Clinical Guideline for Treatment of Childhood Tuberculosis

Dr. Ahmed saeed

Consultant pediatrician

IGMH

Ministry of Health

Male' Republic of Maldives

Author: Dr. Ahmed Saeed, Consultant in pediatrics

Indhira Gandhi Memorial Hospital

Reviewers:

Dr. Ahmed Faisal, Consultant in Pediatrics IGMH

Dr. Sanjaya Shreshtha, Senior Consultant in Pediatrics ADK Hospital

Dr. Amit Bishwakarma, Consultant in Pediatrics Tree Top Hospital

Dr. Mohamed Abdel Wahab Areed, Consultant in Pediatrics IGMH

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List of abbreviations

AFB	Acid-Fast Bacilli
AP	anterior posterior
ART	Anti-retroviral treatment
CBC	Complete Blood Count
CMI	cell mediated immunity
CNS	Central nervous system
CRF	chronic Renal Failure
CXR	Chest x-ray
DM	Diabetes Mellitus
DOTs	Directly observed treatment strategy
DT	Dispersible tablet
e/o	Evidence of
ESR	Erythrocyte sedimentation ratio
f/u	Follow up
FNAC	Fine needle aspiration cytology
FTT	Failure to thrive
GA	Gastric aspirate
h/o	History of
HIV	Human Immunodeficiency Virus
I&D	Incision and drainage
IPT	Isoniazid Preventive therapy
IRIS	immune reconstitution inflammatory syndrome
LFT	Liver function test
LNs	lymph nodes
LTBI	Latent tuberculosis infection
MDR-TB	Multidrug-resistant tuberculosis
MTB	Mycobacterium Tuberculosis
NAATs	Nucleic Acid Amplification Tests
NB	Newborn
NTM	non tuberculosis meningitis
PCR	Polymerase chain reaction
PPD	Purified protein derivative
PTB	pulmonary tuberculosis
Rx	Treatment
s/o	sign of
STAC	SAARC Tuberculosis and HIV/AIDS centre

Susp	Suspension
Tab	Tablet
TB	Tuberculosis
TST	Tuberculin Skin Test
TU	Tuberculin unit
WHO	World health organization

I. Introduction

A. Epidemiology

Tuberculosis (TB) is an infectious disease caused by five closely related species of mycobacteria in which Mycobacterium Tuberculosis (MTB) is the most important cause of tuberculosis disease in human. MTB is an airborne infectious disease that is preventable and curable. It is among the top 10 causes of death among children worldwide. Children can present with TB at any age, but the most common age is between 1 and 4 years. According WHO, at least half a million children become ill with TB each year.

Maldives had estimated TB prevalence and incidence rate of all forms of TB respectively of 56 and 41 per 100 000 population. Total 131 notified new and relapse cases were detected, among the notified new and relapse cases 14 (11%) cases aged less than 15 years. Treatment success rate among new smear-positive cases was 84% for the cohort of patients registered in 2013.

Childhood TB (under 5 years) has been almost zero until recent years due to the high BCG coverage of infants. However due to the increased exposure rates of children to adults with active TB disease both locally and to the high TB prevalent countries in the region, childhood TB is on the rise.

Accurate diagnosis of MTB in children has long been difficult and current technologically advanced diagnostic tools available for adults fail to address the problems experienced in diagnosing TB in children. Similarly, trials of new drugs and development of pediatric formulations of standard first and second line drugs are lagging behind.

B. Tuberculosis in Children

TB is spread from person to person through the air by droplet nuclei with particles of 1 to 5μm in diameter that contain Mycobacterium tuberculosis. Droplet nuclei are produced when persons with pulmonary or laryngeal tuberculosis cough, sneeze, speak, or sing. They also may be produced by aerosol treatments, sputum induction and during bronchoscopy. However, only a small percentage of children who inhale the TB organism actually develop active disease.

C. Four factors determine the likelihood of transmission of MTB, following an exposure

a. Number of organisms being expelled into the air,
b. Concentration of organisms in the air,
c. Length of time an exposed person breathes the contaminated air and
d. Immune status of the exposed individual.

After inhalation, the droplet nucleus is carried down the bronchial tree and implants in a respiratory bronchiole or alveolus. Before the development of cellular immunity, tubercle bacilli spread via the lymphatics to the hilar lymph nodes and then through the bloodstream to more distant sites.

The tubercle bacillus grows slowly, dividing approximately every 25 to 32 h within the macrophage. MTB has no known endotoxins or exotoxins; therefore, there is no immediate host response to infection. The organisms grow for 2 to 12 wk, until they reach 10^3 to 10^4 in number, to elicit a cellular immune response.

Latent tuberculosis infection (LTBI) occurs after the inhalations of MTB, which is characterized by a reactive Tuberculin Skin Test (TST) and absence of clinical and radiological

manifestation of the Tuberculosis Disease. Infants and children with LTBI but not active tuberculosis disease are not infectious and thus cannot transmit the organism. But if left untreated LTBI have up to a 40% likelihood of developing in to active BT disease.

D. Key factors that put children at risk of acquiring TB

The risk of developing active TB disease in children following infection with M. tuberculosis is mainly determined:

a. Close contact with a known case of infectious TB (parents, siblings, close relative, caregivers, neighbors or teacher)
b. Immunosuppressive conditions (such as severe malnutrition, following Measles in the past 3 months, HIV/AIDS, receiving immunosuppressive therapy.
c. Age of the child.

Table 1: Age specific risk to progress to active TB disease, following primary infection with MTB in immunocompetent children

Age at primary infection(year)	Risk of progressing to active TB disease
<1	No disease, 50% Pulmonary TB, 30-40% Disseminated TB or TB meningitis 10-20%
1-2	No disease, 75-80% Pulmonary TB, 10-20% Disseminated TB or TB meningitis 2-5%
2-5	No disease, 95% Pulmonary TB, 5% Disseminated TB or TB meningitis <0.5%
5-10	No disease, 98% Pulmonary TB, 2% Disseminated TB or TB meningitis <0.5%
>10	No disease 80-90% Pulmonary disease 10-20% Disseminated TB or TB meningitis <0.5%

II. Case definitions of TB in children

- **Tuberculosis (TB)** is caused by Mycobacterium tuberculosis.
- **TB infection** is when a person carries the Mycobacterium tuberculosis bacteria inside the body. A positive tuberculin skin test indicates infection but a negative tuberculin skin test 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.
- **Index Case:** Usually an adult with smear positive pulmonary TB.
- **Close contact** is defined as living in the same household as, or in frequent contact with (e.g. child minder, school staff), an index case with PTB.
- **Pulmonary tuberculosis (PTB)** refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree.
- **Smear Positivity**

A child is defined as smear positive if any of the following is true:

a. AFB is detected via microscopy on either a sputum or gastric lavage sample.
b. MTB is isolated by culture on either a sputum or gastric lavage sample.
c. MTB is detected by MTB/RIF Gene X-pert on either a sputum or gastric lavage sample.

- **Extra-pulmonary tuberculosis (EPTB)** refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs.
- **Children** refers to 1 to 16 year age group
- **Infant** is a child of less than 1 year of age (0-12 month age group)

A. The complete case definition of TB is determined by

1. Confirmation of TB,
2. Site of TB
3. Result of any bacteriological results
4. Severity of TB disease
5. History of previous ATT
6. HIV status

All children with TB should be registered with NTP as pulmonary (smear positive or smear negative) or extra pulmonary TB and as either new case or previously treated cases.

WHO categories children as suspected, probable and confirmed cases of TB, based on exposure, poorly defined symptoms and CXR interpretation and bacteriology.

