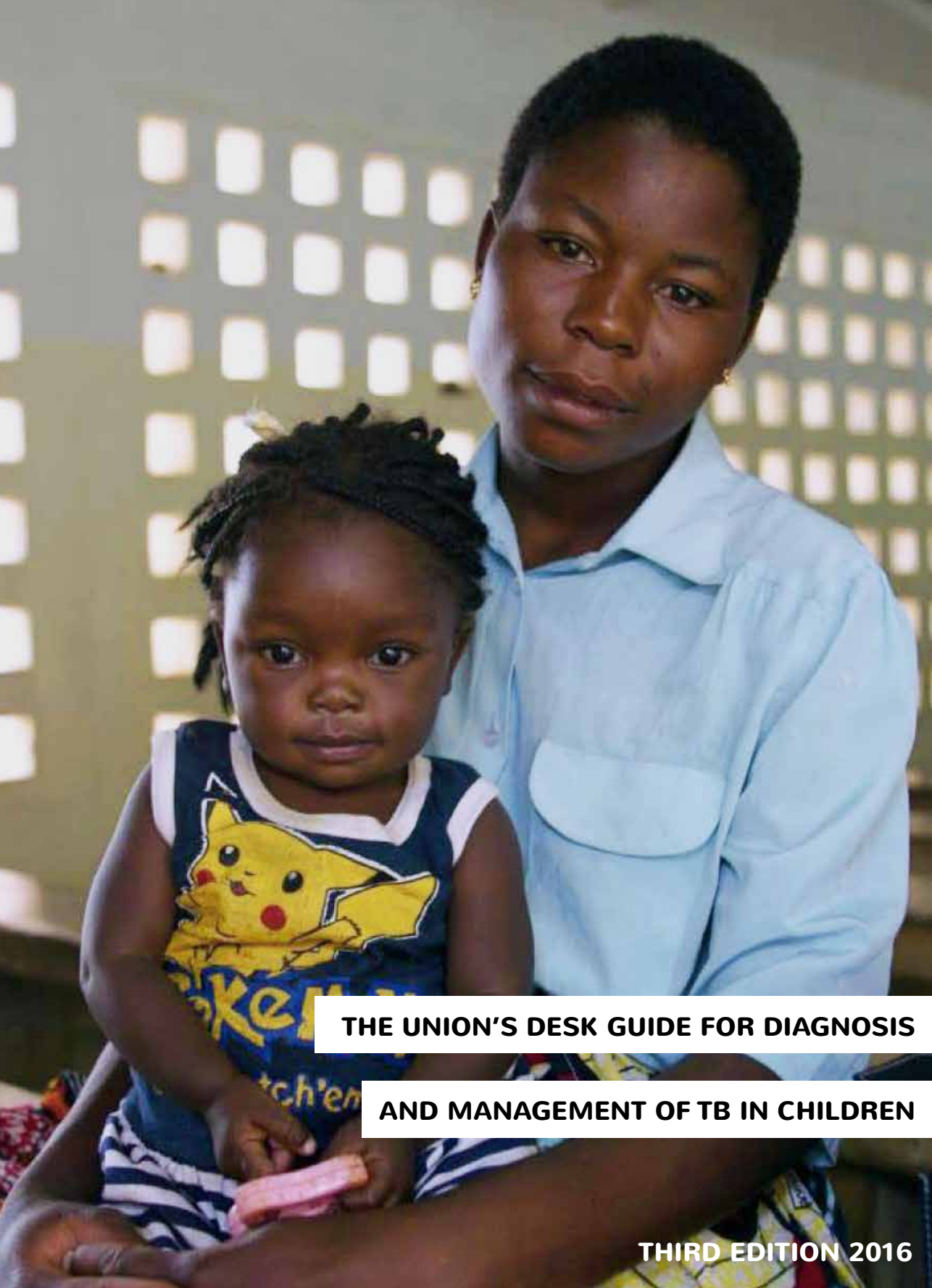


THE UNION'S DESK GUIDE FOR DIAGNOSIS AND MANAGEMENT OF TB IN CHILDREN

THIRD EDITION 2016

The Union's desk guide for diagnosis and management of TB in children

Third edition

2016

USAID FROM THE AMERICAN PEOPLE

The Union International Union Against Tuberculosis and Lung Disease
Health solutions for the poor

CHALLENGE TB

68 Boulevard Saint-Michel, 75006 Paris, France
Third edition, 2016

Photo credit (cover) : Gary Hampton / The Union

ISBN: 979-10-91287-14-2

The Global Health Bureau, Office of Health, Infectious Disease and Nutrition (HIDN), US Agency for International Development, financially supports this guide through Challenge TB under the terms of Agreement No. AID-OAA-A-14-00029. This guide is made possible by the generous support of the American people through the United States Agency for International Development (USAID).

The contents are the responsibility of Challenge TB and do not necessarily reflect the views of USAID or the United States Government.

The first edition of this desk guide was developed under USAID's TB CAP project and was published in 2010.

List of contents

This guide is based on NTP and WHO childhood TB and HIV case management guidelines. This guide is a decision-aid and does not cover all possible situations and/or solutions related to the management of childhood TB. The clinical judgment of the health worker remains the basis for final decision-making, and this aid is not a substitute for clinical expertise and individual assessment. It aims to provide guidance for the more common and straightforward cases presenting for care in the resource-limited setting.

Acknowledgements

This desk guide represents a consensus document originally developed by members of a workshop - Dr C Chabala (Zambia), Ms P Enarson (The Union), Dr SM Graham (Australia), Dr YK Haile (TB CAP), Dr L Muhe (WHO, Geneva), Dr E Obimbo (Kenya), Dr C Puta (Uganda) - convened by the International Union Against Tuberculosis and Lung Disease (The Union) and comments received from a wider audience including National Tuberculosis control Program (NTP) managers and child TB experts from The Union's Child TB Training Working Group (especially Prof BJ Marais and Prof HS Schaaf), and Dr Anna Nakanwagi of The Union, Uganda.

The second and this third edition have been revised with additional input from Dr Valérie Schwoebel, Dr Arnaud Trébucq and Dr Kobto Ghislain Koura of The Union. This third edition includes dosage tables for the newly available fixed-dose combinations of first-line treatments for young children, the inclusion of the Xpert assay in the diagnostic approach, and a section on multidrug-resistant tuberculosis (MDR-TB) in children.

Lead author

Stephen M. Graham
International Union Against Tuberculosis and Lung Disease, France; and
Centre for International Child Health, University of Melbourne Department of Paediatrics, Australia.

Introduction

Tuberculosis (TB) is an important cause of illness and death in children, especially in TB endemic countries

The diagnosis of TB can be made in most children in an outpatient setting based on careful clinical assessment

Contact history is a very important part of assessment for child TB diagnosis and prevention

Any child with suspected or confirmed TB should be tested for HIV infection

Children with TB respond well to treatment and tolerate TB treatment

All children (0-14 years) with TB should be routinely registered with and reported by the NTP

Desk guide is for :

1. health worker who manages sick children in first level health facilities or outpatient settings at any level of care
2. NTP worker who manages children as part of NTP work.

Desk guide aims to improve :

1. early and accurate case detection of children with TB
2. management and outcome of children with TB
3. child contact screening and management.

Desk guide will focus on :

1. diagnosis of common forms of TB in children
2. how to treat
3. when to refer
4. management of children who are close contacts of TB cases.

