

THE UNITED REPUBLIC OF TANZANIA



**MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT,
GENDER, ELDERLY AND CHILDREN**

**NATIONAL GUIDELINES FOR THE MANAGEMENT OF
TUBERCULOSIS IN CHILDREN**

**NATIONAL TUBERCULOSIS AND LEPROSY PROGRAMME
(NTLP)
Third Edition, 2016**

TABLE OF CONTENTS

ABBREVIATIONS.....	5
ACKNOWLEDGEMENTS.....	6
FOREWORD.....	7
1 GENERAL INFORMATION ABOUT TUBERCULOSIS IN CHILDREN.....	8
1.1 Epidemiology of tuberculosis in children: globally and in Tanzania	8
1.2 Tuberculosis in children and the need for specific guidelines	8
1.3 Natural history and pathogenesis of tuberculosis	9
2 DIAGNOSIS OF TUBERCULOSIS DISEASE IN CHILDREN.....	12
2.1 Pulmonary tuberculosis	13
2.2 Diagnosis of extrapulmonary tuberculosis	19
2.3 Classification based on anatomical site of disease	25
3 MANAGEMENT OF TUBERCULOSIS DISEASE IN CHILDREN.....	27
3.1 Treatment regimens for tuberculosis disease.....	27
3.2 Medications and dosages	28
3.3 Fixed-dose combination tablets	28
3.4 Practical guidance for administering medicines to children.....	29
3.5 Steroid use for tuberculosis.....	30
3.6 Management of adverse reactions to anti-tuberculosis medications.....	30
3.7 Management of cutaneous reactions.....	31
3.8 Management of drug-induced hepatitis	32
3.9 Monitoring treatment and directly observed therapy	33
3.10 Clinical and bacteriologic response.....	34
3.11 Treatment failure (confirming failure and management).....	35
3.12 Managing treatment interruption	35
3.13 Ancillary and supportive care.....	36
3.14 Nutrition for children with tuberculosis	36

3.15	Counseling for children with tuberculosis	37
4	PREVENTION OF TUBERCULOSIS IN CHILDREN.....	40
4.1	Bacille Calmette-Guérin immunisation	40
4.2	Management of latent TB infection in children.....	41
4.3	Tuberculosis infection control	45
5	PAEDIATRIC TUBERCULOSIS IN SPECIAL SITUATIONS.....	46
5.1	TB/HIV in children	46
5.2	Drug-resistant tuberculosis in children.....	52
6	RECORDING, REPORTING AND USE OF DATA FOR CHILDREN WITH TUBERCULOSIS	58
6.1	Introduction	58
6.2	TB Recording and Reporting Tools in Children	58
6.3	Recording and Reporting of Outcomes of Child TB Cases	60
7	ROLES AND RESPONSIBILITIES OF THE HEALTH SYSTEM IN DIAGNOSIS AND MANAGEMENT OF CHILDREN WITH TUBERCULOSIS.....	64
7.1	Introduction.....	64
7.2	Community Level TB care	64
7.3	Health facility level TB care.....	64
7.4	Integration of TB services into Reproductive and Child Health services	65
ANNEX 1:	SPUTUM INDUCTION	66
ANNEX2:	GASTRIC ASPIRATION.....	68
ANNEX 3:	DIAGNOSIS AND MANAGEMENT OF MALNUTRITION	70
ANNEX 4:	Drug Re-introduction Challenge following drug-induced hepatitis for children based on weight-bands.....	72
ANNEX 5:	DIAGNOSIS OF HIV INFECTION IN INFANTS AND CHILDREN LESS THAN 18 MONTHS	74
ANNEX 6:	TUBERCULOSIS SCREENING AND IPT ELIGIBILITY TOOL FOR USE WITH HIV/AIDS PATIENTS	76
ANNEX 7:	TUBERCULOSIS DIAGNOSTIC TOOLS AND THE IMPACT OF HIV ON THEIR INTERPRETATION	80
ANNEX 8:	CAUSES OF LUNG DISEASE IN HIV-INFECTED INFANTS AND CHILDREN	81

References 83

ABBREVIATIONS

AFB	Acid-fast bacillus
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine aminotransferase
ART	Antiretroviral therapy
AST	Aspartate aminotransferase
BCG	Bacille Calmette-Guérin
CDC	United States Centers for Disease Control and Prevention
CPT	Cotrimoxazole preventive therapy
CSF	Cerebral spinal fluid
CT	Computed tomography
CTC	Care and treatment clinic
CTRL	Central Tuberculosis Reference Laboratory
CXR	Chest x-ray
DOT	Directly observed therapy
DST	Drug susceptibility testing
DTLC	District Tuberculosis and Leprosy Coordinator
FDC	Fixed-dose combination
HIV	Human Immunodeficiency Virus
IGRA	Interferon gamma release assay
IPT	Isoniazid preventive treatment
IRIS	Immune Reconstitution Inflammatory Syndrome
LFT	Liver function test
LTBI	Latent tuberculosis infection
MDRTB	Multidrug-resistant tuberculosis
MoHCDGEC	Ministry of Health, Community Development, Gender, Elderly and Children
MRI	Magnetic resonance imaging
NTLP	National Tuberculosis and Leprosy Programme
PATH	Program for Appropriate Technology in Health
RTL	Regional Tuberculosis and Leprosy Coordinator
RUTF	Ready-to-use therapeutic food
TB	Tuberculosis
TSH	Thyroid-stimulating hormone
TST	Tuberculin skin test
WHO	World Health Organization

Anti-tuberculosis drug abbreviations

E	Ethambutol
H	Isoniazid
PAS	Para-aminosalicylic acid
R	Rifampicin
S	Streptomycin
Z	Pyrazinamide

HIV drug abbreviations

3TC	Lamivudine
ABC	Abacavir
AZT	Zidovudine
EFV	Efavirenz
LPV/r	Lopinavir/ritonavir
NRTI	Nucleoside reverse transcriptase inhibitor NNRTI Non-nucleoside reverse transcriptase inhibitor NVP Nevirapine
SMZ	Sulfamethoxazole
TMP	Trimethoprim

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Dr. Neema Rusibamayila

Director of Preventive Services

January, 2017

FOREWORD

According to the Ministry of health, Community Development, Gender, Elderly and Children (MoHCDGEC) – NTLP annual reports, the notification for childhood TB for the past 4 years is approximately 10 percent of all TB cases notified in the country. WHO has estimated in epidemic countries including Tanzania, almost 15% – 20% of notified TB cases are likely to be children . The first guideline was developed in 2012 and was then revised in 2013.

The revision of the Guidelines for the management of Tuberculosis in children follows evidence that has been generated globally from randomized controlled trials, observational studies, operational research, and best practices from programmatic implementation. TB alliance has introduced and launched a new pediatric formulation which will be adopted by many countries including Tanzania. This new formulation is believed to have better adherence by both mothers and children.

The revised guidelines demonstrate the commitment of the Ministry to fight against tuberculosis in children in order to reduce morbidity and mortality. National TB and Leprosy Programme (NTLP), the National AIDS Control Programme (NACP), and other stakeholders will work synergistically to reduce the burden of TB/HIV co-infection.

The Ministry engaged a wide range of stakeholders that participated in a lengthy process to revise the document. The principles presented here reflect the substantial input, informed expert opinions, content, and quality of work that were contributed by all of the stakeholders throughout this process.

The Ministry is satisfied that this document reflects national and international standards for guidelines. Because of the extensive process to involve a wide range of stakeholders and various organizations, the Ministry is confident that the appropriate implementation of the guidelines will bring the anticipated positive impact for children affected by the TB and HIV epidemics.

It is important to note that this policy is just one dimension of the Government of Tanzania's efforts to combat the dual epidemics and should not be regarded as a panacea to the TB and HIV epidemics. Other dimensions that the Government of Tanzania is considering include increasing the availability of resources to implement the policy, supporting the 7ilitary7ion7l structure through which the policy guidelines will be practiced, developing the overall management system of collaborative TB/HIV activities, and supporting a system of policy implementation as well as actual service delivery.

Finally, it is the hope of the MoHCDGEC that every one of the stakeholders will effectively comply with the policy guidelines. Let everyone play their part and it will be accomplished.

Prof. Muhammad Bakari Kambi
Chief Medical Officer
January, 2017

1 GENERAL INFORMATION ABOUT TUBERCULOSIS IN CHILDREN

1.1 Epidemiology of tuberculosis in children: globally and in Tanzania

Tuberculosis (TB) is among the top 10 causes of illness and death among children worldwide. Globally in 2015, there were an estimated 10.4 million incident cases of TB. Among those 1.0 million (10%) were children. In 2015, WHO estimated that TB killed 1.4 million people with an additional of 0.4 million deaths due to TB among people living with HIV.

The magnitude of TB disease amongst children in Tanzania is difficult to ascertain due to challenges of diagnosis and reporting. However, data from the NTLP show that paediatric cases were 5,699 (9.4%) of all cases notified in 2015. As the overall incidence of TB infection is decreasing in Tanzania, the greater number of paediatric diagnoses likely reflects improvements in recognition of the disease in children. (See Figures 1.1 and 1.2 on the following page)

1.2 Tuberculosis in children and the need for specific guidelines

Despite several interventions which have been made, still there is gradual increase of TB case notification among children. Infants and young children are highly susceptible to TB. The diagnosis of pulmonary TB (PTB) in children is a common clinical challenge because of the atypical nature of TB symptoms and the rapid progression of TB infection to TB disease. Bacteriological confirmation is also rarely possible and according to the NTLP report of 2015, bacteriological confirmed pulmonary TB in children aged <15 years accounted for 9.3% of all reported paediatric TB cases. Significant number of cases of TB in children are missed and remain undetected because of the diagnostic challenges thereby contributing to the high TB related morbidity and mortality in this age group. These challenges include, lack of knowledge and skills among health care workers to detect and manage TB in children, under utilization of screening tools, unavailability of diagnostic tools, inadequate contact tracing and insufficient operational research in this area. This paediatric guideline has been developed to guide the health care workers on prompt management of TB in children.

Figure 1.1. Proportion of children amongst new TB cases notified; 2006 to 2015

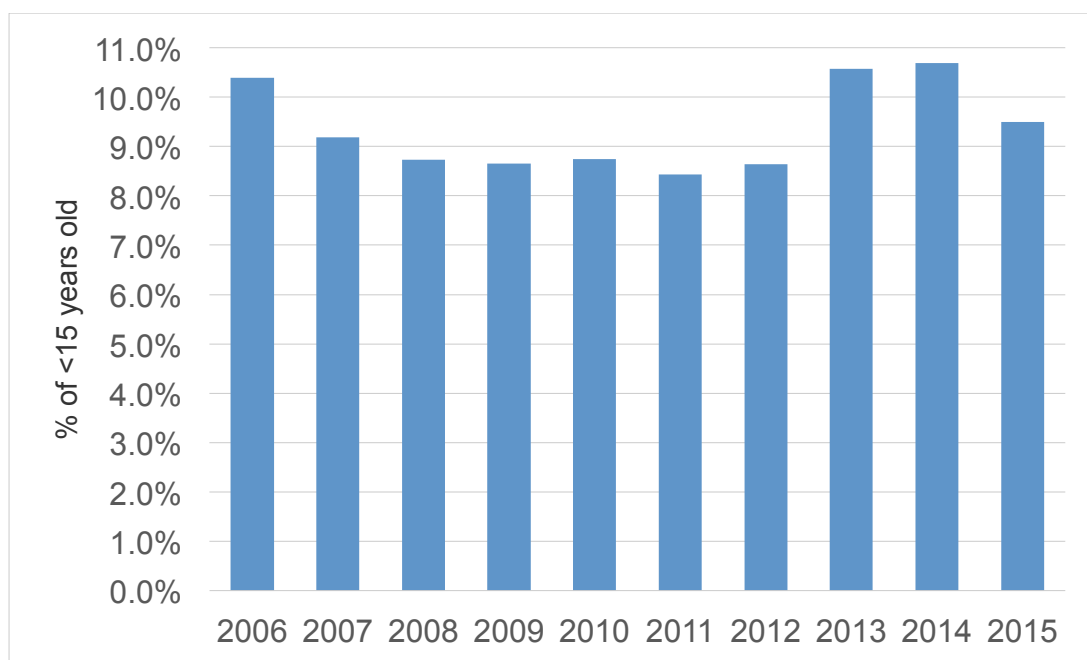
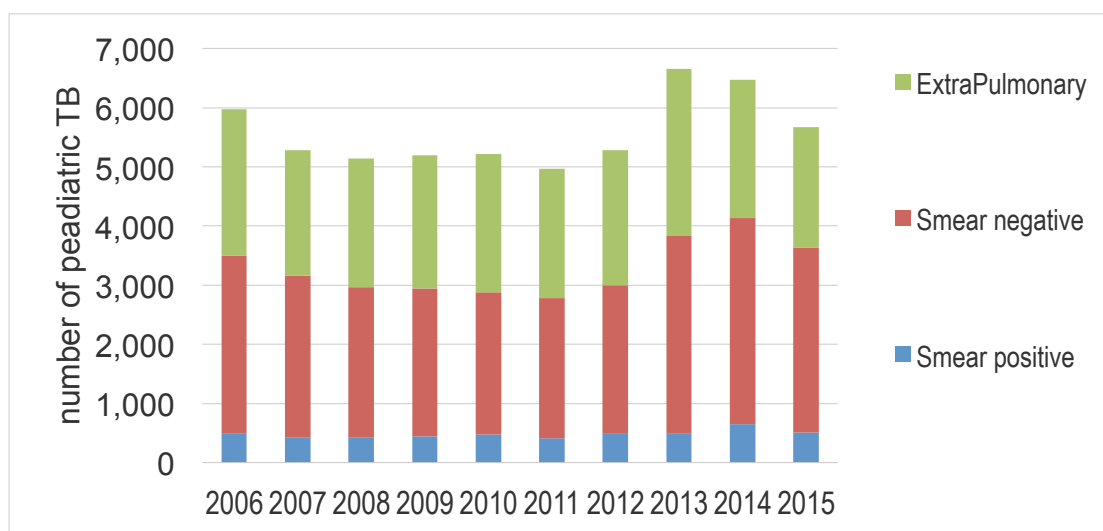


Figure 1.2 Trends in paediatric (<15 years) TB case notification (new cases); 2006 to 2015



According to the drug resistance survey conducted in 2006/2007 amongst smear-positive notified cases, the prevalence of multidrug-resistant tuberculosis (MDR TB) in Tanzania was 1.1 percent and 3.1 percent amongst new and retreated TB cases respectively. In 2014, there were an estimated 600 MDR TB cases in the country and only 34 MDR TB cases were notified (NLP data, 2014). No available data for children with MDR TB; this is largely attributed by difficulties in diagnosis.

1.3 Natural history and pathogenesis of tuberculosis

Tuberculosis is caused by *Mycobacterium tuberculosis*, an acid-fast bacillus

(AFB). A child is exposed to the tubercle bacilli when in contact with an adult or adolescent with infectious TB (AFB smear positive). Upon inhalation, the tubercle bacilli are deposited in the lungs and multiply initially within the terminal alveoli. This primary lesion is called a Ghon focus. Some of the bacilli are phagocytosed but not killed by macrophages that carry the organisms through lymphatic channels to the regional lymph nodes, mainly in the hilar region. Lymphatic and haematogenous spread of the bacilli to almost any organ in the body can occur and cause disseminated disease such as meningitis or miliary disease.

The incubation period between when tubercle bacilli are inhaled and the development of delayed hypersensitivity in children is most often 4 to 8 weeks. This is demonstrated by the development of a positive tuberculin skin test (TST, also called a Mantoux test). In the majority of children infected, the immune response stops the multiplication of *M. tuberculosis* bacilli at this stage and the infection remains latent for many years, possibly a lifetime. Children with latent tuberculosis infection (LTBI) have no signs or symptoms of TB disease. However, reactivation TB may occur in individuals with a weak immune system due to malnutrition, malignancy, chronic or recurrent infections, or HIV/AIDS. In some individuals, the immune response is not sufficient to contain the primary infection and disease occurs within a few months. Progression to disease is highest in the first 6 months after infection but remains high for 2 years. Risk of progression is increased when primary infection occurs before adolescence (less than 10 years of age)—particularly in the very young (0–4 years)—and in immunocompromised children. Diagnosis of TB disease in young children represents recent transmission of *M. tuberculosis*, and efforts should be made to identify and treat the source case (usually an adult in the household or a family member).

Most children who develop TB disease experience pulmonary manifestations. Young children (less than age 4) and immunosuppressed children can develop complicated and unusual forms of intrathoracic TB due to altered or deficient immune responses to *M. tuberculosis*. Children younger than 10 years generally have paucibacillary disease and a nonproductive cough. Thus, they present a low risk for transmission of infection to others. However, children with laryngeal disease can be infectious, even at a very young age.

Infants and children less than 2 years are at very high risk for progression from LTBI to TB disease due to their immature immune systems. Once these children develop TB disease, they are more likely to rapidly progress to a more serious form of TB, such as TB meningitis or miliary (disseminated) TB. These forms can be life threatening and therefore always warrant immediate evaluation and initiation of therapy. Children in this age group often have non-specific symptoms such as loss of appetite, poor weight gain or weight loss, and lethargy.

M. tuberculosis is a slow-growing organism, so long treatment courses are necessary to achieve eradication. Treatment also requires the use of multiple

antibiotics to prevent the development of drug-resistant strains. Due to the length and complexity of treatment regimens, poor adherence to medication is a barrier to successful treatment. Use of fixed-dose combinations (FDCs) and directly observed therapy (DOT) programs greatly improve outcomes.

2 DIAGNOSIS OF TUBERCULOSIS DISEASE IN CHILDREN

Diagnosing TB disease in children is challenging because it is difficult to achieve bacteriologic confirmation. The diagnosis therefore combines a history of exposure to an infectious TB source, clinical presentation, and laboratory and radiologic examinations.

To evaluate a child suspected of having TB, the MoHCDGEC recommends conducting the following:

- Complete history, including a history of TB contact and symptoms consistent with TB disease.
- Clinical examination and use of a scoring chart (including growth assessment) to look for the various signs of TB disease.
- Tuberculin skin test whenever available.
- Bacteriologic confirmation whenever possible.
- Investigations relevant for suspected pulmonary and extra-pulmonary TB, including chest radiography for pulmonary TB.
- HIV testing for all TB suspects.

All findings must be considered carefully, but when a history of close contact with a case of TB, especially an infectious (smear +/ MTB +) case, is present, this strongly supports a diagnosis of TB in a child, especially in those younger than 5 years.

