NOT be given IPT.
- The following categories of index TB cases should have contact investigation conducted.
  - i. Bacteriologically confirmed PTB
  - ii. MDR-TB or XDR-TB (proven or suspected)
  - iii. Person living with HIV
  - iv. Child <5 years of age

CHAPTER 8:
INTEGRATION OF TUBERCULOSIS CARE SERVICES INTO ROUTINE AND OTHER HEALTH CARE SERVICE POINTS

As mentioned, children are more at risk for TB disease, and severe forms of disease when exposed to TB. This is worse if the child is HIV infected. These children often present at other entry points including HIV clinics; maternal, newborn, and child health (MNCH) clinics as well as lower level health facilities rather than specialized TB clinics. Integration of TB care services at the various health care service points enhances early childhood TB case finding, treatment, prevention, and improves outcomes.

The TB care services include:

a. TB health education
b. TB screening using the ICF guide
c. HIV testing
d. TB evaluation and management
e. TB treatment
f. TPT for under five TB contacts and HIV positive children (>12months) and adolescents
g. TB Contact screening and management
h. TB Infection control
i. TB/HIV Documentation
j. Continuous Quality Improvement

8.1 Integration of TB Care Services into Routine Health Facility Care Service Points

The following are routine health care service points into which the above TB care services should be integrated:

a. Out Patient Department (OPD)
b. Young Child Clinic (YCC)
c. Nutrition Unit
d. In-Patient
e. Antenatal Care (ANC)
f. Maternity
g. Post Natal Care (PNC)

8.2 Integration of TB Care Services Into Other Health Facility Care Service Points

The following are the other health care service points into which TB care services should be integrated:

a. HIV/ART clinic
b. Mother-Baby care point (which is also integrated into MNCH)

8.3 Integration of TB Care Services into the Community Healthcare Service Point

Engaging the community and family through existing structures (village health teams, community health workers) provides an opportunity to:

a. Strengthen early identification of TB cases and those who require TPT through TB symptom screening and referral.
b. Strengthen treatment adherence by enhancing DOT.
c. Promptly identify and refer TB contacts in need of clinical evaluation for TB and asymptomatic children under the age of five years who will benefit from TPT.
d. Follow up of patients on TB treatment and have missed their clinic appointments (including follow up sputum smears).

Community outreach programs (such as immunization, deworming) also provide an opportunity for TB symptom screening.

CHAPTER 9:

RECORDING AND REPORTING DATA ON TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

The NLTP is responsible for ensuring that all TB cases and their treatment outcomes (which includes children) are appropriately recorded and reported. For NLTP to have complete and accurate data on TB, it is very important that timely and correct recording and reporting is done. The national TB recording and reporting (R&R) tools are used to capture data on both children and adults. All children diagnosed with TB (including their HIV status, TB disease type, treatment outcomes) should routinely be recorded and reported to the NLTP using the national recommended TB R&R tools.

9.1 Recording Data on TB in Children

➲ Health Facility Level

i. All children presumed to have TB should be recorded in the presumptive TB and information on TB status updated in the appropriate registers where the child has been evaluated e.g. OPD, child, nutrition, in-patient, Pre-ART/ ART registers.
ii. Health workers should endeavour to obtain a TB specimen from children with presumptive TB and once this specimen is submitted the laboratory, the details of the child and specimen should be recorded in the Unit Laboratory TB register.
iii. All children diagnosed with TB should be accurately registered in the Unit TB register at each health facility. If the child has TB/HIV co-infection, the same information should be recorded in the ART card and Pre-ART/ART registers.
iv. All children diagnosed with TB should have a TB treatment card accurately completed by the health worker, and their care givers (or child in case of older children) educated on how to complete the card.
v. For each bacteriologically confirmed PTB, case, the number of contacts under five years of age and those that are started on Isoniazid should be documented in the Unit TB register.
vi. The MOH has introduced an TPT register that will be used to capture infor- mation on children initiated on TPT.