B. Suspected Tuberculosis

1. An ill child with a history of contact with a confirmed case of pulmonary tuberculosis
2. Any child
   - Not regaining normal health after measles or whooping cough
   - With loss of weight, cough and wheeze not responding to antibiotic therapy for respiratory disease
   - With painless swellings in a group of superficial nodes

C. Probable Tuberculosis

A suspect case and any of the following

- Positive (>10 mm) induration on TST
- Suggestive appearance on chest radiograph
- Suggestive histological appearance of biopsy material
- Favorable response to specific anti tuberculous therapy

D. Confirmed Tuberculosis

Detection by microscopy, culture, or MTB/RIF Gene X-pert from secretions or tissues

E. Contact with an Index Case

Defined as any child who lives in a household with an adult taking ATT or has taken such treatment in the past 2years

F. Drug resistant TB

Drug-resistant TB is a laboratory diagnosis and should be suspected in any child with the following features:

1. **Feature in the index case suggestive of drug resistant TB**
    - Contact with a known case of drug resistant TB
    - Previously treated for TB
    - Remains sputum smear positive after 3 months of treatment
    - History of treatment interruption

2. **Features in the child suggestive of drug resistant TB**

- Contact with a known case of drug resistant TB
- Not responding to standard ATT regimen
- Recurrence of TB after adherence to treatment is assured

III. Diagnosis of TB in Children

Diagnosis of childhood tuberculosis requires careful and thorough assessment of all the evidence derived form careful history, clinical examination and relevant investigations. Pulmonary TB is the most common form of TB is children. However, the majority of children with tuberculosis infection develop no signs or symptoms at any time and there are no specific features that can confirm the presence of TB in children.

A. Who should be evaluated for TB

1. Any child with history of exposure to an adult with Pulmonary TB or with evidence of documented TB infection (TST positive)
2. Any child with pneumonia, pleural effusion, a cavity or mass lesion in the lungs that does not improve with a course of standard antibiotics
3. Any child with fever of unknown origin, failure to thrive, significant weightless, severe malnutrition
4. Any child with a known immunosuppressive condition such as Measles in the past 3 months; whooping cough, HIV/AIDS, under immunosuppressive medications
5. Unexplained lymphadenopathy

B. Challenges in the diagnosis of TB in children

1. Symptoms are often non –specific
2. Disease is paucibacillary and microbiological diagnosis is often not possible
3. Difficult to obtain sputum
4. TST is often negative in malnourished children and disseminated TB
5. X-rays are often non specific

C. Recommended approach for diagnosing TB in children

a. History (focusing on contact, symptoms /signs suggestive of TB)

b. Clinical examination (including serial weight)

c. Specific Diagnostic modalities

- TST/IGRA
- Chest X-ray
- Bacteriological confirmation
  - MTB/RIF Gene X-pert
  - Microscopy, Culture
- Investigation for relevant EPTB
- Screening
  - HIV
  - Diabetes mellitus (new recommendation from STAC)

Although bacteriological confirmation of TB is not always feasible, it should be sought whenever possible by microscopy, culture or Xpert MTB/RIF of respiratory or non-respiratory samples as indicated by clinical presentation. A trial of treatment with anti-TB medications is not recommended as a method of diagnosing TB in children.

1. Symptom based diagnostic approach

Unlike adults, clinical Features of childhood TB are very vague and non-specific like poor appetite or poor growth. TB infection in children can progress to severe disease more rapidly in infants and young children.

2. Symptom criteria for diagnosing Pulmonary TB

Table 2. Symptoms based criteria for diagnosing TPB

1. Persistent non remitting cough for >2 weeks, not responding to a course of antibiotic and /or bronchodilators

AND/OR

2. Persistent documented fever (of >38C/100F) for >2 weeks after common causes are excluded.

AND/OR

3. Documented weight loss of >20% or not gaining weight during the past 3 months (specially if not responding to de-worming, and food and micronutrient supplementation) OR severe malnutrition

AND/OR

4. Fatigue and reduced playfulness

3. Symptoms and signs suggestive of extra pulmonary TB

Table.3 clinical features of extra-pulmonary tuberculosis

Symptoms and signs	Extra pulmonary TB
Painless, enlarged, mattered LN (>2x2cm), not fixed to underlying tissues usually in neck, not responding to a course of antibiotic	TB lymphadenitis. (Commonly cervical)
Cough shortness of breath	Pleural TB, Pericardial TB
Reduced playfulness, irritability, weight loss, headache, vomiting, drowsiness, altered sensorium	TB meningitis
Abdominal pain, altered bowel habits mass or ascites	Abdominal TB
Gibbus	Spinal TB
Chronic pain and swelling of joints usually single	TB arthritis

a. TB lymphadenitis

Tuberculous lymphadenitis usually occurs in the neck (cervical neck glands) but may involve axillary and inguinal lymph nodes. The enlarged nodes are usually painless and have developed over time (two weeks or more). They may be firm and discreet nodes at the beginning and become fluctuant and matted together. Later an abscess may form which may break through the overlying skin to form a chronic sinus.

Consider TB lymphadenitis in a child who has;

- Painless enlargement of cervical nodes

- No lesion on the head that could cause the lymph gland enlargement
- No response to antibiotics.

b. TB meningitis

TB meningitis is a very serious form of TB in children and characterised by gradual onset of symptoms. Complications include obstruction of cerebrospinal fluid flow, hydrocephalus, inappropriate anti-diuretic hormone secretion, hemi- or quadriplegia, convulsions, deafness, blindness and mental retardation.

Typical history and symptoms

- Contact with a person who has infectious TB.
- Lack of interest in playing or change in behaviour.
- Headache, especially if accompanied by early morning vomiting.
- Irritability, drowsiness, convulsions.
- Weight loss.

Physical signs

- Neck pain and resistance to neck flexion due to meningeal irritation (Kernig's sign).
- Cranial nerve palsies.
- Altered level of consciousness.

Investigations

1. Lumbar puncture

- CSF has raised protein, low glucose, low chloride, predominantly lymphocytes; the gram stain is negative and acid fast bacilli are seldom found.

2. GeneXpert for MTB detection and Rifampicin susceptibility testing
3. Mantoux skin test – The Mantoux can however be negative
4. Chest x-ray- may be normal in children with TBM

Always consider TB meningitis in children diagnosed with meningitis and not responding to treatment. These children should be URGENTLY referred to a hospital for management.

c. Miliary TB

This is a complication of primary TB in young children. It results from widespread blood borne dissemination of TB bacilli. Patients may present with systemic features such as low-grade fever, weight loss, fatigue and malaise. The patient may have a history of cough and respiratory distress.

Physical signs

- Lymphadenopathy,
- Hepatosplenomegaly,
- Fever, tachypnea, cyanosis, and respiratory distress.
- Other signs - papular, lesions on the skin or choroidal tubercles in the retina.

Investigations

- Chest x-rays
    - diffuse, uniformly distributed, small military shadows, “millet seed” appearance

d. Pleural effusion

Inflammatory tuberculous effusions may occur in any serous cavity of the body i.e. pleural, pericardial, peritoneal. They are common in older children and adolescents. Patients with pleural effusions may present with chest pains, breathlessness

Physical signs

- Decreased chest movement
- Stony dullness

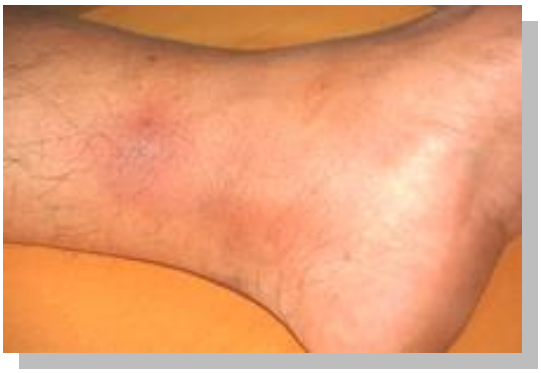
Investigations

- Chest x-rays
    - Tracheal/ mediastinal shift away from side of effusion
    - Unilateral or bilateral uniform, white opacity with a concave upper border
- Pleural aspirate
    - exudate, straw colored, high protein, high WCC, raised Adenosine
- Deaminase (ADA)
- Pleural biopsy and Gene Xpert

e. TB and diabetes Mellitus

People with diabetes are at higher risk of developing tuberculosis than those without diabetes. The link between tuberculosis and diabetes requires interventions that address both diseases. For example, screening for tuberculosis in people with diabetes and screening for diabetes in people with tuberculosis could offer opportunities to increase detection and prevent diabetes or tuberculosis-related complications.

