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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 (caseating granulomas with Langerhans giant cells, epithelioid cells & lymphocytes)
- 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

Microbiologically confirmed TB case

- 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 → Rif resistance +ve follow DRTB pathway; Rif resistance -ve Give 1st line ATT

→ 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
  - Rif resistance +ve$ → **FL-LPA SL - LPA***
    - Rif resistance -ve → Repeat NAAT
    - FQ and/or SLI Resistance
    - H Resistant (inhA and/or KatG mutation) Eto resistance (inhA mutation) → **FL-LPA****
      - H Resistant Not detected
      - No response in 4 weeks → Treat with standard regime 2HRZE/4RHE

$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
- 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

- 2 weeks: For adherence, correct dose, combination & 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 (Educate & 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

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