Bacteriologic confirmation is achievable in only about 30 – 40% of cases; therefore, a diagnosis of TB (pulmonary or extra-pulmonary) in a child is often based on the presence of the classic tetrad:

1. History of close contact with an infectious case (AFB smear + or MTB +).
2. Signs and symptoms of TB disease from history and physical examination.
3. A positive TST.
4. Suggestive findings of TB disease on indicated laboratory or radiologic investigations (chest radiograph, fine needle aspiration, spinal radiograph, abdominal ultrasound, etc.).

2.1 Pulmonary tuberculosis

Clinical presentation in infants

Infants with pulmonary TB are more likely to be symptomatic because of their small airway diameters relative to the parenchymal and lymph node changes. The most common pulmonary symptoms are nonproductive cough and difficulty breathing. Systemic symptoms such as fever, anorexia, poor weight gain, weight loss, and failure to thrive may also occur. Infants with TB often present as a case of severe pneumonia with fast breathing, chest indrawing, and respiratory distress. Infants may present with decreased activity, increased irritability or lethargy.

Clinical presentation in children

Pulmonary disease and associated intra-thoracic (hilar) adenopathy are the most frequent findings of TB in preschool and school-aged children. Common symptoms of pulmonary TB in children in this age group include:

- History of close contact with TB.
- Cough for 2 or more weeks (or any cough for HIV-positive children).
- Fever for at least 2 weeks without other obvious cause and not improving with antibiotics/antimalarials.
- Weight loss, weight faltering, failure to gain weight, or failure to thrive.
- Reduced activity and irritability.

Although these symptoms are nonspecific, their presence supports a diagnosis of pulmonary TB.

There are no specific features on clinical examination that can confirm that the presenting illness is due to pulmonary TB. However, persistent fever (temperature $>38^{\circ}\text{C}$ daily for more than 14 days), chronic cough that does not respond to antibiotics, and failure to gain weight are common.

Clinical presentation in adolescents

The presentation of pulmonary TB in adolescents is similar to the presentation in adults. The typical symptoms of TB—cough lasting more than 2 weeks, fever for 2 or more weeks, weight loss, anorexia, malaise, excessive night sweats, chest pain, and haemoptysis are more likely to be present in adolescents than in children.

Clinical assessment

Taking a good medical history is the first step to diagnosing TB in a child. Ask the patient or caregiver to describe:

- When symptoms started.
- About appetite and weight gain or loss.
- History of coughing, or coughing blood.
- History of TB contact.
- Other medical conditions that predispose to TB, such as HIV.
- Fever/ cough which is not responding to normal antibiotics
- History of reduced activities and/or irritability
- History and details of any prior TB disease/treatment.

Perform a thorough physical examination to assess:

- Appearance: thin or wasted.
- Temperature: normal or elevated.
- Lymph nodes: enlarged, painless, maybe matted or with discharging sinus.
- Chest:
 - Respiratory rate may be normal or high.
 - Trachea: may be displaced in massive pleural effusions.
 - Breath sounds may be normal, but there may be bronchial breathing, crepitations
 - (crackles), rales, and wheezing.
 - Dullness on percussion (in the case of pleural effusions).
 - Distant heart sounds in pericardial effusion.
- Abdomen: masses, ascites, or distension.
- Joints: may be swollen or with effusion; angulation of the spine (Gibbus)

Specimen collection

In children of all ages with presumptive pulmonary TB, sputum should be collected for AFB microscopy. Sputum specimens may be collected by means of expectoration, sputum induction, or gastric aspiration. In many cases, laboratory confirmation is difficult to establish because pulmonary TB in children is typically paucibacillary and specimens may be difficult to obtain. Nonetheless, attempt bacteriologic confirmation for all presumptive cases.

Expectorated sputum

Obtaining expectorated sputum from children younger than 5 years may be difficult, while most adolescents can produce expectorated sputum spontaneously. In children, examination of expectorated sputum has a low yield (<15% for AFB smear positivity and <30% for positive mycobacterial culture). For children who are able to produce sputum, send two specimens for smear microscopy. Collect one spot specimen at the visit and give a specimen cup to the parent or caregiver and explain how to collect an early morning specimen the following day and bring it to the clinic. Collect an additional specimen for mycobacterial culture when indicated. Sputum induction or gastric aspiration (described below) can be used to obtain specimens in children unable to expectorate.

Induced sputum

Sputum induction is the preferred method for collecting sputum from young children who are not able to expectorate. Induced sputum has a higher diagnostic yield than expectorated sputum in children and is comparable to or better than inpatient gastric aspirate specimens. It is a safe and effective procedure in children as young as 1 month of age in centres with adequate training and suitable equipment. It is recommended that this procedure be performed at district, regional, and zonal referral hospitals where appropriate equipment is available, and by trained personnel who are able to respond to any complications. Send two spot samples for analysis. (See Annex 1 for a description of the procedure.)

Gastric aspiration

Gastric aspiration using a nasogastric feeding tube should be used to obtain material for smear and culture from young children who are unwilling or unable to expectorate sputum.

Early morning gastric contents contain sputum swallowed during the night. The child should be hospitalized and two early morning samples collected on different days before the child eats, drinks, or gets out of bed, to suitably specimen yield.

Note: Gastric aspiration should only be undertaken where culture facilities are available nearby because culture specimens need to be processed within 4 hours of collection because the acidic juices in the stomach will kill the bacteria quickly. It is recommended that this procedure be performed at district, regional, and referral hospitals by trained personnel. (See Annex 2 for a description of the procedure.)

Diagnostic methods

Smear

Conventional light microscopy using Ziehl-Neelsen (ZN) stained smears and light-emitting diode fluorescence microscopy are the main diagnostic tests for TB widely available in Tanzania.

Culture

Mycobacterial culture is more sensitive than smear; however, Tbcacilli growth on traditional solid media requires 4 to 8 weeks and in liquid culture systems requires 2 to 4 weeks. Currently in Tanzania, culture is available in the following referral laboratories: Central Tuberculosis Reference Laboratory (CTRL, Muhimbili National Hospital), Bugando Medical Centre, Kilimanjaro Christian Medical Centre, Dodoma Referral Hospital, Kibong'oto National Tuberculosis Hospital, Southern highlands Zonal Hospital (Mbeya Zonal Referral Hospital), and Pemba Public Health Laboratory.

Always send sputum for culture and sensitivity in retreatment cases. For children who are not retreatment cases, culture should be done at the discretion of the TB clinic where the diagnostic work-up occurs. In these cases, specimen transport will need to be arranged in consultation with the medical officer in charge of the facility.

Other diagnostic tests

Xpert[®] MTB/RIF is now available in Tanzania for rapid TB diagnosis and detection of rifampicin resistance. It is a semi-automated polymerase chain reaction test that can be used on sputum samples. At least two sputum samples are recommended.

Line probe assay technology, such as the Hain test, is available in Tanzania, at the CTRL, NIMR- Mbeya, NIMR – Mwanza, Kibong'oto National TB Hospital and Dodoma Regional Referral Hospital for rapid detection of drug resistance.

Other serum tests such as ESR or blood counts and serological test are not sensitive or specific enough and are therefore not recommended for diagnosis of TB.

The tuberculin skin test is intended for diagnosis of LTBI, but a positive TST can be used as an adjunct tool during investigation for the diagnosis of TB disease in children. Criteria for a positive TST are provided in Table 2.1. However, a positive TST alone is never diagnostic of TB disease, as it only indicates TB exposure.

Table 2.1. Interpretation of TST results

Patient characteristic	Positive TST result
HIV infected	≥5 mm diameter induration
Severely malnourished (marasmus or kwashiorkor)	≥5 mm diameter induration
Contact to a case of infectious TB (smear positive)	≥5 mm diameter induration
All other children (regardless of whether they have received a Bacille Calmette-Guérin vaccination or not)	≥10 mm diameter induration

False-positive results can occur from prior vaccination with Bacille Calmette-Guérin (BCG), infection with non-tuberculous mycobacteria, and improper administration or interpretation. Similarly, a negative TST does not rule out TB disease, since false-negative results can occur in the following situations: incorrect administration or interpretation of the TST, age less than 6 months, severe malnutrition, advanced HIV disease, immunosuppression by disease or medication, certain viral illnesses or recent live-virus 17ilitary17ion, or even overwhelming TB disease.

Contraindications to TST administration are a previous severe or blistering reaction to tuberculin or a previous positive result. See Section 4, “Prevention of tuberculosis in children,” for more details.

Blood tests such as erythrocyte sedimentation rate or blood counts (e.g., full blood picture) to diagnose anaemia are not recommended because they are not specific to TB.

Chest radiography

Obtain chest radiography (anterio-posterior and lateral views) on all children suspected to have pulmonary TB. Indications for a chest X-ray include:

- Cough not responding to normal antibiotics and present for more than 2 weeks (or any cough in HIV-positive children).
- Fever for more than 2 weeks without other source.
- Concerns of extrapulmonary TB (to look for concomitant pulmonary TB).
- Presumptive Tuberculosis with negative smears.

Most children with pulmonary TB will have abnormal findings on chest radiography. The most common chest radiograph findings in a child with TB disease include:

- Perihilar, peritracheal, or subcarinal lymphadenopathy.

- Persistent opacification (any lobe).
- Advanced adenopathy causing bronchial compression leading to secondary infection or lung collapse.
- A miliary pattern of opacifications.
- Other opacification that does not improve or resolve following a course of antibiotics.

Adolescents with TB generally present with typical adult disease findings of upper lobe infiltrates, pleural effusions, and cavitations on a chest radiograph.

Clinical diagnosis in the absence of bacteriologic confirmation

Tuberculosis in children is often diagnosed clinically because bacteriologic confirmation, when available, is only achievable in about 30 to 40 percent of cases (Figure 2.1 provides an algorithm for diagnosing pulmonary TB in children). In the absence of bacteriologic confirmation, use the “Score Chart for Diagnosis of TB in Children” (Table 2.2) for clinical diagnosis. Refer a child with a score of 7 or more for TB treatment.

*Table 2.2. Score Chart for Diagnosis of TB in Children**

SCORE IF SIGN OR SYMPTOM PRESENT	0	1	2	3	4	Score
General features						
Duration of illness	Less than 2 weeks	2-4 weeks		More than 4 weeks		
Failure to thrive or weight loss	Weight gain	No weight gain or weight faltering		Weight loss		
TB contact	None	Reported (but no documentation) smear-negative or EPTB		Smear positive (with documentation)		
TST	Negative, not done			Positive		
Malnutrition not improved after four weeks of therapy				Present		
Unexplained fever not responding to appropriate therapy			Positive			
Local features						
Chest x-ray				TB-suggestive features like infiltration, cavity, or hilar lymph nodes		
Painless, enlarged lymph nodes		Any non-cervical lymph nodes		Positive cervical lymph nodes		
Swelling of bones or joints				Positive		
Unexplained ascites or abdominal mass				Positive		
Central nervous system findings: meningitis*, lethargy, irritability and other behavior changes				Positive		

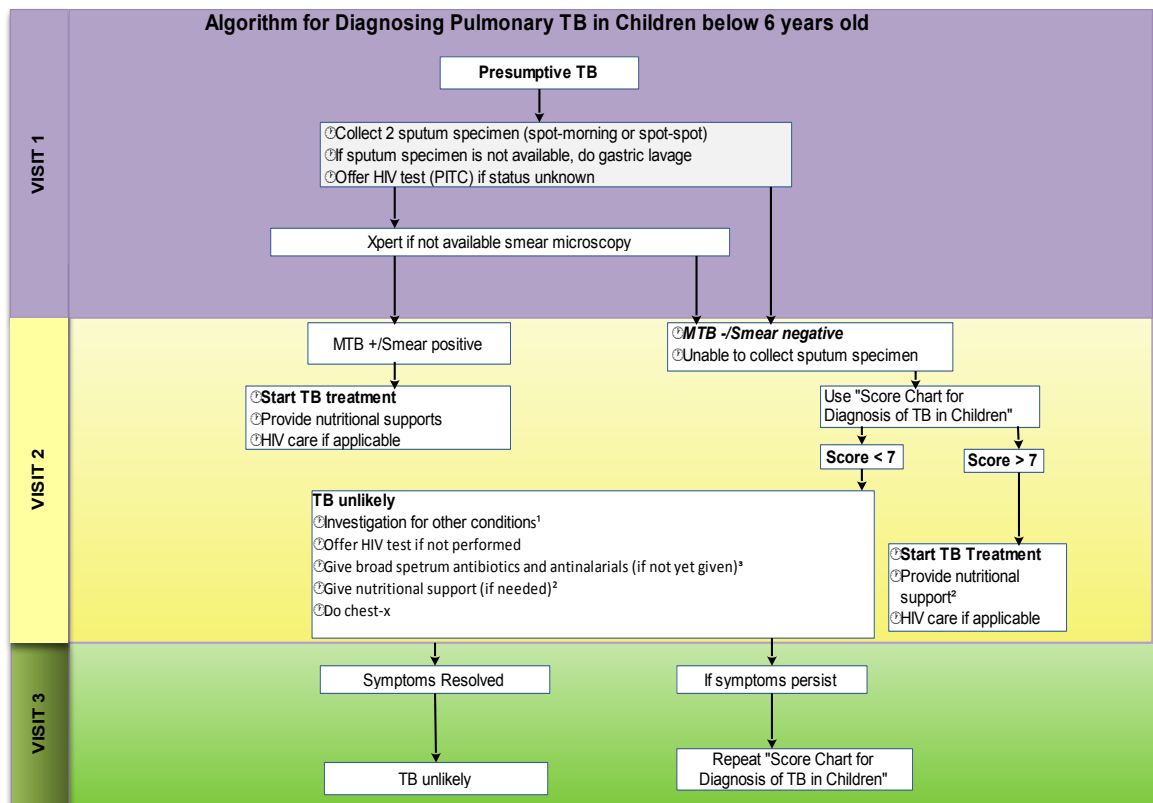
Angle deformity of the spine					Positive	
TOTAL SCORE A score of 7 or more indicates a high likelihood of TB. Refer the child for TB treatment.						

*Meningitis not responding to conventional antibiotics. Other causes of meningitis e.g bacterial must be excluded

HIV infection, sickle cell disease, or rheumatologic diseases alone (in the absence of TB disease) can cause scores of >7. Therefore, best clinical judgment must be used when using this scoring system (see Section 5.1, "TB/HIV in children" for further guidelines). Do not use aminoglycosides and fluoroquinolones, as they are active against M. tuberculosis complex and, thus, may cause transient improvement in persons with TB.

Scoring adapted from: Edwards K. The diagnosis of childhood tuberculosis. P N G Med J. 1987;30(2):169-178.

Figure 2.1. Algorithm for diagnosing pulmonary TB in children younger than 6 years



NOTES

1. Other conditions might include cardiac disease, congenital lung disease, fungal infections (including pneumocystis pneumonia), and chronic lung diseases such as asthma or bronchiectasis, parasitic infections, or oncologic disease.
2. Nutritional support may include nutritional 19ilitary19i, provision of supplemental or therapeutic feeds.
3. Antibiotics should treat common causes of chest bacterial infections. Consider continuing with other investigations if child has already received antibiotics without improvement. Avoid aminoglycosides and fluoroquinolones, as they have anti-Tb effects.

Diagnosis of extrapulmonary tuberculosis

The clinical presentation of extrapulmonary TB depends on the site of disease. The most common forms of extrapulmonary disease in children are

TB of the superficial lymph nodes and of the central nervous system. Neonates have the highest risk of 20ilitary TB and TB meningitis.

To diagnose extrapulmonary TB, collect specimens for smear and/or culture from any site where disease is suspected. The most common extrapulmonary specimens include tissue specimens such as lymph node or bone, cerebrospinal fluid, urine, bone marrow, and pleural fluid.

If any child suspected having extrapulmonary TB is also coughing, perform investigations for pulmonary TB (sputum, chest radiography) according to the guidelines in the previous section.

Tuberculosis lymphadenitis

Tuberculosis lymphadenitis typically presents with:

- Painless, fixed, matted, enlarged lymph nodes, especially in the cervical region, with or without fistula formation.
- Enlarged nodes persisting for several weeks and not associated with symptoms of upper respiratory infection, or they remain once the respiratory symptoms have resolved.

Perform fine needle aspiration of a superficial lymph node. If this is not feasible or is non-diagnostic, perform an excisional biopsy (refer to the nearest regional hospital if the procedure is not available at your site). Send the specimen for AFB smear microscopy, culture, and histopathology examination. The presence of caseating granulomas on histopathology is highly suggestive of TB.

In the absence of a positive smear or culture result, with or without suggestive histopathology findings, a clinical diagnosis may be made using the Score Chart for Diagnosis of TB in Children (Table 2.2).

Tuberculous meningitis

The clinical presentation of TB meningitis depends on the age of the child and the stage of the disease. The evolution of symptoms is usually gradual over a period of 3 weeks. Occasionally the onset is abrupt.

First stage: Personality/Behaviour change, irritability, anorexia, listlessness, fever.

Second stage (after 1 to 2 weeks): Presents with typical meningitis symptoms of headache, neck pain, neck stiffness, fever, lethargy, and convulsions resulting from increased intracranial pressure and damage to the brain.

Third stage: Loss of consciousness, irregular pulse and respirations, rising fever, and death.

Tuberculous meningitis should be suspected in cases of meningitis not responding to antibiotic treatment, with subacute onset, cranial nerve involvement, communicating hydrocephalus, stroke, and/ or elevated intracranial pressure. If there are no signs of increased intracranial pressure, perform a lumbar puncture to obtain cerebral spinal fluid (CSF) for white blood cell count (total and differential), protein, glucose, AFB smear microscopy, and mycobacterial culture.

In the CSF of a child with TB meningitis, during early stages, the white blood cell count reveals a high proportion of neutrophils; later, there is a greater proportion of lymphocytes. CSF glucose is at the lower limit of normal, and protein initially is normal but rises steadily to very high concentrations. Yield from CSF AFB smear microscopy is usually low.

If TB meningitis is suspected, start treatment *immediately*. Do not delay treatment while waiting for CSF smears and culture results. Where possible, perform serial examination of the CSF for AFB smear microscopy and culture to improve definitive diagnosis. Culture has the highest yield of diagnostic confirmation. Where available, molecular diagnostic techniques such as line probe assay and Xpert® MTB/ RIF can also be performed on CSF to confirm the presence of *M. tuberculosis*, though its sensitivity is not well studied.