➲ District/ Division Level

i. All children diagnosed with TB should be accurately documented in the District TB register.
ii. For each bacteriologically confirmed PTB, case, the number of contacts under five years of age and those that are started on Isoniazid should be documented in the district TB register.

9.2 Reporting Data on TB in Children

Health Facility Level

Each health facility should complete and submit monthly HMIS 105 and quarterly HMIS 106a reports to the district. These reports capture data on TB in children.

District Division level

The health facility quarterly HMIS 106a report is entered into DHIS2 at the district level.

National level

Completed quarterly reports for all the districts / divisions are routinely sub- mitted to the NLTP central office by the regional TB and Leprosy focal persons and MoH resource center through the District Health Information System (DHIS2). These reports should include data on children.

9.3 TB Treatment Outcomes

The following are outcomes for all patients (including children) started on TB treatment and should be routinely recorded and reported.

Table 9.1: TB Treatment Outcomes

Treatment Outcomes	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.
Lost 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 whom the treatment outcome is unknown to the reporting unit.
Treatment success	The sum of cured and treatment completed.

9.3.1 Childhood TB Indicators

Indicators are parameters used in monitoring and evaluating any program performance. The following are the childhood TB indicators that will be used to monitor and evaluate the childhood TB at national and can also be applied at regional, district, and facility levels.

Table 9.1: TB Treatment Outcomes

Output Indicator	Significance
i. Proportion of children with TB among all new cases of all forms of TB	Effectiveness of paediatric TB case finding efforts.
ii. Number of household contacts under five who are initiated on TPT out of all those eligible for TPT	Implementation of TPT.
Process Indicator	**Significance**
i. Proportion of TB cases in age groups 0–4, 5-9, 10-14, 15-19.	Age distribution of child and adolescent TB disease.
ii. Proportion of bacteriologically confirmed TB, clinically diagnosed TB, EPTB among all childhood TB cases.	Distribution of disease type category.
iii. Proportion of childhood TB cases that received HCT.	Quality of care
iv. Proportion of childhood TB cases that are HIV infected.	Magnitude of HIV among children with TB disease.
v. Proportion of children with TB /HIV co-infection initiated on ART.	Quality of care
vi. Proportion of children with TB that completed treatment.	Quality of care
vii. Proportion of children with TB that died.	Quality of care
viii. Proportion of children with TB that were lost to follow up.	Quality of care
ix. Proportion of children with TB that were not evaluated.	Quality of care

APPENDIX

APPENDIX A:
PROTOCOLS FOR SPECIMEN COLLECTION

All sputum specimen produced by children should be sent for a GeneXpert and, where not available, smear microscopy. A negative laboratory test for TB does not exclude TB.

Expectoration

Background

Children who can produce a sputum specimen may be infectious, so, as with adults, they should be asked to do this outside and not in an enclosed space (such as a toilet) unless there is a room especially equipped for this purpose.

Give the child confidence by explaining to him or her (and any family members) the reason for sputum collection. Instruct the child to rinse his or her mouth with water before producing the specimen. This will help to remove food and any contaminating bacteria in the mouth. Instruct the child to take two deep breaths, holding the breath for a few seconds after each inhalation and then exhaling slowly. Ask him or her to breathe in a third time and then forcefully blow the air out. Ask him or her to breathe in again and then cough. This should produce sputum from deep in the lungs. Ask the child to hold the sputum container close to the lips and to spit into it gently after a productive cough.

If the amount of sputum is insufficient, encourage the patient to cough again until a satisfactory amount of sputum is obtained. Give the child sufficient time to produce an expectoration that he or she feels is produced by a deep cough. If the child does not produce a sample at that particular time, request the primary care taker to try and obtain a sample in the early morning.

