

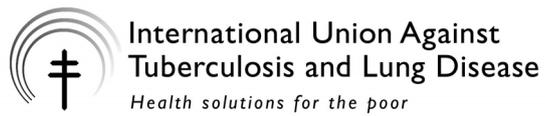
Desk-guide for diagnosis and management of TB in children



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

Desk-guide for diagnosis and management of TB in children

2010



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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.

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Participants of workshop:

Dr Chishala Chabala (Zambia), Ms Penny Enarson (The Union), A/Prof Stephen Graham (Australia), Dr Yared Kebede Haile (TB CAP), Dr Lulu Muhe (WHO, Geneva), Dr Elizabeth Obimbo (Kenya) and Dr Chilunga Puta (Uganda).

Lead author

Stephen M Graham, 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 sub-Saharan Africa

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 anti-TB treatment

Children (0-14 years) 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 setting 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 up to one-third of all TB cases

Most cases are pulmonary TB (PTB) cases

Extrapulmonary 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

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: PTB

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 case of TB living in the same household
- ❖ Contact may be with a source case of TB 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
- ❖ 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

Clinical examination

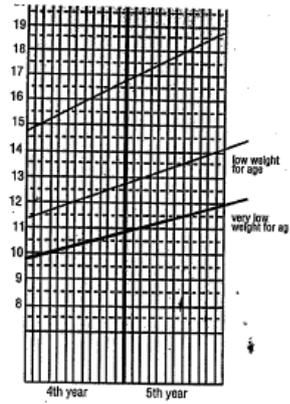
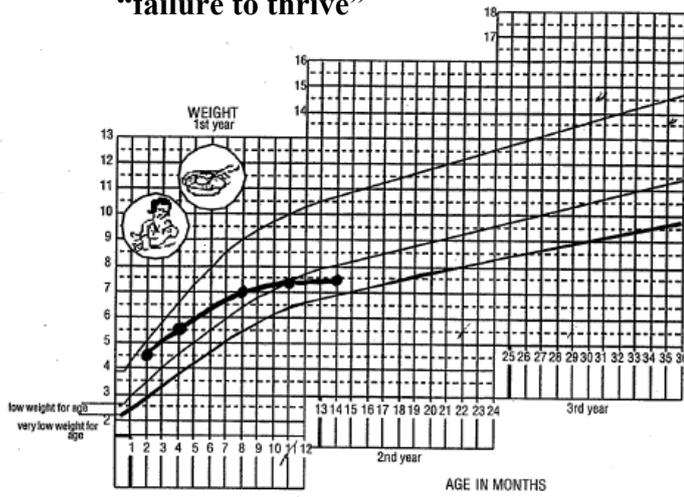
- ❖ Weigh child accurately and compare to previous weights:
 - Look for weight loss or poor weight gain
 - Check for evidence of growth faltering
- ❖ Vital signs
 - Look for fever and increased respiratory rate
- ❖ Respiratory system
 - May have signs of respiratory distress
 - Auscultation and percussion: 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
 - Generalised lymphadenopathy, oral thrush, parotid enlargement suggest HIV infection
 - Finger clubbing (LIP or bronchiectasis, page 17)
 - Recurrent cough and/or wheeze responsive to bronchodilators suggests asthma