Epidemiology of TB in children

Children (0-14 years) account for around 10-20% of all TB cases in TB-endemic countries
- Most cases are pulmonary TB (PTB) cases
- Extra-pulmonary TB (EPTB) is also common and presentation varies with age

Important to always consider
- Age and nutritional status
- Risk factors for TB infection: history of contact with a TB patient
- Risk factors for TB disease: young age, HIV-infected, malnourished, recent measles, recent contact

Most TB cases occur in children less than 5 years of age
- The younger the child, the more likely to identify a close contact with TB disease
- TB disease can be more severe and of rapid onset in infants and young children

Children with TB disease usually have poor weight gain, may lose weight or be malnourished

The presentation and approach to diagnosis of pulmonary TB in older children (> 10 years) and adolescents is similar to that for adults

Any child with suspected or confirmed TB should be tested for HIV
- TB-HIV co-infection is common in children in sub-Saharan Africa
- HIV-infected children are at greater risk for TB infection and for TB disease
- Diagnosis and management can be more challenging in HIV-infected

BCG is not fully protective against TB disease in children

THE DIAGNOSIS OF TB CAN BE MADE WITH CONFIDENCE IN THE MAJORITY OF CHILDREN USING CAREFUL CLINICAL ASSESSMENT

Clinical Diagnosis : Pulmonary TB

The most common clinical presentation of pulmonary TB is persistent respiratory symptoms and poor weight gain. Note that in at-risk groups such as infants or HIV-infected, pulmonary TB can also present as acute pneumonia. The approach to diagnosis of TB in HIV-infected children is similar to that for HIV-uninfected children.

Typical symptoms

- Cough especially if persistent and not improving
- Weight loss or failure to gain weight
- Fever and/or night sweats
- Fatigue, reduced playfulness, less active

Especially if symptoms persist (>2-3 weeks) without improvement following other appropriate therapies (e.g. broad-spectrum antibiotics for cough; anti-malarial treatment for fever; or nutritional rehabilitation for malnutrition)

History of contact

- Close contact : such as with a source TB case living in the same household
- Contact may be with a source TB case from outside the household (e.g. neighbour, relative) with whom the child has had frequent contact
- A source case with sputum smear-positive PTB is more likely to infect contacts than cases with sputum smear-negative PTB
- Determine the treatment regimen of the source case and treatment response
- If no source case is identified, always ask about anyone in household with chronic cough – if so, request assessment of that person for possible TB
- In older children the contact with a TB source case may be outside the household e.g. school
- Timing of contact : children usually develop TB within 2 years after exposure and most (90%) within the first year

CHECK WEIGHT, RECORD WEIGHT AND COMPARE TO PREVIOUS WEIGHTS

Importance of follow-up assessment

- Most children with suspected TB present as outpatients and do not have features of severe illness (e.g. respiratory distress, severe malnutrition) that require them to be hospitalized.

- In such children there is less urgency to make a diagnosis on first presentation, and so if you are uncertain about diagnosis and persistence of symptoms, arrange for the child to return for a follow-up evaluation in 2 to 4 weeks to reassess weight and persistence or improvement of symptoms.
- This decision will be influenced by other factors such as likelihood of child to return for reassessment (such as living proximity, transport). Always encourage child to return earlier if there is any deterioration of symptoms.

Clinical examination

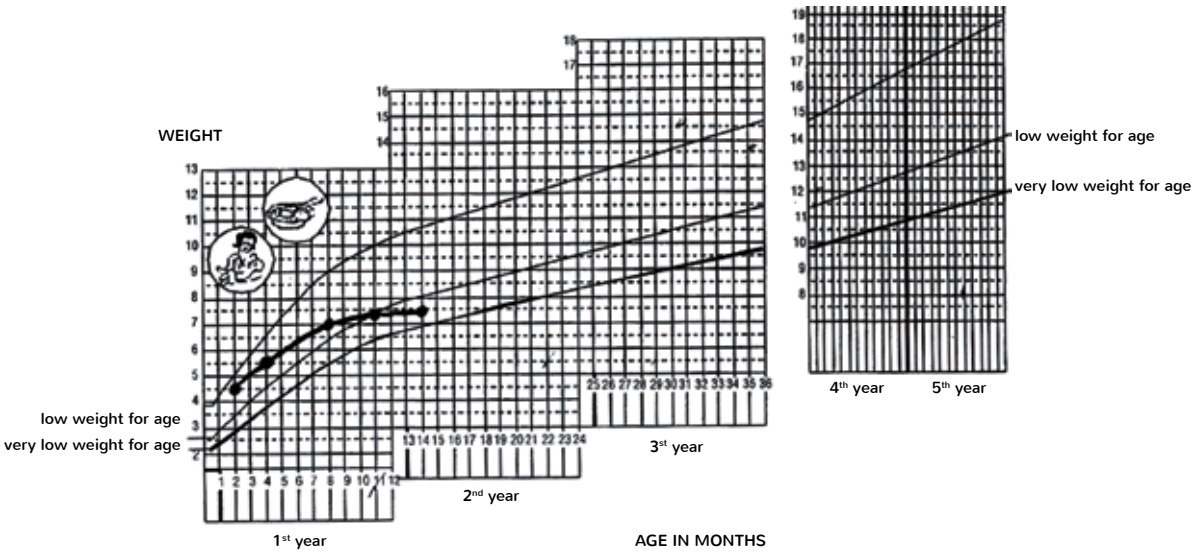
- Weigh child accurately and compare to previous weights
  - Look for weight loss or poor weight gain
  - Check for evidence of growth faltering
- Vital signs
  - Look for fever and increased respiratory rate
- Respiratory system
  - May have signs of respiratory distress
  - Auscultation and percussion: usually normal but may reveal lung disease (e.g. crackles, bronchial breathing) or pleural effusion (dullness and reduced breath sounds)
- Clinical features that might suggest other causes of chronic lung disease
  - Generalized lymphadenopathy, oral thrush, parotid enlargement suggest HIV infection
  - Finger clubbing (lymphoid interstitial pneumonitis [LIP] or bronchiectasis, pages 13)
  - Recurrent cough and/or wheeze responsive to bronchodilators suggests asthma

Atypical clinical presentations of PTB

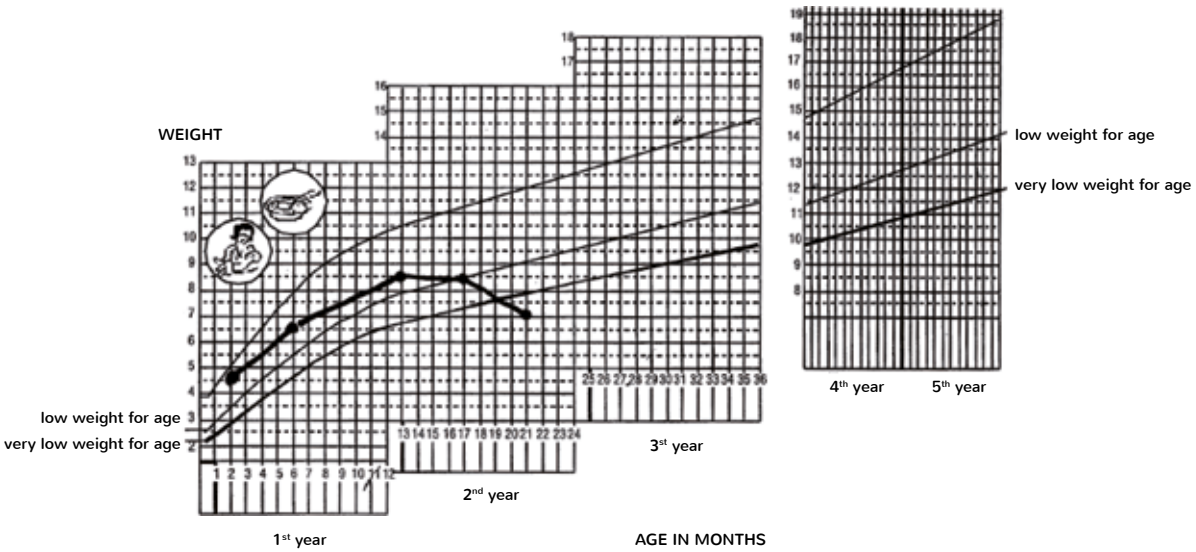
- Acute pneumonia
  - Presents with fast breathing and chest indrawing
  - Occurs especially in infants and HIV-infected children
  - Suspect PTB if poor response to antibiotic therapy – if HIV-infected also suspect other HIV-related lung disease e.g. Pneumocystis (carinii) jirovecii pneumonia (PcP)
- Wheeze
  - Asymmetrical and persistent wheeze can be caused by airway compression due to enlarged tuberculous hilar lymph nodes
  - Suspect PTB when wheeze is asymmetrical, persistent, not responsive to bronchodilator therapy and associated with other typical features of TB*