If smear and culture are not available, CSF findings of low glucose concentration, elevated protein, and elevated lymphocytes are suggestive of TB meningitis. **If these are present and TB meningitis is suspected, start treatment *immediately*,** even in the absence of bacteriologic confirmation.

In the setting of TB meningitis and a neurological deficit, perform a CT scan or MRI of the head to diagnose tuberculomas, infarcts, vasculitis, and hydrocephalus. Chest radiography may reveal pulmonary involvement or may be normal.

Miliary/Disseminated tuberculosis

Miliary or disseminated TB is more common in very young children (age 2 and younger). Children usually present very ill, appearing with failure to thrive, lethargy, loss of appetite, weight loss/failure to gain weight, and in severe cases, coma. Signs and symptoms of TB meningitis may be present, as dissemination to the meninges and central nervous system is common, and these two conditions often present concomitantly (in approximately 30 percent of cases). Mycobacterial dissemination to major organs can result in multi-organ failure and sepsis. Consider diagnosis of disseminated TB in patients with poor response to antibiotics for presumed sepsis.

Perform a lumbar puncture to look for evidence of disseminated/miliary TB. The patient is usually too ill to provide sputum specimens. Perform a chest radiograph, as it may show the characteristic scattered millet seed pattern (see below). **Due to the high risk of death or disability from miliary TB, start**

treatment *immediately.*

Pleural tuberculosis

Pleural effusion is excess fluid that accumulates in the pleural space. Excessive amounts of fluid can impair breathing by limiting the expansion of the lungs during respiration. Signs and symptoms include:

- Coughing, fast breathing, and chest indrawing.
- Stony dullness to percussion, decreased air entry, decreased tactile and vocal fremitus, and diminished chest excursion on the affected side.
- Displacement of the trachea and cardiac apex to the contralateral side.

Homogeneous opacification of the whole hemithorax or obliteration of the costophrenic angle in small effusion.

Perform a pleural tap for laboratory analysis: glucose, protein, and white blood cell count with differential. Fluid is usually yellow (straw coloured), with elevated protein and lymphocyte levels. Bloody fluid or pus indicates other conditions. Send fluid for AFB smear and mycobacterial culture. Culture provides greater diagnosis. Pleural biopsy may show granulomas on histopathology.

Pericardial tuberculosis

Pericardial effusion is excess fluid that accumulates in the pericardial space. Excessive amounts of fluid can impair efficient cardiac function. Signs and symptoms include:

- Dull ache in the left chest.
- Abdominal pain.
- Shortness of breath, fatigue, and cold extremities in severe cases.

When skilled 22ilitary22 are available, perform a pericardial tap, preferably with ultrasound guidance, and send the fluid for laboratory analysis: glucose, protein, and white blood cell count with differential. If infected with *M. tuberculosis*, pericardial fluid usually has elevated protein and lymphocyte levels. Send fluid for AFB smear and mycobacterial culture. Smear microscopy is low yield, and culture provides greater diagnosis.

Abdominal tuberculosis

Tuberculosis can involve any part of the gastrointestinal tract and can result in enlarged and matted mesenteric lymph nodes; ulcers, fibrosis, or strictures of the bowel wall; and peritoneal tuberculomas. Ascites (excess fluid in the peritoneal cavity) is also possible. The most common site of involvement is

the ileocecal region, and can present with a palpable mass in the right lower quadrant and/or signs of obstruction, perforation, or malabsorption.

Perform an abdominal ultrasound or CT scan to evaluate for lymphadenopathy, tuberculomas, or fibrosis. In cases of ascites, perform an ascetic tap for laboratory analysis: glucose, protein, and white blood cell count with differential. Expect infected fluid to have elevated protein and lymphocyte levels. Send fluid for mycobacterial culture.

Tuberculosis of the spine/bones/joints

Tuberculosis disease of the spine, bones, or joints (osteoarticular TB) typically occurs within 6 to 36 months of primary infection. The most common site is the spine (also called Potts Disease), followed by the knee, hip, and ankle joints. The following signs suggest TB in the bones or joints:

- Acute onset of angulation of the spine (Gibbus deformity).
- Progressive weakness of limbs.
- Joint effusions.
- Progressive disease may result in joint destruction with or without abscess or sinus formation.
- Retropharyngeal mass (cold abscess from infected cervical vertebra).
- Psoas abscess (cold abscess from infected lumbar vertebra).

Perform a radiograph of the affected area, with review by a radiologist. In patients with joint effusions, perform a joint tap for laboratory analysis: protein, white blood cell count with differential, AFB smear, and mycobacterial culture. Synovial biopsy may show characteristic granuloma formation.

Neonatal tuberculosis

Congenital TB is when the neonate acquires TB in utero through haematogenous spread via the umbilical vessels, or at the time of delivery through aspiration or ingestion of infected amniotic fluid or cervico-vaginal secretions. Neonatal TB is when the newborn is infected after birth by being exposed to an infectious case of TB, which is usually the mother or may be another close contact. It is often difficult to distinguish between congenital and neonatal TB, and management is the same for both. Both forms will be referred to here as neonatal TB.

The TB-exposed neonate may be asymptomatic or symptomatic. Symptoms and signs of TB in the neonate are usually nonspecific and include the following:

- Lethargy.

- Poor feeding.
- Low birth weight and poor weight gain.
- Respiratory distress.
- Non-resolving pneumonia.
- Hepatosplenomegaly.
- Lymphadenopathy.
- Abdominal distension with ascites.
- A clinical picture of “neonatal sepsis” with disseminated TB.

The diagnosis of neonatal TB should be included in the differential diagnosis of chronic neonatal infection with a poor response to antimicrobial therapy, congenital infections, and atypical pneumonia. The most important clue to the diagnosis of TB in the newborn is a maternal history of TB or TB/HIV co-infection.

The following investigations should be carried out:

- Tuberculin skin test.
- Chest radiography.
- Lumbar puncture.
- Blood, CSF, and gastric aspirate cultures, performed promptly.
- If possible, examination of the placenta histologically for granulomata and AFB, and culture of a specimen for *M. tuberculosis*.

Disseminated Bacille Calmette-Guérin disease

Prolonged fever or other systemic symptoms in an HIV-infected or HIV-unknown infant within weeks or months of BCG 24ilitary24ion should raise the index of suspicion for life-threatening disseminated BCG, which occurs in as many as 1 percent of HIV-infected infants. Perform a complete physical examination, as many infants will also have signs of local BCG disease, which includes swelling, redness, ulceration at the injection site, and enlarged axillary lymph nodes.

Table 2.3. Summary of investigations for Extra pulmonary TB

Anatomical site	Recommended investigations
TB adenitis (especially from cervical region)	Lymph node biopsy or fine needle aspiration; sputum if coughing.
Miliary TB	Sputum and chest x-ray. Perform additional diagnostic tests as appropriate for associated symptoms and signs (e.g., lumbar puncture to test for meningitis).
TB meningitis	Lumbar puncture (cerebrospinal fluid for white blood cell count with differential; biochemical analysis for protein and glucose concentration, Xpert® MTB/RIF where available, AFB smear and mycobacterial culture; chest x-ray and sputum.
Pleural effusion	Chest x-ray, pleural tap for biochemical analysis (protein and glucose concentration, white blood cell count, Xpert® MTB/RIF where available, AFB smear and mycobacterial culture, sputum.
Abdominal TB	Abdominal ultrasound and 25ilitar tap for white blood cell count total and differential; biochemical analysis for protein and glucose concentration, Xpert® MTB/RIF where available, AFB smear and mycobacterial culture; sputum and chest x-ray if coughing.
TB of the spine/bones/joints (osteoarticular TB)	x-ray, joint tap for white blood cell count total and differential; biochemical analysis for protein and glucose concentration, Xpert® MTB/RIF where available, AFB smear and mycobacterial culture; synovial biopsy; sputum if coughing.
Pericardial TB	Chest x-ray, chest ultrasound, pericardial tap for white blood cell count total and differential; biochemical analysis for protein and glucose concentration, Xpert® MTB/RIF where available, AFB smear and mycobacterial culture; sputum if coughing.
Neonatal TB	Chest x-ray, lumbar puncture, cerebrospinal fluid and gastric aspirates, Xpert® MTB/RIF where available; for AFB smear and mycobacterial cultures, histopathology examination of the placenta for AFB and granulomata; evaluation of mother for TB.
Drug-resistant TB any anatomical site	Mycobacterial culture and DST of relevant specimens.

2.3 Classification based on anatomical site of disease

PTB: Refers to a case of TB involving the lung parenchyma. Miliary TB is classified as PTB because there are lesions in the lungs. Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of EPTB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of PTB.

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). EPTB cases can be either bacteriologically confirmed or clinically diagnosed. Identification of *M. tuberculosis* (as opposed to histology) should be the basis of bacteriological confirmation of EPTB. The case definition of an EPTB case with several sites affected depends on the site representing the most severe form of disease.

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

pulmonary TB.

For detailed information please refer NTLP manual section 3.4: on TB case definition and classification.

Key points

- Bacteriologic confirmation should be attempted in all children with presumptive children
- Sputum can be collected by expectoration (coughing into a cup), sputum induction, or gastric aspiration
- Check for the classic tetrad of TB: contact history, signs and symptoms, positive TST, and suggestive laboratory and radiographic findings.
- In the absence of bacteriologic confirmation the Score Chart for Diagnosis of TB in Children should be used to make a clinical diagnosis of TB and referral for treatment (Table 2.2)
- Younger children are at greater risk for disseminated or miliary TB.

(4

MANAGEMENT OF TUBERCULOSIS DISEASE IN CHILDREN

Proper management of TB in children involves prescribing the correct doses of the recommended treatment regimen in an appropriate formulation for the right duration; providing counseling and ancillary care as necessary; managing any adverse reactions that arise; and ensuring adherence until treatment is completed. Directly observed therapy is the standard of care for TB treatment. For children, the DOT supervisor can be a parent/caregiver or health care worker. Register all children started on treatment for TB in the unit TB register.

3.1 Treatment regimens for tuberculosis disease

There are two phases to TB treatment: the intensive phase and the continuation phase. During the intensive phase, there is rapid killing of the TB bacilli. Most patients with smear-positive TB become noninfectious after about 2 weeks of effective treatment. During the continuation phase, the drugs kill the remaining bacteria, which prevents relapse after completion of treatment.

Treatment of TB disease in children requires multidrug combination therapy. Anti-TB drugs have a synergistic effect on each other; their combined actions produce a greater effect than the sum of the individual medications.

In general, paediatric treatment regimens are comparable to adult regimens. Because TB in young children can rapidly disseminate with serious sequelae, prompt initiation of therapy is critical. Appropriate regimens, dosing, and duration are outlined in Tables 3.1 and 3.2.

Table 3.1. Recommended treatment regimens for paediatric patients in Tanzania

TB disease category	Recommended regimen	
	Intensive phase	Continuation phase
All forms of new pulmonary and extrapulmonary TB* (<i>except TB meningitis and TB of the spine/bones/joints</i>)	2 months of daily RHZE	4 months of daily RH
TB meningitis; 27ilitary TB; TB of the spine/bones/joints	2 months of daily RHZE	10 months of daily RH
Previously treated TB (relapse, treatment after failure, treatment after lost to follow-up, other previously treated)**	3 months of daily RHZE***	5 months of daily RHE
MDR TB	See Section 5.2, "Drug-resistant tuberculosis in children"	

E: ethambutol; **H:** isoniazid; **R:** rifampicin; **Z:** pyrazinamide.

*30 percent of children with a 27ilitary picture on chest radiography have central nervous system involvement and should be treated with a 12-month regimen (see a section on "Tuberculous meningitis").

**All previously treated TB cases should be evaluated for MDR TB by sending samples for culture and drug susceptibility testing. Relapse cases are those who have been previously treated for TB, were declared cured or treatment completed at the end of the most recent treatment episode, and a now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by re-infection).

Note: If an adolescent is pregnant, refer to the section in the adult guidelines on treatment of TB in pregnancy.

Adapted from: Graham SM et al. Desk-Guide for Diagnosis and Management of TB in Children. Paris, France: International Union Against Tuberculosis and Lung Disease; 2010; and Definitions and reporting framework for tuberculosis – 2013 revision (updated December 2014), WHO/HTM/TB/2013.2

3.2 Medications and dosages

When treating children with TB, calculate all anti-TB medicine doses by weight and use FDC tablets. It is important to weigh the child at each visit and adjust medication dosages as needed. Anti-TB medications, daily dose and range, maximum dose, and potential adverse reactions are provided in Table 3.2 below.

When available, give pyridoxine supplementation to children receiving TB treatment at a prophylactic dosage of 1-2 mg/kg per day.

Table 3.2. Drug dosing and adverse reactions for the treatment of TB in children

Drug	Daily dose and range mg/kg	Maximum daily dose	Adverse reactions
Isoniazid	10 (7-15)	300 mg	Mild hepatic enzyme elevation, hepatitis, peripheral neuritis, hypersensitivity
Rifampicin	15 (10-20)	600 mg	Orange discolouration of secretions or urine, vomiting, hepatitis, influenza-like reaction, thrombocytopenia, pruritus
Pyrazinamide	35 (30-40)	-	Hepatotoxic effects, hyperuricemia, arthralgias, gastrointestinal tract upset
Ethambutol	20 (15-25)	-	Optic neuritis (usually reversible), decreased red-green colour discrimination, gastrointestinal tract disturbances, hypersensitivity

Adapted from WHO, Stop TB Department. Rapid Advice: Treatment of Tuberculosis in Children. WHO/HTM/TB/2010.13; and WHO, 2014. Guidance for National TB Programmes on the Management of TB in Children, 2nd Edition.

3.3 Fixed-dose combination tablets

Use FDC tablets whenever possible to facilitate adherence and simplify regimens. The FDCs available for use in children in Tanzania include rifampicin, isoniazid, and pyrazinamide (R/H/Z, 75/50/150 mg) and rifampicin and isoniazid (R/H, 75/50 mg). Children below 25 kg will need to receive ethambutol as a separate medication, but older children 25 kg and above can be treated using adult FDC tablets of rifampicin, isoniazid, pyrazinamide, and

ethambutol (RHZE, 300/150/400/275 mg). Table 3.3 lists the pediatric FDC dosage needed to achieve the correct dose by weight in children <25 kg.

Guidelines for using TB dosing charts:

- If child is less than 25 kg: use pediatric FDC dosing chart (Table 3.3)
- If child is ≥25 kg: use adult FDC dosing chart (see NTLP Manual)

Table 3.3. Weight-based dosing of anti-TB drugs for children (0-24.9 kg body weight)

Weight (kg)	Intensive phase * (2 months)		Continuation phase (4 months)
	RHZ (paediatric) 75/50/150 mg	Ethambutol 100mg	RH (paediatric) 75/50 mg
<4 kg**	For infants below 4 kg, consult a pediatric specialist, DTLC, and RTLC for treatment advice		
2 - 2.9 kg	½ tablet	½ tablet	½ tablet
3 – 3.9 kg	1 tablet	½ tablet	1 tablet
4 – 7.9	1 tablet	1 tablet	1 tablet
8 - 11.9 kg	2 tablets	2 tablets	2 tablets
12 - 15.9 kg	3 tablets	3 tablets	3 tablets
16 - 24.9 kg	4 tablets	4 tablets	4 tablets
≥25 kg	use adult FDCs		

H: isoniazid; R: rifampicin; Z: pyrazinamide.

*WHO recommends four-drug therapy during the intensive phase for all children.

**For children < 4kg, recommend referral to pediatric specialist/DTLC/RTLC to assist with dosing and treatment in this high-risk group.

3.4 Practical guidance for administering medicines to children

Pediatric FDCs (RHZ and RH) are dispersible in liquid and fruit-flavored as to be more palatable to children to improve ease of administration for parents and children. In addition to dissolving in liquid, the pediatric FDC tablets can also be swallowed normally.

For paediatric RHZ and RH, advise parents/caregivers to:

- Dissolve the tablets in clean, safe water (approximately 50mL); it will then be ready to drink after 10 seconds
- Once dissolved, it should be drunk within 10 minutes
- Entire volume of liquid must be finished by the child to ensure entire dose is given
- If the child spits up or vomits their dose less than 30 minutes after receiving it, re-administer another dose immediately by mixing it with a different liquid.
- If the child vomits more than 30 minutes after receiving the dose, it has already been absorbed and should not be re-administered

For paediatric ethambutol (film-coated), advise parents/caregivers to:

- Attempt to have child swallow ethambutol tabs; if child is unable to swallow, ethambutol can be crushed and mixed with liquid (but crushing may reduce its effectiveness and potency)
- If the child spits up or vomits their dose less than 30 minutes after receiving it, re-administer another dose immediately.
- If the child vomits more than 30 minutes after receiving the dose, it has already been absorbed and should not be re-administered

3.5 Steroid use fortuberculosis

Corticosteroid therapy is generally indicated as adjuvant therapy when treating children with the following conditions:

- Tuberculous meningitis (steroid use can decrease mortality and long-term neurologic complications).
- Severe miliary/disseminated TB.
- Tuberculosis pericarditis with effusion.
- Pleural TB with massive effusions.
- Pulmonary TB with mediastinal lymph glands obstructing the airways.

Prescribe oral prednisolone at a dose of 1-2 mg/kg/day up to 4mg/kg, with a maximum dosage of 60 mg/day for 4 to 6 weeks, followed by a slow tapering over 2- 4 weeks (or more) while monitoring for any symptoms of corticosteroid withdrawal. Corticosteroid doses may need to be adjusted upward to account for the increased steroid metabolism induced by rifampicin. Treating clinicians should provide necessary information about adverse events to their District Tuberculosis and Leprosy Coordinator (DTLC).

3.6 Management of adverse reactions to anti-tuberculosis medications

In general, a patient who develops minor adverse effects should continue TB treatment and be given symptomatic treatment. *If a child develops a major side effect, stop treatment immediately and urgently refer the patient to a hospital for further assessment and treatment.*

Since FDCs are used in Tanzania, all drugs will be stopped at once when the FDC is discontinued. Contact the DTLC or Regional Tuberculosis and Leprosy Coordinator (RTLTC) if single anti-TB drugs are needed to treat a child. Table 3.4 below provides guidelines for management of adverse reactions to anti-TB medications, based on symptoms.