Atypical clinical presentations of PTB

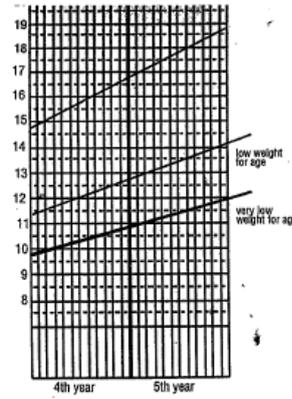
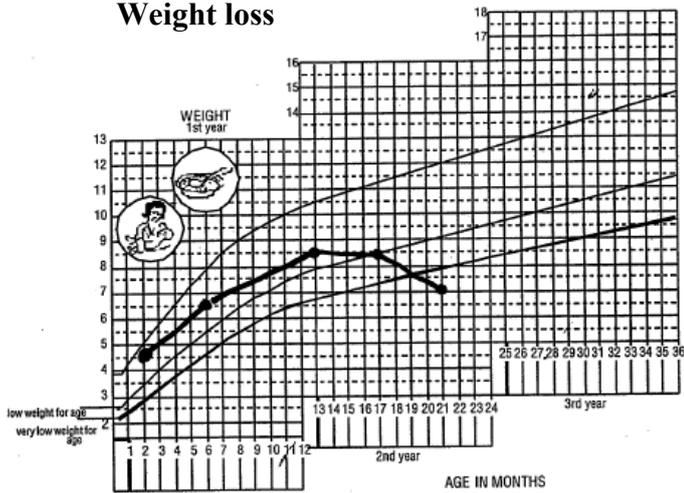
- ❖ Acute severe pneumonia
 - Presents with fast breathing and chest indrawing
 - Occurs especially in infants and HIV-infected children
 - Suspect PTB if poor response to antibiotic therapy – if HIV-infected also suspect other HIV-related lung disease e.g. PcP
- ❖ Wheeze
 - Asymmetrical and persistent 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"

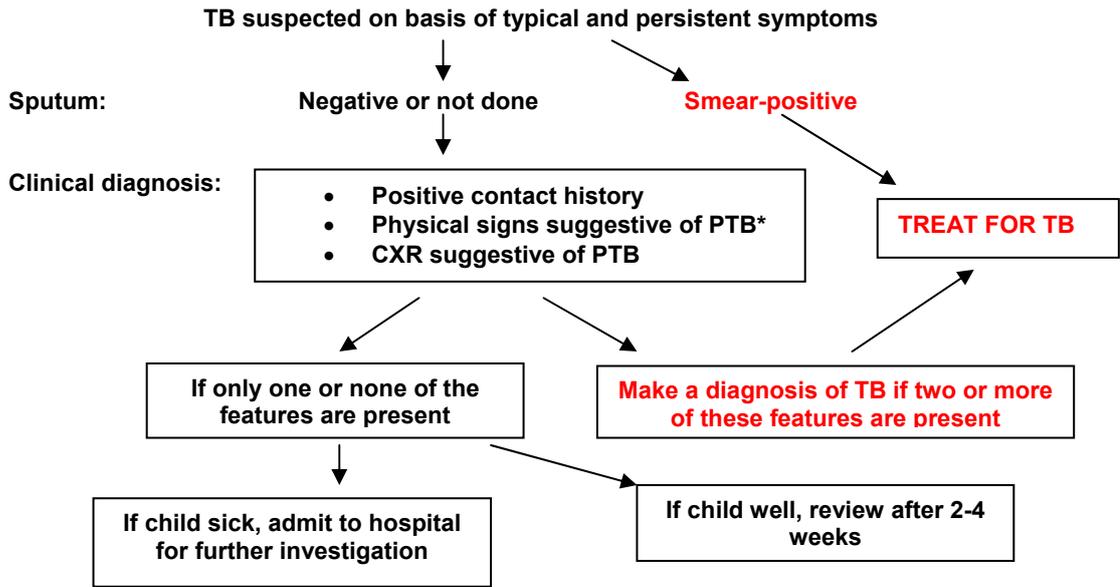


Weight loss



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 anti-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 25).