** Note that wheeze due to asthma is usually recurrent and variable rather than persistent, responsive to inhaled bronchodilator and is not associated with other typical features of TB, such as poor weight gain and persistent fever.*

Growth faltering or "failure to thrive"

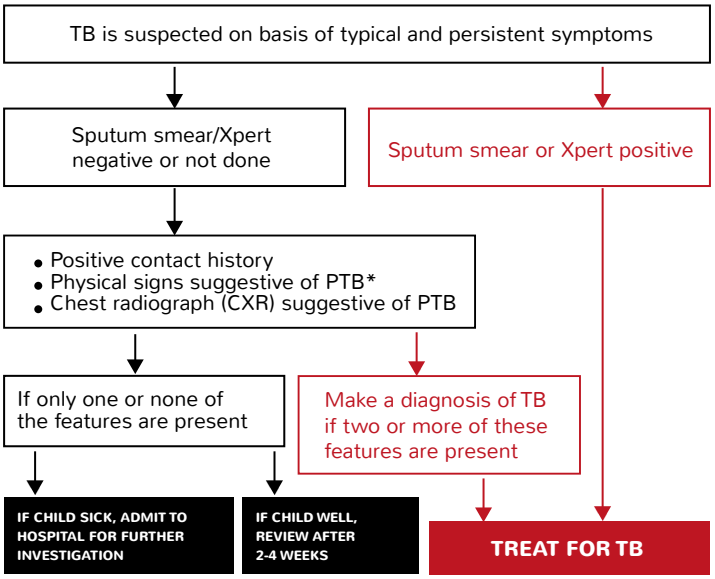


Weight loss



Examples of abnormal growth charts

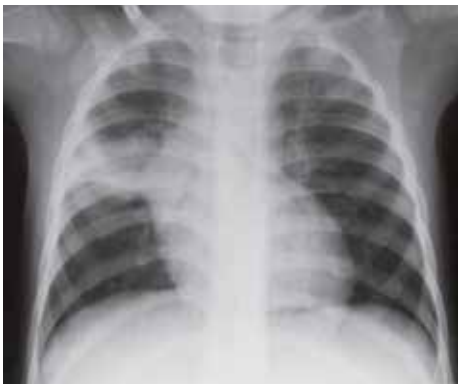
Approach to TB diagnosis in HIV-uninfected child



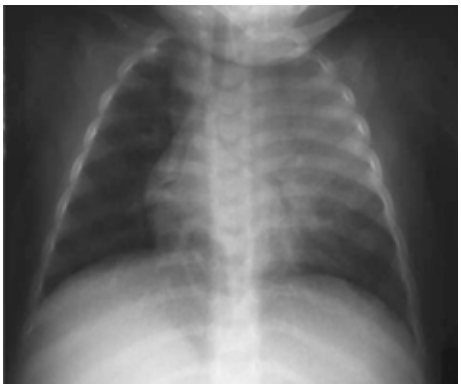
** The clinical and CXR signs suggestive of TB are listed above*

If child does not fit definite criteria to start TB treatment, decision for further review as outpatient or for inpatient management or for referral for further opinion/investigation will depend upon clinical state of the child and available levels of care.

If the child is asymptomatic but has a positive contact history, refer to Appendix 1 (p 34).

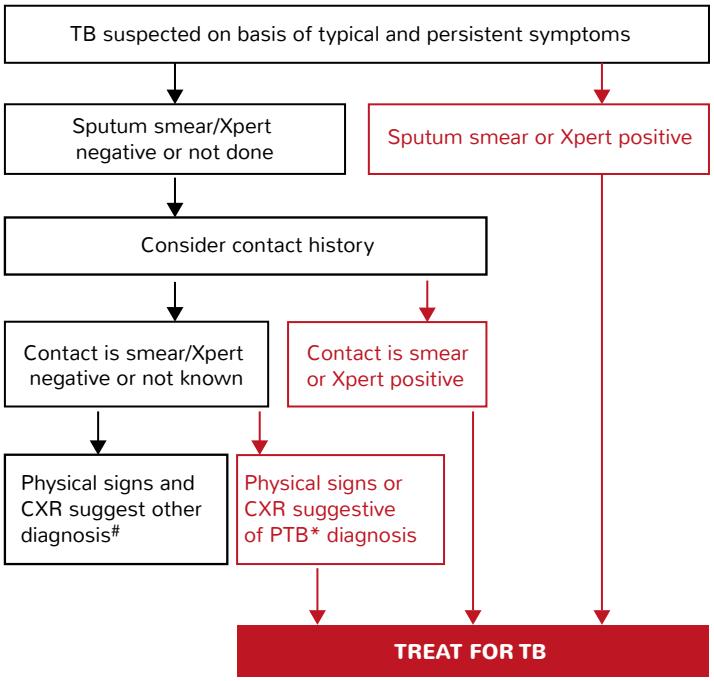


CXR suggestive of PTB: right perihilar lymph node enlargement with opacity in the right mid zone



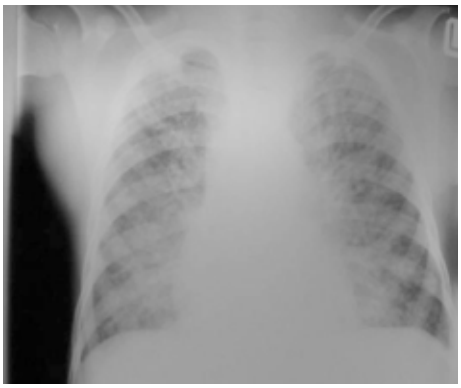
CXR suggestive of PTB: left upper lobe opacification with narrowing and shift of left main bronchus

Approach to TB diagnosis in HIV-infected child

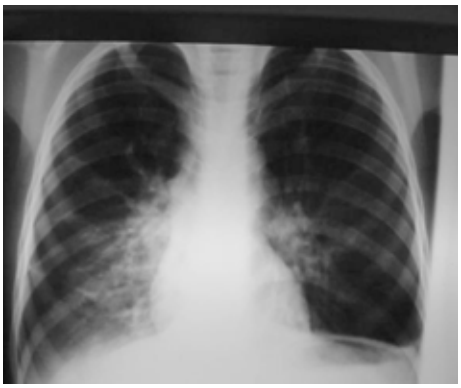


CXR abnormalities of PTB in HIV-infected child are similar to those in HIV-uninfected child.

* It can be difficult to clearly define what is "suggestive of PTB" on clinical or radiological findings in HIV-infected children because of clinical overlap between PTB and other forms of HIV-related lung disease: see Table on page 29 and CXRs below.



