Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Advanced Concepts in Pediatric Tuberculosis: Latent TB Infection

Nizar F. Maraqa, MD, FPIDS

Division of Pediatric Infectious Diseases & Immunology

University of Florida College of Medicine - Jacksonville

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Advanced Concepts in Pediatric Tuberculosis

1. Mycobacteriology, Pathogenesis and Epidemiology
2. Latent TB Infection
3. Clinical Manifestations
4. Diagnosis: Old and New Diagnostic Tools and Challenges
5. TB and HIV
6. Pharmacotherapeutics of TB drugs
7. Treatment of TB, including MDR
8. Infection Control, Source Case and Contact Investigation

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Latent TB Infection
Objectives

At the end of this presentation, attendees should be able to:

- Identify high priority groups of children who should be tested for LTBI.
- Understand the indications for Tuberculin Skin Test (TST) and/or Interferon Gamma Release Assays (IGRAs).
- Correctly interpret result of TST reactions in children, including differential interpretation based on risk factors in the host.
- Interpret correctly results of IGRAs.
- Describe management of children with a positive TST or IGRA.

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

INSTRUCTIONAL CASES

Questions

1. What are this patient's risk factors for TB infection or disease?
2. What is the appropriate management for this patient?

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 1

- 7-year-old Hispanic male
- Moved to U.S. from Guatemala 4 years ago
- Received BCG vaccine at age 1 year
- Known contact of infectious TB case
- TST = 5 mm of induration
- No symptoms of TB disease
- Normal CXR, CBC, AST, and bilirubin

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 2

- 12-year-old Asian female
- Moved to U.S. from Philippines > 5 years ago
- Plans to volunteer at a long term care facility
- TST result negative (0 mm) 1 year ago
- TST prior to volunteering = 26 mm of induration
- CXR normal
- No symptoms of TB disease
- No known contact with a TB patient

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 3

- 16-year-old Asian male
- Moved to U.S. from China < 5 years ago
- Received BCG vaccine in China as an infant
- QFT-GIT result = Positive
- CXR normal
- No symptoms of TB disease
- Known contact with a TB patient

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Latent TB Infection (LTBI)

LTBI is the presence of *M. tuberculosis* organisms (tubercle bacilli) without *signs and symptoms or radiographic or bacteriologic* evidence of TB disease.

- Infection with such a small number of bacilli that is insufficient to produce clinically manifest disease
- LATENCY is an incubation period of undefined duration

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Latent TB Infection (LTBI)

- The best available proxy for diagnosing LTBI is the identification of an <u>adaptive immune response</u> by
  - the tuberculin skin test or an interferon-γ based assay

Eur Respir J 2009; 33: 956–973
DOI: 10.1183/09031936.00120908
Copyright©ERS Journals Ltd 2009

CONSENSUS STATEMENT

LTBI: latent tuberculosis infection or lasting immune responses to *M. tuberculosis*? A TBNET consensus statement

U. Mack, G.B. Migliori, M. Sester, H.L. Rieder, S. Ehlers, D. Goletti, A. Bossink, K. Magdorf, C. Hölscher, B. Kampmann, S.M. Arend, A. Detjen, G. Bothamley, J.P. Zellweger, H. Milburn, R. Diel, P. Ravn, F. Cobelens, P.J. Cardona, B. Kan, I. Solovic, R. Duarte, D.M. Cirillo and C. Lange for the TBNET