Table 3.4. Symptom-based approach to major and minor reactions to anti- TB medications

Adverse reaction(s)	Drug(s) probably responsible	Management
Major	Stop anti-TB drug(s) and refer to a hospital immediately	
Skin rash with or without itching	Isoniazid, rifampicin, pyrazinamide	Stop anti-TB drugs.
Jaundice (other causes excluded), hepatitis, severe vomiting or abdominal pain, confusion	Pyrazinamide, isoniazid, rifampicin	Stop anti-TB drugs.
Visual impairment (other causes excluded)	Ethambutol	Stop ethambutol.
Shock, purpura, acute renal failure	Rifampicin	Stop anti-TB drugs.
Minor	Continue anti-TB drugs; check drug dosages	
Anorexia, nausea, mild abdominal pain	Pyrazinamide, rifampicin, isoniazid	Check LFTs (if possible); if LFTs abnormal refer to clinician. Give drugs with small meals or just before bedtime, and advice patient to swallow pills slowly with small sips of water. If symptoms persist or worsen, or there is protracted vomiting or any sign of bleeding, consider the side effect to be major and refer to a clinician immediately.
Joint pain	Pyrazinamide	Give non-steroidal anti-inflammatory drug or paracetamol.
Burning, numbness, or tingling sensation in the hands or feet (consult paediatrician)	Isoniazid	Give pyridoxine (1-2 mg/ kg/day), especially if HIV positive and/or malnourished. Encourage foods with high amounts of pyridoxine (e.g. potatoes, banana, rice, spinach, nuts, chicken, beef)
Drowsiness	Isoniazid	Provide reassurance. Give drugs before bedtime.
Orange/Red urine	Rifampicin	Provide reassurance. Patients should be told when starting treatment that this may happen and is normal.

Adapted from: World Health Organization, Stop TB Department. Treatment of Tuberculosis Guidelines: Fourth Edition. WHO/HTM/TB/2009.420.

3.7 Management of cutaneous reactions

If a patient develops itching without a rash and there is no other obvious cause, prescribe symptomatic treatment with antihistamines and skin moisturizers. Continue TB treatment while observing the patient closely.

If a skin rash develops (with or without mucosal involvement), stop all anti-TB drugs immediately and refer to the nearest hospital for further management. Once there action has resolved, perform a drug challenge by introducing individual anti-TB drugs one by one, starting with the drug least likely to be responsible for the reaction (as described below)

Drug challenge for cutaneous reactions

1. Start with small doses (one-third to one-quarter of the total dose) of the drug least likely (i.e. ethambutol for cutaneous reactions) to be responsible for the reaction.
2. Gradually increase the dose to the recommended daily dose, over 3 days.
3. Repeat the procedure, adding in one drug at a time (next giving pyrazinamide, if tolerated then isoniazid, and if tolerated finally rifampicin for cutaneous reactions).
4. A reaction after a particular drug is added suggests that this is the drug responsible for the reaction; and this drug should not be used again for treatment
5. Reaction to a small challenge dose will not be as severe as to a full dose.

3.8 Management of drug-induced hepatitis

Many of the first-line anti-TB drugs— pyrazinamide, isoniazid, and rifampicin—can cause liver damage (drug-induced hepatitis). Routine monitoring of serum liver enzyme levels in asymptomatic children is NOT needed, but evaluation for signs and symptoms of hepatitis must be done at each visit for children taking anti-TB. Assess for:

- Nausea, vomiting, loss of appetite, poor weight gain, dark urine.
- Hepatomegaly, jaundice, abdominal pain/tenderness.

If a patient develops liver tenderness, hepatomegaly, or jaundice, immediately stop all potential hepatotoxic drugs, obtain serum liver enzyme levels, assess the child for other causes of hepatitis (other hepatotoxic drugs, viral hepatitis), and refer the child to a hospital for further management. Further management should include assessing the child for other causes of hepatitis (other hepatotoxic drugs, viral hepatitis). Anti-TB drugs should not be reintroduced until liver function has normalized.

If the patient is severely ill with TB and it is considered unsafe to stop TB treatment, consult with the DTLC/RTLTC to arrange to start a non- hepatotoxic regimen.

Once anti-TB treatment has been stopped, recheck serum liver enzymes in 1 to 2 weeks. Consult with your DTLC/RTLTC and do not restart anti-TB drugs until serum liver enzymes have reverted to normal and clinical symptoms (nausea, abdominal pain) have resolved. If it is not possible to perform serum liver enzymes, it is advisable to wait an extra 2 weeks after resolution of jaundice and upper abdominal tenderness before restarting anti-TB treatment. If the signs and symptoms do not resolve and the liver disease is severe, a non-hepatotoxic regimen (e.g. ethambutol, streptomycin, and levofloxacin x 18-24 months) will be selected and initiated with support of DTLC/RTLTC.

Once drug-induced hepatitis has resolved, perform a drug challenge by reintroducing the drugs one at a time. If symptoms recur or liver function tests (LFTs) become abnormal as the drugs are reintroduced, the last drug added should be stopped. Please see (Annex 4) for examples of drug challenges for anti-TB induced hepatitis based on weight band dosing in children.

Drug challenge for hepatitis (to be done by the DTLC/RTLTC)

1. Start with isoniazid at small doses (one-fourth to one-third of the total dose), and gradually increase the dose over 3 days to the recommended daily dose.
2. If no symptoms, next add rifampicin using a rifampicin/isoniazid FDCtablet.
3. If the child can tolerate rifampicin and isoniazid, it is advisable to avoid pyrazinamide. If the patient can tolerate rifampicin and isoniazid and received less than 2 months of pyrazinamide, treat with rifampicin/isoniazid for a total duration of 9months.
4. If the child cannot tolerate rifampicin and isoniazid, then an alternate regimen is required (described below) for 9 to 12 months.

Alternative regimens depend on which drug is implicated as the cause of the hepatitis.

- If rifampicin can not be used, administer 2months of isoniazid, ethambutol, and streptomycin, followed by 10 months of isoniazid and ethambutol.
- If isoniazid cannot be used, 6–9 months of rifampicin, pyrazinamide, and ethambutol can be considered.

If pyrazinamide is discontinued before the patient has completed the intensive phase, the total duration of isoniazid and rifampicin therapy is extended to 9 months.

Reintroducing one drug at a time is the optimal approach, but as FDCs are currently used in Tanzania, efforts should be made by the health facility to order and stock adequate quantities of anti-TB drugs through eLIMS.

The following approach can be applied, depending on whether the hepatitis occurred during the intensive or the continuation phase:

- When hepatitis due to pyrazinamide occurs during the intensive phase of TB treatment:
 - Once hepatitis has resolved, restart RH and individual ethambutol. Send samples for culture and drug susceptibility testing (DST) and modify treatment based on results. Complete the 2-month course of the initial phase, followed by rifampicin and isoniazid for the 6-month continuation phase.
- When hepatitis occurs during the continuation phase:
 - Once hepatitis has resolved, re-challenge with isoniazid and rifampicin, and if no symptoms, then restart isoniazid and rifampicin to complete the 4-months continuation phase of therapy.
 - If hepatitis or symptoms recur during re-challenge, continue to investigate for other causes of hepatitis, and switch to ethambutol and isoniazid to complete a 6-month continuation phase of therapy.

3.9 Monitoring treatment and directly observed therapy

Monitoring patients during anti-TB treatment is vital to ensure patients adhere to and complete their treatment and/or are cured.

Sputa Monitoring and Follow Up Testing

Bacteriologic monitoring using sputum for AFB and culture is needed in

sputum smear- and culture-positive cases. In these smear-positive cases, obtain sputum for smear microscopy (and culture where available) at the end of the intensive phase (second month), at the end of the fifth month, and at the end of treatment. If the sputum smear remains positive at 2-3 months of treatment, conduct Xpert MTB/RIF where available to rule out drug resistant TB, or if Xpert MTB/RIF is not available, send the specimen for culture and DST.

For TB cases that are smear-negative but Xpert MTB positive RIF resistance negative, these patients can be followed clinically without needing to repeat Xpert MTB/RIF testing at 2 months and end of treatment because Xpert can remain positive throughout successful treatment. These bacteriologically confirmed TB patients will then have an outcome of “treatment completed” once finishing their anti-TB therapy.

In children, Xpert MTB/RIF should primarily be used for diagnosis of TB, but not for monitoring of treatment success. However, if the patient is not responding well to anti-TB treatment and there is concern of treatment failure due to MDR-TB, then Xpert MTB/RIF can be repeated in such patients to evaluate for rifampicin resistance.

Clinical Monitoring and Follow Up Visits

Evaluate the child with TB weekly when initiating therapy and every 2 weeks thereafter for the remainder of treatment. Evaluations should include weight measurement and a return to their growth curve, an assessment of response to treatment by checking for signs and symptoms displayed by the child before starting on TB therapy, adherence to their regimen, and any adverse drug reactions or events. Adjust dosages of medicines as needed as children gain weight.

The entire course of treatment for children with TB should be provided under DOT by a health care worker or trained treatment supporter (which can be a parent or caregiver), to prevent the emergence of drug resistance. Adherence is documented on the patient’s treatment card.

3.10 Clinical and bacteriologic response

Evaluating clinical response is very important in children with TB because many lack bacteriologic confirmation.

In all children with TB:

- Assess for improvement or complete resolution of presenting symptoms (e.g., fever, cough) at every follow-up visit.
- Check growth parameters such as weight gain and return to their growth curve on a monthly basis.
- Adjust dosing of anti-TB medications as needed as weight changes.

If the child has smear-negative TB and is not improving clinically by the end of the intensive phase, refer to the next section, “Treatment failure (confirming failure and management).”

Routine follow-up chest radiographs (e.g. monthly) are **not indicated**, as children often have a slow radiographic response. However, if the child is not clinically improving on anti-TB, repeat chest x-rays are recommended.

In children with smear- or culture-positive TB: Collect a sputum specimen at the end of the intensive phase of treatment. If the smear or culture at the end of the intensive phase is negative, start the continuation phase of treatment. If the smear or culture result is positive, conduct Xpert MTB/RIF where available to rule out drug resistant TB, or if Xpert MTB/RIF is not available, send the specimen for culture and DST and refer to the next section, on treatment failure. Start continuation phase with RH while awaiting DST, but ensure close clinical monitoring of the child while waiting for DST results. If child clinically deteriorates while awaiting DST results, refer immediately for MDR-TB treatment.

3.11 Treatment failure (confirming failure and management)

A child who is not responding to treatment either by clinical or bacteriologic measures at the end of the intensive phase should be evaluated for MDR TB by sending a specimen for Xpert MTB/RIF (if available), culture and DST. These patients may have drug-resistant TB, poor treatment adherence, or another condition. These children should be referred to secondary/tertiary centres for further investigations of MDR TB. If these centres are unable to obtain bacteriological confirmation of MDR TB and there is a high suspicion for MDR TB (e.g. child has known MDR TB contact), the child should be referred to the MDR TB treatment centre for further evaluation. See Section 5.2, “Drug-resistant tuberculosis in children,” for further details.

3.12 Managing treatment interruption

Trace patients who miss DOT or an arranged appointment to collect their medicines. Contact within 1 day (or as soon as possible) patients who miss DOT or a medical appointment during the initiation phase, and contact within a week those who miss DOT or a medical appointment during the continuation phase. The patient can be traced using the locating information previously obtained and/or available community resources for tracing. It is important to find out the cause of the patient’s absence so that appropriate action can be taken to prevent further treatment interruptions, and treatment can continue successfully.

If a child misses 2 to 4 weeks of treatment, attempt to collect a sputum sample when the child returns to care. Collect another sputum sample and send for culture and DST if the child meets any of the following criteria:

- The child has positive smear(s) upon returning to treatment.
- The interruption occurred in the intensive phase, rather than the continuation phase.
- The child was responding poorly to treatment before the interruption.
- There is a known drug-resistant TB contact.

If the child misses 2 to 4 weeks of treatment, continue treatment while waiting for sputum results and extend therapy by adding missed doses.

If the child misses more than 4 weeks, the following must be done:

- Send sputum for culture and DST.
- Restart standard TB treatment while awaiting culture and DST results.
- Refer to an MDRTB treatment centre if multidrug-resistant TB is confirmed.

3.13 Ancillary and supportive care

Indications for hospitalizing children with tuberculosis

Admit all debilitated, severely ill children with TB to the hospital for stabilisation and nutritional support as well as initial drug therapy. Examples include a comatose child with TB meningitis, an infant with miliary/disseminated TB, or any child with severe respiratory distress.

Young children, especially infants, often require brief hospitalization to acquire diagnostic specimen by nasogastric aspiration or sputum induction.

Management of the asymptomatic neonate exposed to maternal tuberculosis

Any neonate exposed to infectious maternal TB should be screened for TB disease. Attempt to minimize contact between the mother and her neonate to breast feeding periods only until the mother starts on treatment. Advise the mother to continue breastfeeding. Complete separation of the mother and neonate is only necessary if the mother has possible or confirmed MDR TB.

Exclude TB in the neonate according to the approach described in Section 2, "Diagnosis of tuberculosis disease in children." All household members should also be investigated for TB. Once TB disease has been ruled out, any neonate who was in contact with drug-susceptible TB contact should be started on isoniazid 10 mg/kg orally once daily for 6 months. The neonate should then be followed closely to ensure TB disease does not develop. If TB disease develops, treat the neonate for TB disease. If the infant remains asymptomatic, complete isoniazid treatment for 6 months and if available, perform a TST at end of IPT.

Also test the infant for HIV. If the TST is negative or not done and HIV status is negative, administer the BCG vaccine 2 weeks after completing isoniazid. BCG should not be given while the neonate is on isoniazid because it inhibits the multiplication of BCG organisms. Close monitoring of the exposed neonate is recommended, especially during the first year.

3.14 Nutrition for children with tuberculosis

Maintaining good nutrition throughout childhood is important for healthy development. During TB treatment, proper nutrition is especially important to maximize immune response and treatment outcome. Malnourished children have impaired immune function with reduced cell-mediated immunity. Furthermore, TB disease worsens malnutrition through catabolism, which causes wasting. In a child with LTBI, malnutrition increases the risk of progressing from infection to TB disease. Failure to thrive and weight loss are important clinical features in TB diagnosis in children. Malnutrition is seen frequently in children with TB in Tanzania and contributes to poor outcomes, including death.

Similarly, in HIV-infected children, wasting is associated with increased morbidity and poor survival. Once anti-TB treatment has been started, ensure adequate nutrition is given in order to counteract the prolonged catabolic state that the child has experienced.

Refer to Annex 3 for Diagnosis and Management of Malnutrition.

Breastfeeding infants

Breastfeeding is recommended for all infants irrespective of the mother's TB status. The only exception is when the mother has MDR TB (see Section 5.2, "Drug-resistant tuberculosis in children"). All anti-TB drugs are compatible with breastfeeding. The risk of transmission of TB through breast milk is negligible, and although anti-TB drugs are excreted into breast milk in small amounts, there is no evidence that they induce drug resistance. Separation from the mother is not advisable where establishment of breast feeding is critical for child survival. If TB disease is excluded in the infant, the child is eligible for isoniazid preventive treatment (IPT) (see Section 4, "Prevention of tuberculosis in children").

Assessing malnutrition in children with tuberculosis

Perform a complete assessment of the nutritional status of a child with TB, including the following:

- Detailed dietary history to identify the existence of any feeding problems and support networks, including resources available at home for the family.
- General physical examination to identify features of malnutrition, including taking accurate anthropometric measurements to identify their growth pattern.

Develop an individualized nutritional support plan depending on the severity of malnutrition and the associated complications. Provide supplemental or therapeutic feeding to all malnourished children with TB.

See Annex 3 for guidelines on the management of malnutrition in children. For further details, please refer to recent national guidelines for management of acute malnutrition in children and community-based management of malnutrition.

3.15 Counseling for children with tuberculosis

Counseling helps the child and family cope with the stress of being diagnosed with TB and should be an ongoing process throughout your care of the child with TB. TB carries a stigma and may lead to feelings of shame and fear of social rejection. The child's and parent's/caregiver's perceptions about TB may differ from providers' understanding of the disease process and treatment. Because misinformation and misconceptions about TB increase the likelihood of non-adherence, it is important to identify and address these differences early in treatment. It is important to understand the child's and parent's/caregiver's beliefs about TB and their concerns about being diagnosed with TB and about TB treatment and follow-up care. You should clearly explain the following to the child and family:

- Tuberculosis disease, its cause and symptoms, emphasizing that TB is a curable disease.
- The treatment of TB in the child, including:
 - o Drugs and doses that will be prescribed.

- o Treatment regimen and duration.
- o Possible side effects of the medications and what to do when side effects occur.
- o Importance of taking medications regularly for the full course of treatment.
- o The risk of developing drug-resistant TB if the child misses doses.
- o That the treatment duration for drug-resistant TB is 2 years, the child has to be admitted to the hospital, and there is a high risk of mortality.
- o Options available for DOT/treatment support.
- How to prevent the spread of TB.
- The importance of screening family members for TB.

Ask the parent/caregiver to repeat what she/he has been told. Include children age 7 and older in the counseling sessions.

Counseling about tuberculosis symptoms

Counsel the parent/caregiver about common TB symptoms, including cough, fever, night sweats, weight loss, and breathlessness, and that these should improve on treatment. Inform the parent/caregiver that sometimes the child might experience wheezing due to blockage of the airways by the lymph nodes. **Instruct the parent/caregiver to take the child to the hospital *immediately* if the child has wheezing.** Inform parents/caregivers that some children have no symptoms but that this is not typical.

Points to be considered in adherence counseling

If there are problems with adherence, discuss the following with the child (at an age-appropriate level) and parent/caregiver:

- Identify factors affecting a person's adherence to treatment.
- Describe strategies to enhance adherence.
- Describe the roles of provider, supporter, and patient in adherence to treatment.

Counseling about drug side effects

Counsel parents/caregivers that anti-TB drugs are typically very well tolerated in children and adverse drug reactions are unusual. However, it is important that they understand the possible side effects so they can report them promptly should any occur. Provide information to parents/caregivers and their children (if age appropriate) about the side effects of each drug being prescribed. Emphasise to the parent/ caregiver and child that they should return to care if they experience any adverse reactions. This will allow proper management and ensure the least disruption possible to the treatment course. Unexpected and untreated side effects can cause parents/caregivers and children to experience unnecessary discomfort or more serious consequences, including significant morbidity or death. Alternatively, uninformed parents/caregivers or children may discontinue medicines on their own if they experience side effects, which can also lead to increased morbidity and death.

Psychosocial support

Stress can alter the immune system and make it less proficient; therefore, offering support to reduce stress in these children is important. Stress may result from many factors, such as fear of peer rejection or being different, or being concerned that they can give TB to their friends.

- Encourage parents/caregivers to talk with their children to allow them to verbalize any fears and concerns they may have.
- Suggest participation in a support group. This can allow children to discuss their fears and concerns with peers.
- Encourage proper rest and a balanced diet.
- Link families to social assistance.