4. Uncommon signs indicative of recent TB infection

Phlyctenular conjunctivitis- raised patch at the junction of the sclera and cornea surrounded by a red area of conjunctivitis. 	**Erythema nodosum-** raised, tender, purple patches on the shin 

IV. Investigations

A. Bacteriological confirmation

Every attempt should be made to confirm the diagnosis of TB in children, using whatever specimens and laboratory facilities are available, to demonstrate AFB. Commonly used methods are;

1. Gen-Xpert MTB/RIF

Gen-Xpert MTB/RIF should be offered rather than conventional microscopy and culture as the initial test in all children suspected of having TB, MDR TB or HIV-associated TB

Children suspected of having pulmonary TB but with a single Gen-Xpert MTB/Rif negative result should undergo further diagnostic testing and a child with high clinical suspicion for TB should be treated even if a Gen-Xpert MTB/Rif is negative

Gen-Xpert MTB/RIF would be used as a replacement test for usual practice for testing of specific non-respiratory specimens (lymphnodes and other tissues) from children suspected of having extra pulmonary TB. Suspected children with a single Gen-Xpert MTB/RIF-negative result should undergo further diagnostic testing, and those with high clinical suspicion for TB should be treated even if an Gen-Xpert MTB/RIF result is negative

Gen-Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test in testing cerebrospinal fluid specimens from children suspected of having TB meningitis

For CSF specimens, Gen-Xpert MTB/RIF should be used over culture if the sample volume is low or additional specimens cannot be obtained, in order to reach quick diagnosis. If sufficient volume of material is available, concentration methods should be used to increase yield.

Pleural fluid is a suboptimal sample for the bacterial confirmation of pleural TB using any method. The preferred sample is a pleural biopsy.

2. Smear Microcopy

Common ways of obtaining samples for smear microscopy

- Expectoration
- Gastric aspiration
- Sputum induction
- FNAC

3. Sputum collection for bacteriology

Sputum should always be obtained in children presenting with a chronic cough however, pulmonary TB in young children is usually paucibacillary and the collection of adequate samples is difficult.

4. Culture

Collection of specimen for culture is important in complicated cases or when there is concern of drug resistance TB. The probability of obtaining a positive TB culture increases when more than one sample is taken. Hence it's recommended to take at least 2 samples for culture.

B. Chest X-Ray

Chest radiography is useful in the diagnosis of TB in children. In the majority of cases, children with pulmonary TB have CXR changes suggestive of TB. Good-quality CXRs are essential for proper evaluation. CXRs should preferably be read by a radiologist or a healthcare worker trained in their reading. A lateral chest X- ray is helpful to evaluate hilar lymphadenopathy.

Chest X-ray changes are often non-specific. CXR changes suggestive of TB are summarized below.

1. The most common radiological signs of TB in children

- Increased density in the hilar region due to enlarged hilar lymph nodes, and/or abroad mediastinum due to enlarged mediastinal lymph nodes.
- Persistent opacity in the lung.

2. Less common radiological signs

- Compression of the airways due to enlarged lymph nodes. Partial occlusion may lead to segmental or lobar hyperinflation. Complete airway occlusion may cause collapse of a lung segment or lobe.
- Miliary pattern of opacification.
- Pleural effusions (usually in children > 5 years old).

Adolescent patients with TB often have CXR changes similar to adult patients. Pleural effusions and api- cal infiltrates with cavity formation are the most common presentations.

3. Radiological features require urgent hospital referral

i. Widespread fine millet-sized (1-2 mm) lesions indicative of disseminated or miliary TB.

ii. Severe airway obstruction (always evaluate the airways).

iii. Severe parenchymal involvement.

iv. Acute angulation of the spine (TB spine, gibbus)

Persistent calcification, which does not improve after a course of antibiotics, should be investigated for TB

C. Tuberculin Skin Test (Mantoux Test)

1. Interpretation of TST result

There is no correlation between the size of induration and likelihood of current active TB disease but the **reaction size is correlated with the future risk of developing TB disease**

a. ≥5mm is positive

- HIV-positive person
- Persons with nodular / fibrotic changes on Chest X-ray consistent with old healed TB
- Immunosuppressed patients.
- Patients on long term systemic corticosteroid therapy (> than six weeks) and those on a dose of prednisone ≥ 15 mg/day or equivalent.
- End stage renal disease

b. ≥10mm is positive

- Immigrants from high-prevalence countries
- Residents and employees of high-risk congregate settings (e.g., prisons, hospitals, homeless shelters, etc.)
- Infants, children, and adolescents exposed to adults in high-risk categories

c. ≥15mm is positive

1. Persons with no known risk factors for TB. Reactions larger than 15 mm are unlikely to be due to previous BCG vaccination or exposure to environmental mycobacteria.

2. Mantoux reversion

Reversion is defined as the change to a negative Mantoux result following a previous positive result. Generally this phenomenon is uncommon in healthy individuals, occurring in less than 10% of such people with a previously positive Mantoux.

3. False negative tuberculin reactions

1. Test done in incubation period (<3months) or before the hypersensitivity has developed
2. Severe malnutrition or other immune suppressive conditions
3. Measles within the last 3 months
4. Whooping cough
5. HIV infection
6. Corticosteroid therapy.
7. Overwhelming infection - e.g. TB meningitis, Miliary TB.

8. Wrong technique
9. Inactive tuberculin - Exposure to sunlight, high temp, storage for prolonged period after dilution

4. TST recommendations in Children

a. Children for whom immediate TST is recommended

1. Contact investigation
2. Children with radiographic or clinical findings suggesting TB disease
3. Children immigrating from endemic regions of the world
4. Children with travel histories to countries with endemic infection and substantial contact with indigenous people from such countries

b. Children who should have annual TST

1. Children infected with HIV
2. Incarcerated adolescents
3. Children at increased risk for progression of LTBI to TB disease
4. Children with medical conditions like DM, CRF, severe malnutrition and other immunodeficiencies

c. Situations where TST testing is NOT recommended

1. Past TST reactions ≥15 mm: repeating the test will provide no new diagnostic information and will create more anxiety
2. Previous TB disease: no useful diagnostic information will be gained and significant discomfort is likely

D. Other tests

- Baseline CBC, platelet, liver enzymes, renal function before starting ATT
- ESR is a non specific test for inflammation and has no role in confirming or excluding TB
- Serology and PCR are not recommended for routine diagnosis of childhood TB
- Novel T-cell assays (IGRAs) provide essentially same information as TST

E. Evaluation for suspected extra pulmonary TB

Most of the suspected extra pulmonary TB cases can be confirmed by histopathology or other special investigations. All forms may require an initial TST and Chest X-ray

Table 4: evaluation for common forms of extra pulmonary TB in children

Anatomical site	Investigation/procedure
Peripheral Lymphnodes	FNAC or biopsy
Military (Disseminated) TB	CXR, and LP (to exclude TBM)
TB Meningitis	LP, CT scan Brain
Tuberculoma of Brain	CT scan/MRI Brain
Pleural effusion	CXR, USG, Pleural tapping, Pleural biopsy
Abdominal TB	USG abdomen, Ascitic tapping
TB arthritis or Bone	X ray, USG, Joint fluid study, Bone/synovial biopsy
Pericardial TB	CXR, Echo, Pericardial tapping , biopsy
Skin and subcutaneous TB	Skin biopsy

Criteria for diagnosing sputum smear positive PTB

1. Two or more initial sputum smear examinations positive for AFB **OR**
2. One sputum smear positive for AFB and CXR findings consistent with active PTB **OR**
3. One sputum smear positive for AFB and plus sputum culture positive for M. tuberculosis

Criteria for diagnosing sputum smear negative PTB

1. At least three sputum smear negative for AFB **AND**
2. Presence of diagnostic feature strongly suggestive of PTB **AND**
3. Decision by a clinician to treat with course of ATT

Note:

Children who have both pulmonary and extra pulmonary TB should be classified under case definition of Pulmonary TB

V. Treatment of Tuberculosis in Children

A. Stop TB strategy

The Stop TB Strategy of WHO is aimed at reducing the worldwide burden of disease and thus in protecting children from LTBI and disease. Children usually have paucibacillary pulmonary disease and cavitation is rare. But children develop extra pulmonart forms of TB more often than adults. And severe and disseminated TB (TB meningitis, military TB) occurs specially in children under 5 years.

The management of children with TB should be in line with the Stop TB Strategy, taking into consideration the particular epidemiology and clinical presentation of TB in children. Treatment outcomes in children are generally good.