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

theastern National Tuberculosis Center SHARE • LEARN • CURE

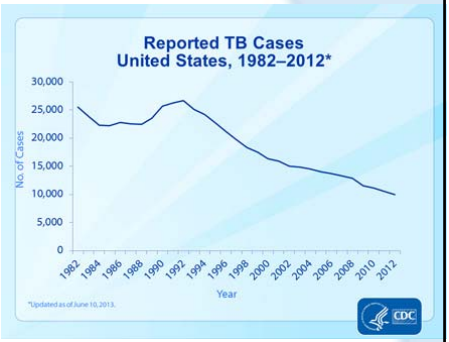
TB: Latent Infection vs. Disease

<u>Latent TB Infection</u>	<u>*Pulmonary* TB Disease</u>
• TST or IGRA: positive	• TST or IGRA: usually positive
• Chest radiograph: normal	• Chest radiograph: usually abnormal
• No symptoms or physical findings suggestive of TB	• Symptoms may include one or more of the following: fever, cough, hemoptysis, night sweats, weight loss, fatigue, decreased appetite
• If done, respiratory specimen are smear & culture-negative	• May be culture-positive (in 50% smear+)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Targeted TB Testing



- As TB disease rates in the U.S. decrease, finding and treating persons at high risk for LTBI has become a priority.
- Targeted TB testing is used to focus program activities and provider practices on groups at the highest risk for TB.

Flexibility is needed in defining "high risk"

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Targeted TB Testing and Treatment of Latent TB Infection

- Treatment of LTBI substantially reduces the risk that persons infected with *M. tuberculosis* will progress to TB disease.
- For more than 3 decades, an essential component of TB prevention and control in the United States has been the treatment of persons with LTBI to prevent TB disease.

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Targeted TB Testing

- ✓ Essential TB prevention and control strategy
- ✓ Detects persons with LTBI who would benefit from treatment
- ✓ De-emphasizes testing of groups that are not at high risk for TB
- ✓ Can help reduce the waste of resources and prevent inappropriate treatment

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment - milestones

1965

American Thoracic Society (ATS) recommends treatment of LTBI for those with

- previously untreated tuberculosis,
- tuberculin skin test (TST) converters, and
- young children

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

1965: ATS recommends treatment of LTBI for those with previously untreated TB, tuberculin skin test (TST) converters, and young children

1967

Recommendations expanded to include all TST positive reactors (≥ 10 mm)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

LTBI - milestones

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

1965: ATS recommends treatment of LTBI for those with previously untreated TB, tuberculin skin test (TST) converters, and young children

1967: Recommendations expanded to include all TST positive reactors (≥ 10 mm)

1974

CDC and ATS guidelines established for pretreatment screening to decrease risk of hepatitis associated with treatment

Treatment recommended for persons ≤ 35 years of age

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

LTBI - milestones

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

1965: ATS recommends treatment of LTBI for those with previously untreated TB, tuberculin skin test (TST) converters, and young children

1967: Recommendations expanded to include all TST positive reactors (≥ 10 mm)

1974: CDC and ATS guidelines established for pretreatment screening to decrease risk of hepatitis associated with treatment (treatment recommended for persons ≤ 35 years of age)

1983

CDC recommends clinical and laboratory monitoring of persons ≥ 35 who require treatment for LTBI

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

LTBI - milestones

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

1965: ATS recommends treatment of LTBI for those with previously untreated TB, tuberculin skin test (TST) converters, and young children

1967: Recommendations expanded to include all TST positive reactors (≥ 10 mm)

1974: CDC and ATS guidelines established for pretreatment screening to decrease risk of hepatitis associated with treatment (treatment recommended for persons ≤ 35 years of age)

1983: CDC recommends clinical and laboratory monitoring of persons ≥ 35 who require LTBI treatment

1988

CDC recommends 2 months of rifampin (RIF) plus pyrazinamide (PZA) as an option for HIV-infected patients (later changed)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

LTBI - milestones

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

1965: ATS recommends treatment of LTBI for those with previously untreated TB, tuberculin skin test (TST) converters, and young children

1967: Recommendations expanded to include all TST positive reactors (≥ 10 mm)

1974: CDC and ATS guidelines established for pretreatment screening to decrease risk of hepatitis associated with treatment (treatment recommended for persons ≤ 35 years of age)

1983: CDC recommends clinical and laboratory monitoring of persons ≥ 35 who require LTBI treatment

1988: CDC recommends 2 months of rifampin (RIF) plus pyrazinamide (PZA) as an option for HIV-infected patients (later changed)

