National Guidelines for the Management of Tuberculosis in Children

NATIONAL TUBERCULOSIS AND LEPROSY PROGRAMME (NTLP)
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ABBREVIATIONS

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<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AFB</td>
<td>Acid-fast bacillus</td>
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<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
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<td>ALT</td>
<td>Alanine aminotransferase</td>
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<tr>
<td>ART</td>
<td>Antiretroviral therapy</td>
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<tr>
<td>AST</td>
<td>Aspartate aminotransferase</td>
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<tr>
<td>BCG</td>
<td>Bacille Calmette-Guérin</td>
</tr>
<tr>
<td>CDC</td>
<td>United States Centers for Disease Control and Prevention</td>
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<tr>
<td>CPT</td>
<td>Cotrimoxazole preventive therapy</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebral spinal fluid</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>CTC</td>
<td>Care and treatment clinic</td>
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<tr>
<td>CTRL</td>
<td>Central Tuberculosis Reference Laboratory</td>
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<tr>
<td>CXR</td>
<td>Chest x-ray</td>
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<td>DOT</td>
<td>Directly observed therapy</td>
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<tr>
<td>DST</td>
<td>Drug susceptibility testing</td>
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<tr>
<td>DTC</td>
<td>District Tuberculosis and Leprosy Coordinator</td>
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<td>FDC</td>
<td>Fixed-dose combination</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<tr>
<td>IGRA</td>
<td>Interferon gamma release assay</td>
</tr>
<tr>
<td>IPT</td>
<td>Isoniazid preventive treatment</td>
</tr>
<tr>
<td>IRIS</td>
<td>Immune Reconstitution Inflammatory Syndrome</td>
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<tr>
<td>LFT</td>
<td>Liver function test</td>
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<td>LTBI</td>
<td>Latent tuberculosis infection</td>
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<td>MDR TB</td>
<td>Multidrug-resistant tuberculosis</td>
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<tr>
<td>MoHSW</td>
<td>Ministry of Health and Social Welfare</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<td>NTLP</td>
<td>National Tuberculosis and Leprosy Programme</td>
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<td>PATH</td>
<td>Program for Appropriate Technology in Health</td>
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<tr>
<td>RTLC</td>
<td>Regional Tuberculosis and Leprosy Coordinator</td>
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<td>RUTF</td>
<td>Ready-to-eat therapeutic food</td>
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<tr>
<td>TB</td>
<td>Tuberculosis</td>
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<tr>
<td>TSH</td>
<td>Thyroid-stimulating hormone</td>
</tr>
<tr>
<td>TST</td>
<td>Tuberculin skin test</td>
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<td>WHO</td>
<td>World Health Organization</td>
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</table>
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
According to Tanzanian Ministry of Health and Social Welfare (MoHSW) epidemiological data for the past six years, childhood tuberculosis (TB) contributes, on average, 9 percent of all TB cases notified in the country annually. However, children may be suffering from TB in greater numbers than what is reported due to diagnostic challenges. It is believed that with accurate diagnosis and a strong recording and reporting system, it would be discovered that children likely contribute 15–20 percent of all cases notified in areas where TB is poorly controlled. A combination of ill-defined symptoms and clinical manifestations, lack of paediatric TB-specific guidelines, and inadequate capacity of health care workers are amongst the reasons many children go undiagnosed or misdiagnosed.

The MoHSW, through the National Tuberculosis and Leprosy Programme (NTLP), is now in the process of rectifying the current situation to improve the management of TB in children. The NTLP, under the fourth Health Sector Strategic Plan (2009–2015), is pursuing expansion of high-quality directly observed therapy, with special focus on gender, children, and marginalized populations. The MoHSW has developed paediatric TB guidelines to improve programmatic diagnosis and management of children suspected of or suffering from TB. These guidelines target workers at all levels of the health care system (national, regional, district, health centre, and dispensary), and provide technical approaches to the management of TB, TB/HIV, and multidrug-resistant tuberculosis in children, including TB prevention and infection control and the roles and responsibilities of health care workers.

These simple, straightforward guidelines were developed based on existing national and international guidelines to meet national standards. The MoHSW encourages all stakeholders and partners to comply with the guidelines and to support their implementation in the country, and will update the guidelines as new technology in paediatric TB is generated.

I welcome all stakeholders to fully implement these guidelines to improve the diagnosis, management, and control of TB in children.

Regina L. Kikuli
Acting Permanent Secretary,
October, 2012.
These operational paediatric tuberculosis (TB) guidelines were developed by the National Tuberculosis and Leprosy Programme (NTLP) of the Ministry of Health and Social Welfare (MoHSW) in close collaboration with the National AIDS Control Programme (NACP), paediatric TB experts from Dartmouth Medical School, PATH, and others.

The MoHSW acknowledges the technical and financial support from the United States Agency for International Development, through PATH, for supporting the initial preparations by holding stakeholder meetings and writing the initial drafts of the guidelines. Special gratitude is extended to NTLP staff for their tireless efforts to oversee the development process, notably Dr. S. M. Egwaga (Manager), Dr. M. Nyamkara (TB/HIV Coordinator), Dr. J. Lyimo (Multidrug-Resistant Tuberculosis Coordinator), Dr. S. Matiku (Monitoring and Evaluation Coordinator), Dr. R. Christopher (TB/HIV Paediatric Coordinator), and Mr. E. Nkiligi (Data Analyst); as well as NACP staff, particularly Dr. A. Ramadhani (Manager) and Dr. A. Rwebembara (Paediatric Coordinator).

In addition, the MoHSW deeply thanks the following individuals and organisations for their valuable technical inputs toward finalisation of the guidelines: Dr. N. Simkoko (World Health Organization); Dr. H. Swai, Dr. P. Swai, and Dr. J. Kimaro (Muhimbili National Hospital); Dr. M. Fataki and Dr. H. Naburi (Muhimbili University of Health and Allied Sciences); Dr. D. Carpenter and Dr. G. Munuo (United States Centers for Disease Control and Prevention [CDC], Tanzania); Dr. Z. Mkomwa, Dr. R. Olotu, Dr. Vishnu Mahamba, Mr. Y. Bunu, and Mr. M. Chonde (PATH); Dr. L. Adams, Dr. E. Talbot, Dr. P. Palumbo, and Dr. C. Fordham von Reyn (Dartmouth Medical School); Dr. Jason Bacha, Dr. J. E. Sanders, and Dr. E. Samuel (Baylor College of Medicine Children’s Foundation, Tanzania); Dr. Stella Chale and Dr. Julius (International Training & Education Center for Health); Dr. G. Lyatuu (Dar-Dar Paediatric Clinic); Dr. C. Casalini and Dr. M. Ndolichimpa (International Center for AIDS Care and Treatment Programs); Dr. N. Kapalata and Dr. A. Swai (NTLP); Dr. F. Lwilla (Ifakara Research Centre).

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Since it is not possible to mention each individual and organisation that supported the development of these guidelines, the MoHSW extends its gratitude to all who contributed in one way or another to make these paediatric TB guidelines available in Tanzania.

Dr. Donan W. Mmbando
Acting Chief Medical Officer,
October, 2012
1 GENERAL INFORMATION ABOUT TUBERCULOSIS IN CHILDREN

1.1 Tuberculosis in children and the need for specific guidelines

Estimating the burden of tuberculosis (TB) disease in children is difficult due to the lack of a standard case definition, the difficulty in establishing a definitive diagnosis, and the frequency of extrapulmonary TB in young children. These same features present challenges to the clinician who suspects TB in a paediatric patient. Previous National Tuberculosis and Leprosy Programme (NTLP) guidelines emphasised management of adult TB for control purposes. These current guidelines have been expanded to include management of TB in children to assist the clinician in evaluating and treating children from birth to 15 years of age with suspected or confirmed TB. Age-specific considerations are included throughout, and a section on children younger than 2 years describes their unique manifestations and high risk for progression to severe forms of TB.

