TUBERCULOSIS INFECTION IN CHILDREN AND ADOLESCENTS: TESTING AND TREATMENT

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CLINICAL REPORT

Tuberculosis Infection in Children and Adolescents: Testing and Treatment

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FACULTY DISCLOSURE

- I do not have any financial disclosures

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OBJECTIVES OF PRESENTATION

- Epidemiology of pediatric tuberculosis (TB)
- Change in terminology: Tuberculosis infection (TBI)
- Available tests for TBI
- Regimens for treatment of TBI

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Mycobacterium tuberculosis (Mtb) is still a problem in pediatrics

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TUBERCULOSIS REMAINS AN IMPORTANT DISEASE

- Medical practitioners who care for children and adolescents have questions about tuberculosis (TB) testing and treatment
- High-risk patients who require testing
  - Close contacts of individuals with TB disease
  - Children <2 years and post-pubertal adolescents
  - Individuals with current or planned immunocompromising conditions

TABLE 1 Age-Associated Risk of Progression From TBI to TB Disease

Age	Risk of Progression from TBI to Disease if Untreated, %
<12 mo	40–50
1–2 y	25
School-aged	5–10
Adolescents	10–15
Adults	5–10

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~~LTBI~~

Call it → Tuberculosis infection (TBI)

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CHANGE IN TERMINOLOGY

- A variety of outcomes may occur for an individual who encounters Mtb
  - Rapid progression to symptomatic disease –or-
  - Immune control of the bacilli
- Under immune control, the bacilli are still viable and persistent
- Removal of the term "latent" will
  - Better represents the pathogenesis of tuberculosis –and-
  - Reduce confusion when discussing treatment goals with patients and families
- **Tuberculosis infection (TBI)** will describe asymptomatic individuals who are infected (have a positive test), and have a negative chest radiograph

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Available Tests To Detect Mtb

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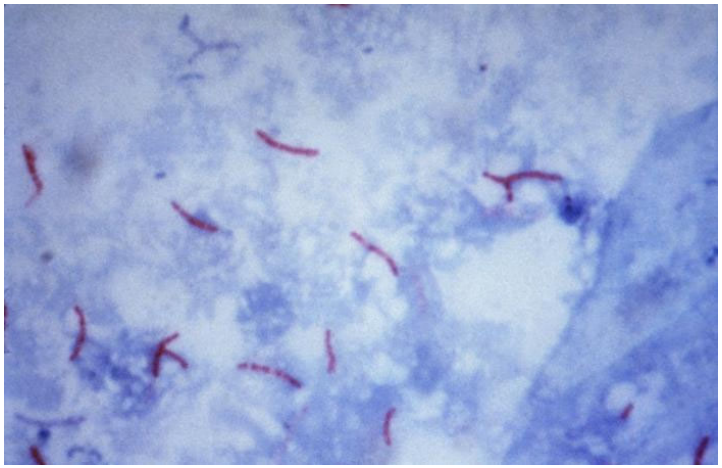
NO "GOLD STANDARD" FOR TB TESTING

- Two available but imperfect methods for identification
  - Tuberculin skin test (TST)
  - Interferon-gamma release assay (IGRA)
- Both depend on cell-mediated immunity and provide immunologic evidence of host sensitization to Mtb
- Neither method can distinguish between TBI and TB disease



This photomicrograph reveals Mycobacterium tuberculosis bacteria using acid-fast Ziehl-Nelsen stain (magnification ×1,000). Courtesy of Centers for Disease Control and Prevention

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TUBERCULIN SKIN TEST (TST)

- Intradermal injection of purified protein derivative (PPD), which contains dozens of TB antigens
- Advantages: Wealth of experience in using this test to aid diagnosis
- Disadvantages: Logistical issues are undesirable to medical staff, patients and families
  - False POSITIVE TST results may occur because PPD antigens in environmental NTM and BCG vaccine
  - Experienced personnel are needed for placement and interpretation
  - Results are not binary (need to consider presence of risk factors when interpreting significance of induration)
  - A return visit is needed

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IGRA IS PREFERRED FOR CHILDREN ≥2 YR

- Test of whole blood that detect interferon-gamma (IFN-γ) release from T lymphocytes
- IGRA is preferred over the TST for several reasons
  - Less false-positive results: TB antigens in the IGRA are NOT found in environmental NTM or BCG vaccine
  - There is one cut-off value for designating a positive vs negative result
  - Only 1 visit is needed (blood draw)
- Caveats
  - Expensive – BUT IGRA may be more cost-effective than TST because only 1 visit is needed for IGRA
  - Experience in children <2 years of age is not as robust as in older individuals
- Neither method has a clear advantage in sensitivity