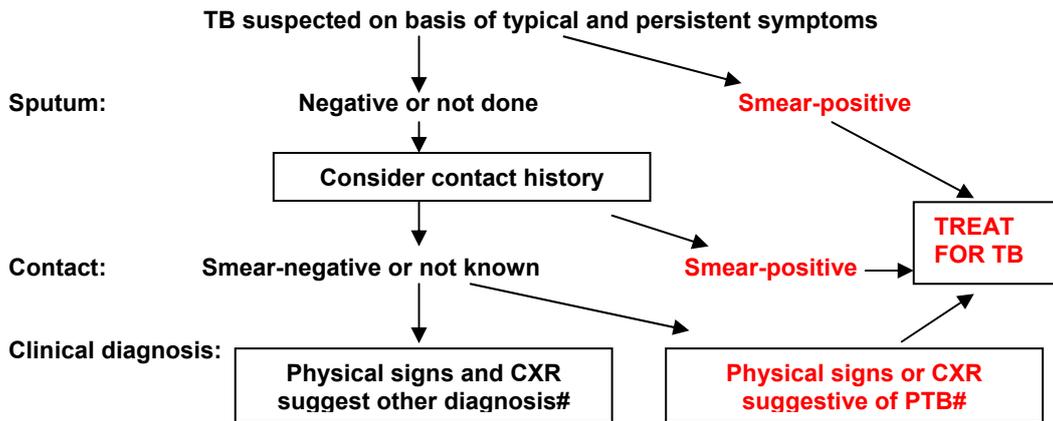


CXR suggestive of PTB: right perihilar lymph node enlargement with opacity in the right mid zone



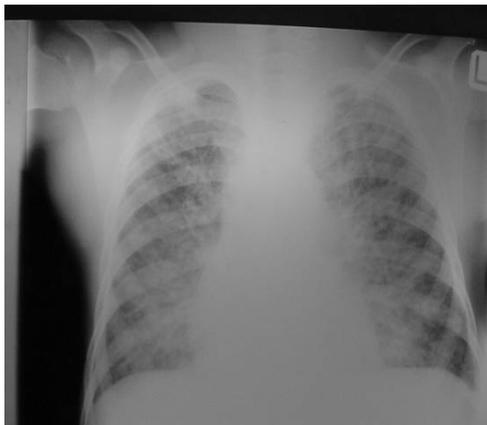
CXR suggestive of PTB: left upper lobe opacification with narrowing and shift of left main bronchus

Approach to TB diagnosis in HIV-infected child



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 22 and CXRs below.

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



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 suspected TB should have an HIV test***
- ❖ A positive HIV test also directs the need for other HIV-related care for the child and possibly other family members

Sputum

- ❖ Do two sputum smears for acid fast bacilli (AFB) microscopy, and culture if available
- ❖ Usually children older than 10 years (sometimes as young as 5 years) can produce sputum

Chest X-Ray

- ❖ 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 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 immunisation
 - 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

Gastric aspirate or induced sputum

- ❖ Usually performed in children unable to provide sputum by coughing
- ❖ Perform AFB microscopy and TB culture if available (culture increases likelihood of identifying TB bacteria)
- ❖ Especially useful in child with diagnostic uncertainty or suspicion of MDR TB

Investigations such as TST and sputum culture are often not available.

Clinical Diagnosis: EPTB

Extrapulmonary 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

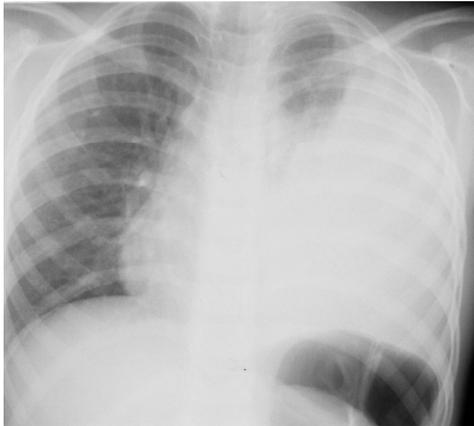
Clinical assessment in all cases should consider:

- ❖ **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** if cough and sputum is available
- ❖ **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 area	Fine needle aspiration when possible for culture 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 behaviour, vomiting (without diarrhoea), lethargic/reduced level of consciousness, convulsions, neck stiffness, bulging fontanelle, cranial nerve palsies	Lumbar puncture obtain CSF# CXR	Hospitalise for TB treatment §
Miliary TB	Non-specific, lethargic, 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