Lymphoid interstitial pneumonitis: typical features are bilateral, diffuse reticulonodular infiltration with bilateral perihilar lymph node enlargement



Bronchiectasis: focal opacification in right lower zone with thickening of bronchial walls and honeycomb appearance

Investigate : who, when and if (available)

HIV test

- Any child with presumptive TB should have an HIV test
- A negative HIV test increases the certainty that the persistent symptoms are due to TB (and not HIV)
- A positive HIV test also directs the need for antiretroviral treatment and other HIV-related care for the child and possibly other family members

Sputum

- Usually children older than 10 years (sometimes as young as 5 years) can produce sputum
- Do two sputum smears for acid fast bacilli (AFB) microscopy
- If available, do one Xpert test on the sputum

Gastric aspirate, nasopharyngeal aspirate or induced sputum

- Usually performed in children unable to provide sputum by coughing
- Perform AFB microscopy, and Xpert test if available
- Especially useful in child with diagnostic uncertainty or suspicion of MDR-TB

Chest X-Ray (CXR)

- CXR remains an important tool for diagnosis of PTB in children who are sputum smear-negative or who cannot produce sputum
- The following abnormalities on CXR are suggestive of TB
    - Enlarged hilar lymph nodes and opacification in the lung tissue
    - Miliary mottling in lung tissue
    - Cavitation (tends to occur in older children)
    - Pleural or pericardial effusion – though seen on CXR – are forms of extra pulmonary TB that tend to occur in older children
- The finding of marked abnormality on CXR in a child with no signs of respiratory distress (no fast breathing or chest indrawing) is supportive of TB

Tuberculin skin test (TST)

- TST is useful to support a diagnosis of TB in children with suggestive clinical features who are sputum smear-negative or who cannot produce sputum
- A positive TST indicates infection:
    - positive in any child if ≥ 10 mm irrespective of BCG immunization
    - also positive if ≥ 5 mm in HIV-infected or severely malnourished child

- A positive TST is particularly useful to indicate TB infection when there is no known TB exposure on clinical assessment i.e. no positive contact history
- Caution
    - A positive TST does not distinguish between TB infection and active disease
    - A negative TST does not exclude TB disease

Limitations of diagnostics

All of the above diagnostic investigations for TB in children have recognized limitations.

TST is often unavailable in primary or secondary healthcare settings. Therefore, the abovementioned suggested diagnostic approaches have not included TST so that they can still be used when TST is unavailable. TST does not distinguish between TB infection and active disease, and a negative TST does not rule out the possibility of TB.

CXR abnormalities in children with pulmonary TB are often non-specific which means that children with other common forms of lower respiratory tract infection (or pneumonia) can have the same abnormalities, and so it cannot alone determine the correct treatment for the child. CXR is used to add further support to a clinical diagnosis of pulmonary TB when TB is suspected and smear microscopy or Xpert is negative.

The diagnostic yield of **smear AFB microscopy** from sputum obtained by any method in young children with TB is very low.

Xpert is more likely to be positive than smear microscopy but will only be positive in less than one-third of children with TB. Therefore, a negative result from either test does not mean that the child does not have TB.

An advantage of Xpert is that if positive, it also provides information on whether the child might have MDR-TB or not. Therefore, it is strongly recommended to obtain suitable samples for Xpert testing in children for whom MDR-TB is suspected as this will determine choice of appropriate treatment regimen for the child.

For children with EPTB, (see page 16) Xpert provides a high positive yield from lymph node aspiration or cerebro-spinal fluid (CSF), but not from pleural, pericardial or peritoneal fluid. Again, a negative Xpert result does not rule out the diagnosis.

Xpert test can detect dead bacilli. Therefore this test should not be used to determine treatment response

Clinical Diagnosis : Extra-pulmonary TB

Extra-pulmonary TB is common in children and presentation varies with age. The table below lists typical clinical features of forms of EPTB and suggested investigations for each category. Symptoms vary depending on site of disease and characteristically are persistent, progressive and may be associated with weight loss or poor weight gain.

Clinical assessment in all cases should consider:

- History of contact (see above). Time lapse from exposure to disease presentation can be quite variable – shorter for young children with disseminated disease, longer for other forms that present in school-aged children
- Sputum for smear microscopy (and Xpert test where easily accessible)
- HIV test

Site of EPTB	*Typical clinical presentation*	*Investigation*	*Comment*
TB adenitis	Asymmetrical, painless, non-tender lymph node enlargement for more than one month +/- discharging sinus Most commonly in neck	Fine needle aspiration when possible for AFB microscopy, Xpert (if available) and histology TST usually positive - not necessary for diagnosis	Treat If axillary node enlargement on same side as BCG, consider BCG disease and refer
Pleural TB	Dullness on percussion and reduced breath sounds +/-chest pain	CXR Pleural tap#	Treat If pus in pleural tap, consider empyema and refer
Usually young (< 5 years) with disseminated disease and severely ill			
TB meningitis	Headache, irritability/ abnormal behavior, vomiting (without diarrhoea), lethargic/reduced level of consciousness, convulsions, neck stiffness, bulging fontanelle, cranial nerve palsies	Lumbar puncture obtain CSF#	Hospitalize for TB treatment §
Miliary TB	Non-specific, lethargic, persistent fever, wasted	CXR	Treat and refer §

Usually 5 years and older			
Abdominal TB	Abdominal swelling with ascites or abdominal masses	Ascitic tap#	Refer §
Spinal TB	Deformity of spine May have lower limb weakness/paralysis/ unable to walk	X-ray spine	Refer §
Pericardial TB	Cardiac failure Distant heart sounds Apex beat difficult to palpate	CXR Cardiac ultrasound Pericardial tap#	Refer §
TB bone and joint	Swelling end of long bones with limitation of movement Unilateral effusion of usually knee or hip	X-ray bone/joint Joint tap#	Refer §

 # typical findings: straw colored fluid, exudate with high protein, white blood cells predominantly lymphocytes on microscopy, positive culture

§ Referral may be necessary for investigation procedure and laboratory support as well as clinical care. If all options for referral have been explored and referral is not possible, start TB treatment. Start TB treatment immediately if TB meningitis suspected

TB adenitis

Tuberculous lymphadenitis is the commonest form of EPTB in children, usually representing around 10% of total child TB caseload. Enlargement of regional lymph nodes occurs after infection via lymphatic drainage from the site of infection. TB adenitis may or may not be associated with other symptoms of TB. Sinus and discharge may develop.

The cervical lymph nodes are the commonest site of clinical presentation. The usual age of presentation is 2-10 years.

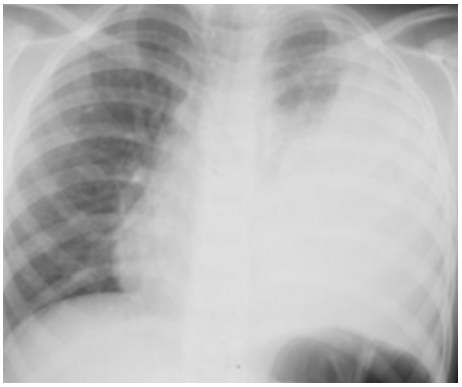
Lymph node enlargement due to TB is typically :

- large (>2 x 2 cm) i.e. visibly enlarged not just palpable
- painless and asymmetrical - often multiple, discreet or matted
- persistent (>1 month) and not responsive to other treatment such as antibiotics.