B. Objectives of treatment of T in children

1. Cure individual patients
2. Prevent death from active TB or its late effects
3. Prevent relapse of TB
4. Reduce transmission
5. Prevent development of drug resistant TB

C. Important things to do in a child diagnosed with TB

1. Assess for co-infections
2. Screen for diabetes mellitus
3. Screen for HIV infection
4. Provide psycho-social support to child and parents
5. Complete the TB Register
6. Ask about other children or adults in the household and screen them for TB

D. Pharmacokinetics of first line Anti-TB drugs

Rapid reduction of bacilli load is important to limit disease progression, terminate transmission and prevent drug resistance. This is achieved by bactericidal drugs that kill active bacilli and bacteriostatic drugs that kill dormant bacilli. This approach justifies the use multiple drugs for prolonged duration, yet with minimal toxicity

Table *5*: Pharmacokinetics of first line Anti-TB drugs

Drug	Pharmacokinetics	Common side effects
Isoniazid(H)	Bactericidal, rapidly metabolizing extra-cellular bacilli	Hepatitis, peripheral neuritis
Rifampicin(R)	Bactericidal, sterilizing, rapidly metabolizing intra-cellular bacilli	Hepatitis, thrombocytopenia
Ethambutol(E)	Bacteriostatic, rapidly metabolizing extra cellular bacilli	Optic neuritis
Pyrazineamide (P)	Sterilizing, extracellular bacilli that persist within the acidic centres caseating granulomas	Hepatitis, arthralgia
Streptomycin(S)	Bacteriostatic	Oto and nephrotoxic

Table 6: Dosages of first line Anti-TB drugs for children

Generic	Dose mg/kg	Range mg/kg	Max. dose mg/day	Available strength
Isoniazid	15	5-15	400	100mg 300mg
Rifampicin	20	10-20	600	100mg/5ml 150mg, 300mg
Ethambutol	20	15-25	750	400mg,600mg
Pyrazinamide	35	30-40	2000	400mg,500mg

- Pyridoxine: tablets 40mg

Regular weight-based dose adjustment is important in children during the course of treatment, as most of the children gain weight, especially during the intensive phase.

Table 7: Weight band tablet for FDCs in children

Weight bands (Kg)	Number of tables		
	Intensive phase		Continuation phase
	HRZ (mg/tablet)	E (mg/tablet)	HR (mg/tablet)
	75/50/150	100	75/50
4-7	1	1	1
8-11	2	2	2
12-15	3	3	3
16-24	4	4	4
25+	Children weighing more than 25kg are routinely treated with adult dosages and preparation		

E. Treatment regimens

1. Intensive phase

- Eliminate the bacterial load and prevent the emergence of drug resistant cases
- At least 3 bactericidal drugs used

2. Continuation phase

- Eradicates the dormant bacilli
- At least 2 bactericidal drugs used to continue and complete the Rx

1. Treatment regimen

- During the initial intensive phase a combination of four drugs (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol HRZ(E) are administered under observation daily for a period of two months (sixty doses).
- When the patient has completed the initial intensive phase of two months, first follow up sputum test is done, and continuation phase will start irrespective of sputum smear result.
- Similarly for smear negative cases, initial intensive phase HRZ(E) is administered for two months.
- Sputum smear is done at the end of 2 month, if smear is negative, the continuation phase will start.
- However if sputum smear is positive, then X-pert test will be done and if Mycobacterium is detected but RR not detected by test result, continuation phase will start.
- During the continuation phase, isoniazid and rifampicin (HR) are administered daily for 2 to 4 months

2. Treatment regimen for re-treatment cases

- During the initial intensive phase Rifampicin, Isoniazid, Pyrazinamide and Ethambutol, (HRZE) are given for the first two months, followed by the same drugs without streptomycin (HRZE) for another one month administered daily under observation. The initial intensive phase should be continued for three months.
- If the sputum smear is negative at the end of 3rd month, the continuation phase is started.
- If the sputum smear is positive at the end of 3rd month, X-pert test will be done. If RR is detected, patient will be shifted to DR register and if RR is not detected, the patient should then start the continuation phase.
- During the continuation phase, Isoniazid, Rifampicin, and Ethambutol (HRE) are administered daily for five months under observation.
- If the patient remains smear-positive after the end of five months, he/she is no longer eligible for the re-treatment regimen. Such patients are regarded as treatment failure & refer as MDR presumptive cases.

Table 9: Recommended treatment regimens for TB in children under 16years of age

TB diagnostic category	ATT regimen	
	Intensive phase	Cont. phase
Non severe, presumed drug-susceptible TB		
Smear negative pulmonary TB	2HRZ	2HR
Intrathoracic lymph node TB		
TB peripheral Lymphadenitis		
Severe, presumed drug-susceptible TB		
Extensive pulmonary Disease	2HRZE	4HR
Smear positive pulmonary TB		
Severe forms EPTB (other than TBM, osteoarticular TB)		
TB meningitis and osteoarticular TB	2HRZE	10HR
Relapse, Defaults, Treatment failure	2(HRZ)E/1(HRZ)E	4(HR)E
TB prophylaxis	3HR	
DR-TB	Individualized	regimens

Steroids

- Steroids are used for the management of complicated forms of TB, to improve survival and decrease morbidity.
- Prednisolone 1-2mg/kg/day
- Miliary TB, pleural effusion pericarditis or peritonitis- 4-8wks
- TB meningitis – 8-12wks

F. Retreatment

Treatment failure in children is rare but should be managed in the same way that treatment failure is managed in adults. The most likely cause for treatment failure or relapse within 6 months of treatment completion is failure to adhere to treatment. In children when anti-TB treatment fails or a relapse occurs, every effort should be made to find the most likely cause for the failure or relapse. Non-adherence is the commonest cause. There are multiple (psychosocial, social taboo, false feeling of cure, economic and practical) reasons why people are nonadherent.

G.Immune reconstitution

- Temporary exacerbation of symptoms, signs or radiographic manifestations sometimes occurring after starting ATT due to the recovery of immune system.
- Commonly occurs after initiation of ART in HIV infected children with TB, and is known as the immune reconstitution inflammatory syndrome (IRIS).
- ATT should be continued, although in some cases the addition of corticosteroids might be useful.

H. Referral to RMC, IGMH

The following children receiving treatment from DOT centers in islands should be referred to IGMH through NTP for assessment

a. All children with severe from of TB, (TBM, miliary TB, TB pericarditis and peritonitis, spinal and skeletal TB)
b. Poor response to ATT (no weight gain, persistent of symptoms after 2-3 months)
c. Side effects of drugs or severe and persistent symptoms of IRIS
d. Children suspected of having drug resistant TB

I. Follow up during treatment

- Treatment outcomes in children are generally good provided that treatment starts promptly and adherence is maintained until completion.
- The risk of serious adverse events in children associated with use of the recommended treatment regimens very low.
- Severe disseminated disease such as tuberculous meningitis is associated with high mortality and with high morbidity among survivors.
- All children receiving treatment for TB should be reviewed monthly for the first three months.

a. Assess for resolution of signs symptoms
b. Assess for side effects and toxicities of ATT
c. Monitor weight, and adjust drug dosage as per increased weight
d. Sputum examination at 2, 5 and 6 months of treatment for smear positive PTB
e. Follow up X-rays are advisable in all children with
    - Persistent symptoms or poor response to treatment

- Any new symptoms develop

f. Routine CBC, RFT or LFT are not required if no side effects observed.

g. Repeat of TST in not required during or after treatment.

J. Causes of deterioration during TB treatment

Whenever deterioration of symptoms are observed, ensure that Children may sometimes deteriorate or experience a worsening of symptoms or signs or radiological features despite adequate therapy. The most important questions to answer are:

- Is the drug dosage correct?
- Is the child taking the drugs as prescribed (good adherence)?
- Is the child HIV-infected?
- Is the child severely malnourished?
- Is there a reason to suspect drug-resistant TB (the index case has drug resistant TB or is a re-treatment case or is also not responding to therapy)?
- Is there another reason for the child's illness other than TB?