Instruct families not to segregate children from other family members, as this can stigmatise and affect children psychologically

4 PREVENTION OF TUBERCULOSIS IN CHILDREN

4.1 Bacille Calmette-Guérin immunisation

The BCG vaccine is a live attenuated vaccine and is administered according to the Expanded Programme on Immunisation and NTLP guidelines. The vaccine is effective in protecting against TB meningitis and other severe forms of TB. However, it is not 100 percent effective and so TB must still be considered in BCG-vaccinated children with symptoms suggestive of TB.

All infants should be given BCG vaccine at birth regardless of HIV status; however, BCG should not be given to HIV-exposed infants who present with clear signs and symptoms of HIV disease or full-blown AIDS.

Infants born to mothers with tuberculosis disease

If the infant is born to a mother with TB disease, do not give BCG vaccine. The infant first must be evaluated for TB disease (see a section on “Neonatal tuberculosis”). If the neonate has TB disease, treat. If TB disease is ruled out, give IPT for six months. If the infant remains asymptomatic and is HIV negative at the end of six months of treatment, give BCG vaccine two weeks after completing IPT. During the course of IPT, the infant should be monitored on a monthly basis.

Side effects of Bacille Calmette-Guérin vaccination Common and minor side effects

Local redness, swelling, and pain occur in most infants at the site of injection and may last several weeks. In 1 to 2 percent of vaccinated infants, local skin infection may spread to the regional lymph nodes, causing a suppurative lymphadenitis. Some children with persistent localized reactions may benefit from surgical excision.

Severe side effects

A small number of children develop more severe complications following BCG vaccination. These most commonly include local abscesses, secondary bacterial infections, suppurative adenitis, and local keloid formation. Most reactions will resolve over a few months.

BCG immune reconstitution: Vaccine site abscess formation and/or ipsilateral lymphadenitis with or without systemic illness may develop within weeks to months of initiation of antiretroviral therapy (ART) (see a section on “Immune Reconstitution Inflammatory Syndrome,”).

Disseminated BCG: Disseminated BCG is a life-threatening infection that occurs in as many as 1 percent of HIV-infected infants vaccinated with BCG. HIV-infected or HIV-unknown infants who develop prolonged fever or other systemic symptoms within weeks or months of BCG immunisation should be investigated for immunodeficiencies and treated for TB using the first-line TB regimen, with the exception of pyrazinamide, to which *Mycobacterium bovis*

is resistant.

Key points

- BCG vaccine is effective in preventing serious forms of TB in very young children.
- BCG vaccine should be given to infants born to HIV-infected mothers at birth.
- BCG vaccine should be administered to HIV-negative/unexposed infants and asymptomatic HIV-exposed infants.
- BCG vaccine should not be given to infants who are confirmed as HIV infected.
- BCG vaccine should not be given to infants born to mothers with active TB disease until infants complete IPT.

Effect of Bacille Calmette-Guérin on tuberculin skin test and interferon gamma release assay

Most infants vaccinated with BCG will develop a positive TST but not a positive interferon gamma release assay (IGRA).

4.2 Management of latent TB infection in children

Latent tuberculosis infection (LTBI) is a state of persistence immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB.

The lifetime risk of reactivation TB for a person with documented LTBI is estimated to 5-10% with majority developing TB diseases within the first five years after initial infection. Children and adolescents have a higher risk than adults for progression to TB disease (with potential for disseminated disease). Most cases of progression to TB disease occur within 2 to 12 months of initial infection. IPT has proven to prevent progression of LTBI to TB disease. This supports the overall recommendation for the wide use of IPT within comprehensive HIV prevention, care, and treatment services.

Diagnosis of latent tuberculosis infection in children

Testing for LTBI in children is targeted to specific groups most at risk for progressing from LTBI to TB disease.

Tuberculin skin test

A TST is performed to diagnose TB exposure. Issues related to dosing, administration, false-positive, and false-negative results in children are discussed in Section 2, “Diagnosis of tuberculosis disease in children.” A child with a positive TST should prompt screening of all members of the household using the national TB screening questionnaire.

Contact screening and management

Numerous studies have found that contact investigations are a valuable means of identifying new TB cases. Young children living in close contact with a person with smear-positive pulmonary TB are at particular risk of TB infection and

disease. The initial steps of the evaluation include taking a history and conducting a thorough physical examination. It is recommended that household contacts of a smear-positive TB case be screened for signs and symptoms of TB and IPT given to children without TB disease. Routine assessment of exposed contacts does not require CXR or TST. These tests have limitations and are often not readily available or possible in low- and middle-income settings. In the absence of TST or CXR, clinical assessment alone is sufficient to decide whether the contact is well or symptomatic. Children diagnosed with TB disease should immediately be registered for anti-TB treatment under DOT. An algorithm for assessing child household contacts of an adult with smear-positive pulmonary TB is provided in Figure 4.1.

Definitions used in contact screening

Source case: A case of pulmonary TB, usually sputum smear positive, who is a source of infection.

Contacts for screening: All children younger than 5 years and children 5 years or older with signs and symptoms of TB who are in close contact with a source case.

Household contact: Living in the same household with the source case.

Source case investigation for children with TB disease: Many children are infected by household contacts with TB disease, so the caregiver of any child identified with TB should be asked whether there is anyone else in the house who has been coughing for more than 2 weeks. If so, these household contacts should be told to come in to the clinic for TB screening.

TB screening of siblings: The caregiver of a child with TB should also be asked whether there are any other children in the home. If so, they should be brought to the clinic for TB screening and consideration of IPT. A symptom screen and/or chest x-ray should be used for TB screening.

Screening for LTBI: LTBI is most likely to progress to TB disease in very young children, so it is important to identify and treat them early. Any household contacts of a child with TB disease who is younger than 5 years and who have TB disease excluded should be treated with daily isoniazid for 6 months. An HIV- infected child older than 12 months should receive IPT for 6 months as part of the comprehensive HIV care package.

Isoniazid preventive treatment

Isoniazid is the regimen of choice for treatment of LTBI amongst children exposed to known TB patients. IPT prevents progression of LTBI to active disease. Isoniazid dosing for LTBI is the same as for treatment of TB disease at 10 mg/kg daily (range 7-15 mg/kg daily) for 6 months. Where available, pyridoxine supplementation (1-2 mg/kg/day) should be administered together with isoniazid for patients with conditions that can predispose to neuropathy, including HIV infection, malnutrition, and diabetes. It should also be

administered if the patient is pregnant.

In HIV-infected children exposed to a TB contact, IPT should be given irrespective of immune status and whether or not the child is on ART. Initiation or completion of IPT should not be the cause of delay in starting ART.

Give IPT to the following children:

- All newborns with no symptoms of active TB disease that are born to mothers with active TB disease.
- All HIV-infected children less than 12 months with no symptoms of active TB disease and with a known TB contact.
- All HIV-infected children who are 12 months or older with no symptoms of active TB disease.
- All children younger than 5 years with no symptoms of active TB disease and with a known TB contact.

Note: LTBI treatment should be initiated only after TB disease has been ruled out (see Section 2, “Diagnosis of tuberculosis disease in children”).

Counselling for children on isoniazid preventive treatment

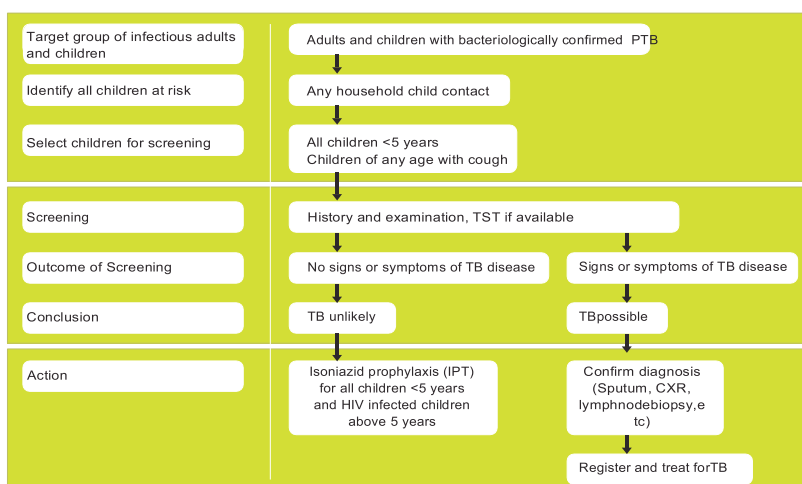
Explain to the child (if age appropriate) and parent/caregiver that treatment with the medicine isoniazid is essential to prevent the child from becoming very sick with TB disease. Describe the potential side effects and that they should return to the clinic if any adverse reactions occur.

Emphasise to the parent/caregiver and/or child that:

- The full duration of treatment is 6 months.
- The child must adhere to and complete their treatment.
- The child should return to the clinic if they feel ill whilst on IPT, or if they develop TB symptoms such as cough, fever, and poor appetite.
- The parent/caregiver does not need to limit the child’s activities in any way.

Figure 4.1. Algorithm for assessing child household contacts

ALGORITHM FOR ASSESSING CHILD HOUSEHOLD CONTACTS



PTB: pulmonary tuberculosis, CXR: chest x-ray, IPT: Isoniazid prophylactic therapy

Counselling for children with latent tuberculosis infection

See Section 3.15, “Counselling for children with tuberculosis.”

Adherence to and monitoring of isoniazid preventive treatment

Ideally, children on LTBI treatment should be monitored by a health care worker to reinforce adherence, assess for possible drug toxicity, and evaluate for potential progression to TB disease. Monitoring is done every 4 weeks for the entire duration of treatment. LFTs do not need to be monitored routinely unless the child has underlying liver disease or is taking other potentially hepatotoxic medications.

Isoniazid is usually well tolerated, although adverse reactions such as drug-induced hepatitis, gastrointestinal disturbances, peripheral neuropathy, and skin rashes can occur. The risk for developing isoniazid-induced hepatitis is increased in the setting of malnutrition, pre-existing liver disease, and use of other hepatotoxic drugs. Under these circumstances, baseline liver function assessment should be performed prior to initiation of isoniazid. The presentation of hepatotoxicity due to isoniazid is variable. If signs and/or symptoms of hepatitis (e.g., nausea/vomiting, poor appetite, abdominal pain, and yellow sclera) are present, isoniazid should be discontinued and LFTs obtained. Usually hepatitis resolves after the discontinuation of isoniazid. In this case, isoniazid should not be restarted.

Rarely, a child will develop symptoms of TB disease while taking IPT. In this case, the child may have developed breakthrough TB disease. Stop the isoniazid and evaluate the child for TB disease according to Section 2, “Diagnosis of tuberculosis disease in children.” IPT can be resumed if TB disease is ruled out.

Completion of IPT is important for good individual and programme outcomes, but IPT should be discontinued in the rare instance of breakthrough TB disease or drug toxicity.

Secondary isoniazid preventive treatment

IPT protects against TB for approximately 2 years. Thereafter, the risk of TB re-infection from new exposures gradually returns. Therefore, if there is known close contact of an adult with infectious TB 2 or more years after a completed course of IPT, a repeat IPT course is recommended.

Managing treatment interruption

In general, 6 months or 180 doses of isoniazid should be administered for LTBI treatment. If the interruption is 3 months or less, the remaining doses should be given and treatment duration extended as needed (upto 9 months). If the interruption is more than 3 months, treatment should be restarted.

Key points

- Give IPT, once active TB disease is ruled out, to:
 - Children younger than 5 years with known active TB contacts.
 - HIV-infected children more than 12 months of age.
 - HIV-infected children less than 12 months with known active TB contacts.
- Children with presumptive TB should be referred for investigation of TB.
- Treat LTBI in children with 6 months of isoniazid (IPT).
- Isoniazid preventive treatment protects against TB for about 2 years.

4.3 Tuberculosis infection control

Contrary to popular beliefs, children with TB may transmit TB and therefore infection control is important, even in health facilities or areas dedicated only to the management of children. Every health care facility must develop a TB infection control plan, which ensures that patients suspected of having TB are rapidly investigated, appropriately isolated, and rapidly treated to prevent TB transmission.

The clinical presentation of TB in children is variable and often overlaps with the presentation of pneumonia, HIV, and malnutrition, so infection control measures are relevant to all outpatient and inpatient areas with sick children.

Principles of infection control

The goal of infection control is to detect TB disease early and provide prompt treatment to children to prevent transmission of the disease in the general community. Health care workers should know priority policies and practices addressing infection prevention control in both children and adults. These include administrative, environmental, and respiratory control measures. The details are found in the National Guidelines for Tuberculosis Infection Control.

Key points specific for children

- Children can transmit TB infection to others, especially to those with HIV/AIDS and with malnutrition.
- Children with presumptive or confirmed TB should be cared for in a separate, well-ventilated room, away from HIV-infected children.
- Infants born to mothers with MDRTB should be separated at the earliest opportunity to minimize risk of contracting the infection.

5 PAEDIATRIC TUBERCULOSIS IN SPECIAL SITUATIONS

5.1 TB/HIV in children

The complex interactions between TB and HIV require health care workers to be knowledgeable about the management of patients with both TB and HIV. The available evidences indicate that TB has a significant adverse effect on outcomes in HIV-infected children.

Diagnosing HIV in children diagnosed with tuberculosis disease

Perform HIV testing on all children who are presumptive TB or diagnosed TB cases. Children found to be HIV infected should be referred to HIV care and treatment facilities for further management. Refer to the national HIV guidelines for further details on HIV testing procedures and management of HIV infection in children (see Annex 4 for more information on HIV testing of children younger than 18months).

Diagnosing tuberculosis disease in children with HIV

Screen all HIV-infected children for TB disease at the time of their HIV diagnosis and at every visit to an HIV care and treatment clinic, using the national TB screening questionnaire (refer to Annex 6). Diagnosis of children who screen positive for TB should follow the normal protocol for diagnosing TB in children as described in Section 2, “Diagnosis of tuberculosis disease in children.”

Since the most common means of transmission of HIV in children is from mother to child, the peak age prevalence for HIV is less than 5 years old. This is also the most difficult age group in which to confirm a diagnosis of TB.

Diagnosing TB in HIV-infected children is further complicated by the following:

- An overlap of clinical and radiological findings of pulmonary TB and that of other forms of HIV-related lung diseases.
- HIV-infected children with TB disease often have fewer TB bacteria than non-HIV-infected children, further increasing the likelihood of negative sputum smear results.
- Extrapulmonary TB and disseminated disease are more common in HIV-infected children.
- Difficulty interpreting the usual diagnostic tools because they are less specific in HIV-infected children (see Annex 7) for a summary of the impact of HIV on TB diagnostic test interpretation).
- Signs and symptoms of TB are less specific in children with HIV because symptoms of TB can overlap with symptoms of HIV (see Annex 8) for common causes of lung diseases in HIV-infected infants and children).

Clinical presentation of TB/HIV in children

As in adults, the natural history of TB in a child infected with HIV depends on

the stage of HIV disease. Before HIV infection advances and the child's immunity is good, the signs of TB are similar to those in a child without HIV infection. However, infants have immature immune systems so their immune status is already somewhat compromised. As HIV disease progresses and immunity declines, dissemination of TB becomes more common and TB meningitis, miliary TB, and widespread TB lymphadenopathy can occur.

Treatment of tuberculosis disease in HIV-infected children

Compared to HIV-uninfected children with TB, HIV-infected children with TB have worse outcomes of TB treatment and higher rates of mortality. This is likely due to a combination of factors, including severe immune suppression, co-existing malnutrition, HIV-related co-infections, Immune Reconstitution Inflammatory Syndrome, and greater problems with adherence to treatment. The majority of deaths in HIV-infected children receiving treatment for TB occur in the first 2 months(intensive phase) of TB treatment.

Important treatment issues to consider:

- Start TB treatment first for all HIV-infected children with TB disease and who are not yet on ART.
- Prescribe the same dosages and regimens of anti-TB treatment to HIV-infected children with TB disease as are used in HIV- uninfected children.
- Start ART as soon as possible in all HIV-infected children with TB regardless of CD4 levels once TB treatment is tolerated ideally within the first 2 to 8weeks of starting TB treatment.
- Monitor treatment and conduct follow-up in a care and treatment clinic (CTC) and a TB clinic, respectively, as per national recommendations (refer to Section 3, "Management of tuberculosis disease in children," for details on TB follow-up, and refer to national HIV guidelines for details on HIV follow-up).
- Once TB disease has been excluded, evaluate all HIV-infected children for IPT (refer to Section 4, "Prevention of tuberculosis in children," for further details).

Simultaneous treatment of both tuberculosis disease and HIV in children

All HIV-infected children with TB disease fulfill criteria for initiation of ART regardless of their CD4 levels, as per national guidelines. ART will reduce mortality in HIV-infected children with TB and the risk of recurrent TB following completion of anti-TB treatment. ART decreases the risk of developing TB disease in HIV-infected children who are TB exposed and infected. HIV-infected children with LTBI are candidates for IPT (refer to Section 4, "Prevention of tuberculosis in children," for details).

Children with TB and HIV who are receiving both ART and anti-TB treatment need special consideration because of the potential drug-drug interactions between rifampicin and non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors, the high pill burden, adherence concerns, and an increased likelihood of drug toxicity. Rifampicin reduces drug levels of NNRTIs and protease inhibitors when they are co-administered. This can

lead to sub-therapeutic ART drug levels and thereby increase the risk for developing ART drug resistance and ART treatment failure.

Below are regimens recommended for use in children with TB/HIV. Efavirenz is the preferred NNRTI to be used concurrently with rifampicin; however, it can only be used in children older than 3 years and weighing more than 10 kg. Nevirapine and lopinavir/ritonavir (LPV/r) should be avoided when the child is taking rifampicin because the levels of nevirapine and LPV/r will decrease significantly, which can compromise virologic suppression.

Recommended ART Regimens for Children Receiving Standard TB Treatment

For children <3 years of age on Anti-TB –

- *If on NVP based regimen, continue NVP ensuring that dose is 200mg/m² (optimized dose), if on LPV/r based regimen double the dose of LPV/r*

For children >3 years of age - ABC/3TC+EFV

- *It is recommended to give 2 NRTIs with EFV and if on LPV/r based regimen double the dose of LPV/r*

Key: *ABC: abacavir; AZT: zidovudine, 3TC:Lamivudine,EFV: efavirenz, NRTI: nucleoside reverse transcriptase inhibitor, , LPVr: Lopinavir/Ritonavir*

When to start antiretrovirals in infants and children receiving standard anti-tuberculosis treatment

Earlier ART treatment is associated with better outcomes. Children with TB/HIV not yet on ART who have been initiated on anti- TB treatment should be started on ART as soon as they are tolerating their anti-TB medicines. ideally within 2weeks after the start of anti-TB and definitely by 8weeks.