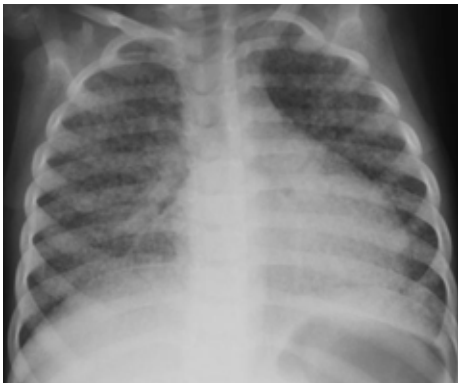
TST (if available) usually strongly reactive but not necessary for diagnosis. Fine needle aspiration for AFB microscopy, Xpert (if available) and histology should be done whenever possible.



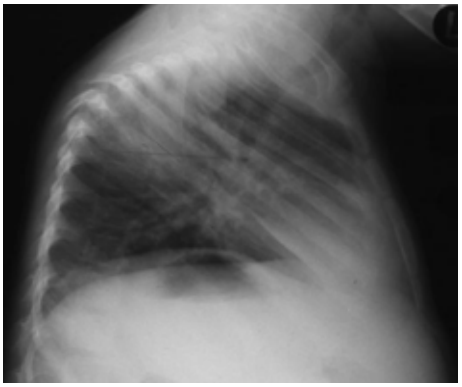
TB adenitis



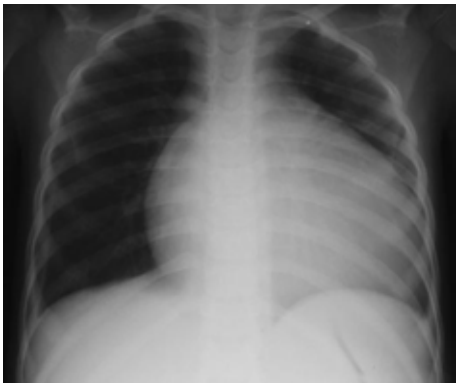
TB pleural effusion: large left-sided effusion. Pleural tap to differentiate from empyema



Miliary TB: typical bilateral diffuse micronodular pattern. Note differences to LIP X-ray above



Spinal TB: collapse of thoracic vertebra causing angulation



Pericardial TB: enlarged cardiac shadow. Ultrasound to differentiate from other causes of cardiac failure

TB Treatment

Some important rules

- Treatment regimens by disease category for new patients are listed in Table 1 on page 20
- Drug dosages according to weight are presented in Table 2 on page 20
- New drug formulations providing the correct dosage for children are available
- Number of tablets by weight bands are presented in Table 3a for the new formulations and in Table 3b for the old formulations (page 21)
- All HIV-infected children require four drugs in the intensive phase of treatment
- HIV-infected children should not be treated with intermittent (three times or twice weekly) regimens including during the continuation phase
- Register all children receiving TB treatment in the health unit TB register
- Record diagnostic category, treatment regimen and date of commencement in road-to-health book, TB treatment card and health unit TB register
- Record weight at each visit in road-to-health book and TB treatment card
- Children gain weight while receiving TB treatment and dosages should be adjusted accordingly
- Weight is important for monitoring of treatment response
- Once treatment starts it must be completed; "trial of TB treatment" should not be used as a diagnostic tool
- A caregiver should be identified as the treatment supporter for all ages including older children
- Adherence to the full course of treatment should be emphasized and reinforced
- TB drugs are very well tolerated in almost all children. Adverse events (side-effects) are unusual and the most important is hepatotoxicity
- Ethambutol can be safely used in all ages of children at recommended dosages

CXR SHOULD NOT BE USED TO MONITOR TREATMENT RESPONSE

Table 1. *Recommended treatment regimens for new patients (WHO, 2014)*

TB disease category	*Recommended regimen*	
	Intensive phase	*Continuation phase*
Non-severe forms of TB (smear-negative PTB, intra-thoracic lymph node TB, peripheral lymph node TB)	2 HRZ	4 HR
More severe forms of PTB (smear-positive PTB, cavitation, extensive parenchymal disease) and EPTB except TB meningitis and osteoarticular TB	2 HRZE	4 HR
TB meningitis Osteo-articular TB	2 HRZE	10 HR

H=Isoniazid. R=Rifampicin. Z=Pyrazinamide. E=Ethambutol
Numeral refers to number of months of the regimen e.g. 2 HRZE refers to two months of daily isoniazid, rifampicin, pyrazinamide and ethambutol

Note : Streptomycin no longer recommended for children with TB

Table 2. *Recommended dosages according to weight (WHO, 2014)*

Drug	*Daily dosage in mg/kg*
Isoniazid (H)	7-15 (300 mg)
Rifampicin (R)	10-20 (600 mg)
Pyrazinamide (Z)	30-40 (2000 mg)
Ethambutol (E)	15-25 (1200mg)

Table 3a.

Numbers of tablets by weight band for new FDC (RHZ 75/50/150)

Weight bands	*Recommended regimen*		
	Intensive phase		*Continuation phase*
	RHZ	*E #*	*RH*
	75/50/150	*100*	*75/50*
4-7 kg	1	1	1
8-11 kg	2	2	2
12-15 kg	3	3	3
16-24 kg	4	4 *	4

E is given only for severe forms of TB

*alternatively (preferably) give one 400mg tablet of ethambutol

Table 3b.

Numbers of tablets by weight band for "old" FDC (RHZ 60/30/150)

Weight bands	*Recommended regimen*		
	Intensive phase		*Continuation phase*
	RHZ	*E #*	*RH*
	60/30/150	*100*	*60/30*
4-6 kg	1	1	1
7-10 kg	2	2	2
11-14 kg	3	2	3
15-19 kg	4	3	4
20-24 kg	5	4 *	5

E is given only for severe forms of TB

*alternatively (preferably) give one 400mg tablet of ethambutol

It should be noted that at 25 kg or greater, children can adopt adult dosage recommendations and use adult preparations.

Additional management decisions

- Hospitalization
  - Severe forms of PTB and EPTB for further investigation and initial management
  - Severe malnutrition for nutritional rehabilitation
  - Signs of severe pneumonia (i.e. chest in-drawing)
  - Other co-morbidities e.g. severe anaemia
  - Social or logistic reasons to ensure adherence
  - Newborns (< 4 kgs)
  - Severe adverse reactions such as hepatotoxicity

- For all HIV-infected children
  - Commence cotrimoxazole preventive therapy (CPT)
  - Commence antiretroviral therapy (ART)
  - Conduct family-based care/screening

- Referral should be considered if
  - Diagnostic uncertainty
  - Necessary for HIV-related care e.g. to commence ART
  - Failure to respond to treatment despite good adherence to TB treatment
  - MDR-TB contact

- Nutritional support should be provided for malnourished children if available

- Breastfeeding infants and children should continue to breastfeed while receiving TB treatment

- Pyridoxine is not routinely given but is recommended for severely malnourished and HIV-infected children

Follow-up

HIV-uninfected : monthly during intensive phase and 2-monthly on continuation phase
HIV-infected : review at 2 weeks and 4 weeks following commencement of TB treatment and then monthly thereafter

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

Important practice points

- Weigh the child at each follow-up, document and adjust dosage if necessary
- Adherence for the full course of treatment may be a challenge
  - Explain and emphasize to care-giver and child why they must take the full course of treatment even if they are feeling better
  - Note risk factors for poor adherence such as distance/transport; orphan (especially if mother has died) or primary care-giver unwell; adolescents
  - Education and adherence support especially TB-HIV
- Explain that TB drugs in children are well tolerated and safe
- CXR is not required in follow-up if the child is responding well to TB treatment

THE MOST IMPORTANT ADVERSE EFFECT IS HEPATITIS WHICH USUALLY PRESENTS WITH JAUNDICE, NAUSEA AND VOMITING. THERE MAY BE ABDOMINAL PAIN, JAUNDICE AND TENDER, ENLARGED LIVER.