Suspect drug resistance in a child who fails to convert at 7 or 11 weeks after excluding non compliance to treatment and first line DST should be conducted. In cases where there was no initial bacteriological confirmation of disease, suspect failure when clinical symptoms are not improving or worsen and x-rays show disease progression. Any child with persistent symptoms or who deteriorates on TB treatment should be referred to Respiratory medicine clinic at IGMH for further assessment and care

K. Treatment adherence

All children should receive daily DOT by a trained DOT provider (community or family health worker or nurse involved in TB services) throughout the entire treatment as per the policy of NTP.

If this arrangement is not convenient for the family, trained and responsible non health care persons who do not have strong emotional ties with the patient (not the childs parents or immediate family) can provide DOT in such situations.

These arrangements must be approved in advance by the supervisory clinician and should be monitored closely to ensure that there are no problems.

Family members should be used to provide DOT only as a last option if a child or family does not agree to any of the above arrangements and there is a possibility for the caregivers not to report to NTP but obtain ATT from pharmacies from neighboring countries and do self administered therapy. This must again be decided by the supervisory clinician and should be very closely monitored by NTP. Not more than 2 weeks of medicines should be handed over to the family or work supervisor at a time

Family members should not be used as DOT providers in patients with drug resistant TB and patients at a high risk for non adherence

Children, their parents, other family members and other caregivers should be educated about TB and the importance of completing treatment. The support of the child's parents and immediate family is vital to ensure a satisfactory outcome of treatment.

Whenever possible, FDCs of drugs should be used to simplify drug administration and adherence. Patient treatment cards are recommended for documenting treatment adherence.

Adherence to the full course of therapy is frequently a challenge, especially as clinical improvement can be rapid; most children with TB will start to show signs of improvement after 2-4 weeks of anti-TB treatment.

On assessment at 2 months after the start of treatment, the possibility of treatment failure should be considered if a child who is receiving anti-TB treatment:

- has no symptom resolution or has worsening symptoms;
- shows continued weight loss;
- is sputum smear-positive

VI. Common side effects of first line Anti-TB drugs

Table 10: Adverse reactions of first line ATT

Drug	Adverse reaction	Monitoring	Comments
INH	Rash Hepatitis Peripheral neuropathy Inhibits cytochrome P450	Baseline hepatic enzymes Repeat if - baseline results are abnormal - adverse reactions	Hepatitis risk increases with age Pyridoxine 10-15 mg/kg may prevent peripheral neuropathy and CNS effects
RIF	Induce cytochrome – p450 GI upset, Rash Hepatitis Bleeding problems Flu-like symptoms Renal failure	Baseline CBC, platelets, and hepatic enzymes	Contraindicated or used with caution when administered with PIs and NNRTIs Colors body fluids orange
EMB	Optic neuritis Rash	Baseline and monthly tests of visual acuity and color	Not recommended for children too young

		vision	
PZA	Hepatitis Rash GI upset Hyperuricemia	Baseline uric acid and hepatic enzymes	Treat hyperuricemia only if patient has symptoms May make glucose control difficult in diabetics
SM	Ototoxicity Renal toxicity	Baseline hearing and renal function tests	Ultrasound and warm compresses to injection site may reduce pain

A. Hepatotoxicity

Drug induced hepatotoxicity is defined as

1. AST/ALT >= 3x upper limit of normal (ULN) with the presence of symptoms; OR
2. AST/ALT >5x ULN in the absence of symptoms; OR
3. Disproportional increase in alkaline phosphatase and total bilirubin.

It usually occurs during the first 3 months of treatment.

The incidences of hepatotoxicity are ranged as the following (from high to low): INH>PZA>RIF.

EMB can be used safely in patients with hepatic disease.

INH is contraindicated in patient with active hepatitis and end stage liver disease.

Management

1. Stop all anti-TB therapy

2. Perform serum liver enzyme levels: severe involvement indicated by - ALT >3 times (with symptoms suggestive of liver disease)

3. Screen for viral hepatitis

4. F/up the Symptoms Biochemical ALT level

5. When the ALT<2 times upper limit and symptoms resolved

6. Reintroduce medicines

a. RMP- gradual reintroduce in 48-72 hours (5mg/kg on Day-1, 10mg/kg on Day-2, 15mg/kg on Day-3)

b. Repeat ALT, if no rebound elevation gradually add in INH

c. Repeat ALT, if no rebound elevation occurs RMP/INH

7. Avoid PZA

8. Start alternative non-hepatotoxic drugs- Ethambutol + Streptomycin + Fluroquinolones especially in severe disease e.g. TBM, disseminated TB

9. A suggested regimen is 2SHE/10HE.

An expert should be involved in the further management of these cases.

B. Gastrointestinal intolerance

- GI upset symptoms are very common and usually occur in the first few weeks of therapy
- Any anti-TB drugs can cause GI upset

Management

- Recommend changing hour of drug administration, preferably closer to meal time
- If patient is not on DOT, medication can be taken at bedtime
- Take medication with a light snack.
- Avoid antacid 1 hour before and 2 hours after INH administration (aluminum salt-containing antacid reduces INH bioavailability)
- If GI symptoms persist or worsen;

- Rule out other possible causes of hepatotoxicity
- drugs induced GI upset
- Perform LFTs. If ALT/AST >=3x ULN, assume it is liver toxicity. Stop antituberculosis drugs.
- HYDRATION! Important to encourage patients to increase fluid intake.

D. Rash

All anti-TB drugs can cause rash. Management depends on its severity:

- Mild rash or itching →antihistamine (Benadryl) 30 minutes before ATT and continue ATT
- Petechial rash →CBC, if the platelet count is below normal, stop RIF and never restart it again. Monitor the platelet count until it returns to baseline.
- Erythematous rash with fever, and/or mucous membrane involvement:
    - STOP ALL drugs immediately
    - Rule out anaphylaxis and Stevens-Johnson Syndrome
- If severely ill with tuberculosis, try second-line drugs such as injectable streptomycin, amikacin) and any 2 oral agents
- If rash has improved substantially, restart ATT one by one and after every 3 days.
- start with RIF followed by INH, PZA and EMB
- If rash recurs at any point; STOP last added

E. Peripheral neuropathy

- The primary agent that causes peripheral neuropathy is INH.

- Commonly seen in the malnourished (vitamin B6 deficiency), diabetes, HIV, renal failure and breastfeeding women.
- It is dose related and uncommon at conventional INH dosage.
- Commonly observed in:
    - Malnourished,
    - HIV-infected
    - Breastfeeding infants

Management

- Prevention is the key!
- Pyridoxine (vitamin B6) prophylaxis 10 mg Pyridoxine for every 100 mg INH is recommended

F. Optic neuritis

Causes a decrease in visual acuity and may lead to irreversible blindness

Management

- Baseline and monthly visual acuity tests while on EMB
- More than 10% visual loss is considered significant
- If there is a defined fluctuation of 2 lines of the Snellen chart, STOP the EMB immediately and permanently if decrease in visual acuity is confirmed.
- EMB is not recommended in children under 5 years old and children whose visual changes are difficult to monitor.

VII. Drug Resistant Tuberculosis

Even though there is no drug resistant TB documented in children in Maldives, drug resistant Tb is increasing among the adult population. Drug resistant TB in children usually develops within 12 months of infection. Contact tracing and close follow up of children exposed to drug resistant TB should be done with high priority.

