Paediatric DRTB DIAGNOSIS

Diagnosing DRTB in children

#1: Clinical

Screen for TB symptoms

STRONGLY suspect DRTB in children with a DRTB household contact and presenting with TB symptoms (persistent cough / not playing / fever and failing to thrive)**.** Examine the child for any signs of TB. Look for lymphadenopathy and determine z-score for weight and for height.

#2: Immunological - help determine risk

Higher risk in HIV +ve children (ALWAYS TEST FOR HIV) and Children <5 years. Children in primary school who are HIV negative have relatively low risk of developing active TB in comparison.
Mantoux test can be helpful to confirm child has been TB EXPOSED. A positive Mantoux does NOT confirm active TB and a negative Mantoux does NOT exclude it.

#3 Radiological CXR

Do A CXR – this is an essential investigation for TB in children. Look for hilar lymphadenopathy and other features suggestive of TB.

#4 Bacteriological Confirmation

ALWAYS send a sample for bacterial confirmation: do a GXP and DRTB reflex

- Induced sputum (best yield)
- Gastric aspirate
- FNAB of significant lymph nodes

#6 Antibiotics

ALWAYS give a trial of antibiotics (Amoxycillin 30mg/kg tds for 5 days) and review symptoms and repeat CXR before starting Rx.
Do not rush to start a symptomatic child on DRTB treatment.

Prophylaxis for exposed children:

Asymptomatic child of confirmed MDRTB contact and < 5 year or HIV positive

Ethambutol (20-25mg/ kg)
Levofloxacin(15-20mg/kg)
INH (10-15mg/kg)
For 6 months

Key: Am (Amikacin) / Lvx (Levofloxacin) / Mox (Moxifloxacin) / Cfz (Clofazamine) Eto (Ethionamide) / Z (PZA) / Hh (High dose INH) E (Ethambutol)

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Nkqubela TB Hospital

RRTB / MDRTB Short Regimen 9-11 months
Children<12yrs

Inclusion criteria

- Children <12 years or <30kg with RR / MDRTB single mutation / Rif Mono
- Uncomplicated disease PTB / EPTB e.g. lymphadenopathy, Pleural effusion

Exclusion criteria

- Prior exposure to 2nd line anti-TB agents >1 month
- PreXDR/ XDR / MDRTB with dual mutation
- Contact has XDR / PreXDR / MDR Dual mutation / Treatment failure
- Complicated / Severe EPTB (disseminated TB / TBM / TB osteoarticular)
- Extensive lung disease e.g. bilateral severe cavitation
- If clinician unsure if the patient meets the criteria for short regimen
- HB <8g/dl or neutrophils <0.75 or platelets <50 (cannot use LZD) – discuss with expert at LZD cannot be used

Children 6-12 years (weight 15-30kg)

4-6 months (Intensive phase)

$LZD_{(2m)}$ +(DLM^{*}_{6m} or PAS) + LFX + CFZ + Z + H^{h} + E

5 Months (continuation phase)

LFX + CFZ + Z + E

- *Delamid preferred age 6-12 (weight 15-30kg) Apply through NCAC
- Children < 6years use PAS
- Use PAS if DLM not accessible
- Delamanid >35kg 100mg bd / 20-35 kg: 50mg bd / 10-25kg 25mg bd (dosing not confirmed)

Children <6 years (weight <15kg)

4-6 months (Intensive phase)

$LZD_{(2m)}$ + PAS + LFX + CFZ + Z + H^{h} + E

5 Months (continuation phase)

LFX + CFZ + Z + E

Delamanid and BDQ may not be used in children <6 years old

Principles

- Always consult with an expert
- Linezolid can be omitted if uncomplicated TB (non-cavitory /unilateral):
  - 5-15 kg 15mg/kg od; 16-24kg 12mg/kg od; >24 kg 10mg/kg od
- Do monthly FBCs in children on LZD
- Intensive phase is 4 months and may be extended to 6 months depending on smear conversion.
- INH: If Kat G or InhA mutation: continue for full four to six months.
- Also see adult guidelines for more details