Monitoring during therapy and management of adverse reactions

Infants and children in general tolerate anti-TB treatment considerably better than adults. The biggest therapeutic challenge is the potential for drug-drug interactions between anti-TB medicines and ART, and achieving proper drug levels. In general, additional laboratory monitoring of LFTs is not required in children with TB/HIV unless there are signs and symptoms of liver toxicity (refer to Section 3, “Management of tuberculosis disease in children,” for further details). Table 5.1 presents overlapping side effects of anti-TB treatment and antiretroviral medications.

*Table 5.1. Overlapping side effects of anti-TB treatment and antiretroviral medications**

Side effect	Possible causes	
	Anti-TB drugs	Antiretroviral drugs
Peripheral neuropathy	Isoniazid, cycloserine	None
Skin rash	Rifampicin, isoniazid, pyrazinamide, cycloserine	Nevirapine, efavirenz, abacavir
Gastrointestinal symptoms	All	All
Hepatitis	Pyrazinamide, rifampicin, isoniazid, ethionamide	Nevirapine, protease inhibitors
Anaemia	Rifampicin	Zidovudine

*For management of adverse reactions, refer to Section 3, “Management of tuberculosis disease in children.”

Immune Reconstitution Inflammatory Syndrome

Immune Reconstitution Inflammatory Syndrome (IRIS) is an inflammatory process characterized by transient worsening of clinical disease following initiation of treatment due to restoration of the body’s capacity to mount an inflammatory immune response. This condition may arise when ART is initiated in a patient with very low CD4 levels and/or a high viral load. Onset is usually within the first 3 months after starting ART. IRIS develops in 5 to 20 percent of children starting ART.

When IRIS occurs, it is commonly associated with TB (current or undiagnosed) or recent BCG vaccine. 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. Typically, a patient who was doing well and responding to therapy suddenly gets much worse or has new symptoms or signs; hence, this is also referred to as a paradoxical reaction. In addition, sometimes ART start alone can unmask prior quiescent TB, so a few months after starting ART, signs and symptoms of TB appear.

Symptoms of TB IRIS include worsening TB symptoms and chest x-ray 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 fistulae and cold abscesses or worsening central nervous system disease due to enlarging cerebral tuberculosis).

When IRIS is detected, the following actions should be taken:

- Rule out TB/HIV treatment failure, side effects of TB and HIV treatment, and pre-existing untreated opportunistic infections.
- Continue both ART and anti-TB treatment unless severe toxicity is

- suspected or confirmed (e.g., elevated LFTs).
- In severe cases, give prednisolone at a dose of 1-2mg/kg for 1 to 2 weeks; and thereafter, gradually decrease the dose.
- Provide other supportive measures as warranted.

Appropriate use of cotrimoxazole preventive therapy

Cotrimoxazole preventive therapy (CPT) is a safe and cost-effective strategy and should be universally administered to all HIV-infected infants and children who do not have prior contraindication to its use. CPT prevents several secondary bacterial, fungal, and parasitic opportunistic infections, and significantly reduces morbidity and hospitalization from opportunistic infections.

Provide CPT to all children with TB/HIV, and to HIV-exposed infants if not already given as per national HIV guidelines. Cotrimoxazole is provided at a prophylactic dose of 4 mg/kg of trimethoprim once daily. In Tanzania, cotrimoxazole is available in a combination tablet of trimethoprim 80mg/sulfamethoxazole 400mg and as a syrup in the same ratio, containing 40 mg trimethoprim/200 mg sulfamethoxazole per 5 ml (see Table 5.2 for recommended dosages by weight).

Table 5.2. Recommended doses of cotrimoxazole by age

Age range	Trimethoprim/Sulfamethoxazole (TMP/SMZ) (Septrin®, Bactrim®)	
	<i>4 mg/kg once daily (for prophylaxis against opportunistic illnesses; higher doses will be required for treatment)</i>	
	Syrup: 40 mg/200 mg/5	Single-strength tablet: 80 TMP/400 SMZ
Birth to 6 months	2.5 ml	¼ tablet
6 months-5 years	5 ml	½ tablet
5 years-14 years	10 ml	1 tablet
≥14 years		2 tablets

HIV counselling (provider-initiated testing and counselling)

Tell the parent/caregiver (or child depending on age) that about 36% of TB patients have HIV, then advise HIV testing for the child and parents. Also inform the parents that by knowing HIV sero status earlier, prompt treatment and better outcomes are possible. Obtain HIV test at TB clinic or refer to RCH if early infant diagnosis is needed.

Treatment adherence to anti-tuberculosis and antiretroviral medications

Inform parents/caregivers and children that:

- By adhering to treatment, a patient can manage HIV, cure TB, and prevent the development of resistance, thereby improving their overall health and protecting the health of their community.
- Tuberculosis treatment is long but will cure their TB and can help prevent others from getting sick with TB.
- HIV treatment is lifelong that can keep them healthy as well as prevent the transmission of HIV to others.

Give enough age-appropriate information to the child to ensure adherence to TB/HIV treatment. Counseling is an ongoing and lifelong activity, so more information and support must be provided as children mature. Help the parent/caregiver become a knowledgeable adviser and advocate for their children, and be sure to review the following with the patient and parent/caregiver:

- TB and HIV transmission
- Clinical care and treatment
- Good nutrition, exercise, hygiene, and rest
- Psychosocial care

Adherence to treatment manages HIV, cures TB, and prevents resistance, thus improving the child's health and protecting others

Disclosure of TB/HIV status to the child

The most important counselling moment for children with TB/HIV is disclosure of their TB and HIV status. Be aware that parents/caregivers and children may have strong emotions at this time, particularly when the child's HIV infection is the result of mother-to-child transmission. Very often, parents are terrified of the idea of telling their child that they have TB and HIV and that the parent(s) has/have partly contributed to it. Parents/Caregivers often do not know where to begin, or how to deal with their child's self-isolation, sorrow, and withdrawal that may follow after the disclosure. Many parents feel tremendous guilt and shame, and worry that their child will become angry or reject them. Discuss these issues with parents/caregivers before disclosure to the child is undertaken.

Better outcomes are achieved when a disclosure process targets both children and their parents/caregivers and when both parties are included in primary counselling from the beginning of the disclosure process. Sharing of experiences from other parents—ideally by providing a parent support group—can be helpful to reassure parents/ caregivers that while their child may be initially angry and upset, they may also feel great relief at finally knowing the truth. Having the information will allow them to address these feelings, with the goal of being able to come to an acceptance of their diagnosis. While the best age at which to disclose depends very much on the individual child, in general, school-aged children can handle age-appropriate information about TB and HIV.

Making sure that parents/caregivers are well prepared and supported throughout the disclosure process will ensure a successful disclosure process that will not negatively affect the child's clinical and psychosocial well-being and the relationship with their parent/ caregiver.

Key points

- When TB and HIV interact, they intensify and worsen each other.
- If a child has HIV infection, they need to be screened for TB, and if a child has TB, they need to be tested for HIV.
- Start ART as soon as possible in all HIV-infected children with TB regardless of CD4 levels once TB treatment is tolerated ideally within the first 2 to 8 weeks of starting TB treatment.
- Immune Reconstitution Inflammatory Syndrome is not treatment failure but a recovery of the immune system and exaggerated presentation of unmasked infection.
- Continue anti-TB medicines and ART when HIV-infected children develop IRIS, unless severe toxicity occurs.
- Cotrimoxazole preventive therapy is universally recommended for HIV-infected children.

5.2 Drug-resistant tuberculosis in children

Drug-resistant TB is defined as TB caused by a strain that is resistant to one or more anti-TB medicines. This may be grouped into:

- **Mono-resistant TB:** Resistance to a single drug, most commonly isoniazid. This pattern of resistance is not usually associated with a worse outcome and does not require modification of the treatment regimen, as long as there are 4 drugs in the initial phase and rifampicin is included throughout the full duration of treatment. Rifampicin mono-resistance occurs, but is uncommon and is seen mainly in patients with HIV infection.
- **Poly-resistant TB:** Resistance to more than one drug, but *not* the combination of isoniazid and rifampicin.
- **MDR-TB:** Resistance to *at least* isoniazid and rifampicin. MDR has a major adverse effect on treatment outcome, and infected patients will generally require treatment with second-line regimens.
- **RR-TB:** Resistance to rifampicin detected using molecular tests or culture (phenotypic or genotypic methods), with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, in the form of monoresistance, multidrug resistance, polydrug resistance, or extensive drug resistance.
- **XDR-TB:** MDR-TB, plus resistance to fluoroquinolones, and at least 1 of 3 injectable agents (amikacin, kanamycin, capreomycin). XDR-TB cases are often also resistant to all 4 first-line agents, making patients significantly more difficult to treat.
- **Primary drug-resistance:** “*New Cases*”: Drug resistance in a patient who has never been treated for TB, or received less than 1 month of TB therapy. Drug-resistant TB in children is usually primary and due to contact with an infectious adult case.
- **Acquired drug-resistance:** “*Previously Treated Cases*”: Drug resistance in a patient who has received at least one month of anti-TB therapy

Multidrug-resistant tuberculosis (MDR-TB) is defined as resistance to both isoniazid and rifampicin with or without resistance to other first-line anti-TB drugs (streptomycin, pyrazinamide, and ethambutol). In adults, MDR TB is more common in previously treated TB cases (acquired drug resistance); however, in children, MDR TB is usually the result of direct transmission of *M. tuberculosis*-resistant strains (primary drug resistance) from an adult sickperson.

Diagnosis of multidrug-resistant tuberculosis in children

Children usually have paucibacillary or extrapulmonary TB disease, furthermore, sputum samples may be difficult to obtain in younger children and bacteriologically confirmation of drug resistant TB diagnosis may be difficult to obtain.

In view of these gaps, a high index of clinical suspicion is needed when diagnosing MDR TB in children and the following will be investigated for MDR TB:

- A child who is a close contact of an infectious MDRTB case including house or school contact.
- A child who is a close contact of a TB patient, who has failed treatment, was lost to follow up or died during treatment.
- Failure to improve clinically after 2-3 months of first-line TB treatment, including persistence of positive smears or cultures, persistence of symptoms, and failure to gain weight
- A child with proven TB who is still bacteriologically positive after five months of appropriate treatment with first-line anti-TB medications (treatment failure).
- History of previous treatment within the past 6-12 months

Despite the diagnostic challenges, every efforts should be made to obtain specimens from all possible sources, like gastric aspiration, sputum induction, or lymph node aspiration for bacteriologic confirmation of drug resistant TB through Xpert/MTB/Rif or culture and DST or Line Probe Assay (LPA) tests, because DR TB is a microbiological diagnosis even in children. Culture results can be available within two weeks (Liquid Media), and DST results are available after at least 6 weeks. Xpert MTB/Rif is a rapid molecular test and the results can be obtained in 3 hours' time. The diagnosis of DR TB in children is made by a review panel of experts on DR TB based on history, physical examination, and laboratory findings. Children diagnosed with DR TB should be reported to the DTLC for recording and referred to a DR TB treatment centre for further management as stipulated in the Operational Guidelines for the Management of Drug-Resistant TB in Tanzania.

Pretreatment screening and evaluation

Before referral for DR TB treatment, the following interventions should be performed:

- Inform the parent/caregiver and family about DR TB, its treatment and duration.
- Evaluate nutritional status, and inform the mother on proper feeding

- practices and maintenance of a feeding chart.
- Counsel and test for HIV, if HIV status is unknown.
- Ensure the child has a baseline chest radiograph.

The MoHCDGEC recommends using a **standardized treatment regimen** approach for all identified paediatric DR TB cases, so that all patients receive the same regimen. Children should be managed under the same principles as adults, the duration of therapy for standardized treatment regimen of DR TB in children is 20 to 24. All treatment should be given daily and under facility DOT. Treatment consists of two phases:

- **Intensive phase**, in which the child takes at least four effective drugs, including an injectable, for 8 months. Paediatric MDR TB patients should only be hospitalized when they have other co-morbid conditions* associated with MDR TB and/or have under nutrition so as to receive nutritional care and treatment. These patients should be transferred to the community for continuation of treatment once they reach the early discharge criteria (as early as two weeks after initiating treatment). Majority of patients not meeting above criteria should be initiated treatment on an outpatient basis in their communities.
- **Continuation phase**, in which the child takes the same drugs except for the injectable at a health facility close to their home for a total of 12 months.

**Common co-morbid conditions seen in children with MDR-TB include; HIV, diabetes mellitus, orthopedic problems, and reactive airway disease.*

Tables 5.3 below provides a list of the drugs for each treatment phase, and Table 5.4 provides details on paediatric dosages for second-line anti-TB drugs.

Table 5.3. Standardized MDR TB medicines and duration of treatment regimen

Treatment phase	Drugs	Duration
Intensive phase	Amikacin or kanamycin Ofloxacin or levofloxacin Pyrazinamide Ethionamide Cycloserine Ethambutol	8 months
Continuation phase	Levofloxacin Ethionamide Pyrazinamide Cycloserine Ethambutol	12 months

Table 5.4. Paediatric dosing and adverse reaction of second-line anti-TB drugs

Drug	Daily dose (mg/kg)	Frequency	Maximum daily dose	Adverse reactions
Amikacin	15-22.5	Once daily, 5 times a week	1 g	Ototoxicity, nephrotoxicity
Kanamycin	15-30	Once daily	1 g	Ototoxicity, nephrotoxicity
Capreomycin	15-30	Once daily	1 g	Ototoxicity, nephrotoxicity
Moxifloxacin	7.5-10	Once a day	400 mg	Arthropathy, arthritis
Levofloxacin ^f	7.5-10	Once a day	750 mg	Arthropathy, arthritis
Ethionamide	15-20	Twice a day	1 g	Vomiting, gastrointestinal upset

Cycloserine	10-20	Once or twice a day	1 g	Central nervous system manifestations (psychosis, depression), neurological
PAS	200 - 300	Twice or thrice daily	12 g	Vomiting, gastrointestinal upset
Pyrazinamide*	30-40	Once daily	2 g	Hepatotoxicity, hyperuricemia, arthralgias, gastrointestinal upset
Ethambutol*	15-25	Once daily	2.5 g	Optic neuritis (usually reversible), decreased red-green colour discrimination, gastrointestinal upset, hypersensitivity

PAS: para-aminosalicylic acid. *First-line anti-TB drugs.

^fLevofloxacin is dosed twice daily for children 5 years of age and under (total daily dose: 15-20mg/kg/day) and once daily for children over 5 years of age (total daily dose: 7.5-10mg/kg/day). This is done because children under five metabolize the levofloxacin faster than those older than five. (Source: *Management of Drug-Resistant Tuberculosis in Children: A Field Guide. Boston, USA: The Sentinel Project for Pediatric Drug-Resistant Tuberculosis; November 2012*)

Adverse effects of second-line anti-tuberculosis drugs in children

Children generally tolerate second-line medicines well, with adverse events occurring less frequently than in adults. Caregivers should be made aware of possible adverse events and told to immediately report any possible adverse event. No second-line anti-TB drugs are absolutely contraindicated in children unless hypersensitivity or an intractable adverse reaction has been documented.

Monitoring of children on MDR treatment

Children in the continuation phase of MDR TB treatment should be monitored for simple adverse effects with support from the DTLC, as shown in the table below.

Table 5.5. Treatment monitoring of children with MDR TB

Parameter	Frequency
Fever, cough, and loss of appetite	Monitor daily.
Sputum for smear, culture	Monthly.
Weight	Daily in hospital, monthly in the continuation phase.
Height	Monthly.
Full blood picture	Baseline and quarterly.
Creatinine	Twice monthly for the first month, then monthly in the intensive phase and in the continuation phase if indicated.
Potassium	Monthly. If low, obtain calcium and magnesium.
AST, ALT, total bilirubin	Monthly.
TSH	Baseline, then quarterly.
Audiometry and vestibular function	Monthly in the intensive phase then quarterly
X-ray investigation	At baseline, every 6 months, and at end of therapy

ALT: alanine aminotransferase; **AST:** aspartate aminotransferase; **TSH:** thyroid-stimulating hormone.

Monitoring treatment efficacy

Obtain a sputum specimen for smear, culture, and DST monthly until the child's sputum converts to smear and culture negative. Sputum conversion is defined as two consecutive negative smears and cultures taken 30 days apart. After conversion, obtain smears at least monthly and cultures every 2 months.

In children who are not culture positive initially, treatment efficacy or failure is difficult to assess. **Always monitor weight carefully in children to adjust dosages as the child gains weight.** The following are the first (or only) signs of treatment failure

- Failure to gain weight adequately ;or
- Failure to thrive; or
- Weight loss.

The short MDR TB Regimen

Currently, the Ministry is in the process of introducing short term DR-TB treatment regimen which will shorten the duration of treatment from 18 to 24 months down to 9 to 11 months.

The regimen is endorsed by WHO and comprises of the following drug combinations;

4-6 Km, Mfx, Pto, Cfz, z, H high dose, E/5 Mfx, Cfz, z, E

[i.e Km= Kanamycin, Mfx= Moxifloxacin, Pto= Prothionamide, Cfz = Clofazimine, z = Pyrazinamide, H = Isoniazid, E = Ethambutol]

The intensive phase: This will be given daily for **four months**. The Kanamycin, clofazimine, Moxifloxacin, ethambutol, high dose isoniazid, pyrazinamide and prothionamide will be extended until smear and/or culture conversion if smear conversion is not achieved within four months, with a maximum of **6 months**. Kanamycin will be given thrice-weekly from the fourth month onwards. Failure might be declared at 6 months for those who have both positive smear at 6 months and poor clinical response to treatment.

The continuation phase: Moxifloxacin, ethambutol, pyrazinamide and clofazimine given daily for a further **five months**.

The recommended dosage by weight, can be used in **people living with HIV**, including those who are receiving antiretroviral treatment and in **children under 15 years**. However the regimen is not recommended in patients with resistance to any of the two drug classes (Pre-XDR; FQs, second line injectables (SLinj)) or who have extensively drug-resistant TB (XDR-TB; MDR-TB plus additional resistance to a fluoroquinolone and a second-line injectable). The short MDR TB regimen should be provided in accordance with existing National MDR TB guidelines.