1.2 Epidemiology of tuberculosis in children: globally and in Tanzania

Worldwide in 2009, 47,635 cases of smear-positive TB in individuals younger than 15 years were reported to the World Health Organization (WHO), representing an increase from 44,592 cases reported in 2005. Since many children present with smear-negative and extrapulmonary TB, these figures surely underestimate the true burden of childhood TB. From 2003 to 2008, an average of 9.4 percent of all TB cases registered worldwide was in children younger than 15 years. More recently, WHO estimated that childhood TB constitutes between 9.6 percent and 11 percent of all incident cases, with the majority occurring in high TB-burden countries.

Tanzania ranks number 20 amongst the 22 high TB-burden countries in TB incidence rate, according to WHO’s Global Tuberculosis Control 2011 report. More than 60,000 cases of TB were identified in 2010, with an incidence rate of 177 cases per 100,000 population. 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 for the past 8 years show that paediatric cases have constituted an average of 10 percent of all TB case notifications. In 2010, there were 5,216 notifications of TB cases in children (less than 15 years of age), which accounted for 8.7 percent of the total new case notifications. 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.)

**Figure 1.1. Proportion of children amongst new TB patients notified; 2003 to 2010**

![Figure 1.1](image)

**Figure 1.2. Trends in paediatric (<15 years) TB case notification (all forms); 2003 to 2010**

![Figure 1.2](image)
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 2010, there were an estimated 510 MDR TB cases amongst 63,453 TB cases. No data are available on children with MDR TB; this is largely attributed to 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 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 nonspecific 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.
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 MoHSW 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 extrapulmonary 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-positive) 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 to 40 percent of cases; therefore, a diagnosis of TB (pulmonary or extrapulmonary) in a child is often based on the presence of the classic tetrad:

1. History of close contact with an infectious case (AFB smear-positive sputum).
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 intrathoracic (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°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 first started.
- About appetite and weight gain or loss.
- If coughing, about sputum production and whether there is blood present.
- History of TB contact.
- Other medical conditions that predispose to TB, such as HIV.
- 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 suspected pulmonary TB, sputum should be collected for smear 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 suspected cases.

Expectorated sputum
Obtaining expectorated sputum from children younger than 6 years may be difficult, while most adolescents can produce expectorated sputum spontaneously. In children, examination of expectorated sputum has a low yield (<15 percent for AFB smear positivity and <30 percent 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 specialised 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 optimise 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 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, TB bacilli 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 Regional Hospital, Kibong’oto Tuberculosis Hospital, Mbeya Regional 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
GeneXpert® MTB/RIF is now available in a few sites 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 also available in Tanzania, at the CTRL, for rapid detection of drug resistance.

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

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

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 immunisation, 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 (anterioposterior and lateral views) on all children suspected to have pulmonary TB. Indications for a chest x-ray include:

- Cough not improving 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).
- Tuberculosis suspect 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**

<table>
<thead>
<tr>
<th>SCORE IF SIGN OR SYMPTOM PRESENT</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Score</th>
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<tr>
<td><strong>GENERAL FEATURES</strong></td>
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<tr>
<td>Duration of illness</td>
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<tr>
<td>Less than 2 weeks</td>
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<td>2-4 weeks</td>
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<td>Failure to thrive or weight loss</td>
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<td>Weight gain</td>
<td></td>
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<tr>
<td>No weight gain or weight faltering</td>
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<tr>
<td>Weight loss</td>
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<tr>
<td>TB contact</td>
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<tr>
<td>None</td>
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<tr>
<td>Reported (but no documentation), reported smear negative or extrapulmonary TB</td>
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<tr>
<td>Smear positive (with documentation)</td>
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<td>TST</td>
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<tr>
<td>Negative, not done</td>
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<tr>
<td>Positive</td>
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<tr>
<td>Malnutrition not improved after 4 weeks of therapy</td>
<td></td>
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<tr>
<td>Present</td>
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<tr>
<td>Unexplained fever not responding to appropriate therapy**</td>
<td></td>
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<tr>
<td>Positive</td>
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<tr>
<td><strong>LOCAL FEATURES</strong></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Painless, enlarged lymph nodes*</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Any non-cervical lymph nodes</td>
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<tr>
<td>Positive cervical lymph nodes</td>
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<tr>
<td>Positive</td>
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<tr>
<td>Swelling of bones or joints*</td>
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<tr>
<td>Positive</td>
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<tr>
<td>Unexplained ascites or abdominal mass*</td>
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<tr>
<td>Positive</td>
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<tr>
<td><strong>LOCAL FEATURES</strong></td>
<td></td>
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<tr>
<td>Central nervous system findings: meningitis***, lethargy, irritability and other behaviour changes</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>Positive</td>
<td></td>
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<tr>
<td>Angle deformity of the spine</td>
<td></td>
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<tr>
<td>Positive</td>
<td></td>
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</tbody>
</table>

**TOTAL SCORE** A score of 7 or more indicates a high likelihood of TB. Refer the child for TB treatment.
*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. Meningitis not responding to conventional antibiotics. Other causes of meningitis (e.g., bacterial) must be excluded.


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

**NOTES**

1. 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.
2. Nutritional support may include nutritional counselling, provision of supplemental or therapeutic feeds.
3. 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.
2.2 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 miliary 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 of 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 GeneXpert® 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 personnel 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 immunisation 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. Extrapulmonary TB: summary of presentations and investigations

<table>
<thead>
<tr>
<th>Anatomical site</th>
<th>Signs and symptoms</th>
<th>Recommended investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural TB (pleural effusion)</td>
<td>Cough, fast breathing, decreased breath sounds, decreased tactile and vocal fremitus, displaced trachea and cardiac apex, homogeneous opacification of whole hemithorax or obliteration of costophrenic angle</td>
<td>Chest x-ray, pleural tap for: protein, glucose, cell count, AFB smear, mycobacterium culture, sputum (smear AFB positive in &lt;10%)</td>
</tr>
<tr>
<td>Pericardial TB</td>
<td>Shortness of breath, cough, chest pain, fainting/dizziness, increased heart rate</td>
<td>Chest x-ray, chest ultrasound, pericardial tap for white blood cell count, protein, glucose, AFB smear, mycobacterium culture, sputum</td>
</tr>
<tr>
<td>Abdominal TB</td>
<td>Increased abdomen size, abdominal discomfort, shortness of breath</td>
<td>Abdominal ultrasound, tap ascites looking for white blood cell count, protein, glucose, AFB smear, mycobacterium culture, chest x-ray, sputum if coughing</td>
</tr>
<tr>
<td>TB of spine, bones, joints</td>
<td>Acute angulation of spine, weakness in limbs, joint effusions, joint destruction, retropharyngeal mass, psoas abscess</td>
<td>X-ray, joint tap for white blood cell count, protein, glucose, AFB smear, mycobacterium culture, synovial bi</td>
</tr>
</tbody>
</table>

2.3 Paediatric case definitions and disease classification

World Health Organization guidance on TB in children provides the following standard language with regard to the diagnosis of TB in children:

The diagnosis of TB refers to the recognition of an active case, i.e. a patient with symptomatic disease (due to M. tuberculosis). Beyond the diagnosis of TB disease, the type of TB case should also be defined to
enable appropriate treatment to be given and the outcome of treatment evaluated. The case definition is determined by the: (i) site of disease, (ii) result of any bacteriological tests, (iii) severity of TB disease, and (iv) history of previous anti-TB treatment. All children with TB should be registered with the NTP as smear-positive pulmonary, smear-negative pulmonary TB or extrapulmonary TB, and as a new case or a retreatment (i.e., previously treated) case.