Gastric Aspiration

Background

Children with TB may swallow mucus that contains the TB bacteria. Gastric aspiration is a technique used to collect gastric contents to try to confirm the diagnosis of TB by GeneXpert, microscopy, and TB culture. Gastric aspirates

are used for collection of samples in young children who cannot cough out sputum on their own. The highest yield of specimen is obtained in the morning. Performing the test properly requires 2 people (one doing the procedure and an assistant). The child should have fasted for at least 4 hours (3 hours for infant) before the procedure. Children with a low platelet count or bleeding should undergo the procedure.

Educate the care giver of the child on the procedure and obtain informed consent.

Requirements

i. Gloves
ii. Nasogastric tube (size 6 or 8)
iii. Syringe of capacity 5, 10, 20 or 30 ml, with appropriate connector for the nasogastric tube
iv. Specimen containers
v. Pen (to label specimen)
vi. Laboratory requisition forms
vii. Normal saline
viii. Sodium bicarbonate (8%)
ix. Alcohol or Chlorhexidine

Procedure

Gastric aspiration can be carried out as an inpatient procedure first thing in the morning when the child wakes up, or as an outpatient procedure. The child should have fasted for at least 4 hours (infants for 3 hours) before the procedure.

i. Find an assistant to help.
ii. Prepare all equipment before starting the procedure.
iii. Position the child on his or her back or side. The assistant should help to hold the child.
iv. Measure the distance between the nose and stomach, to estimate how far the tube will need to be inserted to reach the stomach.
v. Attach a syringe to the nasogastric tube.
vi. Gently insert the nasogastric tube through the nose and advance it into the stomach.
vii. Withdraw (aspirate) gastric contents (2 – 5 ml) using the syringe attached to the nasogastric tube.
viii. To check that the position of the tube is correct, push some air (3 – 5 ml) from an empty syringe into the stomach and listen with a stethoscope over the stomach. If the tube is in the airway, bubbles will be seen when the outerend of the tube is immersed into a dish of water. In such a case, remove the tuber immediately.
ix. If no fluid is aspirated, insert 5 – 10 ml of sterile water or normal saline and attempt to aspirate again. If still unsuccessful, repeat the procedure.
x. Do not repeat the procedure more than 3 times.
xi. Withdraw the gastric contents (at least 5 – 10 ml).
xii. Transfer the gastric fluid from the syringe a sterile sputum container.
xiii. Add an equal volume of sodium bicarbonate solution to the specimen in order to neutralize the acidic gastric contents and so prevent de- struction of the TB bacterias.

After the Procedure

i. Wipe the specimen container with alcohol/chlorhexidine to prevent cross-infection and label the container.
ii. Fill out the laboratory requisition forms.
iii. Transport the specimen to the laboratory for processing as soon as pos- sible (within hours).
iv. It if is likely to take more than 4 hours for the specimens to be transported, place the specimen in a refrigerator (4-8°c) and store until transported.
v. Give the child his or her usual food.

Safety

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

Sputum Induction

Background

It is important to note that, unlike gastric aspiration, sputum induction is an aerosol – generating procedure. Where possible, therefore, this procedure should be performed in an isolation room that has adequate infection control precautions.
Sputum induction is regarded as a low risk procedure for the child to be evalu- ated for TB. The reported adverse events included:- coughing spells, mild wheezing, and nose bleeds. The procedure can safely be performed in young infants though requires specialized training and equipment.

Children with the following characteristics should not undergo sputum induction:

i. Inadequate fasting (postpone the procedure if the child has not fasted for at least 3 hours)
ii. Respiratory distress (including fast breathing, wheezing, hy- poxia)
iii. Asthma
iv. Intubation
v. Low platelet count
vi. Bleeding tendency
vii. Nosebleeds (symptomatic or platelet count < 50 cells/ml)
viii. Reduced level of consciousness

Educate the care giver of the child on the procedure and obtain informed consent.