A. Type of drug resistances

1. **Mono drug resistance:** MTB is resistant to only one of the first line ATT
2. **Poly drug resistance:** MTB is resistant to more than one of the first line ATT other than both INH and Rifampicin
3. **Multi drug resistance (MDR-TB):** MTB is resistant to both isoniazid and rifampicin with or without resistance to other first line ATT
4. **Extensively drug resistant (XDR-TB):** MDR-TB that is also resistant to any one of the fluoroquinolones and to at least one of three injectable second line ATT (Amikacin, Capreomycin, Kanamycin)

B. Feature of Drug Resistant TB

Drug resistant TB should be suspected in any child with the following features

1. Index case

- Remaining smear positive after 3 months of first line ATT
- H/O previous ATT interruption or recurrence after completion of treatment

2. Child

- H/O contact with a know case of MDR-TB

- Not responding to adhered standard first line ATT
- Recurrence after completing ATT

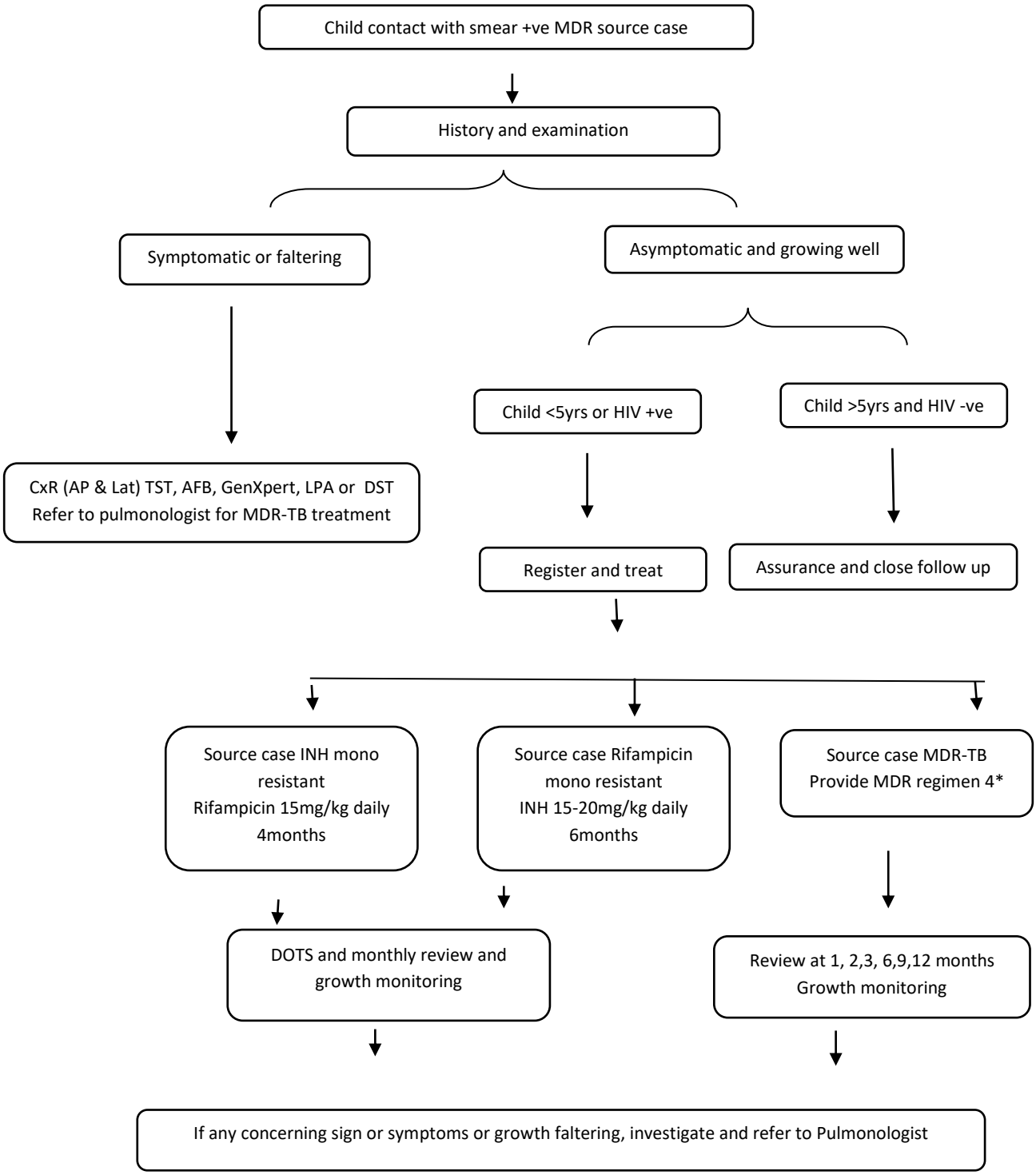
C. Diagnosis of MDR-TB in children

MDR-TB is a laboratory diagnosis. Younger children may not be able to produce specimen, but every effort should be made to obtain specimens for culture. Appropriate specimens for culture include induced sputum, tissue biopsy, gastric aspirate, urine and /or stool.

D. Duration of treatment

There is little evidence on treatment of MDR-TB in children; typically, therefore, programmes treating children with MDR-TB use WHO guidelines for treatment of adult patients. Treatment duration depends on the extent of the disease; in most cases, the intensive phase will last at least 8 months and total duration of treatment will be at least 18 months. All treatment should be given daily and under direct observation. The optimal duration of treatment for MDR-TB in children is unknown. It may be that children with early, non-extensive disease require treatment for shorter periods than adults, but this is an area that requires research. Making the MDR -TB regimen in detail is beyond the scope of this guideline

Figure 1. Management of child contacts of MDR TB



VIII. TB in children living with HIV

Globally, TB is the most common opportunistic infection and leading cause of mortality in people living with the human immunodeficiency virus. Children living with HIV infection have increased risk of TB exposure, infection, progression to disease, and TB-related morbidity and mortality. This risk is influenced by the degree of immune suppression

A. Treatment of TB in HIV-Infected Children

- TST is less sensitive in children living with HIV than in HIV-negative children; induration of >5 mm is considered positive if the child is living with HIV
- Children living in settings where the prevalence of HIV is high should be treated with a four-drug regimen (HRZE) for 2 months followed by a two-drug regimen (HR) for 4 months at the dosages.
- should not be treated with intermittent regimens
- Each child should be assessed 2 weeks after the start of ATT then reviewed monthly with clinical monitoring, which should include symptom assessment, weight measurement, assessment of adherence to treatment
- All children should receive isoniazid for an additional 6 months after completion of treatment
- Additional therapy recommended for HIV-infected children with TB, which may help to improve TB treatment outcomes, includes co-trimoxazole preventive therapy, the early start of ART

B. Co-trimoxazole preventive therapy

Daily prophylaxis – co-trimoxazole preventive therapy (CPT) - prolongs survival in children living with HIV and reduces the incidence of co-morbidities. It also reduces the risk of co-infections such as pneumocystis pneumonia in HIV- exposed infants and children

Table 11: Cotrimoxazole prophylaxis

Age	Recommended daily cotrimoxazole prophylaxis
Under 6 months of	20 mg trimethoprim (TMP) + 100 mg sulfamethoxazole (SMX)
Under 5 years	40 mg TMP + 200 mg SMX
5 years or older	80 mg TMP + 400mg SMX

C. Antiretroviral therapy

Antiretroviral therapy (ART) in children living with HIV aims to

- improve the length and quality of life
- reduce HIV-related morbidity and mortality by reducing the incidence of opportunistic infections
- reduce the viral load, restore and preserve immune function
- preserve normal growth and development.

ART improves TB treatment outcomes for children living with HIV.

TB treatment should be started first, followed by ART as soon as possible thereafter (and within 8 weeks of the start of TB treatment). For those with a CD4 count below 50 cells/mm3, ART should be provided within 2 weeks of the start of TB treatment.

Table 12: first-line ART

Age	Treatment
Children younger than 3 years	Protease inhibitor (PI)-based regimen in combination with ABC or zidovudine (AZT)
Adolescents and children older than 3 years	Regimens comprising a non-thymidine nucleoside reverse-transcriptase inhibitor (NRTI) backbone (tenofovir disoproxil fumarate (TDF) or abacavir (ABC) + lamivudine (3TC)) and one non-nucleoside reverse-transcriptase inhibitor (NNRTI) efavirenz (EFV)

Table 13: When to start ART in children

Age	When to start
Infants (<1 year)	Treat all individuals regardless of CD4 count
1 year to <5 years	Treat all individuals (children ≤2 years or with WHO stage 3 or 4 or CD4 count ≤750 cells/mm^3 or <25% as a priority)
5 years and above	WHO stage 3 or 4 or CD4 ≤500 cells/mm^3 (CD4 ≤350 cells/mm^3 as a priority)

IX. Maternal Tuberculosis

All pregnant women who are exposed to a person with smear positive TB should be thoroughly assessed and a clear distinction has to be made between LTBI and active TB disease.

