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

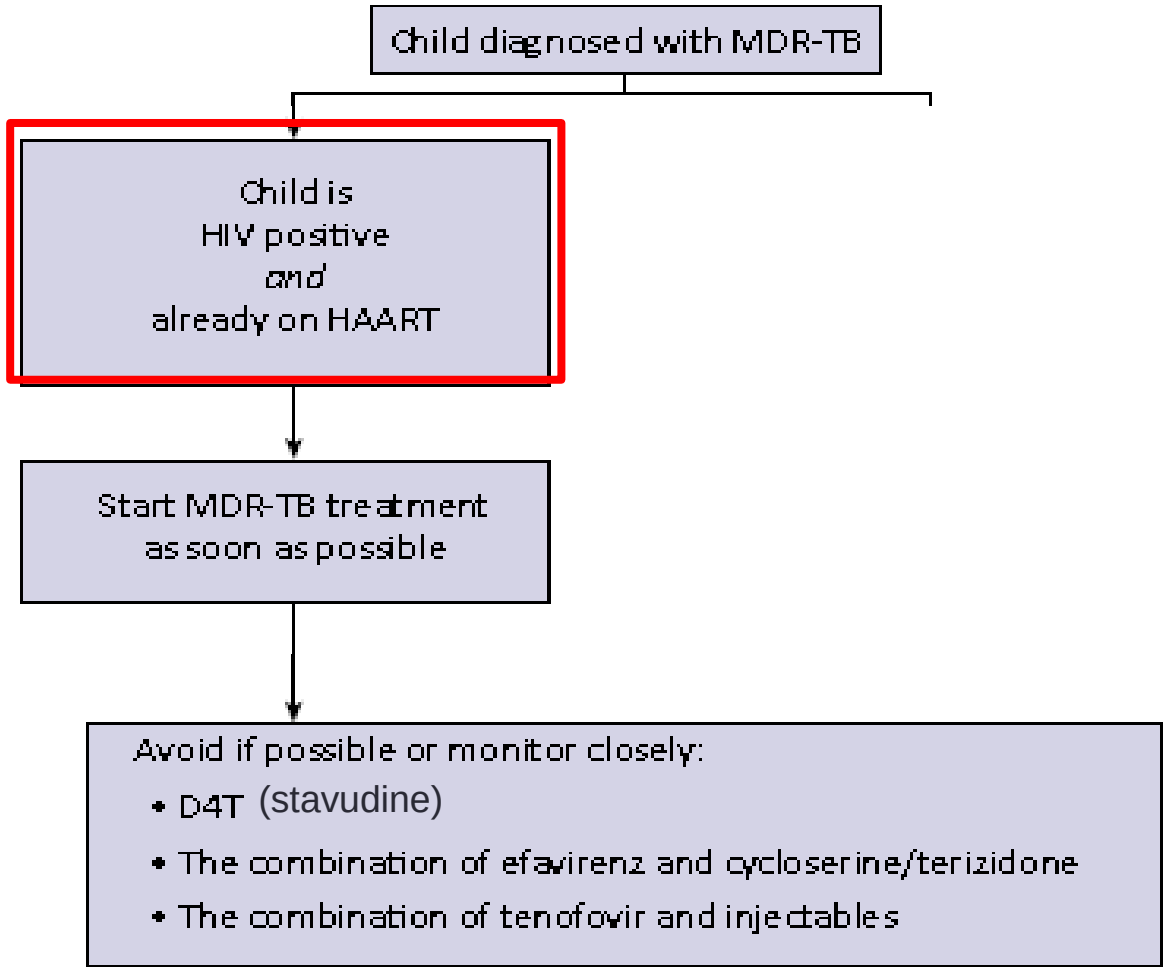
- High prevalence (22.2%) of MDR-TB seen in HIV exposed and infected children in South Africa (Hesseling et al., IJTLD, 16:192-5, 2012.
- Excellent outcomes can be achieved if HIV treated within days to weeks after starting MDR-TB treatment (Satti et al., PLoS ONE, 7(5):e37114, 2012)
- Poor outcomes (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

TB and HIV



Treatment focus on co-morbidities

Algorithm for Management of Children on Treatment for MDR-

Child diagnosed with MDR-TB

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

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

Watch for signs of IRIS:

- Worsening symptoms or signs (respiratory or lymphadenopathy)
- Fever
- Weight loss
- Abdominal pain

Treat with steroids if IRIS detected

If severe or life-threatening consider stopping HAART and restarting when MDR-TB more established

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.