Procedure

i. Administer a bronchodilator (e.g salbutamol) to reduce the risk of wheezing
ii. Administer nebulized hypertonic saline (3% NaCl) for 15 minutes or until 5 ml of solution has been fully administered.
iii. Carry out chest physiotherapy if necessary; this is useful to mobilize secre- tions.
iv. For older children who are able to expectorate, follow procedures as de- scribed under "expectoration" above to collect sputum.
v. For younger children who are unable to expectorate, carry out suction the nasopharynx to collect a suitable sample
vi. Any equipment that will be reused must be disinfected and sterilized before use in a subsequent patient

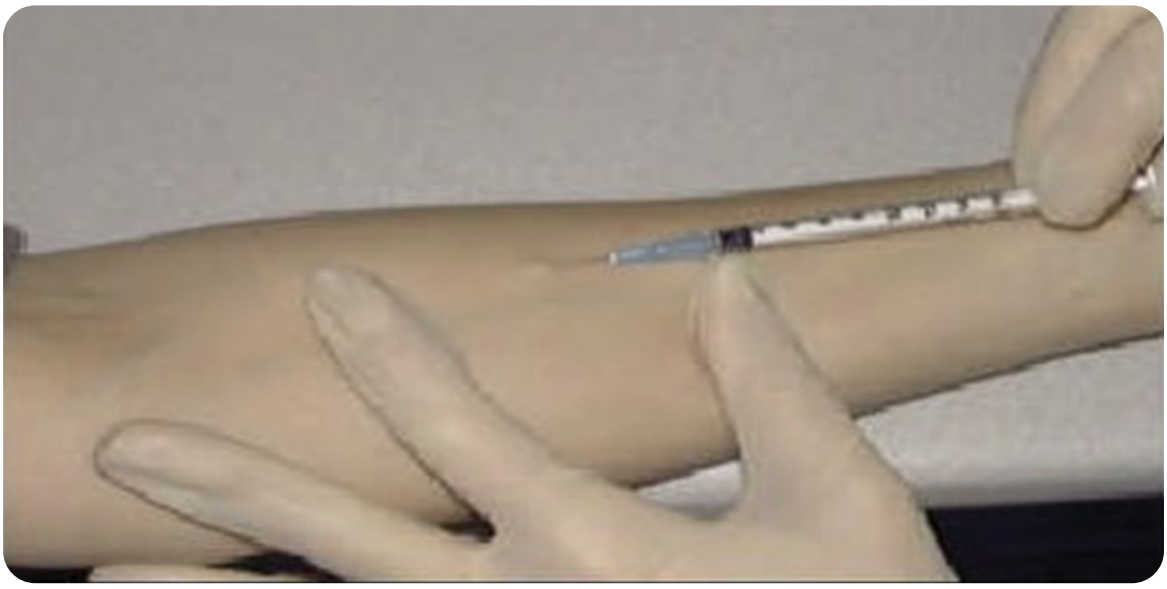
APPENDIX B:
PROTOCOL FOR TUBERCULIN SKIN TEST (MANTOUX TEST)

Background

A TST is the intradermal injection of a combination of mycobacterial antigens which elicit an immune response (delayed-type hypersensitivity), represented by induration, which can be measured in millimetres. The TST using the Man- toux method is the standard method of identifying people infected with M. tuberculosis. Multiple puncture tests should not be used to determine whether a person is infected, as these tests are unreliable (because the amount of tuberculin injected intradermally cannot be precisely controlled).

Administration

1. **Locate and clean injection site 5–10 cm (2–4 inches) below elbow joint**
   - Place forearm palm-side up on a firm, well-lit surface.
   - Select an area free of barriers (e.g. scars, sores) to placing and reading
   - Clean the area with an alcohol swab.
2. **Prepare syringe**
   Fill the syringe with 0.1 ml tuberculin.
3. **Inject tuberculin (see figure below)**
   - Insert the needle slowly, bevel up, at an angle of 5–15 °.
   - Needle bevel should be visible just below skin surface.
4. **Check injection site**
   After injection, a flat intradermal wheal of 8–10 mm diameter should appear. If not, repeat the injection at a site at least 5 cm (2 inches) away from the original site.
5. **Record information**



Reading

The results should be read between 48 and 72 hours after administration.