2000

CDC & ATS issue updated guidelines for targeted testing and LTBI treatment[1]

- 9-month regimen of INH is preferred
- 2-month regimen of RIF and PZA and a 4-month regimen of RIF recommended as options (later changed)

[1] *MMWR* June 9, 2000; 49(No. RR-6) http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

LTBI - milestones

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

1965: ATS recommends treatment of LTBI for those with previously untreated TB, tuberculin skin test (TST) converters, and young children

1967: Recommendations expanded to include all TST positive reactors (≥ 10 mm)

1974: CDC and ATS guidelines established for pretreatment screening to decrease risk of hepatitis associated with treatment (treatment recommended for persons ≤ 35 years of age)

1983: CDC recommends clinical and laboratory monitoring of persons ≥ 35 who require LTBI treatment

1988: CDC recommends ~~2 months of rifampin (RIF) plus pyrazinamide (PZA)~~ as an option for HIV-infected patients (later changed)

2000: CDC & ATS updated guidelines for targeted testing and LTBI treatment 9-month regimen of (INH) is preferred ~~2-month regimen of RIF and PZA~~ and a 4-month regimen of RIF recommended as options (later changed)

2001

Due to liver injury and death associated with 2-month regimen of RIF and PZA, use of this option de-emphasized in favor of other regimens[2]

[2] *MMWR* August 31, 2001; 50(34): 733-735

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

LTBI - milestones

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

1965: ATS recommends treatment of LTBI for those with previously untreated TB, tuberculin skin test (TST) converters, and young children

1967: Recommendations expanded to include all TST positive reactors (≥ 10 mm)

1974: CDC and ATS guidelines established for pretreatment screening to decrease risk of hepatitis associated with treatment (treatment recommended for persons ≤ 35 years of age)

1983: CDC recommends clinical and laboratory monitoring of persons ≥ 35 who require LTBI treatment

1988: CDC recommends ~~2 months of rifampin (RIF) plus pyrazinamide (PZA)~~ as an option for HIV-infected patients (later changed)

2000: CDC & ATS updated guidelines for targeted testing and LTBI treatment 9-month regimen of (INH) is preferred ~~2-month regimen of RIF and PZA~~ and a 4-month regimen of RIF recommended as options (later changed)

2003

2-month regimen of RIF and PZA generally not recommended — to be used only if the potential benefits outweigh the risk of severe liver injury and death[3]

[3] *MMWR* August 8, 2003; 52(31): 735-739

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

LTBI - milestones

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

1965: ATS recommends treatment of LTBI for those with previously untreated TB, tuberculin skin test (TST) converters, and young children

1967: Recommendations expanded to include all TST positive reactors (≥ 10 mm)

1974: CDC and ATS guidelines established for pretreatment screening to decrease risk of hepatitis associated with treatment (treatment recommended for persons ≤ 35 years of age)

1983: CDC recommends clinical and laboratory monitoring of persons ≥ 35 who require LTBI treatment

2000: CDC & ATS updated guidelines for targeted testing and LTBI treatment 9-month regimen of (INH) is preferred and a 4-month regimen of RIF (6-mo for children) recommended as an option

2011

CDC recommends 12-doses (3 months) of isoniazid (INH) and rifapentine (RPT) as an option equal to the standard 9-month INH regimen for certain groups*

**MMWR* December 9, 2011 / 60(48);1650-1653. Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

LTBI - milestones

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

IDENTIFYING RISK FACTORS FOR PROGRESSION TO TB DISEASE

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Risk of Progression from LTBI to TB Disease

The risk declines exponentially ~10 fold over the first few years…

- Initial years: cumulative risk is 2-5% (1 per 100 person-years)
- Subsequent risk is 1 in 1000 person-years
- Lifetime risk of 10-15%
  - The risk increases substantially to 5-15% **annually** in the immune compromised

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Persons at Risk for Developing TB Disease

Persons at high risk for developing TB disease fall into 2 categories:

