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# Standard Treatment Workflow (STW) for the Management of PAEDIATRIC INTRATHORACIC TUBERCULOSIS (PULMONARY, PLEURAL, MEDIASTINAL)

## ICD-10-A15

## WHEN TO SUSPECT?

- Documented, persistent unexplained fever for 2 weeks or more
- Unremitting cough for 2 weeks or more
- Unexplained documented weight loss of ≥ 5% in last 3 months
- No weight gain despite adequate nutrition
- Unexplained loss of appetite
- Chest pain (specific to pleural effusion)
- Contact with TB patients in past 2 years

## EXAMINATION

- Temperature, Weight, Mid Arm Circumference (MAC), Lymphadenopathy, cold abscess, discharging sinus
- Chest examination findings depend upon underlying pathology like consolidation, pleural effusion etc.

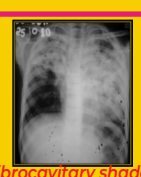
## INVESTIGATIONS

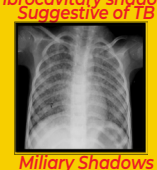
### Essential

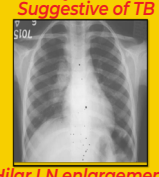
- Chest x-ray
  - › TB suggestive: Hilar/ paratracheal lymph nodes, fibrocavitory disease, Miliary pattern
  - › Non Specific : effusion, consolidation, bronchopneumonia, other shadows etc.
- Sputum/Induced Sputum/Gastric Lavage/ Aspirate /pleural fluid for NAAT
- Smear examination **(if NAAT unavailable)**
- If facilities exist, send aliquot of sample for culture, **if NAAT negative for MTB**
- Pleural tap**: Gross, Cytology, Biochemistry, NAAT, MGIT/LJ, ZN if NAAT not available

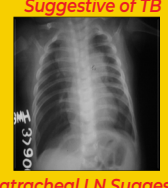
**If can't be done at primary level then refer

**Do HIV testing for all cases with TB**


Fibrocavitary shadows Suggestive of TB


Miliary Shadows Suggestive of TB


Hilar LN enlargement Suggestive of TB


Paratracheal LN Suggestive of TB

### Desirable

- Chest x-ray of family members

### Optional (to be done in institutions)

- CECT scan
- Pleural Biopsy
- Image guided (USG/CT) mediastinal LN biopsy
- Bronchoscopy & BAL

### DO NOT DO

- TST/Mantoux test
  - › Overemphasized, supportive only
  - › Not to diagnose TB or to start ATT on basis of +ve TST ONLY
- Serological tests- IGRA (Quantiferon/Quantiferon-Gold etc)
- Pleural fluid ADA

## DIAGNOSTIC ALGORITHM

### ALGORITHM FOR PEDIATRIC INTRATHORACIC TB AMONG CHILDREN WITH NO RISK FACTORS FOR DRUG RESISTANCE

- Persistent Fever ≥2weeks, without a known cause and/or
- Unremitting cough for ≥2weeks and/or
- Weight loss ≥5%; or no weight gain in past 3 months despite adequate nutrition; or failure of nutritional rehabilitation in babies with SAM
- With or without contact with patient with Pulmonary TB in past 2 years

**Chest X-ray**

- **CXR suggestive** → Sputum/GA/IS for approved NAAT for *MTB*
  - **MTB +ve** → **Microbiologically confirmed TB case** → Rif resistance +ve follow DRTB pathway; Rif resistance -ve Give 1st line ATT
  - **MTB -ve** → Persistent shadow & symptoms → Give antibiotics (Amoxyclav or Amoxicillin & avoid quinolones, linezolid) Skip if already taken → Sputum/GA/IS for approved NAAT for *MTB*
- **CXR Non specific shadows** → Give antibiotics (Amoxyclav or Amoxicillin & avoid quinolones, linezolid) Skip if already taken → Sputum/GA/IS for approved NAAT for *MTB*
- **Pleural Effusion** → Pleural fluid for NAAT, cytology, biochemistry & Sputum/GA/IS for NAAT for MTB
  - **MTB +ve** → **Microbiologically confirmed TB case**
  - **MTB -ve** → Straw colored, exudative effusion → **No alternative diagnosis treat as clinically diagnosed probable TB case**
- **CXR Normal**
  - Check for EPTB
  - Needs detailed investigation for TB/ alternate diagnosis. May need CECT chest / other investigations as per symptoms
  - Consider referral to higher center for further investigations

- Look for significantly enlarged peripheral LN & test LN aspirate for MTB
- Repeat NAAT with good sample/ alternative sample (BAL/aspirate) as per feasibility
- May seek review from a higher centre

→ MTB +ve → **Microbiologically confirmed TB case**
→ MTB -ve or if repeat test not feasible → **No alternative diagnosis treat as clinically diagnosed probable TB case**

### PEDIATRIC TB FURTHER WORK-UP ALGORITHM UNDER U-DST

**Presumed TB cases** → **NAAT**

- **MTB -ve** Clinically diagnosed TB case with no risk factors for DRTB → Treat with standard regime 2HRZE/4RHE; Add Pyridoxine 10 mg/day
- **MTB +ve**
  - **Rif resistance -ve** → Reinvestigate for nonresponse including for DRTB → **Repeat NAAT**
    - No response in 4 weeks → Treat with standard regime 2HRZE/4RHE; Add Pyridoxine 10 mg/day
    - Rif resistance -ve → FQ and/or SLI Resistance
  - **Rif resistance +ve$** → **FL-LPA SL - LPA***
    - **FL-LPA****
      - H Resistant Not detected → Treat with standard regime 2HRZE/4RHE; Add Pyridoxine 10 mg/day
      - H Resistant (inhA and/or KatG mutation) Eto resistance (inhA mutation)