1. Inspect site
2. Palpate induration
3. Mark induration
4. Measure diameter of induration using a clear flexible ruler.
5. Record diameter of induration.

Interpretation

1. Diameter of induration of ≥5 mm is considered positive in:
   a. HIV-infected children.
   b. Severely malnourished children (with clinical evidence of oedematous or non oedematous malnutrition).
2. Diameter of induration of ≥10 mm is considered positive in:
   All other children (whether or not they have received BCG vaccination).

APPENDIX C:
SOS STOOL PROCESSING METHOD

Principle

The SOS stool processing method uses one step to release M. tuberculosis from stool. Particulate matter is sedimented by gravity, and it is assumed that this allows TB bacilli to float to the top of the watery solution because of their lipid-containing cell wall (20).

Biosafety Requirements

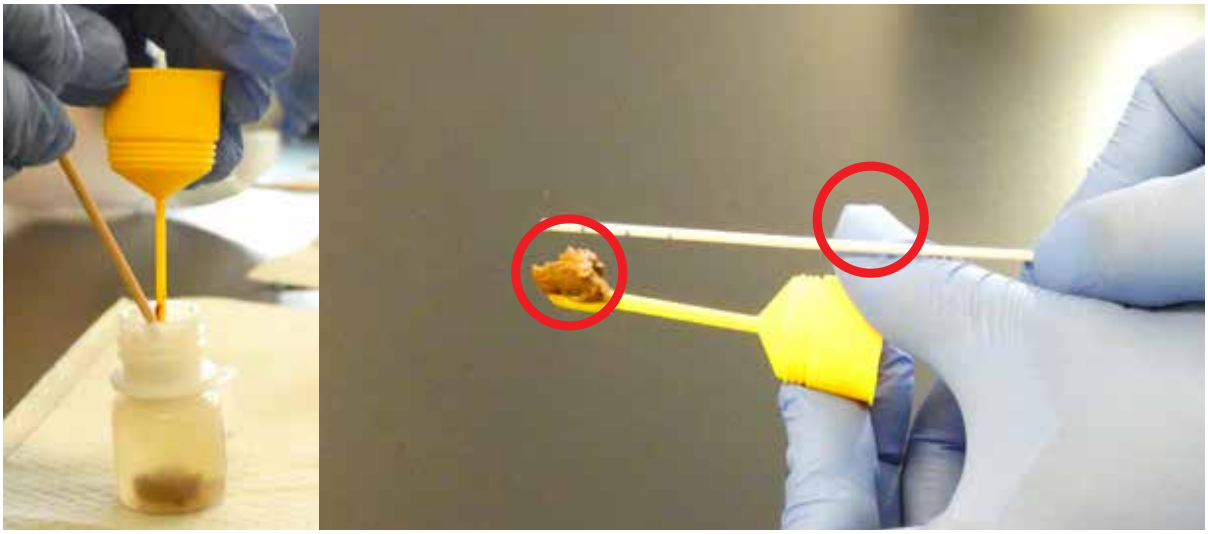
In the SOS stool method, stool is added directly into the SR bottle provided in the Xpert kit; this results in immediate inactivation of the bacteria. Therefore, the SOS stool method can be performed in an open, well-ventilated space with appropriate aerosol reduction practices and appropriate use of PPE.

Procedure

Before stool processing, the consistency of the stool specimen is assessed using the Bristol stool scale (30). For stool with the appearance of Bristol type 1 to 5 (formed stool), 0.8 g or a thumbnail size amount of stool (Fig. 3) is directly transferred from the stool container into the SR bottle using a wooden stick or applicator (Fig. 4). For stool with the appearance of Bristol type 6 and 7 (liquid stool), 2 mL SR is removed from the SR bottle, then 2 mL of stool is transferred to the SR bottle using a balloon pipette (Fig. 3). For all types of stools, the SR is shaken vigorously for 30 seconds and then incubated for 10 minutes at room temperature. This step is repeated once.

