TREATING TUBERCULOSIS IN CHILDREN

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All existing diagnostic tests for TB in children have significant shortcomings. Most tests are not available in settings where the vast majority of TB cases are diagnosed. The utility of most tests is further diminished in children with immune compromise [especially HIV infection].
DIAGNOSTIC TESTS FOR CHILDHOOD TUBERCULOSIS

The sensitivity and specificity of the available tests are inherent in the tests.

However, the positive and negative predictive values are inherent in the population on whom the tests are used.

Therefore, all tests are more accurate when used on children with a high index of suspicion [epidemiology – HISTORY OF RECENT CONTACT TO A TB CASE - or suspicious symptoms]
MANTOUX TUBERCULIN SKIN TEST

- Uses 5 TU [2 TU if R23] of purified protein derivative
- Interpret in 48 – 72 hours
- Record size of induration in mm
- If it makes a reaction at >72 hrs, it counts!
- False negatives: 10% to 20% in disease
FACTORS THAT CAUSE DECREASED RESPONSE TO TUBERCULIN

Host-related
- Infections, vaccines
- Chronic disease, malnutrition
- Immunosuppressive diseases (HIV, malignancy, CVD)
- Drugs (corticosteroids)
- Extremes of age, stress
- **Overwhelming tuberculosis**

Tuberculin - related
- Improper storage or dilution
- Adsorption to glass or plastic

Administration - related

Reading - related
Interferon $\gamma$ tests

- MTB specific antigens:
  - Genes in region of difference (RD1) on MTB genome
  - Culture filtrate protein 10 (CFP-10)
  - Early secretory antigen target 6 (ESAT-6)

- Identify LTBI &/or disease

- Do not cross react with BGC vaccine or most other mycobacteria

- Require:
  - single medical visit
  - blood collection
  - laboratory equipment and personnel

- Results in 24-48 hrs
IGRAs – WHERE ARE WE NOW?

- FDA approved – limitation for children
- Major use – employee health
- Strategies: IGRA only or follow positive TST results with an IGRA
- Best pediatrics use - lower risk, BCG-vaccinated children
- Be careful in: children < 5 yrs old, immune compromised patients, children with suspected TB disease
HOW IS TUBERCULOSIS DIAGNOSED?

**Children**
- Positive sputum or gastric AFB smear - 10%
- Positive sputum or gastric culture - 10% - 40%
- Positive tuberculin skin test - 50% - 80%
DIAGNOSIS OF TUBERCULOSIS

Even in developed countries, the “gold standard” for the diagnosis of tuberculosis in children is the triad of:

1. a positive TST
2. an abnormal CXR and/or physical exam
3. a history of recent contact to an infectious adult case of TB
OBTAINING CULTURE AND AFB SMEAR SAMPLES FROM CHILDREN

- Traditional method is gastric aspiration, performed as an inpatient on 3 consecutive mornings – expensive, invasive
- Bronchioalveolar lavage has no advantage
- Nasopharyngeal aspiration – few studies
- Other sites – yields usually 0% - 25% culture positive, <10% smear positive
INDUCED SPUTUM COLLECTION IN CHILDREN

- Can be done inpatient or outpatient
- Infection control precautions important
- Salbutamol, followed by 15 minutes of 5% hypertonic saline solution
- Sputum obtained via suction with a nasopharyngeal catheter
- Yield: 30% to 40% culture positive

INTERPRETING CHILDREN’S CHEST RADIOGRAPHS FOR TB

- Rarely available in highest prevalence areas
- Marked inter- and intra- observer variability
- Reliable in expert hands and in the presence of suspicious symptoms
- Commonest picture is persistent opacification together with enlarged hilar or subcarinal lymph nodes [though nodes not always discernable]
- **The x-ray is usually sicker than the patient!**
TREATMENT OF LTBI IN CHILDREN

- 9 months of isoniazid (daily or twice weekly under DOT) is only accepted regimen

- INH-resistance or intolerance – rifampin for 6 months

- Multidrug-resistance – consult an expert

- Use isoniazid unless there is documented exposure to a specific case of drug-resistant TB
PEARLS OF WISDOM FOR TREATING LTBI IN CHILDREN

- Use INH suspension only in children ≤ 5 kg
- Compliance with 9 months of INH averages 50%
  - be vigilant and skeptical
- Use DOT for: recent contacts, infants, immune compromised
- When children aren’t tolerating INH, the problem is more often with the parent than the child
- Routine LFTs only for: other liver toxic drugs, liver disease, signs or symptoms of hepatitis
TREATING EXPOSED CHILDREN

- Very high rate of infection

- Takes up to 3 months for the skin test to turn positive

- U.S. studies – 10% to 20% of childhood TB cases can be prevented if children exposed in a household receive isoniazid

- WHO standards – children <5 years old in a TB household should be treated
TREATMENT OF TUBERCULOSIS
DISEASE IN CHILDREN

Pulmonary
- INH, RIF for 6 months + PZA for first 2 months
- Add EMB initially if risk of INH resistance
- Can be every day or twice/thrice weekly therapy
- INH-resistant: RIF+PZA+EMB for 6 to 9 months
- MDR - depends on susceptibility - at least 18 mo

CNS, Disseminated
- Usually start with 4 drugs (INH, RIF, PZA + ETH or STM)
- Usual length: 9-12 months
- Every day initially, may use twice/thrice weekly later
FOLLOW-UP EVALUATIONS FOR CHILDREN WITH TUBERCULOSIS

- Skin test stays positive “forever”
- Frequent chest x-rays unnecessary - at diagnosis, 1-2 months, end of therapy
- Follow growth & development closely
- Adequate nutrition
- Routine liver enzyme monitoring not necessary
- Routine vitamin B₆ not necessary except breast-feeding, pregnant adolescents, poor diet
WHAT WE REALLY NEED FOR BETTER TB CONTROL IN CHILDREN?

- A better vaccine
- Better diagnostic tests
- New drugs with pediatric pharmacokinetics
- Shorter durations of therapy
- Sustained public health funding for contact investigation and DOT
Summary

- TB Diagnostic tests have limitations – have high index of suspicion
- Treatment is cheap and effective in most children
- Consult ID/public health for assistance with management
Resources

WHO Global TB report Executive Summary:


Trends in Tuberculosis — United States, 2012 MMWR March 22, 2013 / 62(11);201-205
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6211a2.htm