- Those who have an increased likelihood of exposure to persons with TB disease
- Those with clinical conditions that increase their risk of progressing from LTBI to TB disease

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Increased Likelihood of Exposure to Persons with TB Disease

- Close contacts to person with infectious TB disease
- Residents / employees of high-risk congregate settings
  - e.g., correctional facilities, homeless shelters, health care facilities
- Recent immigrants from TB-endemic regions of the world
  - within 5 years of arrival to the United States

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Increased Risk for Progression from LTBI to TB Disease

- Children ≤ 5 years with a positive TST
  - ✓ the risk is largest in the youngest children & drops to one of the lowest in life during primary school to increase again with adolescence to a second peak among young adults
- HIV-infected persons
- Those with a history of prior, untreated TB or fibrotic lesions on chest radiograph
- Underweight or malnourished persons

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Increased Risk for Progression from LTBI to TB Disease

- Those receiving TNF-α antagonists for treatment of rheumatoid arthritis or inflammatory bowel disease
- Injection drug users
- Those with certain medical conditions such as:
  - Chronic renal failure or on hemodialysis
  - Solid organ transplantation (e.g., heart, kidney)
  - Diabetes mellitus
  - Gastrectomy or jejunoilial bypass
  - Silicosis
  - Carcinoma of head or neck

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

METHODS FOR DETECTING *M. TUBERCULOSIS* INFECTION IN THE U.S.

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Testing for *M. tuberculosis* Infection

- Two testing methods are available for the detection of *M. tuberculosis* infection in the United States:
  - Mantoux tuberculin skin test (TST)
  - Interferon-gamma release assays (IGRAs)
- They test the adaptive immune response to *M. tb*
- These tests do not exclude LTBI or TB disease
  - Decisions about medical and public health management should include other information, and not rely solely on TST or IGRA results

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Mantoux Tuberculin Skin Test

Continuously in use for over 100 years in clinical medicine

Skin test that measures delayed-type hypersensitivity reaction to a purified protein derivative of tuberculin

- a crude mixture of antigens shared by *M. tuberculosis, M. bovis, M. bovis* BCG & other environmental mycobacteria species

- Multiple puncture tests (e.g., Tine Test) are inaccurate and not recommended

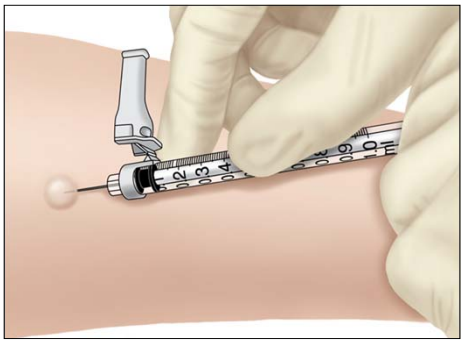
UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Administering the TST

- Inject 0.1 ml (5 TU) of PPD tuberculin solution intradermally on the volar surface of the forearm using a 27-guage needle → produce a wheal 6 to 10 mm in diameter (Mantoux technique)

Universal Precautions

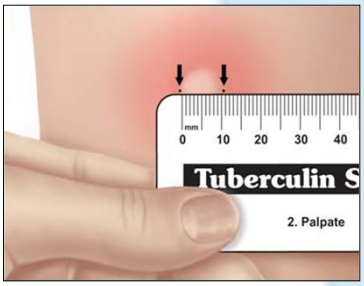


2-8 weeks after exposure

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Reading the TST -1



- ✓ Measure reaction in 48 to 72 hours
- ✓ Palpate and measure induration, not erythema
- ✓ Record reaction in millimeters
  - ✓ not "negative" or "positive" / record "0" if no induration
- ✓ Ensure trained health care professional measures and interprets the TST (~15% variability)

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Reading the TST - 2

- ✓ An induration may start to appear immediately following TST placement (type-I or type-III immune reaction)
- ✓ Histopathology: perivascular extravasation of lymphocytes into the epidermis & interstitium
- ✓ A strongly positive TST may lead to persistent skin discoloration or, rarely, to tissue necrosis