IF CONSIDERED A POSSIBILITY, STOP THE TB DRUGS IMMEDIATELY AND REFER TO HOSPITAL

Treatment failure

Most children with TB will start to show signs of improvement after 2 to 4 weeks of TB treatment. Poor adherence may be the cause of "treatment failure".

Assessment at 1-2 months after treatment, consider treatment failure if child is receiving TB treatment and :

- No symptom resolution or symptoms getting worse
- Continued weight loss
- Smear-positive at 2 month follow-up sputum.

If a child stops TB treatment for more than 2 weeks in the intensive phase or more than 2 months in the continuation phase and becomes symptomatic, then restart first-line TB therapy. If a child stops TB treatment for less than 2 weeks in the intensive phase or less than 2 months in the continuation phase and becomes symptomatic, then continue current regimen.

Treatment failure is more common in HIV-infected children.

Treatment failure suggests the possibility of MDR-TB and needs careful assessment.

REFER CHILDREN WITH TREATMENT FAILURE FOR FURTHER ASSESSMENT

Child contact screening and management

Preventive therapy greatly reduces the risk of an infant or young child with TB infection from developing disease.

Important questions for any person commenced on TB treatment

i. Is the case sputum positive ?
ii. What treatment regimen is the index case receiving and what is the treatment response ?
iii. Is there anyone else in the household who is coughing ?
iv. How many children in the household ?
v. What are the ages of the children ?
vi. Is the child contact sick or well ?
vii. What is the relationship of the index case to the children?

- All close contacts with cases with bacteriologically confirmed TB should be screened for TB including children
- If the TB source case is the child's parent and is HIV-infected, test all the children for HIV
- Screening can be initiated at the primary health or community care level
- Symptoms alone are used to screen child contacts for possible TB disease

Refer to Appendix 1 (page 34) for a recommended approach to assessment of the child contact.

Any contact, including children, with symptoms should be carefully assessed for TB disease

Preventive therapy is indicated for all young children (< 5 years) and HIV-infected children of any age that are household contacts of a case with sputum smear-positive TB AND do not have any evidence of TB disease

There are a number of possible regimens for preventive therapy that are known to be effective. The two most commonly used are :

- Isoniazid daily for a full 6 months – also known as IPT – is the regimen most widely recommended (Table 4a, page 25)
- Rifampicin and isoniazid for 3 months (Table 4b, page 25)

Dosage of isoniazid and rifampicin for preventive therapy is the same as for treatment. Number of tablets by weight bands are presented in Tables 4a and 4b.

Table 4a. *H50 or H100 tablets daily for 6 months duration (IPT – 6H)*

Weight bands	*Isoniazid (mgs)*	*H50 tablet*	*H100 tablet*
4-7 kg	50	1	1/2
8-11 kg	100	2	1
12-15 kg	150	3	1 1/2
16-24 kg	200	4	2

Table 4b. *RH 75/50 FDC daily for 3 months (3RH)*

Weight bands	*RH 75/50 tabs*
4-7 kg	1
8-11 kg	2
12-15 kg	3
16-24 kg	4

For children that are 25 kg and above, use adult preparations: one tablet of H300mg or two RH150/75.

Preventive therapy (or IPT) registers

It is encouraged to register all children that are provided with preventive therapy. This provides important information for the NTP about drug requirements for procurement to avoid stock-outs, as well as monitoring the uptake of, adherence to and outcome from preventive therapy. More and more NTPs are developing such registers, and these should be completed if available.

Challenges for preventive therapy

It takes time and understanding to explain to families why a child should take preventive therapy to protect them from developing TB. It is challenging for parents (and many health workers) to understand that a child who is well needs to take a medicine every day for up to 6 months. For similar reasons, it is challenging to ensure that the child completes the full course of preventive therapy.

There is often concern about the potential toxicity of preventive therapy for a child who is well. However, the risk of serious toxicity using the regimens in Tables 4a and 4b is extremely low, and certainly lower than the risk of the child developing TB.

There are as yet no clear guidelines for the use of preventive therapy in children that are contacts of MDR-TB cases. The regimens listed in Tables 4a and 4b are very unlikely to be effective.

Follow-up is critical

Review every 2 months and continuously re-enforce message of adherence.

Investigate for TB if typical symptoms develop i.e. persistence of cough, fever, fatigue, poor weight gain.

MDR-TB in children

Multidrug-resistant TB (MDR-TB) is a strain of TB that is resistant to at least isoniazid and rifampicin. With increasing numbers of MDR-TB cases in the world, there is also an increasing number of children with MDR-TB. The prevalence of MDR-TB in a community will determine how common MDR-TB is in children in the same community.

The clinical presentation of MDR-TB in a child is similar to the clinical presentation of other forms of TB in a child (as above). Therefore, the diagnosis is often made on clinical and radiological grounds as bacteriological confirmation is not always possible. A high index of suspicion is required in children that fit the criteria listed below.

Important criteria for suspected MDR-TB :

Close contact with a person with known MDR-TB

The child has been taking first-line treatment but has failed to improve clinically by 2 months (completion of intensive phase), i.e. persistence of symptoms, failed to gain weight, or persistence of positive smear

If the child is in close contact with a person that has failed TB treatment or is non-adherent to TB treatment, one should try to get information on whether this person has been confirmed with MDR-TB.

When MDR-TB is suspected, it is important to try as best as possible to get samples for bacteriological confirmation by Xpert and culture whenever possible. Xpert provides rapid information that indicates rifampicin resistance (and therefore MDR) while culture allows testing for susceptibility to a wide range of drugs. If there is a known contact with MDR-TB, it is also important to know which drugs the index case is resistant to.

Treatment for MDR-TB is more complicated than treatment for drug-sensitive TB with more drugs required, longer treatment regimens often with daily injections, and greater risk of serious toxicity with irreversible hearing loss being the main one. Treatment by a 9 months regimen may be administered under specific conditions but still requires intensive follow-up. For this reason and for the need to obtain samples, a child with suspected MDR-TB requires referral to a centre with the management experience and expertise.

Screening of household contacts of an MDR-TB case is recommended, and any contact (of any age) with TB-related symptoms should also be carefully evaluated for MDR-TB. All children in close contact with an MDR-TB case should be evaluated for TB. If they are well and have no evidence of TB, they should be followed-up regularly. However, currently there are no recommended guidelines for choice of appropriate preventive therapy regimen. Therefore, consideration of preventive therapy would require discussion with those that are managing the index case for MDR-TB.

[1]http://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/

TB infection control

Prevention of TB transmission and infection in the household and health facilities are important components of control and management of TB in children.

The following simple procedures are effective in TB infection control at home and clinics

- Early diagnosis and treatment of adult TB cases in the household
- At the clinic promptly identify potential and known infectious cases of TB; separate and treat them with minimal delay by conducting triage and screening
- Provide health education about TB transmission without stigmatizing TB patients
- Encourage proper cough hygiene both at home and at health facilities
- Natural ventilation and sunlight:
  - Keep doors and windows open on opposite sides of the TB clinic and other clinics (effective ventilation- changing air)
  - Where children and adults stay together, open windows
  - Advise TB patients to do the same at home

Newborns are particularly vulnerable and outbreaks of TB among neonates occur in newborn care settings with the source usually being a mother or a staff member. If a mother has TB, she can breast-feed her newborn, provided she is receiving treatment for TB, uses a mask and the newborn should receive preventive therapy if there is no evidence of TB in the newborn. In this case, BCG is delayed until after completion of preventive therapy.