Screening of children in contact with multidrug-resistant tuberculosis patients

Close contacts of drug-resistant TB patients who develop TB disease usually have drug-resistant disease with the same resistance pattern. All children who are contacts of an infectious MDR TB case should be screened for MDR TB disease. Screening should be done even in asymptomatic children, and include:

- Taking a history.
- Physical examination.
- Laboratory findings (sputum for smear and culture, and x-ray investigations).
- HIV counseling and testing if not yet done.

Chemoprophylaxis

Currently, there are no recommendations for chemoprophylaxis for MDR TB contacts in Tanzania. The alternative to chemoprophylaxis in MDR TB contacts is careful clinical follow-up, every 2 to 3 months for the first 6 months, and thereafter, every 6 months for at least 2 years. If active disease develops, refer for MDR TB treatment.

Management of a newborn child of a mother with multidrug-resistant tuberculosis

A newborn should be separated from a mother with untreated MDRTB or who is still smear/culture positive despite treatment. Once a mother is no longer contagious (smear/culture negative), the infant may be cared for by the mother (separation is no longer needed). Advise the mother to consider using breast milk substitutes to avoid possible adverse effects, because most second-line TB medications are excreted in breast milk.

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.

Key points

- Most children are culture negative, making the diagnosis of drug-resistant TB difficult.
- All children who are contacts of an infectious MDRTB case should be screened for MDR TB disease.
- Standardized treatment regimen of Multidrug-resistant tuberculosis requires 18 to 24 months of appropriate treatment (in two phases: intensive and continuation)
- Short Multidrug-resistant treatment regimen of tuberculosis requires 9 to 11 months of appropriate treatment (in two phases: intensive and continuation).
- Always monitor weight carefully in children to adjust doses as the child gains weight.
- Close and extensive monitoring is required for all patients receiving treatment with second-line anti-TB medicines.
- No chemoprophylaxis is indicated for children who are MDR TB contacts.
- Mothers with MDRTB are able to provide care for their newborns once they are no longer infectious (smears and cultures are negative).

6 RECORDING, REPORTING AND USE OF DATA FOR CHILDREN WITH TUBERCULOSIS

6.1 Introduction

Reliable and complete data in the recording and reporting system are essential for monitoring patient outcomes and programme performance. Children with TB should always be included in the routine recording and reporting system. The data collected at any level should be analysed and interpreted locally for reporting, planning, monitoring purposes, making evidence based decisions and accountability.

Definitions

Recording - capturing data on patient management over time and across clinical sites. Information is written directly on paper forms or entered into a computer.

Reporting - routine tracking (monitoring) of priority program management information of summary patient outcome data (evaluation) at facility, district, regional, and national levels over a period of time.

6.2 TB Recording and Reporting Tools in Children

Recording and Reporting of Child Cases

Children with TB should be included in routine recording and reporting. Notify all identified TB cases in children and register the child for treatment. If smear positive, record their smear status at months 2, 5 and at the end of treatment. Record the child's treatment outcome as well.

TB registers are available at facility and district levels. The district registers are in paper and electronic version (in the DHIS2). The paper version is filled out at the district, and then transcribed into electronic version.

TB Forms and Cards

- **TB 01** – Tuberculosis treatment card
The health care worker who manages the patient's treatment fills out this card at every patient visit. It focuses on the diagnosis and clinical aspects of patient care.
- **TB 02** – Kadi ya mgonjwa wa kifua kikuu
The health care worker fills out this card when treatment is started. It is kept by the patient, provides evidence of previous treatment history, and enables the patient to collect their medicines.
- **TB 03** - TB Unit register

This register list of all patients taking TB drugs in the clinic. Data from this register provide the foundation for the District TB register and forms the basis for major decisions. It is filled out by health care workers in TB clinics who provide drugs, treatment, and counselling to patients.

- TB 04 – Tuberculosis district register
Contains the list of all TB patients notified in the district and the transferred in from other district.
- TB 05 - Tuberculosis Laboratory Register
This is a laboratory register where all sputum samples from presumptive TB cases are registered including respective sputum examination results.
- TB 06 - Request and reporting form for TB culture and Drug susceptibility Test
- TB 07 - Tuberculosis Quarterly Case Notification Report Form
- TB 08 - Tuberculosis Drugs and Supplies Calculation and Order Form
- TB 09 - Tuberculosis Quarterly Treatment Results Report Form
- TB 11 – Quarterly report of treatment results of transferred-in TB and TB/HIV patients notified in the quarter ending 12 months earlier.

Community based recording and reporting tools

- TB 12 - Fomu ya watu (wateja) waliofanyiwa uchunguzi wa awali wa TB katika Jamii
- TB 13 - Rejesta ya Wanaohisiwa kuwa na TB katika Jamii
- TB 14 - Fomu ya Taarifa ya Robo Mwaka ya Kikundi cha Jamii cha Huduma za TB
- TB 15: Fomu ya rufaa ya huduma za TB ngazi ya jamii

TB and Leprosy combined forms

- TB/LEP 01 - Request and Report Form for Smear Examination
- TB/LEP 02 - Fomu ya Rufaa / Uhamisho

MDR TB tools

- MDR TB 01: MDR TB Treatment Card
- MDR TB 02: MDR TB Patient Identity Card
- MDR TB 03: MDR TB Suspect Register
- MDR TB 04: MDR TB District Register

HIV Forms and Cards

- CTC1 Card
- CTC2 Card
- Pre ART register
- ART register

6.3 Recording and Reporting of Outcomes of Child TB Cases

Assigning and Evaluating Treatment Outcomes

Health workers at health facility level fill in the treatment outcomes of each patient on treatment card and in the unit register, the DTLC fill in treatment outcome in the district unit and compile quarterly report for notification and treatment outcomes. The NTLP compiles all cases and treatment outcome data for national recording and reporting purposes.

New patient have never been treated for TB or have taken anti-TB drugs for less than 1 month. Outcome assignment is done by the DTLC or health care worker after 6 months of therapy as follows:

- **Treatment completed:** A child with smear negative pulmonary TB or extra-pulmonary TB cases, who has completed treatment after 6 months of continuous therapy, or 168 doses. This includes 56 doses in the intensive phase and 112 doses in the continuation phase. Since most children have sputum smear negative and/or extra-pulmonary TB, it is impossible to show bacteriological cure and most cases will be classified as treatment completed.
- **Cured:** New bacteriologically confirmed patients with negative sputum smear or culture results at 5 months and on at least one previous occasion. However, patient should complete 168 doses (6 months of treatment).
- **Treatment failed:** New bacteriologically confirmed patients with positive sputum smear or culture results at 5 months or later during treatment. Request a sputum specimen for mycobacterial culture and drug susceptibility testing (DST). Close their treatment card (outcome = failure) and open a new treatment card (type of patient = treatment after failure).

Previously treated patients have received 1 month or more of anti-TB drugs in the past. Outcomes for previously treated are reported similar as described above.

Table 6.1. Definitions of treatment outcomes

Outcome	Definition
Cured	A PTB patient with bacteriologically confirmed TB at the beginning of treatment and 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 there is 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 they were not done or because results were not available
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 two consecutive months or more.
Not evaluated	A TB patient for whom no treatment outcome is assigned. (This includes cases “transferred out” to another region and when the treatment outcome is unknown to the reporting district.)
Treatment success	Sum of cured and treatment completed

Age disaggregated Data and Indicators

Age disaggregated Data

Cohort analysis is a key tool for evaluating program effectiveness. It is the review of the outcomes for a cohort or group of patients that were started on treatment during the same timeframe. Type of TB, classification and outcomes for children are analyzed based on the following age groups: under 5 years, from 5 to under 10 years, and from 10 to under 15 years.

TB/HIV programme indicators

TB/HIV programme indicators are used to assess the effectiveness of TB/HIV programme collaboration and integration. Measurement of these indicators can also identify areas of possible programme strengthening.

Table 6.2. Indicators for NTL routine recording and reporting

Indicator	Significance
Proportion of children with TB amongst all TB cases notified	May indicate over- or under-reporting of TB cases in children
Proportion of children with pulmonary TB amongst childhood TB cases	May indicate over- or under-diagnosis of pulmonary TB
Proportion of children with TB who are cured amongst smear-positive childhood TB cases (demonstrated by end-of-treatment smear conversion from positive to negative)	Demonstrates the quality of management of children with TB in the program
Proportion of children who complete treatment amongst smear-positive childhood TB cases (those who complete a full course of anti-TB treatment in whom smear conversion is not demonstrated)	Demonstrates the quality of management of children with TB in the program
Proportion of children who are successfully treated amongst smear-positive childhood TB cases (cured + treatment completed)	Demonstrates the quality of management of children with TB in the program
Proportion of children with miliary TB or TB meningitis amongst childhood TB cases	This proportion should be very low where BCG vaccination coverage is high

TB contacts of index cases being treated for TB should be entered into the TB contact register. This register can serve as a reminder of the importance of contact screening as well as provide important information on contacts, such as age, HIV status, and management. A record should be kept to indicate contact screening has taken place and the outcomes documented.

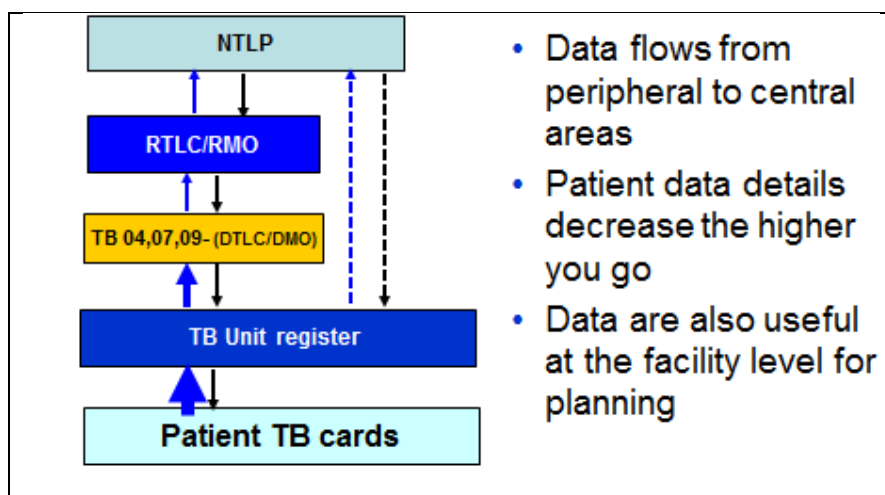
TB clinic setting indicators

- Number and proportion of children counselled and tested for HIV amongst all children notified.
- Number and proportion of children who tested HIV positive.
- Number and proportion of children who tested HIV positive and were referred to a CTC.
- Number and proportion of children who tested HIV positive and were registered at a CTC.
- Number and proportion of children who tested HIV positive and were initiated on CPT.
- Number and proportion of children who tested HIV positive and were initiated on ART.

HIV clinic setting

- Number and proportion of children newly enrolled in HIV care.
- Number of children screened for TB amongst newly enrolled in HIV care.
- Number of children diagnosed with TB amongst newly enrolled in HIV care.
- Number of children initiated on TB treatment amongst newly enrolled in HIV care.
- Number of children initiated on IPT amongst newly enrolled in HIV care

Figure 6.1: Data Flow for TB



Key Points

- Recording and reporting are essential to a facility's success, as they help health care workers to:
 - Assess patient progress
 - Ensure quality of care, sharing of information between patient and health workers
 - Conduct monitoring and evaluation activities
 - Assess program performance
 - Plan programs
 - Demonstrate accountability
- Learning how to use all of the different TB data forms is key to successful reporting
- The more accurate and complete reporting is, the more likely it is that health care workers will meet TB programme objectives.

7 ROLES AND RESPONSIBILITIES OF THE HEALTH SYSTEM IN DIAGNOSIS AND MANAGEMENT OF CHILDREN WITH TUBERCULOSIS

7.1 Introduction

The diagnosis, treatment, and case management of TB in children require that certain services are available at different levels of care. The delivery of services and the responsibilities of staff will differ within the levels of care.

7.2 Community Level TB care

Community TB care approach aim at involving communities and community health workers including former TB patients to improve early TB care-seeking and treatment adherence, increase community awareness around TB symptoms and signs among children, and mitigate TB stigma. The resulting outcome will contribute to increased childhood TB case detection and treatment success.

Community TB care represents a wide range of activities carried out at the community level by community members themselves, in partnership with community health care workers who serve as a link to the health care system. These activities include:

- Recognition of sign and symptoms of childhood TB
- To Identify children with presumptive TB and refer or escort them to health facilities
- To Ensure referral feedback from health facilities
- To Ensure all confirmed TB cases are initiated with treatment
- Conduct contact tracing
- Reducing stigma and discrimination in the communities and within families
- Providing support and advocating for treatment adherence
- Increasing awareness on childhood TB and demand for management

7.3 Health facility level TB care

Primary health facility level of care

This level includes dispensaries and health centres. At this level, staff should be able to:

- Recognise the symptoms and signs of childhood TB
- Recognize the significance of household contact with smear-positive index cases
- Diagnose children with presumptive TB by using Paediatric TB score charts, AFB smear or Xpert MTB/Rif
- Register immediately all children diagnosed with TB and start treatment under DOT following NTLF guidelines
- Perform HIV counseling and testing following National guideline for

management of HIV and AIDS.

- Do counselling on special issues related to children, including the challenges of disclosure of HIV serostatus at different ages

Secondary level of care

This level includes district and regional hospitals. At this level, staff should be trained and be able to perform all activities at the primary health care level as mentioned above. In addition the following activities should be performed:

- Tuberculin skin test (TST)
- Lumbar puncture, pleural tap and ascites tap, Sputum induction and gastric lavage to collect samples for AFB smear microscopy, Xpert MTB/RIF and culture
- Read chest x-rays
- Diagnose and manage complicated TB cases like meningitis, osteoarticular disease, and drug-resistant TB.

Tertiary level of care

This level includes zonal and referral/consultant hospitals and specialized hospitals. In addition to the activities performed at the secondary level, at this level, services should include:

- Culture and DST
- Interferon gamma release assay(IGRA)
- Diagnosis and management of complicated TB cases, including drug-resistant TB in children
- To ensure internal and external quality control of the above procedures at the lower levels of care

7.4 Integration of TB services into Reproductive and Child Health services

All children up to the age of five years are required to attend Reproductive and Child Health Clinic (RCH) for growth monitoring and immunization services. These clinics serve as the opportunity for TB screening in children as health workers in these clinics are mostly the first to realize health issues in children and their mothers while attending routine visits. Linking TB services with RCH services will contribute to increased TB case detection and treatment success in children. Education on TB prevention, diagnosis and treatment should be included in pregnancy and child health care package. These services should include the following:

- TB screening during antenatal, natal and postnatal period (mother and infant), all those who screen positive should be referred for investigation/treatment
- TB screening for all <5 years during their visits
- Contact-tracing for persons with infectious TB in their families and provide IPT prophylaxis for TB exposed infants and children
- Providing TB treatment adherence support
- HIV testing and counseling for TB patients (parents and children)
- Provision of TB education, supervision and support for staff and volunteers

ANNEX 1: SPUTUM INDUCTION

Sputum induction is a procedure in which the respiratory tract is stimulated to produce sputum through the use of inhaled hypertonic saline. Unlike gastric aspiration, sputum induction is an aerosol-generating procedure. Therefore, this procedure should be performed in an isolation room that has adequate infection control precautions (negative pressure, ultraviolet light [turned on when room is not in use], and an extractor fan).

Sputum induction is regarded as a low-risk procedure. Very few adverse events have been reported, and they include coughing spells, mild wheezing, and nosebleeds. Recent studies have shown that this procedure can safely be performed even in infants as young as 1 month old, though staff will need to have specialised training and equipment to perform this procedure in such patients.

Materials needed for sputum induction

- Respiratory face mask (fit-tested N95 mask is recommended if available; N95 mask can be used by the same person for up to 1 month)
- Gloves
- Nebuliser machine (with tubing and mask)
- Suction machine with sputum trap
- Inhaled bronchodilator (e.g., salbutamol inhaler)
- Inhaled hypertonic saline (3-5%)
- Suction catheter (soft, flexible, small caliber and large caliber)
- Supplemental oxygen source
- Log book/forms for the documentation of sputum induction procedure
- Laboratory request form to accompany specimen to laboratory
- Disinfectant solution (for disinfecting materials used)
- *Optional materials (should be used if available)*
 - *Fan (for airflow)*
 - *Goggles or visor (for eye protection)*
 - *Stethoscope*
 - *Pulse oximeter or cardiac monitor*
 - *Nasopharyngeal or oral airways*

General approach

Examine children before the procedure to ensure they are well enough to undergo the procedure.

Children with the following characteristics should not undergo sputum induction:

- Inadequate fasting: If a child has not been fasting for at least 3 hours, postpone the procedure until the appropriate time.
- Severe respiratory distress, including rapid breathing, wheezing, and hypoxia.
- Intubated.
- Bleeding: Low platelet count, bleeding tendency, severe nosebleeds (symptomatic or platelet count <50,000/ml blood).
- Reduced level of consciousness.
- History of significant asthma (diagnosed and treated by a clinician).

Procedure

1. Positioning the child:
 - a. Infants: best held in the feeding position (cradled, supine).
 - b. Older children: held upright or semi-upright in caregiver's arms.
2. Pre-procedure assessment: Verify adequate fasting (no liquids/solids within past 3 hours), assure that none of the contraindications (listed above) apply to the child, check baseline pulse and respiratory rate, and auscultate the lungs to exclude wheezing. Ensure all equipment is ready and set up properly.
3. Intra-procedure monitoring—monitor for the following throughout the

procedure:

- a. Increased respiratory rate or respiratory distress (indrawing, nasal flaring, grunting).
- b. Profuse sweating.
- c. Vomiting.

If any of these symptoms are seen, the sputum induction should be terminated and the patient needs to be assessed by a clinician.

4. Administer a bronchodilator (e.g., salbutamol) to reduce the risk of wheezing:
 - a. After child is seated (or in caregiver's arms), apply the mask to the child.
 - b. Turn on the nebulizer and have the caregiver keep the mask on the child's face.
 - c. Administer the nebulised bronchodilator for 3-5 minutes.
5. Administer nebulised hypertonic saline (e.g., 3% NaCl):

After 3-5 minutes of bronchodilator therapy, add 5-10 ml of hypertonic saline to the nebuliser.