Standard case definitions are provided below.

**Pulmonary tuberculosis, sputum smear positive**
The criteria are:
- One or more initial sputum smear examinations positive for AFB; or
- One sputum smear examination positive for AFB plus chest x-ray abnormalities consistent with active pulmonary TB, as determined by a clinician; or
- One sputum smear examination positive for AFB plus sputum culture positive for M. tuberculosis.

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

**Pulmonary tuberculosis, sputum smear negative**
This is a case of pulmonary TB that does not meet the above definition for smear-positive pulmonary TB. Such cases include those without smear results, which should be exceptional in adults but relatively more frequent in children.

In keeping with good clinical and public health practice, diagnostic criteria for sputum smear-negative pulmonary TB should include:
- At least three sputum specimens negative for AFB; and
- Radiological abnormalities consistent with active pulmonary TB; and
- No response to a course of broad-spectrum antibiotics; and
- A decision by a clinician to treat with a full course of anti-TB chemotherapy.

**Extrapulmonary tuberculosis**
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.
Drug-resistant tuberculosis

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

1. **Features in the source case suggestive of drug-resistant TB:**
   - Contact with a known case of drug-resistant TB.
   - Remains sputum smear or culture positive after 3 months of treatment.
   - History of previously treated TB.
   - History of treatment interruption.

2. **Features of a child suspected of having drug-resistant TB:**
   - Contact with a known case of drug-resistant TB.
   - Not responding to the anti-TB treatment regimen.
   - Recurrence of TB after adherence to treatment.


**Key points**
- Bacteriologic confirmation should be attempted in all children suspected of having TB.
- 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.
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 counselling 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

<table>
<thead>
<tr>
<th>TB disease category</th>
<th>Recommended regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>All forms of new pulmonary and extrapulmonary TB* except TB meningitis and TB of the spine/bones/joints</td>
<td>Intensive phase: 2 months of daily RHZE</td>
</tr>
<tr>
<td></td>
<td>Continuation phase: 4 months of daily RH</td>
</tr>
<tr>
<td>TB meningitis; miliary TB; TB of the spine/bones/joints</td>
<td>Intensive phase: 2 months of daily RHZE</td>
</tr>
<tr>
<td></td>
<td>Continuation phase: 10 months of daily RH</td>
</tr>
<tr>
<td>Previously treated smear-positive pulmonary TB (relapse, return after default, treatment failure)**</td>
<td>Intensive phase: 3 months of daily RHZE***</td>
</tr>
<tr>
<td></td>
<td>Continuation phase: 5 months of daily RHE</td>
</tr>
<tr>
<td>MDR TB</td>
<td>See Section 5.2, “Drug-resistant tuberculosis in children”</td>
</tr>
</tbody>
</table>

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

*30 percent of children with a miliary picture on chest radiography have central nervous system involvement and should be treated with a 12-month regimen (see “Tuberculous meningitis,” page 12).

**All retreatment cases should be evaluated for MDR TB by sending samples for culture and drug susceptibility testing. Relapse cases are those who received anti-TB treatment in the past and were declared cured or treatment completed but now present with another episode of bacteriologically confirmed TB disease. ***Investigate for drug-resistant TB. ***You may use streptomycin in special considerations eg drug re-challenging or when susceptibility is confirmed..

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

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, drug formulations, daily dose and range, maximum dose, and potential adverse reactions are provided in Table 3.2 below.

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug formulation</th>
<th>Daily dose and range mg/kg</th>
<th>Maximum dose</th>
<th>Adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>Scored tablets:</td>
<td>10 (10-15)</td>
<td>Daily: 300 mg</td>
<td>Mild hepatic enzyme elevation, hepatitis, peripheral neuritis, hypersensitivity</td>
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<tr>
<td></td>
<td>100 mg, 300 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Syrup: 10 mg/ml</td>
<td></td>
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<tr>
<td>Rifampicin</td>
<td>Capsules:</td>
<td>15 (10-20)</td>
<td>600 mg</td>
<td>Orange discolouration of secretions or urine, vomiting, hepatitis, influenza-like reaction, thrombocytopenia, pruritus</td>
</tr>
<tr>
<td></td>
<td>150 mg, 300 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Scored tablet:</td>
<td>35 (30-40)</td>
<td>2 g</td>
<td>Hepatotoxic effects, hyperuricemia, arthralgias, gastrointestinal tract upset</td>
</tr>
<tr>
<td></td>
<td>500 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethambutol*</td>
<td>Tablets:</td>
<td>20 (15-25)</td>
<td>1,200 mg</td>
<td>Optic neuritis (usually reversible), decreased red-green colour discrimination, gastrointestinal tract disturbances, hypersensitivity</td>
</tr>
<tr>
<td></td>
<td>100 mg, 400 mg (scored)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Vials: 1 g</td>
<td>15 (12-18)</td>
<td>1,500 mg</td>
<td>Irreversible auditory nerve damage</td>
</tr>
</tbody>
</table>

*Ethambutol was previously omitted from treatment regimens for children due to concerns about optic toxicity, but a review of the literature indicates it is safe and should be used to treat TB in children of all ages at recommended dosages.

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

3.3 Fixed-dose combination tablets

Use FDC tablets whenever possible to facilitate adherence and simplify regimens. The FDCs available for use in children include rifampicin and isoniazid (RimarctazidTM; R/H, 60/30 mg), and rifampicin, isoniazid, and pyrazinamide (R/H/Z, 60/30/150 mg). Very young children will need to receive ethambutol as a separate medication, but older children can be treated using adult FDC tablets of rifampicin, isoniazid, pyrazinamide, and ethambutol (RHZE, 300/150/400/275 mg). Tables 3.3 and 3.4 list the combinations of tablets needed to achieve the correct dose by weight.

Table 3.3. Weight-based dosing of anti-TB medications using paediatric formulations (2-20 kg body weight)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Intensive phase* (2 months)</th>
<th>Continuation phase (4 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RHZ (paediatric) 60/30/150 mg</td>
<td>Ethambutol 100 mg</td>
</tr>
<tr>
<td>2–2.9 kg</td>
<td>½ tablet</td>
<td>½ tablet</td>
</tr>
<tr>
<td>3–3.9 kg</td>
<td>1 tablet</td>
<td>½ tablet</td>
</tr>
<tr>
<td>4–5.9 kg</td>
<td>1 tablet</td>
<td>1 tablet</td>
</tr>
<tr>
<td>6–7.9 kg</td>
<td>1.5 tablets</td>
<td>1.5 tablets</td>
</tr>
<tr>
<td>8–10.9 kg</td>
<td>2 tablets</td>
<td>2 tablets</td>
</tr>
<tr>
<td>11–13.9 kg</td>
<td>3 tablets</td>
<td>2 tablets</td>
</tr>
<tr>
<td>14–19.9 kg</td>
<td>4 tablets</td>
<td>3 tablets</td>
</tr>
</tbody>
</table>

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

*WHO recommends four-drug therapy during the intensive phase for all children.
### Table 3.4. Weight-based dosing of anti-TB medicines using adult FDC formulations (≥5 kg)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Intensive phase* (2 months)</th>
<th>Continuation phase (4 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RHZE (adult) 150/75/400/275 mg</td>
<td>RH (adult) 150/75 mg</td>
</tr>
<tr>
<td>5–9.9 kg</td>
<td>½ tablet</td>
<td>Use paediatric formulation; if not available, ½ tablet adult</td>
</tr>
<tr>
<td>10–14.9 kg</td>
<td>1 tablet</td>
<td>Use paediatric formulation; if not available, 1 tablet adult</td>
</tr>
<tr>
<td>15–19.9 kg</td>
<td>1.5 tablets</td>
<td>Use paediatric formulation; if not available, 1.5 tablets adult</td>
</tr>
<tr>
<td>20–24.9 kg</td>
<td>2 tablets</td>
<td>2 tablets</td>
</tr>
<tr>
<td>25–29.9 kg</td>
<td>2.5 tablets</td>
<td>2.5 tablets</td>
</tr>
<tr>
<td>30–40 kg</td>
<td>3 tablets</td>
<td>3 tablets</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>4 tablets</td>
<td>4 tablets</td>
</tr>
</tbody>
</table>

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

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

#### 3.4 Practical guidance for administering medicines to children

In many instances, paediatric liquid formulations will not be available and patients and/or their parents/caregivers must be instructed to crush tablets to achieve the prescribed dosage.