The child with TB and HIV

- HIV test is indicated in all children with suspected and confirmed TB
- Approach to diagnosis of TB is similar as for HIV-uninfected children
- Treatment for TB is same as for HIV-uninfected children
- All children with TB-HIV should receive CPT and ART
- Nutritional support is often needed for children with TB-HIV
- All HIV-infected children need to be screened for TB disease
- If TB disease is excluded, IPT is given irrespective of age
- The management of children with TB-HIV should be integrated and all family members are counseled and tested for HIV and screened for TB
- The specific needs of each family need to be determined and a plan of action developed to ensure that the family receives comprehensive care using all available services

The diagnosis of PTB can be particularly challenging in HIV-infected child because of clinical overlap with other HIV-related lung disease.

Cause	*Clinical features*
Recurrent pneumonia	Recurrent episodes of cough, fever and fast breathing that usually respond to antibiotics
LIP	Unusual before 1 year of age Associated with generalized symmetrical lymphadenopathy, clubbing, parotid enlargement. Nutritional status variable. CXR: diffuse reticulonodular pattern and bilateral perihilar adenopathy. No compression of airways
Tuberculosis	Persistent respiratory symptoms not responding to antibiotics. Often poor nutritional status; positive TB contact especially in younger children CXR: focal abnormalities and perihilar adenopathy
Bronchiectasis	Cough productive or purulent sputum; clubbing CXR: honeycombing usually of lower lobes Complicates recurrent bacterial pneumonia, LIP or TB
PcP	Common cause of severe, fatal pneumonia especially in infants. Persistent hypoxia is common Unusual after 1 year of age CXR: diffuse interstitial infiltration or hyperinflation
Mixed infection	Common problem: LIP, bacterial pneumonia, TB Consider when poor response to first-line empiric management
Kaposi sarcoma	Uncommon Characteristic lesions on skin or palate

NTP Management Issues

Most of the issues that relate to an effective NTP providing a high quality service for TB control relate to children as well as adults. Early case detection and effective management of TB cases in the community will reduce the burden of TB in children. It is important that NTPs include child TB in funding and resource allocation, in policy guidelines/protocols and training opportunities. NTPs should have a focal person for child TB and a child TB working group for monitoring and evaluation of child TB-related issues.

Registration and reporting

All children receiving TB treatment need to be registered in the district TB register and should be part of the quarterly and yearly cohort analysis and reporting, including when sputum smear or Xpert test are negative or not obtained.

Children are reported in same way as adults: include age, site of TB, gender, disease category (e.g. bacteriologically confirmed, clinically diagnosed), HIV status, outcome.

Major differences to management of adults

Most cases not bacteriologically confirmed i.e. smear or Xpert negative
Drug dosages need to be higher in mg/kg (Table 2, page 20)
Drug dosages may need to be adjusted with weight gain
Children tolerate first-line TB drugs very well

Treatment outcome

It is very important that treatment outcomes are reported by NTP for all children that receive TB treatment as per standard category

i. Treatment completion
ii. Lost to follow-up
iii. Death
iv. Transfer out
v. Cure (for smear-positive)
vi. Failure (for smear-positive)

Engage all care providers

As part of the overall TB control activities, NTPs need to coordinate and engage all relevant care providers to ensure adequate service provision through dissemination and implementation of the International Standards of TB Care. Public-Private Partnership, including community and faith-based organizations, is critical to intensify case finding and support adherence.

Definitions and distinctions

Infection with *Mycobacterium tuberculosis* usually results from inhalation of infected droplets produced by someone who has PTB and who is coughing. The most infectious source cases are those with sputum smear-positive disease. The closer the contact with this source case, the greater the exposure and the greater the risk of getting infected with *Mycobacterium tuberculosis*.

TB infection is when a person carries the Mycobacterium tuberculosis bacteria inside the body. Many people have TB infection and are well. A positive TST indicates infection - but a negative TST does not exclude the possibility of infection.

TB disease occurs in someone with TB infection when the bacteria inside the body start to multiply and become numerous enough to damage one or more organs of the body. This damage causes clinical symptoms and signs and is referred to as "tuberculosis" or active disease.

Close contact is defined as living in the same household as, or in frequent contact with (e.g. child minder, school staff), a source case with PTB.

Children refer to the 0 to 14 year age group.

Infant is a child of less than 1 year of age (0-12 month age group).

Abbreviations

AFB	acid-fast bacilli
ART	anti-retroviral therapy
BCG	Bacillus Calmette-Guérin
CPT	cotrimoxazole preventive therapy
CSF	cerebro-spinal fluid
CXR	chest radiograph
DOT	directly observed therapy
EPTB	extra-pulmonary tuberculosis
HIV	human immunodeficiency virus
IPT	isoniazid preventive therapy
LIP	lymphoid interstitial pneumonitis
MDR	multidrug-resistant
NTP	National Tuberculosis control Program
PcP	Pneumocystis (carinii) jirovecii Pneumonia
PTB	pulmonary tuberculosis
TB	tuberculosis
TST	tuberculin skin test

Resource materials

1. Guidance for national tuberculosis programmes on the management of tuberculosis in children – 2nd edition. World Health Organization, Geneva, 2014.
http://www.who.int/tb/publications/childtb_guidelines/en/

2. Diagnostic atlas of intrathoracic tuberculosis in children. A guide for low income countries. The Union, Paris, 2003.
http://www.theunion.org/what-we-do/publications/technical/english/pub_diagnostic-atlas_eng.pdf

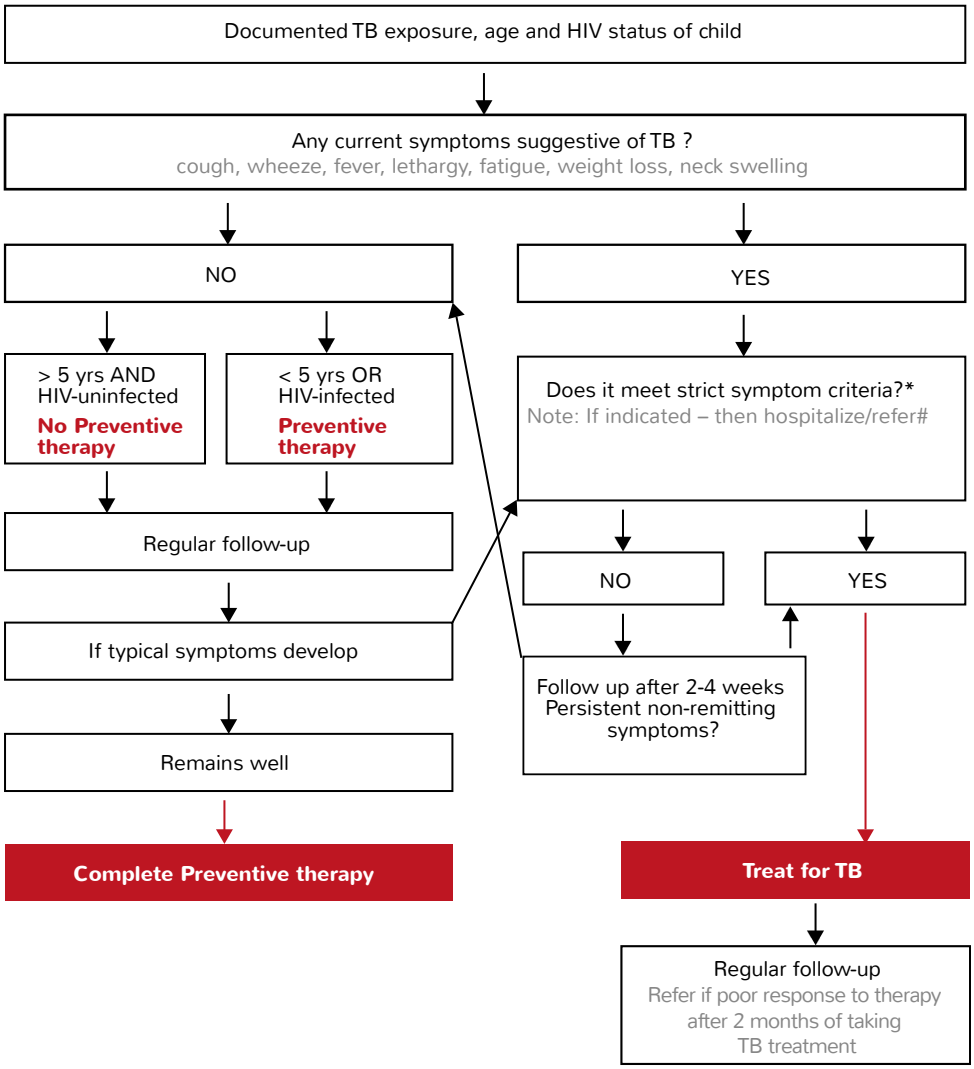
3. Xpert MTB/RIF implementation manual: technical and operational 'how-to'; practical considerations. WHO/HTM/TB/2014.1
http://www.who.int/tb/publications/xpert_implem_manual/en/