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Reading the TST - 3

- ✓ Educate patient and family regarding significance of a positive TST result
  - ✓ an intention to test is an intention to treat
- ✓ Positive TST reactions can be measured accurately for up to 7 days
  - ✓ A delayed reaction is more common in children
- ✓ Negative reactions can be read accurately for only 72 hours

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

TST Interpretation

- TST sensitivity (50-85%) and specificity is influenced by the cut-off used.
- A lower cut-off will result in a higher sensitivity and a lower specificity for M. tuberculosis infection

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

TST Interpretation

≥ 5 mm induration is interpreted as positive in

- HIV-infected persons
- Close recent contacts of infectious TB
- Persons with chest radiographs consistent with prior untreated TB
- Organ transplant recipients
- Other immunosuppressed patients (e.g. , those taking the equivalent of > 15 mg/d of prednisone for ≥1 month or those taking TNF-α antagonists)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

TST Interpretation

≥ 10 mm induration is interpreted as positive in

- Recent arrivals from high-prevalence countries
- Children < 4 years; or children and youth exposed to adults at high risk
- Persons with clinical conditions that place them at high risk of progressing to TB
- Residents or employees of congregate settings
- Injection drug users
- Mycobacteriology laboratory personnel

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

TST Interpretation

≥ 15 mm induration is interpreted as positive in

- Persons with no known risk factors for TB.
  - Although skin testing programs should be conducted only among high-risk groups, certain individuals may require TST for employment or school attendance.
  - Diagnostic interpretation and treatment of LTBI should always be tied to risk assessment.

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Factors That May Cause False-Positive TST Reactions

- Nontuberculous mycobacteria (NTM)
  - Reactions caused by NTM are usually ≤10 mm of induration (<5% may have >15mm TSTs)
- BCG vaccination
  - leaves an immunological imprint for a prolonged period of time (less than 5% after five years; may be *up to 10 years* in some)
  - Reactivity in BCG vaccine recipients generally wanes over time; positive TST result is likely due to TB infection if risk factors are present

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Factors That May Cause False-Negative TST Reactions -1

- Anergy
  - Inability to react to a TST because of a weakened immune system
  - Usefulness of anergy testing in TST-negative persons who are HIV-infected has not been demonstrated

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Factors That May Cause False-Negative TST Reactions - 2

- Recent TB Infection
  - Usually less than 8-10 weeks after exposure
- Overwhelming TB Disease
- Very young age
  - Newborns (< 6 months)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Factors That May Cause False-Negative TST Reactions - 3

- Live virus vaccination
  - Can temporarily suppress TST reactivity
    - e.g., measles or smallpox
- Poor TST administration technique
  - TST injection too shallow or too deep, or
  - wheal is too small

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Boosting

- Some people with LTBI may have a negative skin test reaction when tested years after infection because of a waning response (e.g. older adults).
- An initial skin test may stimulate (boost) the ability to react to tuberculin.
- Subsequent positive "boosted" reaction to TST may be misinterpreted as a new infection.
- "Boosting" may occur in BCG-vaccinated persons.

