PEDIATRIC DR-TB:

Treatment with a Focus on Co-Morbidities and Adherence

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Objectives

- To discuss a general approach to the major comorbid conditions that occur in children with DR-TB
- To review the management of DR-TB and HIV
- To discuss malnutrition and DR-TB
- To review diabetes and DR-TB
- To discuss orthopedic problems seen in DR-TB
- To review other pulmonary problems seen with DR-TB

To discuss adherence strategies in pediatric populations
Children with DR-TB and comorbidities

- Little data on comorbidities in this group (HIV is the exception)
- Data taken from literature on adults with MDR-TB and children with pan-susceptible TB
- Integrated care provides the best possible outcomes
Other Illnesses Occurring with TB

Children with TB often have other illnesses (co-morbid conditions) along with TB. These could be:

• caused by the TB

• occur at the same time as the TB

• present before the child got TB

Children do better with their TB if these other illnesses are aggressively treated
Basic Principles of Treating Co-Morbid Conditions

• Treatment of other illnesses should occur at the same time as treatment for MDR-TB.

• Treatment for both conditions should occur at the same place but care should be taken to separate infectious children with MDR-TB from other sick people.

• Avoid giving medicines that interact or have overlapping toxicities.
Common Co-Morbid Conditions

- HIV
- Malnutrition
- Diabetes mellitus
- Orthopedic problems
- Asthma/Reactive Airway Disease
HIV and MDR-TB in Children

• High prevalence (22.2%) of MDR-TB seen in HIV exposed and infected children in South Africa (Hesseling et al., IJTLID, 16:192-5, 2012).

• Excellent outcomes can be achieved if HIV treated within days to weeks after starting MDR-TB treatment (Satti et al., PLoS ONE, 7(5):e37114, 2012)

• Poor outcomes (25% treatment success) seen in adolescents with co-morbid MDR-TB and HIV (Isaakidis et al., PLoS ONE, 8(7): e68869, 2013)
Treatment of HIV and MDR-TB

- Treatment of HIV and TB can be difficult, due to drug-drug interactions and overlapping toxicities
- Start treatment for HIV and TB as soon as possible
- Assess for other opportunistic infections
Algorithm for Management of Children on Treatment for MDR-TB and HIV

Child diagnosed with MDR-TB

Child is HIV positive and already on HAART

Start MDR-TB treatment as soon as possible

Avoid if possible or monitor closely:
- d4T (stavudine)
- The combination of efavirenz and cycloserine/terizidone
- The combination of tenofovir and injectables

Treatment focus on co-morbidities
Algorithm for Management of Children on Treatment for MDR-TB

1. Child diagnosed with MDR-TB

2. Child is
   - Found to be HIV positive
   - or
   - Known to be HIV positive but not yet on HAART

3. Aim to start HAART two weeks after starting MDR-TB treatment

4. Watch for signs of IRIS:
   - Worsening symptoms or signs (respiratory or lymphadenopathy)
   - Fever
   - Weight loss
   - Abdominal pain

5. Treat with steroids if IRIS detected
   - If severe or life-threatening consider stopping HAART and restarting when MDR-TB more established

6. Avoid if possible or monitor closely:
   - D4T ( stavudine)
   - The combination of efavirenz and cycloserine/terizidone
   - The combination of tenofovir and injectables

Treatment focus on co-morbidities
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Treatment for Malnutrition

- If a child does not show improvement in nutritional status, this may be a sign their TB is not being controlled.

- Children with MDR-TB require more calories because of the high metabolism associated with TB infection.

- Malnutrition centers and wards are high yield screening site for TB.
Monitoring Nutritional Status

• All children should get baseline height, weight and mid-upper arm circumference (MUAC).

• If the MUAC indicates acute malnutrition, acute nutritional interventions are needed.

• Height and weight should be assessed at monthly follow ups.

• Weight-for-age and weight-for-height should be plotted for children less than 5 years old.

• Body mass index (BMI), should be plotted for children 5 to 19 years old.
Treatment focus on co-morbidities

Weight-for-age BOYS
6 months to 2 years (percentiles)

Weight for age gain is acceptable

Weight-for-height BOYS
2 to 5 years (percentiles)

Weight for height loss is worrisome
Improving Nutrition

- Many children with MDR-TB live in poverty, and their families are unable to meet their basic nutritional needs.
- Vitamin B6 should be prescribed for all children undergoing treatment for TB.
- Prescribing a number of other vitamins can increase pill burden and may not be well absorbed.
- It is preferable to give children nutritious foods that have vitamins already naturally in them.
Suggestions for Improving Nutrition

• Provide a family food basket during treatment.

• Know the resources in the community that offer food assistance (e.g. non-governmental organizations, religious organizations and community groups).