Key: H^{h}: Isoniazid / LZD: Linezolid / LFX: Levofloxacin/Eto: Ethionamine /PZA: Pyrazinamide/BDQ: Bedaquiline /E:Ethambutol/ TRD: Terizidone /DLM: Delamanid NCAC: National Clinical Advisory Committee

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RR TB / MDRTB Long Regimen (18-20m) Children <12yrs

Inclusion criteria

- RR / MDRTB with prior exposure to 2nd line anti-TB agents >1 month
- MDRTB with dual mutation (Kat G and inhA)
- PreXDRTB with INJ resistance but sensitive to FLQ
- RR / MDRTB with known contact with MDRTB Dual mutation
- RR / MDRTB Complicated / Severe EPTB (TB spine / pericardial / disseminated)
- RR / MDRTB Extensive lung disease e.g. bilateral severe cavitation
- RR / MDRTB If clinician unsure if the patient meets the criteria for short regimen

Exclusion criteria

- Any patient with FLQ resistance or close contact with FLQ resistance (present to NCAC)
- TB meningitis (see separate regimen)

Children <12 years (weight 15-30kg)

6-8 months (Intensive phase)

(BDQ_{6M} or DLM_{6m} or PAS) +LZD + LFX + CFZ + TRD+(H^h * or Eto*)

12 Months (continuation phase)

PAS (if used in Intensive phase) LFX + CFZ + TRD+(H^h *or Eto*)

- The Intensive phase is 6-8 months depending on **culture conversion** and clinical response.
- Extend intensive phase to 8 months if
  - slow clinical response
  - bilateral pulmonary disease with extensive cavitations
  - delayed culture conversion at 4 months
  - Where 2nd line LPA uninterpretable or FLQ susceptibility not confirmed

Principles

- Culture negative may be treated for shorter duration e.g. 15months depending on effective drugs
- Use DLM as preferred option (until BDQ available for <12years).
  - If neither available use PAS for full duration of treatment
- *If InhA mutation present use INH 15-20mg/kg/day. If Kat G present use Eto. If both mutations present do not use either INH or Eto.
- All children eligible for long regimen must be discussed with an expert

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XDRTB & FLQ resistant TB regimens Individualised Children < 12yrs

Inclusion criteria

- FLQ resistant TB (e.g. PreXDR with FLQ resistance)
- XDRTB
- Treatment failure on RR / MDRTB regimen

Principles: Always discuss with expert

- Treatment regimens should be individualised considering the history and DST result
- Intensive phase with minimum 4 drugs known or predicted to be effective
- Continuation phase minimum 3 drugs known or predicted to be effective
- A history of a drug used for >1month with persistent smears or positive cultures: consider probable resistance to that drug and do not use it as a core drug. This includes a patient who was started on MDRTB regimen but DST results were delayed.
- Drugs exposed to previously > 1year on positive cultures should not be included in regimen

EXAMPLE Children Individualised regimen

6-8 months (Intensive phase)

PAS + DLM_{6m} (or BDQ if possible) +LZD + CFZ + TRD +
+ Z + (Eto or H^h)*

12Months (continuation phase)

PAS + LZD + CFZ + TRD + Z + (Eto or H^h)*

- The Intensive phase is 6-8 months depending on **culture conversion** and clinical response
- In children under 3 omit the Delamanid

Adverse events /Substitutions

- *Use H^h if inhA/mutation / Eto if Kat G mutation / neither in dual mutation

Discuss

- All <12 year old with FLQ resistant TB
- Resistance suspected or detected to core drugs
- Patient or Contact has had treatment >1m with LZD, BDQ, DEL or CFZ in the past
- Core drugs contraindicated or patient cannot tolerate core drugs
- Previously treated for XDR / PreXDR for >1month
- Diagnosed of FLQ resistance >1month on short regimen

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