Advise parents/caregivers to:
- Crush tablets to ensure that the entire pill portion is retained (e.g., crush between two spoons and insert both spoons into a liquid or soft food to collect the powder from both).
- Crush hard tablets by placing the tablet between a clean, folded sheet of paper and rolling a hard round object over it, making certain not to tear the paper. Funnel the powder into a liquid or soft food substance.
- Mix the crushed tablet with clean (ideally, boiled) water (that has cooled to room temperature) or bottled water. Crushed pills can have a bitter taste, and the child may spit up or vomit the dose. Therefore, advise:
• If the child spits up or vomits their dose less than 30 minutes after receiving it, repeat the dose immediately, mixing it with a different liquid or soft food.
• If the child vomits more than 30 minutes after receiving the dose, it should not be re-administered. In both instances, the next dose should be given as scheduled.

3.5 Steroid use for tuberculosis

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 4 mg/kg, with a maximum dosage of 60 mg/day for 4 to 6 weeks, followed by 2 weeks of tapering. Corticosteroid doses should be adjusted upward to account for the increased steroid metabolism induced by rifampicin. Treating clinicians should provide necessary information, including any 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, with the exception of streptomycin, which can be discontinued as a single drug. Contact the DTLC or Regional Tuberculosis and Leprosy Coordinator (RTLC) if single anti-TB drugs are needed to treat a child. Table 3.5 below provides guidelines for management of adverse reactions to anti-TB medications, based on symptoms.
Table 3.5. Symptom-based approach to major and minor reactions to anti-TB medications

<table>
<thead>
<tr>
<th>Adverse reaction(s)</th>
<th>Drug(s) probably responsible</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin rash with or without itching</td>
<td>Streptomycin, isoniazid, rifampicin, pyrazinamide</td>
<td>Stop anti-TB drugs.</td>
</tr>
<tr>
<td>Decreased hearing or deafness (no wax in ear canal)</td>
<td>Streptomycin</td>
<td>Stop streptomycin.</td>
</tr>
<tr>
<td>Dizziness (vertigo and nystagmus)</td>
<td>Streptomycin</td>
<td>Stop streptomycin.</td>
</tr>
<tr>
<td>Jaundice (other causes excluded), hepatitis, confusion</td>
<td>Isoniazid, pyrazinamide, rifampicin</td>
<td>Stop anti-TB drugs.</td>
</tr>
<tr>
<td>Visual impairment (other causes excluded)</td>
<td>Ethambutol</td>
<td>Stop ethambutol.</td>
</tr>
<tr>
<td>Shock, purpura, acute renal failure</td>
<td>Rifampicin</td>
<td>Stop anti-TB drugs.</td>
</tr>
<tr>
<td>Decreased urine output</td>
<td>Streptomycin</td>
<td>Stop streptomycin.</td>
</tr>
<tr>
<td><strong>Minor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anorexia, nausea, abdominal pain</td>
<td>Pyrazinamide, rifampicin, isoniazid</td>
<td>Give drugs with small meals or just before bedtime, and advise 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.</td>
</tr>
<tr>
<td>Joint pain</td>
<td>Pyrazinamide</td>
<td>Give non-steroidal anti-inflammatory drug or paracetamol.</td>
</tr>
<tr>
<td>Burning, numbness, or tingling sensation in the hands or feet (consult paediatrician)</td>
<td>Isoniazid</td>
<td>Give pyridoxine (1-2 mg/kg/day), especially if on high-dose isoniazid and/or malnourished.</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>Isoniazid</td>
<td>Provide reassurance. Give drugs before bedtime.</td>
</tr>
<tr>
<td>Orange/Red urine</td>
<td>Rifampicin</td>
<td>Provide reassurance. Patients should be told when starting treatment that this may happen and is normal.</td>
</tr>
</tbody>
</table>

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, stop all anti-TB drugs immediately and refer to the nearest hospital for further management. Once the reaction 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 of the total dose) of the drug least likely (i.e., ethambutol) 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, then isoniazid, and finally rifampicin).
4. A reaction after a particular drug is added suggests that this is the drug responsible for the reaction.
5. Reaction to a small challenge dose will not be as bad as to a full dose.
6. If possible, while a patient is undergoing drug challenge, give two anti-TB drugs that the patient has not had before.

3.8 Management of drug-induced hepatitis

Any of the first-line anti-TB drugs—isoniazid, pyrazinamide, and rifampicin—can cause liver damage (drug-induced hepatitis). Do not routinely monitor serum liver enzyme levels in asymptomatic children, but evaluate children for signs and symptoms of hepatitis at each visit. 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. 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/RTLC to arrange to start a non-hepatotoxic regimen consisting of streptomycin and ethambutol.

Once anti-TB treatment has been stopped, recheck serum liver enzymes in 1 to 2 weeks. Consult with your DTLC/RTLC 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, start (or continue) the non-hepatotoxic regimen consisting of streptomycin and ethambutol for a total of 18–24 months.

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.

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

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 FDC tablet.
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 9 months.
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 cannot be used, administer 2 months 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.

**Table 3.6. Example of re-introduction of TB drugs following drug reaction in a 15 kg child**

<table>
<thead>
<tr>
<th>Anti TB drug</th>
<th>Day 1 (challenge dose)</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>25 mg (¼ tablet)</td>
<td>50 mg (½ tablet)</td>
<td>100 mg (1 tablet)</td>
<td>125 mg (1 ¼ tablet)</td>
</tr>
<tr>
<td>Rifampicin (using pediRH)</td>
<td>60 mg (1 tablet)</td>
<td>120 mg (2 tablets)</td>
<td>180 mg (3 tablets)</td>
<td>Full dose (4 tablets)</td>
</tr>
<tr>
<td>Pyrazinamide (using pediRHZ)</td>
<td>150 mg (1 tablet)</td>
<td>300 mg (2 tablets)</td>
<td>450 mg (3 tablets)</td>
<td>Full dose (of pediRHZ)</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>50 mg (½ tablet)</td>
<td>100 mg (1 tablet)</td>
<td>200 mg (2 tablets)</td>
<td>Full dose (3 tablets)</td>
</tr>
</tbody>
</table>

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

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

Reintroducing one drug at a time is the optimal approach. FDCs are currently used in Tanzania, so efforts should be made by the DTLC/RTLC to stock limited quantities of single anti-TB drugs for use in such cases. However, if the health unit does not have single anti-TB drugs, the following approach can be applied, depending on whether the hepatitis with jaundice occurred during the intensive or the continuation phase:

- When hepatitis with jaundice occurs during the intensive phase of TB treatment with isoniazid, rifampicin, pyrazinamide, and ethambutol: 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 with jaundice 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 are cured. Bacteriologic monitoring (sputum check for AFB) is needed in sputum smear- and culture-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. 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 (i.e., monthly) are not indicated, as children often have a slow radiographic response.

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, confirm adherence and then add 1 month to the intensive phase. Recheck a sputum smear and culture at the end of the additional month of intensive-phase therapy. If that sputum smear or culture is positive and adherence is confirmed, refer to the next section, on treatment failure.