• Recommend that the child eat several small, high calorie meals a day.
Asthma/Reactive Airway Disease and TB

- Asthma may increase risk of acquiring TB in children (Eisenhunt, M., Peds. All and Imm., 24: 98, 2013)

- TB may lead to the development of asthma/reactive airway disease (Jung, A., Ped. Resp. Reviews, 13: 123-9, 2012)


- Corticosteroid use (inhaled, oral) can be safely used provided patient on adequate therapy for TB (de Benedictis, F. and Bush, A. , Am. Rev. Resp. Dis. and Crit. Care Med., 185: 12-23, 2012)
Asthma (and other reactive airway disease)

- Active MDR-TB can make existing lung disease worse or cause reactive airway disease
- Bronchodilators should be used for maintenance and rescue treatment
- Inhaled corticosteroids can be safely used in children with MDR-TB
Orthopedic Problems

- TB in children can affect the spine (Pott’s disease) or joints.

- If possible, children should be referred to an orthopedic doctor or a physical therapist.

- Children should be evaluated for the need for braces or other support devices.

- The braces could be made from local materials.

- Simple physical therapy regimens can be designed to be done at home.
Diabetes and DR-TB

• DM is a risk factor for MDR-TB (Bates, M. et al., PLOS One, 7(7):e40774, 2012)


• Higher rates of recurrence seen with DM and DR-TB (Franke, M., et al., CID, 56: 770-6, 2013)

Interactions between Diabetes Mellitus and TB

- Blood sugars may fluctuate in people with acute MDR-TB.

- Medications used to treat TB may make controlling glucose more difficult.

- TB medications and diabetes medications may have overlapping toxicities (oral antihyperglycemics).

- TB drugs may make effects of diabetes worse (for example, peripheral neuropathy).
Treatment in Diabetes Mellitus and TB

- More frequent monitoring of blood sugars is necessary.

- Insulin dosing may need to be adjusted for tighter control, especially in the early stages of TB treatment.

- Patients should be provided with adequate calories to ensure a healthy weight gain.
Additional Recommendations

- Simple physical therapy treatments, like cupping (to help the child clear lung secretions) can be done by the family at home.

- All children with MDR-TB should have all of their vaccines. It is important to verify immunizations at each appointment.
Comorbidities

• Common comorbid condition in children with MDR-TB include HIV, malnutrition, DM, orthopedic problems, and asthma.

• Optimal management of comorbid conditions key to ensuring good MDR-TB outcomes.

• All children with any form of TB should undergo HIV testing and start ART in a timely fashion.

• Comorbid conditions may persist even after MDR-TB is cured.
Treatment focus on co-morbidities
Adherence

- Adherence to medications means that the child takes all of their medications at all the times that they should.
- Adherence can be difficult because of the long time needed for treatment and that taking the medications can be difficult.
- Directly observed therapy (DOT) should be used.
- Hospitalization for treatment is not always necessary; community based DOT should be used whenever possible.
Suggested Ways to Improve Adherence

- Explain to the child and caregiver in a way that they both can understand, the importance of taking the medications properly.
- Avoid restraining the child or using nasogastric tubes. If you must use these, recheck every day to decide if they are still needed.
- Try to have a relationship with the child and give them some control over the process. For example, let them hold the medication spoon or decide on the order to take the medications.
Suggested Ways to Improve Adherence

• It may be easy for the health care worker to give all the medications at the same time, but this might be overwhelming for the children.

• Consider dosing medications two or three times a day. Even with once daily dosing, some meds could be given in the morning and some at night, as long as it is not taken more than once every 24 hours.

• The drug that is causing the problem can be changed for another drug, as long as the new drug is still effective against the child’s TB strain.
Suggested Ways to Improve Adherence

• Caregivers must understand how the child should take their medications properly, be involved in treating the child, and help make decisions to improve adherence.
• Incentives should be provided to the child on a daily or weekly basis, depending on age.
• Examples include: wall charts, singing a favorite song, or eating a special food. For older children, cell phone minutes often work well.
• Incentives should also be provided to the person taking care of the child.
Suggested Ways to Improve Adherence

- Remember that children are often far more adherent than health care providers think that they are.
- Non-adherence may be a sign of psychological or emotional distress.
- Try to give good social support and understanding to the child and the caregiver.
Community-Based Care Improves Adherence

- First studies on MDR-TB in children done in the community (Farmer and Kim, 1998; Mukherjee et al., 2000)
- Treatment supports or CHWs provide quality care; should be paid
- Allows for early recognition of problems
- Leads to innovative, community appropriate solutions
Summary Points Regarding Adherence

- Children at different ages will have different adherence needs; adherence needs change over time.
- Age-appropriate partnerships with children and their caregivers are key to improve adherence.
- Some adverse effects are very real and if treatment modifications can be made without affecting regimen integrity, these should be considered.
- Family situations that affect adherence should be addressed.
- Community-based care support adherence.
Thank You!

Treatment focus on co-morbidities