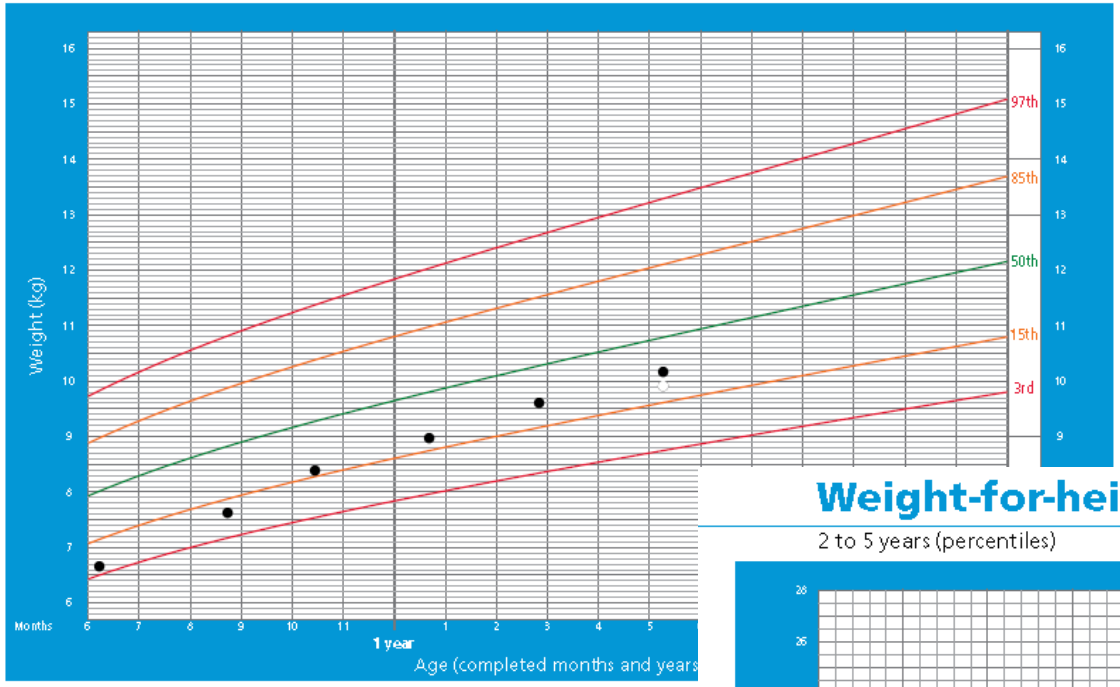
Monitoring Nutritional Status

- 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.

Weight-for-age BOYS

6 months to 2 years (percentiles)

World Health Organization

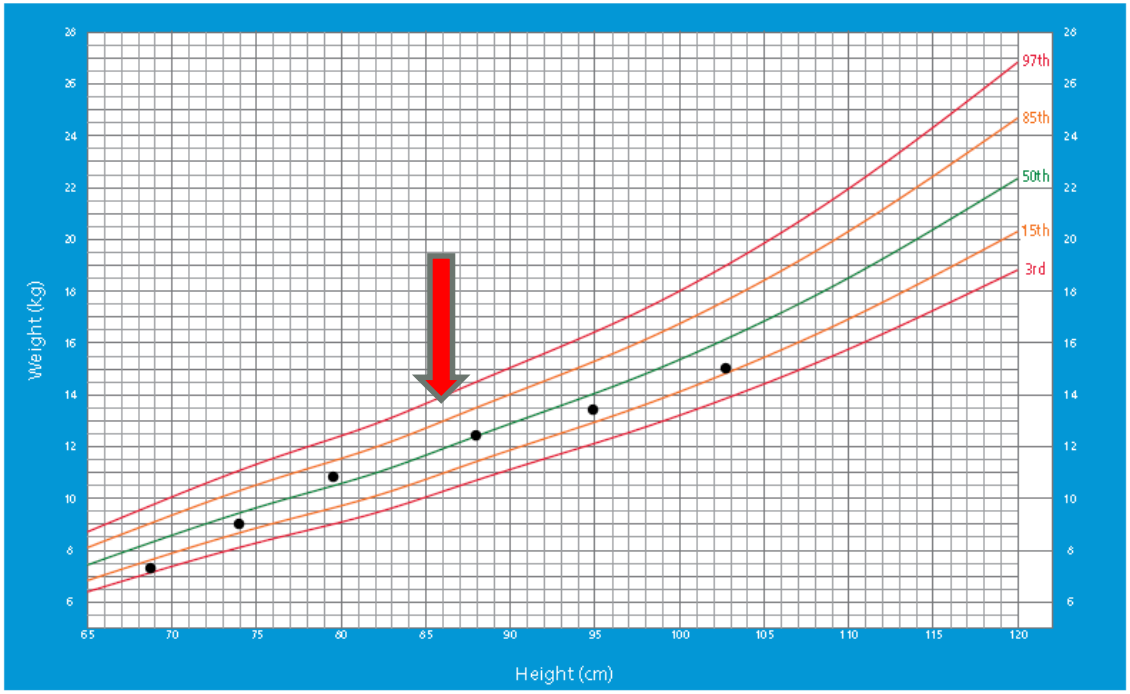


Weight for age gain is acceptable

Weight-for-height BOYS

2 to 5 years (percentiles)

World Health Organization



Weight for height loss is worrisome

Treatment focus on co-morbid

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)
- Co-management of asthma and TB results in improved outcomes in children (Bateman, E., et al., Prim. Care Resp. J., 18: 69-75, 2009)
- 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 corticosteriods 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)
- Patients with DM and DR-TB are slower to convert their sputum (Restrepo, B., et al, Am. J. Trop. Med. And Hyg., 79: 541-4, 2008)
- Higher rates of recurrence seen with DM and DR-TB (Franke, M., et al., CID, 56: 770-6, 2013)
- DR-TB worsens glycemic control (Fisher-Hoch, S., et al., Scan. J. ID, 40: 888-93, 2008)

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.

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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.

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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.

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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.

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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.

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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

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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.

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Thank You!