- TST should be done in all exposed pregnant women (pregnancy does not alter the response to TST and there have been no adverse reactions on women or fetus).
- Whenever the TST is positive, a complete history and physical examination is mandatory and if clinical manifestations of TB disease are present, CXR (with appropriate abdominal shielding) should be obtained.
- IPT is differed till delivery in asymptomatic women
- Pregnant women with active TB should be treated with 2HRE+4HR
- Once on treatment for at least 2–3 weeks, she is generally no longer infectious and it is less likely that the baby will become infected.
- If a pregnant woman is found to have pulmonary TB shortly before delivery, then the baby, and if possible, the placenta should be investigated for evidence of congenital TB infection

A. Congenital Tuberculosis

Neonates are at greater risk of developing serious form of extrapulmonary tuberculosis, including meningitis, miliary TB and bone etc.

B. Signs and symptoms of TB in Neonates

Clinical manifestations of TB neonates are very nonspecific and vary in relation to the duration, mechanism and location in the infant.

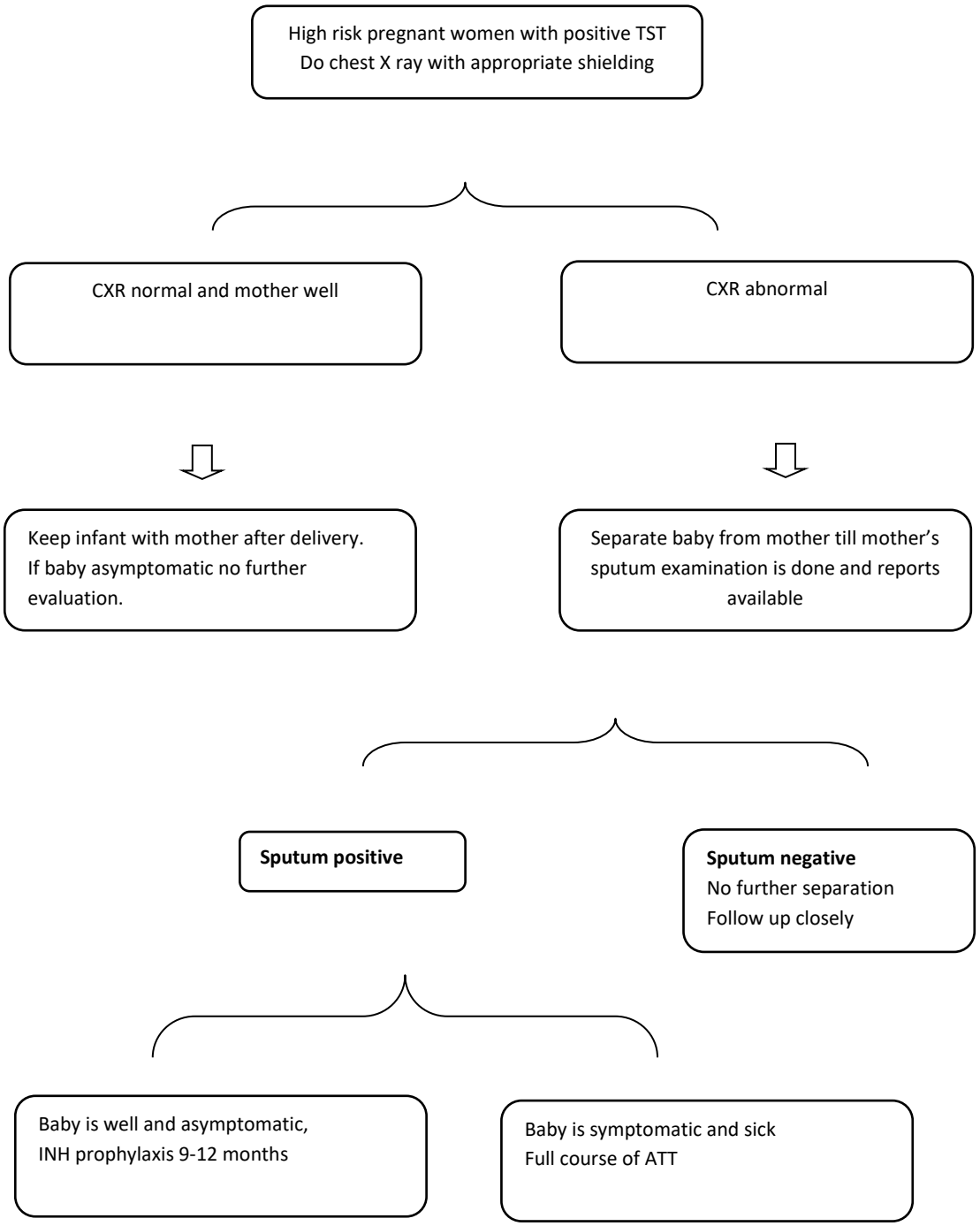
Table 14. Clinical manifestation of TB in new born

Clinical manifestation	Percentage (%)
Live and spleen enlargement	76
Respiratory distress	72
Fever48	48
Lymphadenopathy	38
Abdominal distension	24
Lethargy and irritability	21
Ear discharge	17
Skin papules	14

C. Investigating a newborn for TB

- All neonates with suspected TB should have a TST, CXR, LP and cultures done immediately after birth.
- Placenta should be sent for culture and histopathology

Figure 2. Evaluating high risk women and newborn for congenital TB



D. Treatment for tuberculosis in newborn

- Infants with active disease should receive 2 (HRZ+amikacin) +4HR
- Infants with TB meningitis should receive 2 (HRZ+amikacin) +7 to 10 HR and prednisone 2mg/kg 4-6 weeks

E. Neonates with TB exposure in the nursery

- Neonates exposed to TB in the nursery have a low risk if acquiring TB disease, but they can acquire infection.
- If the exposure is considered significant, do TST and start IPT immediately (no need to wait for TST report)
- If first TST negative, do a second TST at 3 months, if negative stop IPT and give BGC, and closely monitor for symptoms.
- If TST positive, minimum 9 months IPT recommended for neonates.

F. Infant of a breastfeeding mother with smear-positive PTB

- A breastfeeding infant has a high risk of infection from a mother with smear-positive PTB, and has a high risk of developing TB.
- The infant should receive 9 months of isoniazid preventive therapy, followed by BCG immunization.
- An alternative policy is to give 3 months' isoniazid, then perform a TST.
    - If TST is negative, isoniazid should be stopped and BCG vaccination given.
    - If TST test is positive, isoniazid should be continued for another 3 months, after which it should be stopped and BCG given.

- Breastfeeding can be safely continued during this period.

G. When to separate the newborn from the mother?

- Mother has active disease (until infant is receiving IPT and mother is non-infectious).
- Mother is ill enough to require hospitalization
- Mother expected to become non-adherent with her Rx
- Drug resistant TB

X. Prevention of TB in Children

A. Childhood BCG immunization

A single dose of BCG vaccine should be given to all infants as neonatal BCG vaccination provides substantial protection against the more severe types of disseminated TB, such as miliary TB and tuberculous meningitis, to which infants and young children are particularly susceptible

In children who are known to be HIV-infected, BCG vaccine should not be given because of the increased risk, reported from some settings, of severe and often fatal disseminated BCG disease

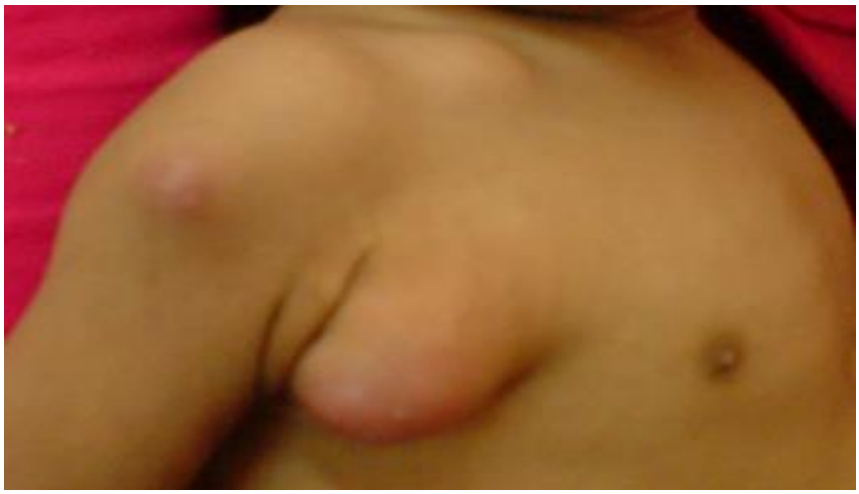
1. BCG (BACILLE CALMETTE-GUÉRIN) VACCINATION

- Strain of M. bovis attenuated by subculture
- Administration – 0.1ml, intra-dermal
- Age – during infancy, single dose, including asymptomatic children.
- Extremely safe in immunocompetent host
- Local ulceration and regional suppurative adenitis – 0.1-1%.