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

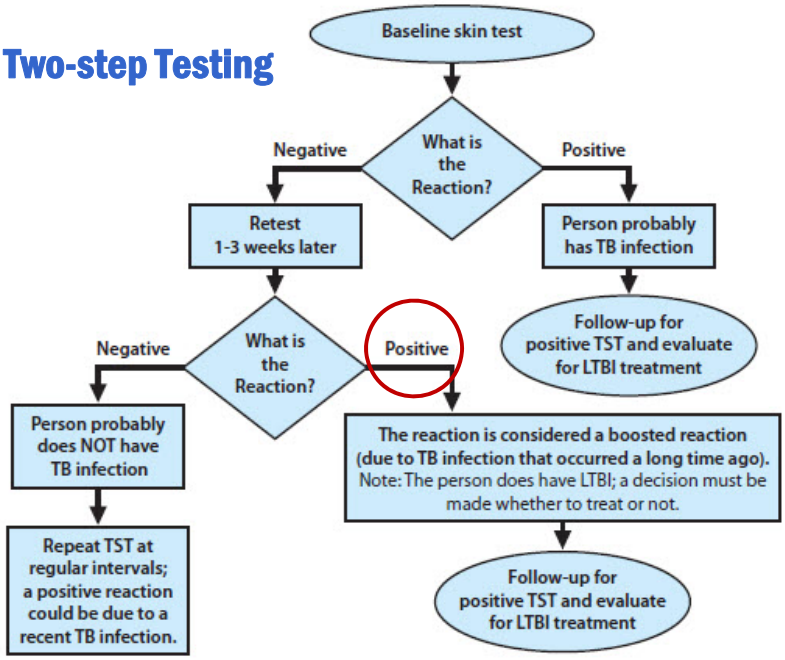
Two-Step Testing

- A strategy to differentiate between boosted reactions and reactions due to recent infection.
  - If 1st test positive, consider infected; if negative, give 2nd test 1–3 weeks later
  - If 2nd test positive, consider infected; if negative, consider uninfected
- Use two-step tests for initial baseline skin testing of adults who will be retested periodically (e.g., health care workers).

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Two-step Testing



TST- special considerations

- Pregnancy
  - TST is safe and reliable for mother & fetus throughout pregnancy
  - Pregnant women who have risk factors for TB infection should be tested
- Occupational exposure (eg Healthcare Workers)
  - Cutoff for TST positivity depends on prevalence of TB in facility and individual's risk factors for TB
  - Test at hire and at intervals determined by annual risk assessment

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

INTERFERON-GAMMA RELEASE ASSAYS (IGRA)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Interferon-Gamma Release Assays (IGRAs)

- Ex-vivo whole-blood tests used to detect the immune response to an *M. tuberculosis* infection
- Two U.S. Food and Drug Administration (FDA) - approved IGRAs are commercially available:
  - QuantiFERON-TB Gold-In-tube (QFT-GIT)® test
  - T-SPOT.*TB*® test

Cellestis
Carnegie, Australia

Oxford Immunotec
Abingdon, UK

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

How IGRAs Work

- tests that measures and compares amount of IFN-γ released by blood cells in response to antigens
- entails mixing blood samples with antigens from *M. tuberculosis* and controls
- T-cells that recognize the antigens release IFN-γ
  - Enzyme-linked immunospot (ELISPOT) or whole blood ELISA
- amount of interferon released in response to *M. tuberculosis* antigens is compared to amount released in response to other antigens & to background signals

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Administering IGRAs

- Confirm and arrange for delivery of blood sample within specific time-frame to ensure viability of blood samples
- Draw blood sample according to test manufacturer's instructions
- Schedule a follow up appointment to receive test results, medical evaluation and possible treatment if needed

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Interpretation of IGRA Test Results

IGRA Test	Results Reported as
QFT-GIT	Positive, negative, indeterminate
T-Spot.*TB*	Positive, negative, equivocal, invalid

Note: Laboratory should provide both quantitative and qualitative results

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

- Children with a positive result from an IGRA should be considered infected with *M tuberculosis* complex. A negative IGRA result cannot be interpreted universally as absence of infection
- Indeterminate IGRA results have several possible causes that could be related to the patient, the assay itself, or its performance. Indeterminate results do not exclude *M tuberculosis* infection and may necessitate repeat testing, possibly with a different test. Indeterminate IGRA results should not be used to make clinical decisions

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Advantages of IGRAs

- Requires a single patient visit to conduct test
- Results can be available within 24 hours
- Does not boost responses measured by subsequent tests
- Have higher specificity than TST in populations with higher prevalence of BCG vaccination
  - BCG vaccination does not cause false-positive IGRA test result
- Very few NTM can cause a false-positive IGRA
  - *M. kansasii, M. marinum, M. szulgai, M. flavescens*

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Disadvantages/Limitations of IGRAs

- Errors in collecting and transporting blood, or in interpreting assays can decrease IGRAs' accuracy
- Tests may be expensive
- Limited data on the use of IGRAs for
  - Children < 5 years of age;
  - Persons recently exposed to *M. tuberculosis*;
  - Immunocompromised persons; and
  - Serial testing
- Limited data on use of IGRAs to predict who will progress to TB disease in the future

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

WHICH TB TEST TO SELECT??