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 culture and DST to the CTRL. 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, the child should be referred to the MDR TB treatment centre in Kibong’oto 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 patients who miss DOT or a medical appointment during the initial 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. It is important to find out the cause of the patient’s absence so that appropriate action can be taken and treatment can continue.
If a child misses 2 to 4 weeks of treatment, collect a sputum sample for smear microscopy 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, rather than the continuation, phase.
- The child was responding poorly to treatment before the interruption.
- Drug-resistant TB is known or suspected.

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 MDR TB treatment centre if Multi drug-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. Limit contact between the mother and her neonate to breastfeeding 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 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 perform a TST if available. Also test the infant for HIV at this time if indicated. 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.

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 breastfeeding 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 (2010 or more recent) and community-based management of malnutrition.

3.15 Counselling for children with tuberculosis
Counselling 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, emphasising that
TB is a curable disease.

- The treatment of TB in the child, including:
  - Drugs and doses that will be prescribed.
  - Treatment regimen and duration.
  - Possible side effects of the medications and what to do when side effects occur.
  - Importance of taking medications regularly for the full course of treatment.
  - The risk of developing drug-resistant TB if the child misses doses.
  - 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.
  - 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 counselling sessions.

**Counselling 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 counselling**
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.

**Counselling 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 “Neonatal tuberculosis,” page 15). 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 supplicative 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, supplicative 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 “Immune Reconstitution Inflammatory Syndrome,” page 42).

**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.

**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).

**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.

### 4.2 Isoniazid preventive treatment: preventing progression of latent tuberculosis infection to tuberculosis disease

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.

**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 10-15 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 who 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.

**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. 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 are younger than 5 years and who have TB disease excluded should be evaluated for LTBI. LTBI screening can be done with the TST, where >5 mm induration is considered positive. A child with a positive TST but no indication of TB disease should be treated with daily isoniazid for 6 months. An HIV-infected child older than 12 months does not need to have a TST and should receive IPT for 6 months if there is evidence of TB disease, as part of the comprehensive HIV care package.

**Figure 4.1. Algorithm for assessing child household contacts**

**ALGORITHM FOR ASSESSING CHILD HOUSEHOLD CONTACTS**

- **Target group of infectious adults**
- **Adults with sputum smear-positive PTB**
- **Identify all children at risk**
- **Any household child contact**
- **Select children for screening**
- **All children <5 years, Children of any age with cough**
- **Screening**
- **History and examination, tuberculin skin test if available**
- **Outcome of Screening**
- **No signs or symptoms of TB disease**
- **Signs or symptoms of TB disease**
- **Conclusion**
- **TB unlikely**
- **TB possible**
- **Action**
- **Isoniazid prophylaxis (IPT) for all children <5 years and HIV infected children above 5 years**
- **Confirm diagnosis (sputum, CXR, lymph node biopsy, etc)**
- **Register and treat for TB**

**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 (up to 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.
- Tuberculosis suspects should be referred for microbiologic TB diagnosis.
- 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
Key points specific for children

- Children can transmit TB infection to others, especially to those with HIV/AIDS and with malnutrition.
- Children with suspected or confirmed TB should be cared for in a separate, well-ventilated room, away from HIV-infected children.
- Infants born to mothers with MDR TB should be separated at the earliest opportunity to minimise 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 limited data available 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 TB suspects or confirmed 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 18 months).

**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 5). 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 6 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 7 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 in all HIV-infected children with TB regardless of CD4 levels once TB treatment is tolerated.
• 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.

See Table 5.1 for 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.

*In situations where the use of nevirapine cannot be avoided, it should be used at a maximum dose (200 mg/m2 twice daily). On ART initiation, do not use nevirapine lead-in dosing since it will lead to sub-therapeutic nevirapine levels and can compromise viral suppression. Refer these children for specialty consultation to determine the most appropriate regimen and dosages. For children on a regimen of lopinavir boosted with ritonavir (LPV/r), consider adding ritonavir in a 1:1 ratio to achieve a fully therapeutic dose of lopinavir. For children with anaemia (Hb <7.5 g/dL), replace zidovudine with stavudine.*


Table 5.1. Recommended ART regimens for children receiving standard TB treatment

<table>
<thead>
<tr>
<th>STATUS</th>
<th>REGIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART regimen in children receiving anti-TB</td>
<td>2 NRTIs + EFV (for children &gt;3 years of age and weighing &gt;10 kg)</td>
</tr>
<tr>
<td>treatment</td>
<td>2 NRTIs + NVP or triple NRTI (for children &lt;3 years of age and/or</td>
</tr>
<tr>
<td></td>
<td>weighing &lt;10 kg)</td>
</tr>
<tr>
<td>Children on anti-TB</td>
<td>For children &lt;3 years of age and/or weighing &lt;10 kg:</td>
</tr>
<tr>
<td>treatment but not yet</td>
<td>Initiate AZT/3TC/NVP; or as an alternative, AZT/3TC/ABC</td>
</tr>
<tr>
<td>initiated on ART</td>
<td>For children &gt;3 years of age and weighing &gt;10 kg:</td>
</tr>
<tr>
<td></td>
<td>Initiate AZT/3TC/EFV</td>
</tr>
<tr>
<td>Children already on ART</td>
<td>Continue ART regimen</td>
</tr>
<tr>
<td>and started on anti-TB treatment</td>
<td>For children &lt;3 years of age and/or weighing &lt;10 kg: substitute NVP</td>
</tr>
<tr>
<td></td>
<td>with ABC</td>
</tr>
<tr>
<td></td>
<td>For children &gt;3 years of age and weighing &gt;10 kg:</td>
</tr>
<tr>
<td></td>
<td>substitute NVP with EFV</td>
</tr>
</tbody>
</table>

3TC: lamivudine; ABC: abacavir; AZT: zidovudine; EFV: efavirenz; NRTI: nucloside reverse transcriptase inhibitor; NVP: nevirapine.

The effect of rifampicin on ART metabolism lasts for 2 weeks after rifampicin is stopped; hence, dose adjustments of ART should be continued for 2 weeks after completion of the rifampicin-containing therapy. After this 2-week period, return to the original ART regimen and dosing. When to start antiretrovirals in infants and children receiving standard anti-tuberculosis treatment

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. Earlier treatment is associated with better outcomes, so start ART once TB treatment is tolerated, ideally 2 weeks after the start of anti-TB and definitely by 8 weeks.

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 5.2 presents overlapping side effects of anti-TB treatment and antiretroviral medications.
Table 5.2. Overlapping side effects of anti-TB treatment and antiretroviral medications*

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Possible causes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anti-TB drugs</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Isoniazid, cycloserine</td>
</tr>
<tr>
<td>Skin rash</td>
<td>Rifampicin, isoniazid, pyrazinamide, cycloserine</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>All</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>Pyrazinamide, rifampicin, isoniazid, ethionamide</td>
</tr>
<tr>
<td>Anaemia</td>
<td>Rifampicin</td>
</tr>
</tbody>
</table>

*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 characterised 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 tuberculomas).
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 1-2 mg/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 80 mg/sulfamethoxazole 400 mg and as a syrup in the same ratio, containing 40 mg trimethoprim/200 mg sulfamethoxazole per 5 ml (see Table 5.3 for recommended dosages by weight).