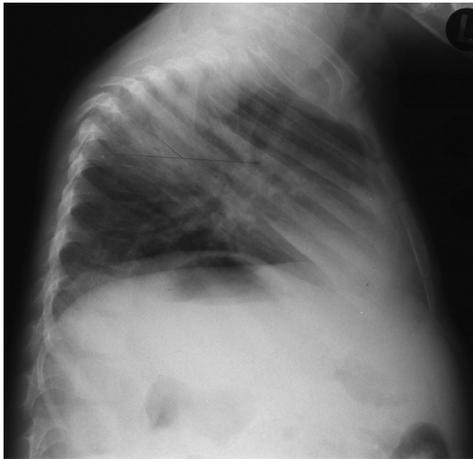
§ Referral may be necessary for investigation procedure and laboratory support as well as clinical care. If all options for referral have been explored and referral is not possible, start anti-TB treatment. Start anti-TB treatment immediately if TBM suspected



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 16
- Drug dosages are calculated according to weight and are listed in Table 2 on page 16
- 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 anti-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 anti-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 DOT provider 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

Table 1. Recommended treatment regimens for new patients in HIV endemic setting# (WHO, 2010)

TB disease category	Recommended regimen	
	Intensive phase	Continuation phase
All forms of PTB and EPTB except TBM and osteoarticular TB	2 HRZE	4 HR
TB meningitis Osteoarticular 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

HIV endemic setting i.e. countries where the HIV prevalence among adult pregnant women is $\geq 1\%$ or among TB patients is $\geq 5\%$

Note:

- Streptomycin no longer recommended for new patients
- Intermittent regimens not recommended in HIV-endemic setting

Table 2. Recommended dosages according to weight (WHO, 2010)

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

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
 - 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 anti-TB treatment

- Nutritional support should be provided for malnourished children if available

- Breastfeeding infants and children should continue to breastfeed while receiving anti-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 anti-TB treatment and then monthly thereafter

This is a critical part of effective TB treatment requiring a clear management plan. There is an example of a TB treatment card (Appendix 2) that could be copied and provided.

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 anti-TB drugs in children are well tolerated and safe.
- CXR is not required in follow-up if the child is responding well to anti-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 anti-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 anti-TB treatment

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

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

Poor adherence is a common cause of “treatment failure”. If a child stops anti-TB treatment for less than 2 weeks in the intensive phase and less than 2 months in the continuation phase and becomes symptomatic, then restart first-line anti-TB therapy.

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

Isoniazid preventive therapy (IPT) greatly reduces the risk of an infant or young child with TB infection from developing disease.

Important questions for any person commenced on anti-TB treatment

- i. Is the case smear positive?***
- ii. How many children in the household?***
- iii. What are the ages of the children?***
- iv. Is the child contact sick or well?***
- v. What is the relationship of the source case to the children?***
- vi. Is there anyone else in the household who is coughing?***

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

Refer to Appendix 1 (page 25) for a recommended approach to assessment of the child contact.

Any child contact with symptoms should be carefully assessed for TB disease

IPT 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

IPT must be given for a full 6 months to be effective. Dosage (10-15 mg/kg) is same as for treatment.

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

If source case is MDR TB, refer the children for contact management advice

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
 - Apply the same in the clinics

The child with TB and HIV

A comprehensive approach to management of both TB and HIV is critical.

- 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 generalised 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 NTP include child TB in funding and resource allocation, in policy guidelines/protocols and training opportunities in NTP. NTP 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 is smear-negative or not obtained.

Children are reported in same way as adults: includes: age, site of TB, gender, disease category, HIV status, outcome

Major differences to management of adults

Most cases not confirmed i.e. "smear-negative"
TST is an important tool for child TB diagnosis
Drug dosages need to be higher in mg/kg (Table 2, page 16)
Drug dosages may need to be adjusted with weight gain
Children tolerate 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. Default
- iii. Death
- iv. Transfer out
- v. Cure (for smear positive)

Engage all care providers

As part of the overall TB control activities, NTP need to coordinate and engage all relevant care providers to ensure adequate service provision through dissemination and implementation of 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 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)