 - a. Administer nebulised hypertonic saline for 15 minutes or until 5 cm³ of solution has been fully administered.
 - b. Give chest physiotherapy as necessary; this is useful to mobilize secretions.
 - c. If the child begins coughing before the full 15 minutes but has provided an adequate specimen, then it is okay to stop the sputum induction.
6. Suctioning of the sputum:
 - a. This is started after the patient begins coughing.
 - b. There are 3 ways to suction:
 - 1) The suction catheter alone (without any airway) can be inserted directly into the nostril or mouth (where mucoid secretions are being produced) and suctioned.
 - 2) Nasopharyngeal airway: Suction catheter is dipped in water and inserted into nostril. Suction catheter is then introduced via the nasopharyngeal airway and airway is suctioned. Catheter should be inserted the approximate length from the child's nostril to earlobe.
 - 3) Oropharyngeal airway: Inserted into the child's mouth to prevent clenching of teeth and biting of catheter. The suction catheter is then introduced into the mouth and the airway is suctioned.
 - c. When correctly inserted, the suction catheter should stimulate an involuntary cough.
 - d. Suction by covering the suction hole on the catheter/trap device.
 - e. Start with negative pressure at 15-20 mm Hg, and only increase the pressure if needed to obtain an adequate sample. (Caution: Very high negative suction pressure can cause tissue damage and airway bleeding.)
 - f. *An adequate sample is 2 ml (or more) of thick mucoid secretions.*
7. Post-procedure assessment: Monitor the child for 10 minutes for increased respiratory rate or increased respiratory distress (provide oxygen if this occurs, and evaluate by clinician).

Any equipment that will be reused will need to be disinfected and sterilised before use with a subsequent patient. Clean the tubing of the nebuliser machine in prepared antiseptic solution, wipe down the chair/equipment with a cloth soaked in antiseptic solution, and discard any disposable equipment. Wash hands at the end of each encounter.

ANNEX2: GASTRIC ASPIRATION

Gastric aspiration is used to collect gastric contents to try to confirm the diagnosis of tuberculosis (TB) by microscopy and mycobacterial culture in young children when sputum cannot be spontaneously expectorated nor induced using hypertonic saline. During sleep, the lung's mucociliary system sweeps mucus up into the throat, where it is swallowed and remains in the stomach until the stomach empties. Therefore, the highest-yield specimens are obtained first thing in the morning. Gastric aspiration on each of 2 consecutive mornings should be performed for each patient. Performing the test properly usually requires two people (one doing the test and an assistant). Children with a low platelet count or bleeding tendency should not undergo the procedure.

Required equipment

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

Procedure

The procedure can be carried out as an inpatient first thing in the morning when the child wakes up, at the child's bedside, or in a procedure room on the ward (if one is available), or as an outpatient (provided that the facility is properly equipped). The child should have fasted for at least 4 hours (infants for 3 hours) before the procedure.

1. Prepare all equipment before starting the procedure.
2. Position the child on his or her back or side. The assistant should help to hold the child.
3. Measure the distance between the nose and stomach, to estimate the distance that will be required to insert the tube into the stomach.
4. Attach a syringe to the nasogastric tube.
5. Gently insert the nasogastric tube through the nose and advance it into the stomach.
6. Withdraw (aspirate) gastric contents (2–5 ml) using the syringe attached to the nasogastric tube.
7. To check that the position of the tube is correct, test the gastric contents with litmus paper: blue litmus turns red (in response to the acidic stomach contents). (This can also be checked by pushing some air [3–5 ml] from the syringe into the stomach and listening with a stethoscope over the stomach.)
8. If no fluid is aspirated, insert 5–10 ml sterile water or normal saline and attempt to aspirate again.
 - a. If still unsuccessful, attempt this again (even if the nasogastric tube is in an incorrect position and water or normal saline is inserted into the airways, the risk of adverse events is still very small).
 - b. Do not repeat more than three times.
9. Withdraw the gastric contents (ideally at least 5–10 ml).
10. Transfer gastric fluid from the syringe into a sterile container (sputum collection cup).
11. Add an equal volume of sodium bicarbonate solution to the specimen (in order to neutralize the acidic gastric contents and to prevent destruction of tubercle bacilli).

After the procedure

1. Wipe the specimen container with alcohol/chlorhexidine to prevent cross-infection and label the container.

2. Fill out the laboratory requisition forms.
3. Transport the specimen (in a cool box) to the laboratory for processing as soon as possible (within 4hours).
4. If it is likely to take more than 4 hours for the specimen to be transported, place it in the refrigerator (4–8°C) and store until transported.
5. Give the child his or her usual food.

Safety

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

ANNEX 3: DIAGNOSIS AND MANAGEMENT OF MALNUTRITION

Diagnosis

Malnutrition can be recognised by clinical manifestations of visible severe wasting (e.g., cachexia and/or presence of swelling of both extremities).

To check for wasting, undress the child and look at the front and back view:

- Is the outline of the child's ribs easily seen?
- Does the skin of the upper arms look loose?
- Does the skin of the thighs look loose?
- Is flesh missing from the buttocks?

To check for **oedema**, grasp the foot so that it rests in your hand, with your thumb on top of the foot. Press your thumb gently for a few seconds. The child has oedema if a pit (dent) remains in the foot when you lift your thumb. To be considered a sign of severe malnutrition, oedema must appear in both feet.

The extent of oedema is commonly rated as follows:

- + mild (grade 1): both feet only
- + + moderate (grade 2): both feet, plus lower legs, hands, or lower arms
- + + + severe (grade 3): generalised oedema, including both feet, legs, hands, arms, and face

Oedema is a characteristic of kwashiorkor.

Malnutrition is confirmed by anthropometric measurements as shown in the table below.

Diagnostic criteria for malnutrition in children aged 6 to 60 months		
Indicator/Measure*	Cutoff	
	Severe acute malnutrition	Moderate acute malnutrition
Weight-for-height/length	Less than -3SD (<70%)	Between -2SD and -3SD (70–79%)
Mid-upper arm circumference	Less than 11.5 cm	11.5–12.5 cm
	Bilateral oedema (any type)	

SD: standard deviation.

*Based on World Health Organization child growth standards, available at www.who.int/childgrowth/standards.

Principles of management

It is important to address all the problems facing the child. In addition to undergoing overall assessment, children with tuberculosis should undergo complete assessment of nutritional status, including the following:

- Detailed dietary history to identify the existence of any feeding problems and support networks, including resources available at home for the family.
- General examination focused on identifying features of malnutrition, including taking of accurate anthropometric measurements to identify the growth pattern and appropriate management plan.
- An individualized nutritional support plan, depending on the severity of malnutrition and the associated complications

Management of severe acute malnutrition

Children who present with severe acute malnutrition (kwashiorkor, marasmus, or marasmic-kwashiorkor) and with any of the following complications need inpatient care immediately for stabilisation and initial management using the Tanzanian National Guidelines for Management of Acute Malnutrition for the inpatient management of severe acute malnutrition (i.e., the ten steps for recovery):

- Severe oedema (bilateral pitting oedema, grade3).
- Anorexia.

- Not alert (lethargic/unconscious).
- Severe co-morbid disease conditions.

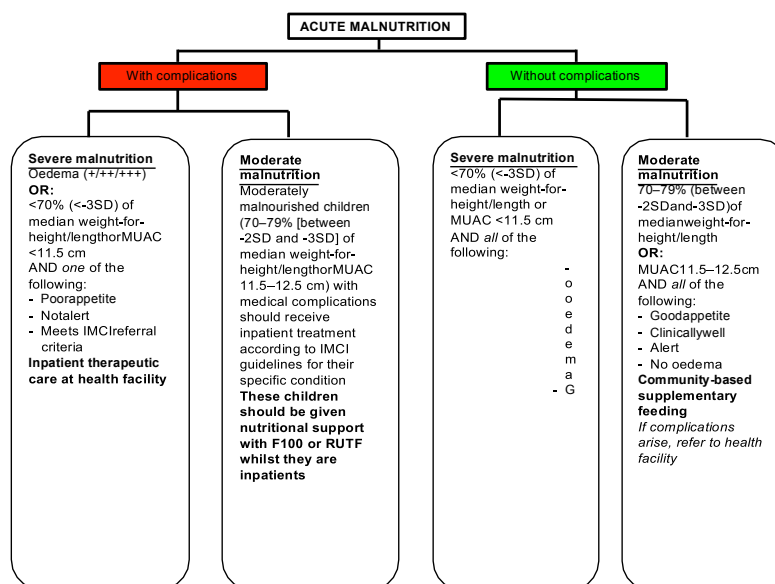
Children with severe acute malnutrition without complications who are alert with a good appetite can be managed on an outpatient basis using ready-to-eat therapeutic food (RUTF) and basic medical care. (These children are given a portion of RUTF, encouraged to eat it, and pass the test if they finish the feed.)

- Provide 200Kcal/kg/day RUTF.
- Prescribe broad-spectrum antibiotics (e.g., amoxicillin) for 1 week.
- Conduct weekly or 2-weekly follow-ups for assessment and refill of RUTF during the intensive phase, followed by long-term follow-up at 4-weekly intervals until the child recovers satisfactorily (weight-for-height is approximately 90 percent of the standard).

Management of moderate malnutrition

Children with moderate malnutrition are managed on an outpatient basis by providing an individual plan to improve dietary intake depending on the resources available to the family. This translates into providing an extra meal in addition to the recommended age-specific feedings. Adding a spoon of oil and different mixes of food including fruits and vegetables increases the energy density of meals and the various nutrients required for catch-up growth. RUTF supplements can also be provided. Long-term follow-up at 4-weekly intervals should be conducted until the child recovers satisfactorily (weight-for-height is approximately 90 percent of the standard). The mother's card can be used to counsel on feeding and feeding problems.

Management algorithm for acute malnutrition



IMCI: integrated management of childhood illness; **MUAC:** mid-upper arm circumference; **SD:** standard deviation.

ANNEX 4: Drug Re-introduction Challenge following drug-induced hepatitis for children based on weight-bands

Weight Band:0-3.9kg **Seek specialist assistance for <4kg weight band**				
Weight Band:4-7.9kg				
Isoniazid (using paediatric isoniazid 100mg tablets)	Day 1	Day 2	Day 3	Day 4
	25mg (¼ tablet)	50 mg (½ tablet)	75 mg (¾ tablet)	100 mg full dose (1 tablet)
Rifampicin (using paediatric RH 75/50 tablets)	Day 5	Day 6	Day 7	Day 8
	18.75mg (¼ tablet)	37.5 mg (½ tablet)	56.25 mg (¾ tablet)	75mg full dose (1 tablet)
Pyrazinamide (using paediatric RHZ 75/50/150 tablets)	Day 9	Day 10	Day 11	Day 12
	37.5mg (¼ tablet)	75 mg (½ tablet)	112.5 mg (¾ tablet)	150mg full dose (1 tablet)
Ethambutol (using paediatric ethambutol 100mg tablets)	Day 13	Day 14	Day 15	Day 16
	25mg (¼ tablet)	50 mg (½ tablet)	75 mg (¾ tablet)	100 mg full dose (1 tablet)
Weight Band:8-11.9kg				
Isoniazid (using paediatric isoniazid 100mg tablets)	Day 1	Day 2	Day 3	Day 4
	50mg (½ tablet)	100 mg (1 tablet)	150 mg (1.5 tablets)	200 mg full dose (2 tablets)
Rifampicin (using paediatric RH 75/50 tablets)	Day 5	Day 6	Day 7	Day 8
	37.5mg (¼ tablet)	75 mg (1 tablet)	112.5 mg (1.5 tablets)	150 mg full dose (2 tablets)
Pyrazinamide (using paediatric RHZ 75/50/150 tablets)	Day 9	Day 10	Day 11	Day 12
	75mg (¾ tablet)	150 mg (1 tablet)	225 mg (1.5 tablets)	300 mg full dose (2 tablets)
Ethambutol (using paediatric ethambutol 100mg tablets)	Day 13	Day 14	Day 15	Day 16
	50mg (½ tablet)	100 mg (1 tablet)	150 mg (1.5 tablets)	200 mg full dose (2 tablets)
Weight Band:12-15.9kg				
Isoniazid (using paediatric isoniazid 100mg tablets)	Day 1	Day 2	Day 3	Day 4
	50mg (½ tablet)	100 mg (1 tablet)	200 mg (2 tablets)	300 mg full dose (3 tablets)
Rifampicin (using paediatric RH 75/50 tablets)	Day 5	Day 6	Day 7	Day 8
	37.5mg (¼ tablet)	75 mg (1 tablet)	150 mg (2 tablets)	225 mg full dose (3 tablets)
Pyrazinamide (using paediatric RHZ 75/50/150 tablets)	Day 9	Day 10	Day 11	Day 12
	75mg (¾ tablet)	150 mg (1 tablet)	300 mg (2 tablets)	450 mg full dose (3 tablets)
Ethambutol (using paediatric ethambutol 100mg tablets)	Day 13	Day 14	Day 15	Day 16
	50mg (½ tablet)	100 mg (1 tablet)	200 mg (2 tablets)	300 mg full dose (3 tablets)
Weight Band:16-24.9kg				
Isoniazid (using paediatric isoniazid 100mg tablets)	Day 1	Day 2	Day 3	Day 4
	100mg (1 tablet)	200 mg (2 tablets)	300 mg (3 tablets)	400 mg full dose (4 tablets)
Rifampicin (using paediatric RH 75/50 tablets)	Day 5	Day 6	Day 7	Day 8
	75mg (1 tablet)	150 mg (2 tablets)	225 mg (3 tablets)	300 mg full dose (4 tablets)
Pyrazinamide (using paediatric RHZ 75/50/150 tablets)	Day 9	Day 10	Day 11	Day 12
	150mg (1 tablet)	300 mg (2 tablets)	450 mg (3 tablets)	600 mg full dose (4 tablets)
Ethambutol	Day 13	Day 14	Day 15	Day 16

(using paediatric ethambutol 100mg tablets)	100mg (1 tablet)	200 mg (2 tablets)	300 mg (3 tablets)	400 mg full dose (4 tablets)
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H: isoniazid; **R:** rifampicin; **Z:** pyrazinamide.

*Always dose anti-TB drugs in children based on weight.

ANNEX 5: DIAGNOSIS OF HIV INFECTION IN INFANTS AND CHILDREN LESS THAN 18 MONTHS

Diagnosis of HIV infection in infants

All infants born of HIV-infected women have passively transferred maternal HIV antibodies that persist until 9 to 18 months of age. These antibodies make interpretation of positive antibody tests difficult in children younger than 18 months.

Assays that detect the virus or its components (i.e., virologic tests) are required in order to positively diagnose HIV infection in children younger than 18 months of age.

The two most commonly used tests for such a diagnosis are DNA or RNA polymerase chain reaction (PCR).

PCR tests should be done at 4 to 6 weeks or at the second reproductive and child health visit (i.e., 8 weeks after delivery):

- For a child who was **never breastfed**, a single negative PCR test after the age of 4 weeks excludes HIV infection.
- For a child who was **weaned for more than 6 weeks prior to virologic (DNA PCR) testing**, a negative PCR test excludes HIV infection.
- If the child is **being breastfed**, a negative virologic test does not exclude infection. Ongoing exposure to HIV through breastfeeding continues to put the child at risk of infection. Confirmatory testing should be done 6 weeks after complete cessation of breastfeeding with DNA PCR as described above to determine final infection status.

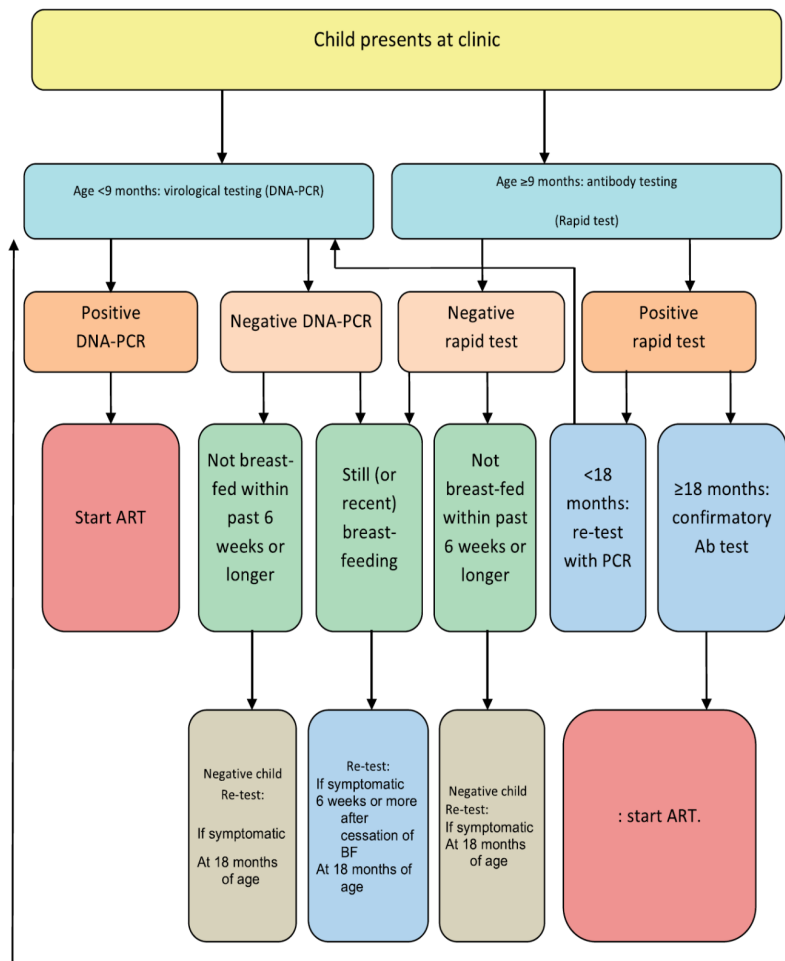
Children between the ages of 9 and 18 months at the first health encounter should have a rapid HIV antibody test since maternal HIV antibodies diminish rapidly between 9 and 18 months of age.

All positive tests should be confirmed with a DNA PCR test.

If the antibody test is negative and the infant is still breastfeeding, the antibody test should be repeated at least 12 weeks after complete cessation of breastfeeding.

However, if the child has a positive rapid HIV antibody test and is symptomatic, *fulfilling World Health Organization stage 3 or 4 criteria*, and virologic tests are not available but HIV antibodies are present, **a presumptive diagnosis should be made and antiretroviral therapy started**. In these children, confirmatory testing with either 1) virologic tests as soon as possible or 2) HIV antibody tests at 18 months age must be performed. However, initiation of ART should not be delayed while waiting confirmatory testing.

Diagnosis of HIV Infection in infants and young children less than 18 months of age



Adapted from United Republic of Tanzania MoHSW NACP National Guidelines for the Management of HIV and AIDS. May, 2015. 5th Edition.

ART: antiretroviral therapy; **PCR:** polymerase chain reaction; **BF:** breast feeding.