Table 5.3. Recommended doses of cotrimoxazole by age

<table>
<thead>
<tr>
<th>Age range</th>
<th>Trimethoprim/Sulfamethoxazole (TMP/SMZ) (Septrin®, Bactrim®)</th>
<th>Syrup: 40 mg/200 mg/5 ml</th>
<th>Single-strength tablet: 80 TMP/400 SMZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 6 months</td>
<td>2.5 ml</td>
<td>¼ tablet</td>
<td></td>
</tr>
<tr>
<td>6 months-5 years</td>
<td>5 ml</td>
<td>½ tablet</td>
<td></td>
</tr>
<tr>
<td>5 years-14 years</td>
<td>10 ml</td>
<td>1 tablet</td>
<td></td>
</tr>
<tr>
<td>≥14 years</td>
<td></td>
<td></td>
<td>2 tablets</td>
</tr>
</tbody>
</table>

HIV counselling (provider-initiated testing and counselling)

Tell patients and parents/caregivers that, currently, 50 percent of TB patients are HIV infected so patients should be HIV tested. By knowing their HIV status, patients have the opportunity to be treated earlier.
Obtain an HIV test at the TB clinic or refer to the reproductive and child health clinic if the patient is less than 18 months of age and 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 a lifelong process that can keep them healthy as well as prevent the transmission of HIV to 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 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.
- If a child has HIV infection and TB disease, the child needs to be started on anti-TB medications, and if not already on ART, start ART 2 to 8 weeks later.
- 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

**Definition:** Multidrug-resistant tuberculosis 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 sick person.

**Diagnosis of multidrug-resistant tuberculosis in children**
Multidrug-resistant tuberculosis should be suspected in the following situations:
- A child who is a close contact of an infectious MDR TB case.
- A child who is a close contact of a TB treatment failure or defaulter.
- A child with proven TB who is still bacteriologically positive after five months of appropriate treatment with first-line anti-TB medications (treatment failure).
Drug-resistant TB should be suspected under these circumstances, but confirming the diagnosis depends on sputum culture for M. tuberculosis strains and results of DST.

Efforts should be made to obtain specimens from all possible sources, like gastric aspiration, sputum induction, or lymph node aspiration, for culture and DST, because MDR 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. The diagnosis of MDR TB in children is made by a review panel of experts on MDR TB based on history, physical examination, and laboratory findings. Children diagnosed with MDR TB should be reported to the DTLC for recording and referred to an MDR 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 MDR TB treatment, the following interventions should be performed:

- Inform the parent/caregiver and family about MDR TB and 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 MoHSW recommends using a **standardized treatment regimen** approach for all identified paediatric MDR TB cases, so that all patients receive the same regimen.

The duration of therapy for MDR TB in children is 18 to 24 months (or at least 18 months after the first negative culture). 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 a minimum of 6 to 8 months while admitted in an MDR TB treatment centre.
- **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.
Tables 5.4 below provides a list of the drugs for each treatment phase, and Table 5.5 (on the following page) provides details on paediatric dosages for second-line anti-TB drugs.

### Table 5.4. MDR TB medicines and duration of treatment

<table>
<thead>
<tr>
<th>Treatment phase</th>
<th>Drugs</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive phase</td>
<td>Amikacin or kanamycin</td>
<td>Minimum of 6-8 months; can be prolonged depending on timing of culture conversion</td>
</tr>
<tr>
<td></td>
<td>Ofloxacin or levofloxacin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethionamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cycloserine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethambutol</td>
<td></td>
</tr>
<tr>
<td>Continuation phase</td>
<td>Ofloxacinor levofloxacin</td>
<td>12 months</td>
</tr>
<tr>
<td></td>
<td>Ethionamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cycloserine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethambutol</td>
<td></td>
</tr>
</tbody>
</table>

### Table 5.5. Paediatric dosing and adverse reaction of second-line anti-TB drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose (mg/kg)</th>
<th>Frequency</th>
<th>Maximum daily dose</th>
<th>Adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>15-22.5</td>
<td>Once daily, 5 times a week</td>
<td>1 g</td>
<td>Ototoxicity, nephrotoxicity</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>15-30</td>
<td>Once daily</td>
<td>1 g</td>
<td>Ototoxicity, nephrotoxicity</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>15-30</td>
<td>Once daily</td>
<td>1 g</td>
<td>Ototoxicity, nephrotoxicity</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>15-20</td>
<td>Twice daily</td>
<td>800 mg</td>
<td>Arthropathy, arthritis</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>7.5-10</td>
<td>Once a day</td>
<td>400 mg</td>
<td>Arthropathy, arthritis</td>
</tr>
<tr>
<td>Ethambutol*</td>
<td>15-25</td>
<td>Once daily</td>
<td>2.5 g</td>
<td>Optic neuritis (usually reversible), decreased red-green colour discrimination, gastrointestinal upset</td>
</tr>
</tbody>
</table>

**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 5.6. Treatment monitoring of children with MDR TB**

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

**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.

**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 counselling 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 MDR TB 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 MDR TB case should be screened for MDR TB disease.
- Multidrug-resistant tuberculosis requires 18 to 24 months of appropriate treatment (in two phases: intensive [inpatient] and continuation [outpatient]).
- 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 MDR TB are able to provide care for their newborns once they are no longer infectious (smears and cultures are negative).
RECORDING AND REPORTING OF CHILDREN WITH TUBERCULOSIS

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.

Health care workers should:
- Register all children diagnosed with TB for treatment.
- Report all registered children to all levels.
- Record smear status at months 2 and 5 of treatment for all children who are smear or culture positive.
- Record the child’s treatment outcome at the end of treatment.

6.1 Assigning treatment outcomes to child tuberculosis cases

Assigning the treatment outcome to a child TB case follows the same procedure used to assign outcomes to adult patients, as shown in Table 6.1 below. The health care worker should assign a treatment outcome to each patient after completing treatment. At the end of treatment, the patient is discharged and the treatment outcome is recorded in the patient treatment card, identity card, and unit and district TB registers.

<table>
<thead>
<tr>
<th>Treatment outcome</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cured</td>
<td>A patient whose sputum smear or culture was positive at the beginning of treatment but who was smear or culture negative in the last month of treatment and on at least one previous occasion.</td>
</tr>
<tr>
<td>Treatment completed</td>
<td>A patient who completed a treatment course but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion. Note: The sputum examination may not have been done or the results may not be available.</td>
</tr>
<tr>
<td>Failure</td>
<td>A patient whose sputum smear or culture is positive at 5 months or later during treatment. Also included in this definition are patients found to harbor a multidrug-resistant strain at any point of time during the treatment, whether they are smear negative or positive.</td>
</tr>
<tr>
<td>Died</td>
<td>A patient who dies for any reason during the course of TB treatment.</td>
</tr>
<tr>
<td>Default</td>
<td>A patient whose treatment was interrupted for 2 consecutive months or more.</td>
</tr>
<tr>
<td>Transferred out</td>
<td>A patient who has been transferred to another recording and reporting unit and whose treatment outcome is unknown.</td>
</tr>
</tbody>
</table>
New child TB cases are assigned outcomes by the DTLC or health care worker after 6 months of therapy as follows:

- A child with smear-negative pulmonary TB or extrapulmonary TB is classified as “treatment completed” if the child took all 168 doses (56 in the intensive phase and 112 in the continuation phase).
- A child with smear- or culture-positive pulmonary TB whose smear or culture results at 5 months and at the end of treatment are negative is classified as “cured” after completing 168 doses (6 months of treatment).
- A child with smear- or culture-positive pulmonary TB whose smear or culture results at 5 months or at the end of treatment are positive is classified as “treatment failure” and the treatment card closed. Request sputum for culture and DST and open a new treatment card listing the patient type as “treatment after failure.”

Retreatment child TB cases are assigned outcomes by the DTLC or health care workers after 8 months of therapy as follows:

- A child whose sputum smear or culture results at 7 months are negative is classified as “cured” after completing 244 doses (8 months of treatment).
- A child whose smear or culture results at 7 months are positive is classified as “treatment failure” and the treatment card is closed. Check results from the sputum culture and DST that were requested previously (see Section 3.11, “Treatment failure (confirming failure and management).” If drug resistance is identified, refer the child to the MDR TB treatment centre.