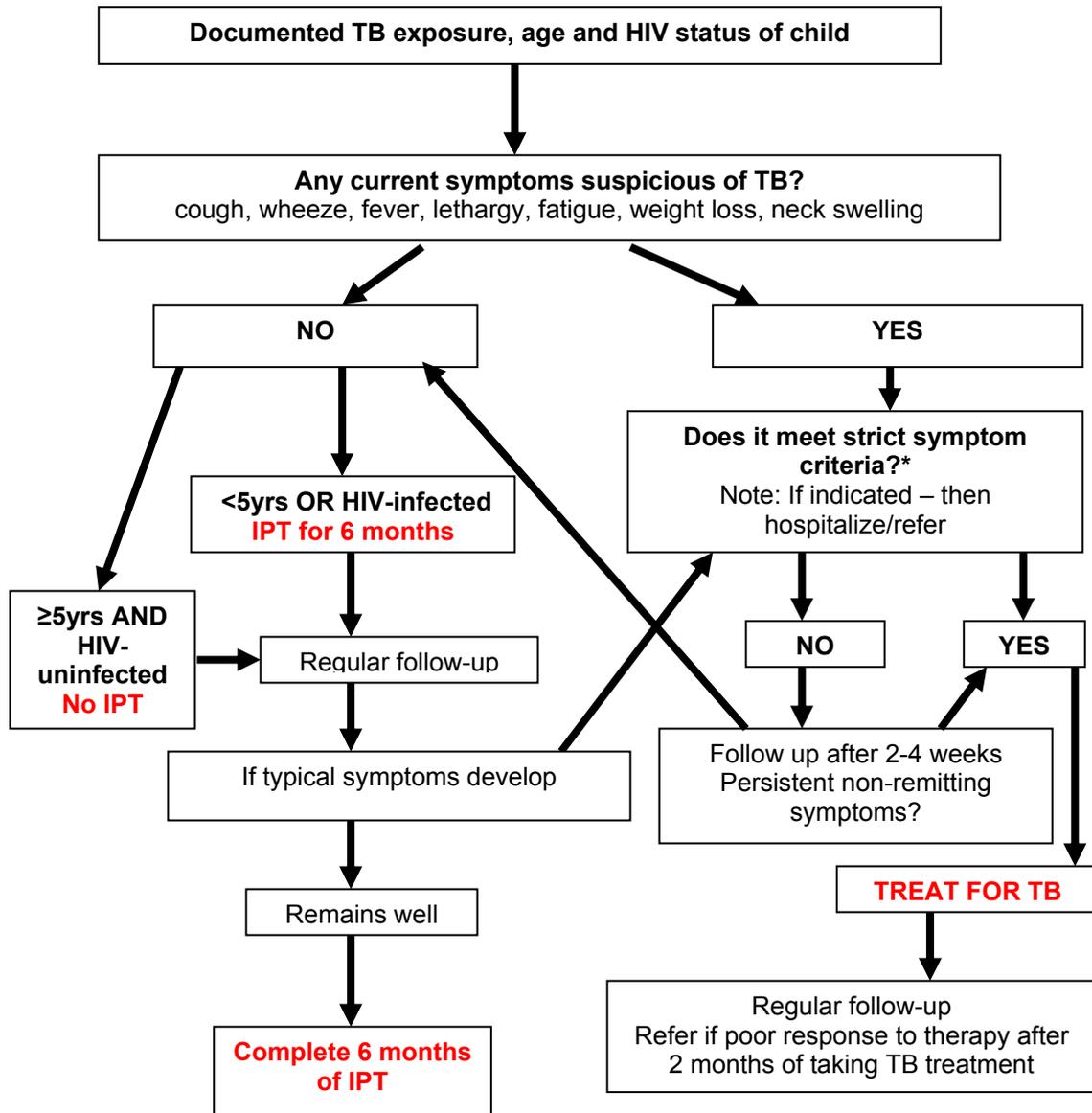
Abbreviations

ART	anti-retroviral therapy
CPT	cotrimoxazole preventive therapy
CXR	chest radiograph
DOT	directly observed therapy
EPTB	extra-pulmonary tuberculosis
HIV	human immunodeficiency virus
IPT	isoniazid preventive therapy
LIP	lymphoid interstitial pneumonitis
MDR	multi-drug resistant
NTP	National Tuberculosis control Programme
PcP	<i>Pneumocystis jirovecii</i> pneumonia
PTB	pulmonary tuberculosis
TB	tuberculosis
TST	tuberculin skin test