$RR detected in new case with no risk factors for DRTB needs retesting if only MTB detected is very low as it makes Rif resistance detection less reliable
*SLLPA may be done directly if smear +ve else send for MGIT followed by SLLPA or LC DST (Mfx 2.0, Km, Cm, Lzd)
**LPA may be done directly if smear +ve else send for MGIT followed by FLPA to evaluate for H (inhA and/ or KatG mutn) and Eto (inhA) resistance

| TYPE OF PATIENTS | TB TREATMENT REGIMENS |
|---|---|
| Microbiologically confirmed RS Pulmonary TB | 2HRZE + 4HRE |
| Clinically diagnosed Pulmonary TB | |
| Drug sensitive previously treated TB (recurrent, failure, treatment after default)* | |

*DR TB algorithm-DST

| | |
|---|---|
| ISONIAZID (H) | 7-15 mg/kg (maximum dose 300mg/day) |
| RIFAMPICIN (R) | 10-20 mg/kg (maximum dose 600mg/day) |
| PYRAZINAMIDE (Z) | 30-40 mg/kg (maximum 2000mg/day) |
| ETHAMBUTOL (E) | 15-25 mg/kg (maximum 1500mg/day) |

| WEIGHT BAND | Number of tablets (dispersible FDCs) | | | |
|---|---|---|---|---|
| | Intensive phase | | Continuation phase | |
| | HRZ 50/75/15 | E 100 | HR 50/75 | E 100 |
| 4-7 kg | 1 | 1 | 1 | 1 |
| 8-11 kg | 2 | 2 | 2 | 2 |
| 12-15 kg | 3 | 3 | 3 | 3 |
| 16-24 kg | 4 | 4 | 4 | 4 |
| 25-29 kg | 3 + 1A* | 3 | 3 + 1A* | 3 |
| 30-39 kg | 2 + 2A* | 2 | 2 + 2A* | 2 |

*A=Adult FDC (HRZE = 75/150/400/275; HRE = 75/150/275)

- Consider steroids in miliary TB with hypoxia, Endobronchial TB massive bilateral effusion with distress
- Prednisone dose 2 mg/kg daily or Dexamethasone 0.6 mg/kg/day for 4 weeks
- Reduce dose gradually over next 4 weeks before stopping
- Pyridoxine 10 mg/day for 6 months
- Nutritional support
- Treat co-morbid conditions: HIV, SAM

## MONITORING

**When to assess**

- Within 2 weeks of starting therapy for checking that- correct dose, combination of drugs is being taken, adherence and tolerance to drugs
- Then every month till completion of treatment

**What to assess**

- Appropriateness of therapy:
  - Correct combination, acceptance/tolerance
  - Counsel about need to complete & not miss on doses (Inform, if doses are missed)
- Response to therapy:
  - Clinical (symptoms, adverse effects, weight, dose revision)
  - X-ray at end of therapy
  - Do X-ray for worsening at any time OR slow resolution OR persistent symptoms at end of IP
  - NAAT is not appropriate follow up tool for monitoring progress of disease
  - Smear examination at end of treatment (to declare outcome)
  - Repeat microbiological test (smear, MGIT, NAAT) at end of IP & at end of therapy, if still symptomatic or any deterioration/failure to respond
- After treatment completion: follow up patients clinically at end of 6, 12, 18 & 24 months

## MANAGING TREATMENT INTERRUPTIONS (NON-ADHERENCE)

- **Interruption up to 4 weeks** → Resume therapy (Restart if missed within 1st 4 weeks)
- **Interruption over 4 weeks** → Reinvestigate for DRTB
  - Rif resistance not detected → Retreat with 1st line drugs and Check for INH resistance and treat
  - Rif resistance detected → Treat as MDRTB

- In case interruption happens in CP & on retrieval, the patient has no clinical evidence of active disease & tests for DRTB are negative, the remaining treatment course to be completed
- Resons for interruption should always be evaluated & addressed in all cases (Address myths/fear or any intolerance)

## ABBREVIATIONS

**ADA**: Adenosine Deaminase
**BAL**: Broncho-alveolar lavage
**CBNAAT**: Cartidge-based Nucleic Acid Amplification test
**CECT**: Contrast enhanced CT
**CP**: Continuation phase
**CT**: Computed tomography
**DRTB**: Drug resistant TB
**DST**: Drug sensitivity test
**EPTB**: Extra-pulmonary TB
**ETO**: Ethionamide
**FDC**: Fixed dose combination
**FL-LPA**: First line - Line probe assay
**FQ:** Fluoroquinolones
**GA**: Gastric aspirate
**H**: Isoniazid
**HIV**: Human Immunodeficiency virus
**HRZE**: Isoniazid; Rifampicin; Pyrazinamide; Ethambutol
**IGRA**: Interferon Gamma Release assay
**IS**: Induced sputum
**LN**: Lymph node
**MAC**: Mid Arm Circumference
**MTB**: Mycobacterium Tuberculosis
**NAAT**: Nucleic acid amplification test
**PPD**: Purified Protein Derivative
**RIF**: Rifampicin
**SAM**: Severe acute malnutrition
**SLI:** Second line injectables
**SL-LPA**: Second line - Line probe assay
**TST**: Tuberculin skin test
**USG**: Ultrasonography
**ZN**: Ziehl Neelson

## REFERENCES


1. *National TB Elimination Programme, Central TB Division. Training Modules for Programme managers & Medical Officers. Ministry of Health & Family Welfare, Government of India https://tbcindia.gov.in/index1.php?lang=1&level=1&sublinkid=5465&lid=3540 Last access on 06 March, 2022.*
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