Other definitions that are not listed as treatment outcomes but are commonly used:

- **Treatment success rate:** The sum of smear- or culture-positive patients who are cured or who have completed treatment over the number of smear- or culture-positive patients who started treatment during the same time frame.
- **Unfavourable treatment outcome:** The sum of patients who died, failed treatment, and defaulted. This should be less than 15 percent of all patients initiated on TB treatment.
The NTLP is responsible for compiling all case and treatment outcome data for national recording and reporting purposes. Table 6.2 below shows the indicators used for recording and reporting child TB cases to determine if programme activities are successful and where improvement might be needed.

Table 6.2. Indicators for NTLP routine recording and reporting

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of children with TB amongst all TB cases notified</td>
<td>May indicate over- or under-reporting of TB cases in children</td>
</tr>
<tr>
<td>Proportion of children with pulmonary TB amongst childhood TB cases</td>
<td>May indicate over- or under-diagnosis of pulmonary TB</td>
</tr>
<tr>
<td>Proportion of children with TB who are cured amongst smear-positive TB cases (demonstrated by end-of-treatment smear conversion from positive to negative)</td>
<td>Demonstrates the quality of management of children with TB in the program</td>
</tr>
<tr>
<td>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)</td>
<td>Demonstrates the quality of management of children with TB in the program</td>
</tr>
<tr>
<td>Proportion of children who are successfully treated amongst smear-positive childhood TB cases (cured + treatment completed)</td>
<td>Demonstrates the quality of management of children with TB in the program</td>
</tr>
<tr>
<td>Proportion of children with miliary TB or TB meningitis amongst childhood TB cases</td>
<td>This proportion should be very low where BCG vaccination coverage is high</td>
</tr>
</tbody>
</table>

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/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.

**TB/HIV programme indicators**

**TB clinic setting**

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

7.1 Levels of care

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.

Primary level of care
This level includes communities, dispensaries, and health centres. At this level, staff should be able to recognise the symptoms and signs of childhood TB. They should also recognise the significance of household contact with smear-positive index cases.

Staff at this level should be able to identify children with symptoms and signs suggestive of TB as well as contacts of newly diagnosed smear-positive TB cases. The TB suspect should be diagnosed by AFB smear microscopy or be referred for diagnosis at the secondary level for radiography and TST. Diagnosed patients should be immediately registered and started on treatment under DOT following NTLP guidelines. All registered TB patients should undergo HIV counselling and testing following National AIDS Control Programme guidelines. Staff should be trained on the use of the validated paediatric scoring chart. Counsellors should have training 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 to perform AFB smear microscopy, TST, lumbar puncture, GeneXpert® MTB/RIF, pleural tap, ascites tap, gastric lavage to collect samples for AFB smear microscopy and culture, and to read chest x-rays. In addition to performing these procedures, staff should be able to diagnose and manage complicated TB cases like meningitis, osteoarticular disease, and drug-resistant TB (continuation phase).
Tertiary level of care
This level includes zonal and referral/consultant hospitals. In addition to the activities performed at the secondary level, at this level, services should include culture and DST, CT scan, and IGRA. Staff should be able to diagnose and manage complicated TB cases, including drug-resistant TB in children. Staff at the tertiary level should ensure internal and external quality control of the above procedures at the lower levels of care.

Key points
- Recording and reporting are essential to patient management and TB programme success. They provide:
  - Patient baseline information.
  - Information for patient management.
  - Information to assess patient progress.
  - Information to assess programme performance.
  - Basis for accountability.
- All cases of TB and TB/HIV in children should be recorded and reported.
- Evaluation of treatment outcomes in children is a valuable indicator of the quality of care for childhood TB.
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 respules)
- 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 air flow)
  - 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 in 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 nebuliser 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):
   a. After 3-5 minutes of bronchodilator therapy, add 5-10 ml of
hypertonic saline to the nebuliser.

b. Administer nebulised hypertonic saline for 15 minutes or until 5 cm³ of solution has been fully administered.

c. Give chest physiotherapy as necessary; this is useful to mobilize secretions.

d. 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 ear lobe.

   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.
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 4 hours).
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.
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:

<table>
<thead>
<tr>
<th>Indicator/Measure*</th>
<th>Severe acute malnutrition</th>
<th>Moderate acute malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight-for-height/length</td>
<td>Less than -3SD (&lt;70%)</td>
<td>Between -2SD and -3SD (70–79%)</td>
</tr>
<tr>
<td>Mid-upper arm circumference</td>
<td>Less than 11.5 cm</td>
<td>11.5–12.5 cm</td>
</tr>
<tr>
<td>Bilateral oedema (any type)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD: standard deviation.
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, grade 3).
• 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 200 Kcal/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

<table>
<thead>
<tr>
<th>Severe malnutrition</th>
<th>Moderate malnutrition</th>
<th>Severe malnutrition</th>
<th>Moderate malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oedema (+/++/+++):</td>
<td>Moderate malnourished children (70–79% [between -2SD and -3SD] of median weight-for-height/length or MUAC 11.5–12.5 cm) with medical complications should receive inpatient treatment according to IMCI guidelines for their specific condition. These children should be given nutritional support with F100 or RUTF whilst they are inpatients.</td>
<td>&lt;70% (&lt;-3SD) of median weight-for-height/length or MUAC &lt;11.5 cm AND one of the following: - No oedema - Good appetite - Clinically well - Alert Community-based therapeutic care If complications arise, refer to health facility.</td>
<td>&lt;70% (&lt;-3SD) of median weight-for-height/length or MUAC &lt;11.5 cm AND all of the following: - No oedema - Good appetite - Clinically well - Alert Community-based supplementary feeding If complications arise, refer to health facility.</td>
</tr>
<tr>
<td>&lt;70% (&lt;-3SD) of median weight-for-height/length or MUAC &lt;11.5 cm AND one of the following: - Poor appetite - Not alert - Meets IMCI referral criteria Inpatient therapeutic care at health facility.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**IMCI:** integrated management of childhood illness; **MUAC:** mid-upper arm circumference; **SD:** standard deviation.
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); however, DNA PCR is the preferred method.

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 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 6 weeks after complete cessation of breastfeeding. However, if the child 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.
ART: antiretroviral therapy; CXT: coltrimoxazole prophylaxis; DBS: dried blood spot; PCR: polymerase chain reaction.
### TB/HIV Activities

#### Tuberculosis Screening Questionnaire for HIV/AIDS Patients

**Date:** ______________  
**Reg. number:** ______________  
**Physical address:** ____________________________

**Patient’s name:** ____________________________  
**Age:** _____  
**Area leader/neighbor:** ____________________________

**Contact telephone (if available):** ____________________________  
**Sex:** Male/Female

#### Adults and children 5 years and older

<table>
<thead>
<tr>
<th></th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
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<th>Y</th>
<th>N</th>
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<tbody>
<tr>
<td>Cough for 2 weeks or more?</td>
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<tr>
<td>Coughing up blood-stained sputum (haemoptysis)?</td>
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<tr>
<td>Fevers for 2 weeks or more?</td>
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<td>Noticeable weight loss for new patients or a 3 kg weight loss in a month (in subsequent visits)?</td>
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</tbody>
</table>
- Excessive sweating at night for 2 weeks or more?
- Children younger than 5 years
  - Any cough?
  - History of household contact with TB?
  - Fever for 2 weeks or more?
  - Reduced activities or irritability for 2 weeks or more?
  - Inadequate weight gain, weight faltering? Weight loss?

- If ‘Yes’ to one or more questions: Do sputum examination and continue evaluation according to the TB diagnostic flowchart of the National Tuberculosis and Leprosy Programme.
- If sputum cannot be obtained from a child, do chest X-ray.
- If ‘No’ to all questions: Stop TB investigations and repeat screening at each subsequent visit (every month).