- 50% effective in preventing pulmonary TB in adults and children.
- Protective effect for disseminated and meningeal TB – 50-80%.
- BCG vaccination administered during infancy has little effect on incidence of TB in adults, suggesting that the effect of vaccine is time limited.

2.BCG adenitis in HIV-negative

- Estimated incidence 3-15%
- Associated with vaccine technique
- No evidence of benefit of systemic or local TB therapy
- Role of surgery:
    - FNAC staining C/S and GenXpert); purulent or non-resolving lesions
    - Small masses – observation
    - Large/painful masses – repeated aspiration or I&D



BCG vaccination in HIV infected children

BCG vaccination SHOULD NOT be given to infants or children with known HIV infection because of the risk of disseminated BCG disease

B. Contact screening and LTBI treatment

Latent tuberculous infection is defined as a state of persistent immune response to stimulation by M. tuberculosis antigens with evidence of clinically manifest TB. TB preventive treatment is one of the key interventions recommended by WHO to achieve the End TB Strategy targets

1. Purposes of screening child contacts

a. Identify symptomatic children (i.e. children of any age with undiagnosed TB disease) and provide prompt treatment
b. Provide preventive therapy for susceptible individuals (i.e. all asymptomatic children under 5 years of age

2. High risk groups who should be routinely screened

- children who live in the same household with a person diagnosed with smear and/or culture positive PTB
- HIV positive children
- children less than five years
- children with severe malnutrition

The systematic screening should include a symptom screen followed by thorough history taking, clinical examination, chest x-ray and bacteriological testing. For all those with a positive symptom screen, a chest x-ray will be done to screen for PTB in children.

If the child is the index case with TB, active case finding should be undertaken to determine the source case.

Information about any person in the household diagnosed with or has symptoms of TB and other possible places of exposure should be obtained from the parent or guardian.

Table 15: Definitions used in contact screening

SOURCE CASE	A case of pulmonary TB (usually smear positive) which results in infection or disease among contacts
CONTACTS FOR SCREENING	All children aged under 5 years (whether sick or well) and children older than 5 years if symptomatic, who are un close contact with the source case.
CLOSE CONTACT	Living in the same household as the source case or in frequent contact with the source case (close relatives, neighbors, friends, teachers etc.), in the past 1 year

Children usually acquire TB from adults with active pulmonary tuberculosis. Children usually develop disease within 2 years of exposure and most (90%) cases develop within the first year. Therefore, **history of close contact with a patient with smear positive pulmonary TB within the last year is a strong indication of possible TB.**

Clinical assessment alone is sufficient to decide whether the contact is symptomatic or not. Hence, routine evaluation of exposed contacts does not require CXR or TST. Enquire if the suspected index case;

- Is receiving TB treatment for the first time?
- is adherent to treatment?
- is responding to the treatment?

3. Method

a. Clinical examination.

b. TST/IGRA

c. Chest x-ray P/A and Lat view.

d. Evaluate for **Window Period** (A second TST should be placed 12 weeks after the last known exposure to infectious TB).

1. Who should receive IPT

a. All infants and children <5 years who have a **positive TST result but with no evidence** of TB disease.

b. All infants and children <5 years of age, even with negative TST (<5mm), **who have been close contacts** of infectious persons within the past 3 months (window Period).

2. TB preventive therapy (TPT) for LTBI

- Initiate therapy even before the TST result is available.
- The recommended duration is HR for 3 months (alternatively, INH alone for 6 to 9 months)
- INH 10mg/kg and Rifampicin 15mg/kg is given daily in a single dose.
- Pyridoxine (vitamin B6) 10 mg for every 100 mg INH is recommended

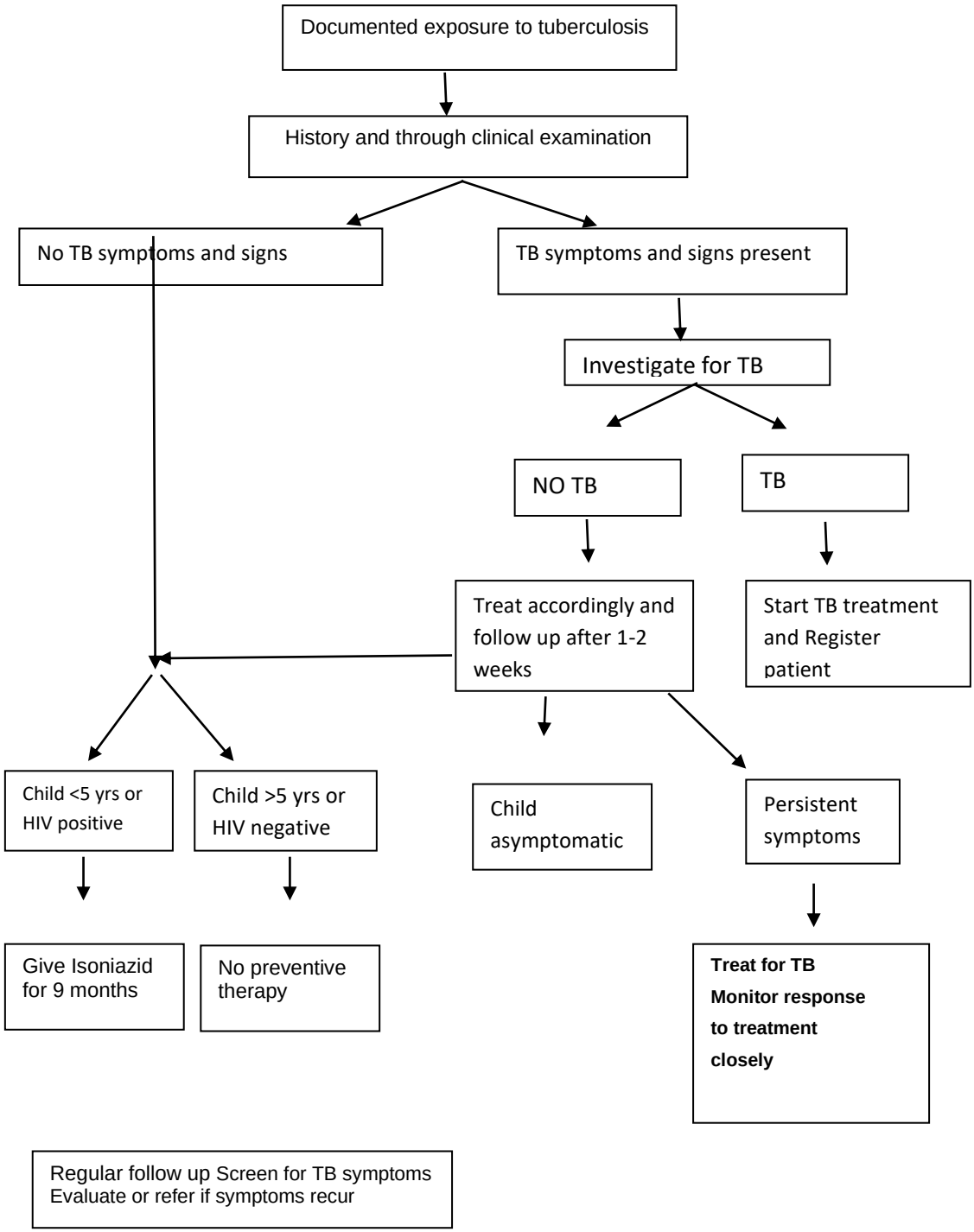
3. When to discontinue IPT

The recommended minimum duration is 3months for all TST positive asymptomatic children < 5 years

4. Prevention of TB in children living with HIV infection

All children living with HIV should be screened for TB and all children (and their families) with TB should be offered HIV testing and counselling.

Figure 3. Contact screening and INH prophylaxis



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