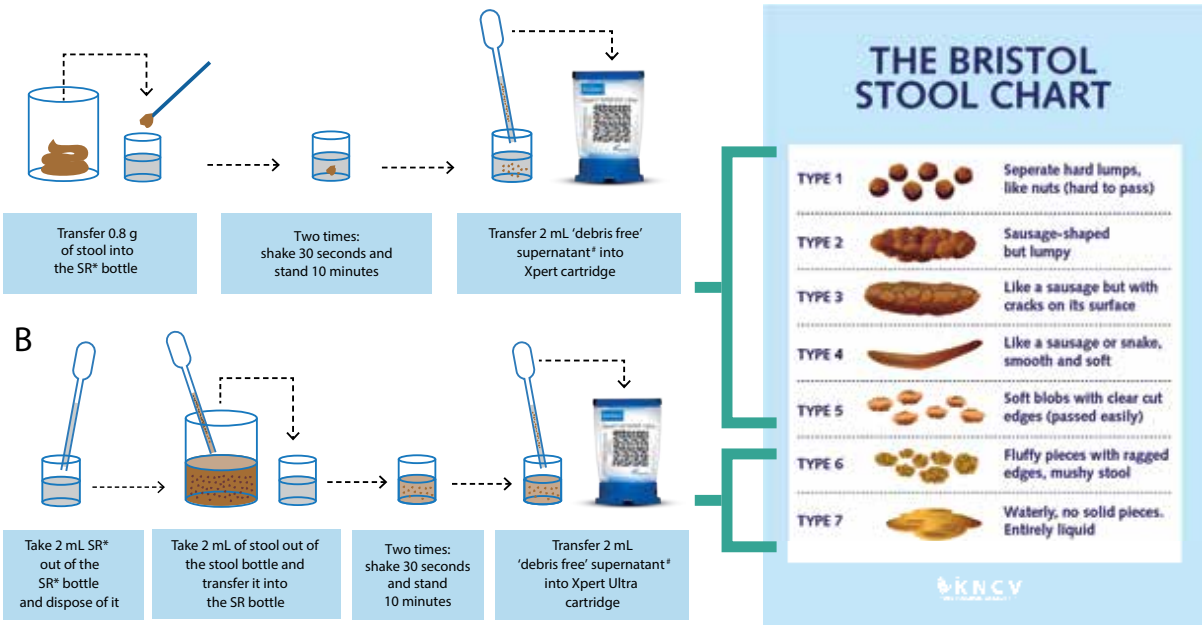
After carefully ensuring that solid particles and debris have settled, 2 mL of the supernatant is then transferred from the SR bottle to the Xpert MTB/RIF or Xpert Ultra cartridge. The cartridge is then inserted into the GeneXpert instrument. Use of the GeneXpert instrument and interpretation of Xpert results is done according to the manufacturer's instructions. A detailed SOP on how to perform the SOS stool processing method can be found in the KNCV stool toolbox on the KNCV website (31).

In the SOS stool processing method, 0.8 g or an amount of stool equal to the size of a thumbnail is used



SOS: simple one-step.

Schematic overview of the SOP of the SOS stool processing method and the Xpert MTB/RIF or Xpert Ultra assay for different types of stools[a]



* sample reagent buffer

SOP: standard operating procedure; SOS: simple one-step; SR: sample reagent.

[a] The upper panel shows the procedure for stool of Bristol type 1–5 (i.e. formed stool) and the lower panel for stool of Bristol type 6 and 7 (i.e. liquid stool).

MINISTRY OF HEALTH

NATIONAL LEPROSY/TB
CONTROL PROGRAMME

NATIONAL GUIDELINES FOR THE MANAGEMENT OF TUBERCULOSIS

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