<table>
<thead>
<tr>
<th>Action taken</th>
<th>Date</th>
<th>Result</th>
<th>Date</th>
<th>Result</th>
<th>Date</th>
<th>Result</th>
<th>Date</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
<td>Sputum smear</td>
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<tr>
<td>Chest x-ray</td>
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<tr>
<td>Refer for clinical assessment</td>
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<td>Started broad-spectrum antibiotics</td>
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<tr>
<td>Started anti-TB treatment</td>
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## TUBERCULOSIS DIAGNOSTIC TOOLS AND THE IMPACT OF HIV ON THEIR INTERPRETATION

<table>
<thead>
<tr>
<th>Diagnostic tool</th>
<th>Impact from HIV</th>
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</thead>
<tbody>
<tr>
<td>Symptoms suggestive of tuberculosis (TB)</td>
<td>Lower specificity: clinical overlap between symptoms of TB- and HIV-related diseases</td>
</tr>
<tr>
<td>Clinical examination, including growth assessment</td>
<td>Lower specificity: malnutrition is common with TB or HIV</td>
</tr>
<tr>
<td>Tuberculin skin test (TST)</td>
<td>Lower sensitivity: TST positivity decreases with increasing immunosuppression and decreasing age</td>
</tr>
<tr>
<td>Sputum smear and culture</td>
<td>Less sensitive in HIV-infected children</td>
</tr>
<tr>
<td>Investigations relevant for suspected pulmonary and suspected extrapulmonary TB</td>
<td>Wider range of diagnostic possibilities because of other HIV-related diseases</td>
</tr>
</tbody>
</table>
### Causes of lung disease in HIV-infected infants (<1 year of age)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Importance</th>
<th>Clinical features</th>
<th>Management (a,b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial pneumonia</td>
<td>Very high incidence</td>
<td>Acute onset of cough, fever and fast breathing Can be very severe with hypoxia</td>
<td>Broad-spectrum antibiotics including coverage of Gram-negative organisms</td>
</tr>
<tr>
<td>e.g. pneumococcus, staphylococcus, Gram negatives</td>
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<tr>
<td>PCP</td>
<td>Common cause of severe, fatal pneumonia especially in 2 to 6 months age group</td>
<td>Severe respiratory distress with hypoxia not improving with broad-spectrum antibiotics; Often asoluble; CXR: diffuse interstitial infiltration or hyperinflation</td>
<td>Add high-dose cotrimoxazole Consider steroids</td>
</tr>
<tr>
<td>CMV pneumonitis</td>
<td>Common co-infection with PCP but few data from resource-poor setting</td>
<td>Severe respiratory distress with hypoxia not improving with broad-spectrum antibiotics and high-dose cotrimoxazole</td>
<td>Add ganciclovir</td>
</tr>
<tr>
<td>Viral pneumonia e.g. RSV</td>
<td>Common and associated with bacterial co-infection</td>
<td>Acute onset of cough, fever, fast breathing; Wheezing less common than in HIV-uninfected</td>
<td>Broad-spectrum antibiotics if suspect bacterial co-infection</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Depends on prevalence of TB/HIV in adult population</td>
<td>TB contact usually identifiable, often mother; Presentation often acute and severe or disseminated</td>
<td>Anti-TB treatment</td>
</tr>
<tr>
<td>Mixed infection</td>
<td>Common problem: PCP, bacterial pneumonia, viral, TB</td>
<td>Consider when poor response to first-line empiric management</td>
<td>Anti-TB treatment plus treatment for additional and presumed respiratory infections</td>
</tr>
<tr>
<td>Measles</td>
<td>In communities with poor measles immunization coverage</td>
<td>Conjunctivitis, typical rash, fever and cough, respiratory distress</td>
<td>Broad-spectrum antibiotics Vitamin A</td>
</tr>
<tr>
<td>LIP</td>
<td>Uncommon in infants and associated with bacterial co-infection</td>
<td>Generalised lymphadenopathy, clubbing, parotid enlargement; CXR: diffuse reticulonodular pattern</td>
<td>If symptomatic and close follow-up, steroids and broad-spectrum antibiotics</td>
</tr>
</tbody>
</table>

**CMV:** cytomegalovirus; **CXR:** chest x-ray; **LIP:** lymphoid interstitial pneumonitis; **PCP:** pneumocystis pneumonia; **RSV:** respiratory syncitial virus.

(a) Oxygen may be indicated irrespective of cause; (b) cotrimoxazole preventive therapy and antiretroviral therapy when indicated for all cases.
### Causes of lung disease in HIV-infected children (1-14 years)

<table>
<thead>
<tr>
<th>Causes</th>
<th>Importance</th>
<th>Clinical features</th>
<th>Management (a,b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial pneumonia e.g. pneumococcus, staphylococcus, Gram negatives</td>
<td>Very high incidence&lt;br&gt;Often recurrent</td>
<td>Acute onset of cough, fever and fast breathing&lt;br&gt;Can be very severe with hypoxia</td>
<td>Broad-spectrum antibiotics including coverage of Gram-negative organisms</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Common in TB-endemic regions</td>
<td>See text. Persistent respiratory symptoms and often poor nutritional status; positive TB contact especially in younger children; CXR: focal abnormalities and perihilar adenopathy</td>
<td>Anti-TB treatment</td>
</tr>
<tr>
<td>LIP</td>
<td>Common especially around 2-6 years and bacterial pneumonia is a common complication</td>
<td>Persistent or recurrent respiratory symptoms&lt;br&gt;Generalised lymphadenopathy, clubbing, parotid enlargement. CXR: diffuse reticulonodular pattern and bilateral perihilar adenopathy</td>
<td>If symptomatic, steroids and broad-spectrum antibiotics</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>Common&lt;br&gt;Complicates recurrent bacterial pneumonia, LIP or TB</td>
<td>Cough productive of purulent sputum; clubbing; CXR: honeycombing usually of lower lobes</td>
<td>Broad-spectrum antibiotics&lt;br&gt;Physiotherapy</td>
</tr>
<tr>
<td>Viral pneumonia</td>
<td>Associated with bacterial co-infection</td>
<td>Acute onset of cough, fever, fast breathing; Wheezing less common than in HIV-uninfected</td>
<td>Broad-spectrum antibiotics if suspect bacterial co-infection</td>
</tr>
<tr>
<td>Mixed infection</td>
<td>Common problem: bacterial pneumonia, viral, LIP, TB</td>
<td>Consider when poor response to first-line empiric management</td>
<td>As above</td>
</tr>
<tr>
<td>Measles</td>
<td>In communities with poor measles immunization coverage</td>
<td>Conjunctivitis, typical rash, fever and cough, respiratory distress</td>
<td>Broad-spectrum antibiotics&lt;br&gt;Vitamin A</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>Especially in tropical Africa</td>
<td>Characteristic lesions on skin or palate</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>PnCP</td>
<td>Rarely described from African region in this age group</td>
<td>Severe respiratory distress&lt;br&gt;not improving with broad-spectrum antibiotics; CXR: diffuse interstitial infiltration</td>
<td>High-dose cotrimoxazole&lt;br&gt;Consider steroids</td>
</tr>
<tr>
<td>Other fungal pneumonia e.g. cryptococcosis, candidiasis</td>
<td>Little clinical data but data from autopsy studies suggests rare</td>
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<tr>
<td>Penicilliosis&lt;br&gt;Melioidosis</td>
<td>Older children in South-East Asia</td>
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</tbody>
</table>

CXR: chest x-ray; LIP: lymphoid interstitial pneumonitis; PnP: pneumocystis pneumonia.
(a) Cotrimoxazole preventive therapy and antiretroviral therapy when indicated for all cases.
References