4. WHO treatment guidelines for drug-resistant tuberculosis 2016 update.
http://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/

5. Management of multidrug-resistant tuberculosis in children: a field guide. Second edition. March 2015. Sentinel Project.
http://sentinel-project.org/wp-content/uploads/2015/03/Field_Handbook_2nd_Ed_revised-no-logos_03022015.pdf

Wall charts (Appendix 1)

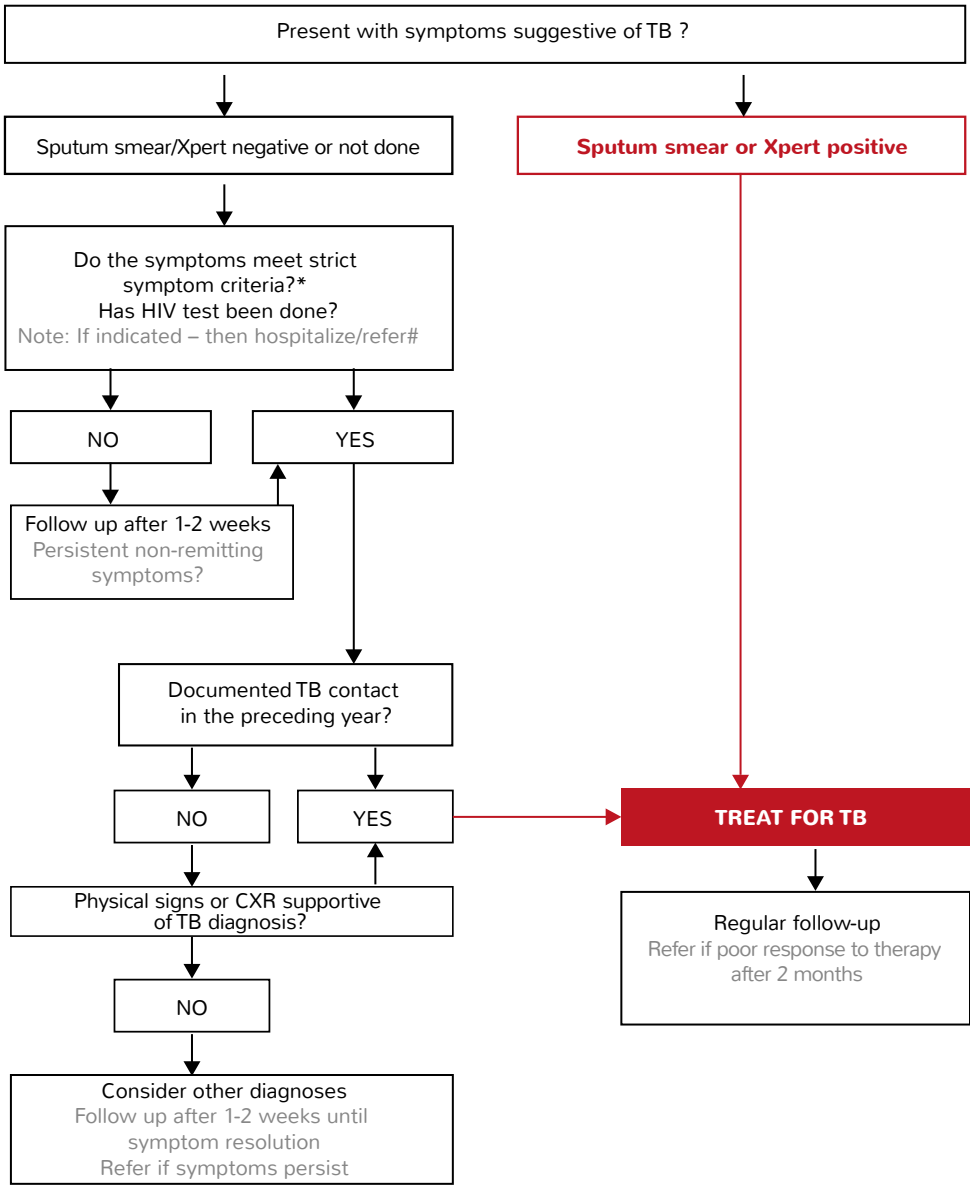
1. Guidance for the screening of children in close contact with bacteriologically confirmed pulmonary TB



Close contact is defined as living in the same household as, or in frequent contact with (e.g. child minder, school staff), a source case with PTB.
** See Appendix 3*
 # See Appendix 4

(Appendix 2)

2. Guidance for the diagnosis of children who present with symptoms suggestive of TB



** See Appendix 3*
 # See Appendix 4

(Appendix 3)

3. Strict symptom criteria

- Persistent, non-remitting cough or wheeze for more than 2 weeks not responding to standard therapy
- Documented loss of weight or failure to thrive during the past 3 months especially if not responding to food and/or micronutrient supplementation, OR severe malnutrition
- Fatigue/reduced playfulness
- Persistent fever > 10 days

TWO OR MORE OF THESE SYMPTOMS ARE HIGHLY SUGGESTIVE OF TB DISEASE

(Appendix 4)

4. Indications requiring hospitalization/referral

- Severe forms of PTB and EPTB for further investigation and initial management
- Severe malnutrition for nutritional rehabilitation
- Signs of severe pneumonia (i.e. chest in-drawing) or respiratory distress
- Other co-morbidities e.g. severe anaemia

Referral should also be considered if :

- Diagnostic uncertainty requiring further investigation at referral level
- Necessary for HIV-related care e.g. to commence ART

About The International Union Against Tuberculosis and Lung Disease (The Union)

For nearly 100 years, The Union has drawn from the best scientific evidence and the skills, expertise and reach of its staff, consultants and membership in order to advance solutions to the most pressing public health challenges affecting people living in poverty around the world. With nearly 17,000 members and subscribers from 156 countries, The Union has its headquarters in Paris and regional offices in Africa, the Asia Pacific, Europe, Latin America, North America and South-East Asia. The Union's scientific departments focus on tuberculosis and HIV, lung health and non-communicable diseases, tobacco control and operational research. For more information, please visit www.theunion.org.


USAID
FROM THE AMERICAN PEOPLE


The Union
International Union Against
Tuberculosis and Lung Disease
Health solutions for the poor


CHALLENGE TB