Resource materials

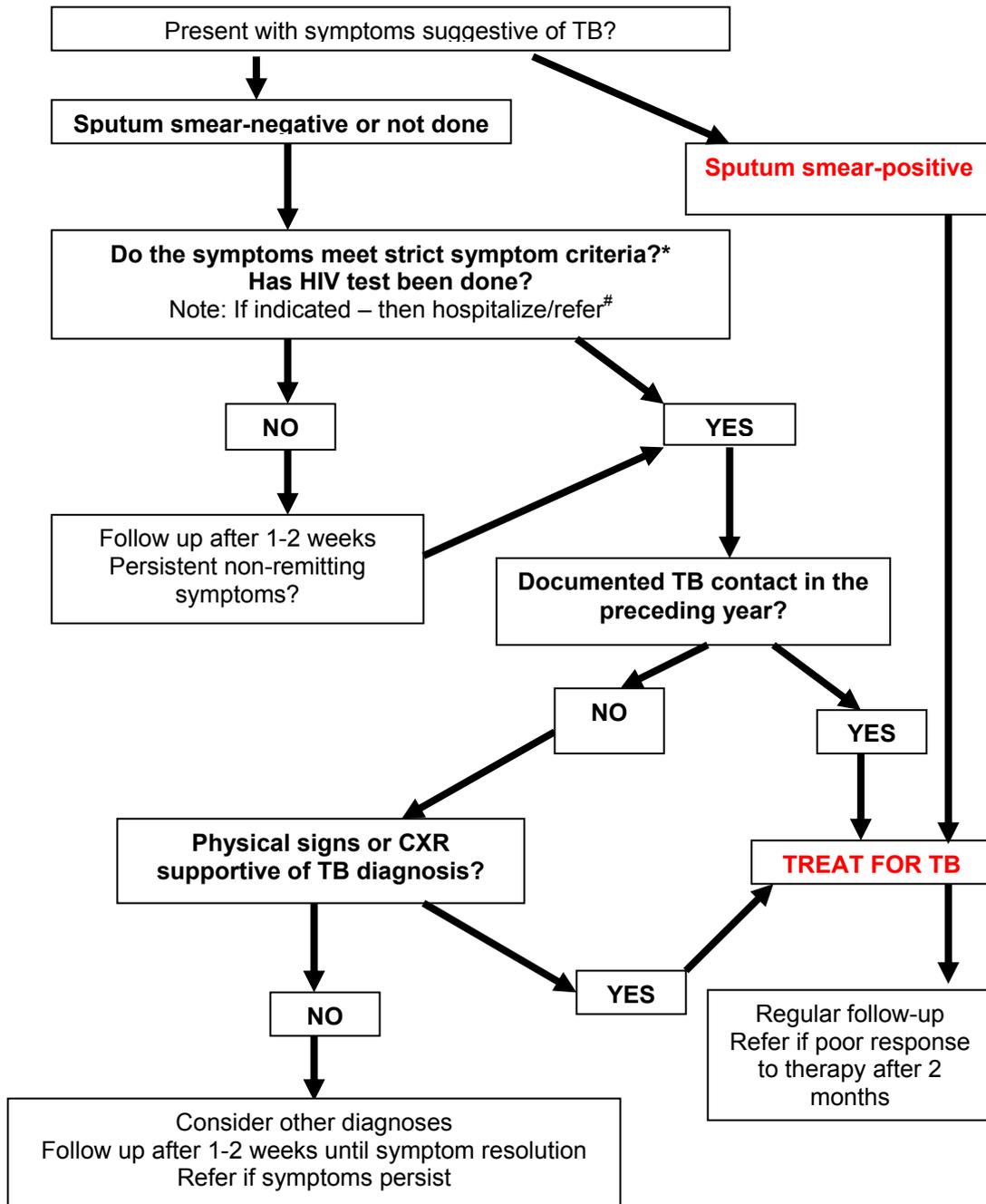
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1. GUIDANCE for the screening of children in close contact with a adolescent or adult with newly diagnosed pulmonary TB**



****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.

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



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

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