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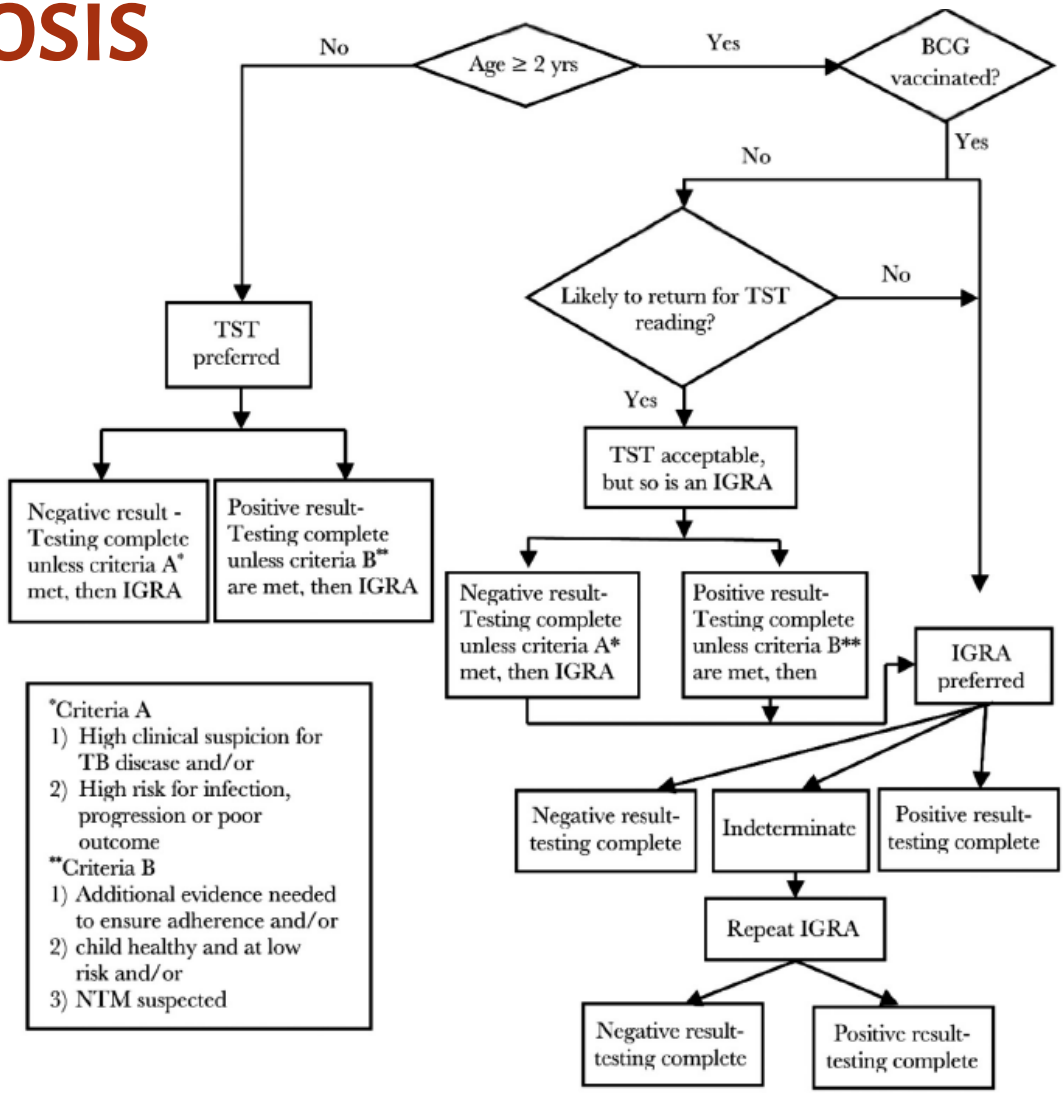
TUBERCULOSIS



Available treatments for TBI

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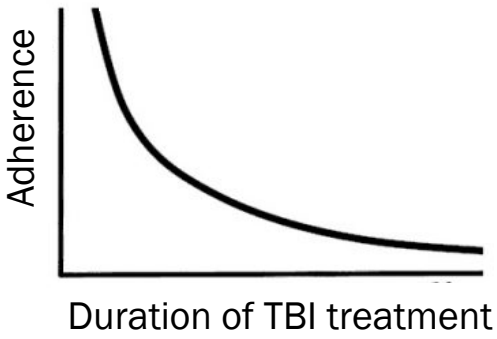
PRINCIPLES OF TBI TREATMENT

- Reducing risk of TBI progressing to TB disease
  - Treatment reduces the risk of developing TB disease by 90% in children who adhere to therapy
- Risk of disease progression is highest in 3 patient groups
  - Close contacts of individuals with TB disease
  - Children < 2 years of age and post-pubertal adolescents
  - Individuals with current or planned immunocompromising conditions
- ADHERENCE to TBI treatment is inversely correlated to DURATION
  - The shorter the duration, the higher the completion rate of therapy



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RIFAMYCIN-CONTAINING REGIMENS ARE FIRST LINE FOR TBI TREATMENT

Infection or Disease Category	Regimen	Remarks
***M tuberculosis* infection** (positive TST or IGRA result, no disease)[a]		
• Isoniazid susceptible	12 weeks of isoniazid plus rifapentine, once a week	Most experts consider isoniazid-rifapentine to be the preferred regimen for treatment of TBI for children 2 years and older
	OR	
	4 mo of rifampin, once a day	Continuous daily therapy is required. Intermittent therapy even by DOT is not recommended.
	OR	
	3 mo of isoniazid plus rifampin, once a day	To be considered if above 2 regimens are not feasible.
	OR	
	6 or 9 mo of isoniazid, once a day	If daily therapy is not possible, DOT twice a week can be used; medication doses differ with daily and twice-weekly regimens.

ASPECTS OF TREATMENT

- Serial evaluations of individuals while on therapy
  - At least monthly, and in-person visits
- Gastro-intestinal upset while on medications
- Interruptions in TBI treatment

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RESOURCES

Information for Pediatricians and Pediatric Health Care Providers

- AAP Clinical Report, "Tuberculosis Infection in Children and Adolescents: Testing and Treatment " https://publications.aap.org/pediatrics/article/148/6/e2021054663/183445/Tuberculosis-Infection-in-Children-and-Adolescents
- Red Book 2021 Tuberculosis Chapter https://publications.aap.org/redbook/book/347/chapter/5757587/Tuberculosis

Information for Patients, Families, and Caregivers

- Healthy Children article Tuberculosis in Children - HealthyChildren.org

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THANK YOU

- Members of AAP and medical providers of children and adolescents

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