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Selecting a Test to Detect TB Infection

- IGRAs are preferred method of testing for
  - ✓ Groups of people who have poor rates of returning to have TST read
  - ✓ Persons who have received BCG vaccination
- TST is the preferred method of testing for
  - ✓ Children under the age of 5 years
    - ✓ 2-5 years (controversial)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Selecting a Test to Detect TB Infection

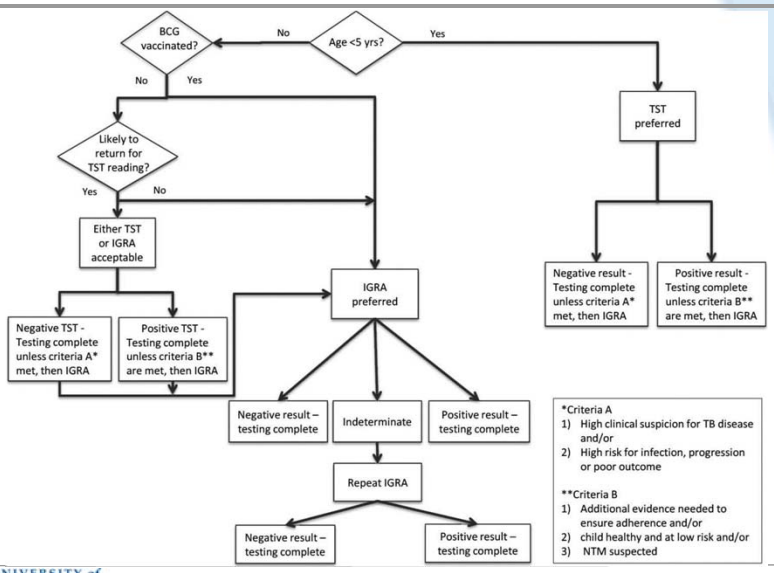
- ❑ Either TST or IGRA can be used without preference for other groups that are tested for LTBI
- ❑ Routine testing with TST and IGRA is *NOT* recommended

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Red Book® Online

Guidance on Strategy for Use of TST and IGRA by age and BCG-Immunization Status



UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Copyright © 2015 American Academy of Pediatrics.
All rights reserved.

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

- Results from both IGRA and TST may be helpful when the initial test is
  - NEGATIVE, and patient has high risk of TB infection or disease
  - POSITIVE, and additional evidence is required/desired
  - Unclear or indeterminate

If a person has low risk of TB infection and progression from infection to TB disease, requiring a positive result from the second test as evidence of infection increases the likelihood that the test reflects infection

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Selecting a Test to Detect TB Infection

- In contact investigations, confirm a negative test via retest 8-10 weeks postexposure
- Use the same test for repeat testing to reduce misclassification errors

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Selecting a Test to Detect TB Infection

- In immunocompromised: IGRAs may be better!!
  - Variability seen with type of immune compromising condition
  - HIV: IGRA has shown superiority over TST especially in high-TB burden populations
  - SOT: no clear advantage for IGRA over TST
  - HSCT: IGRA has the edge over TST (? combined TST/IGRA…)
  - Immunosuppressants (anti-TNF-a, steroids, DMRDs): either test
  - A full analysis of clinical & epidemiologic TB risk factors will increase the PPV and may improve LTBI detection

Sauzullo et al. Curr Opin Infect Dis. 2015;28:275-82

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

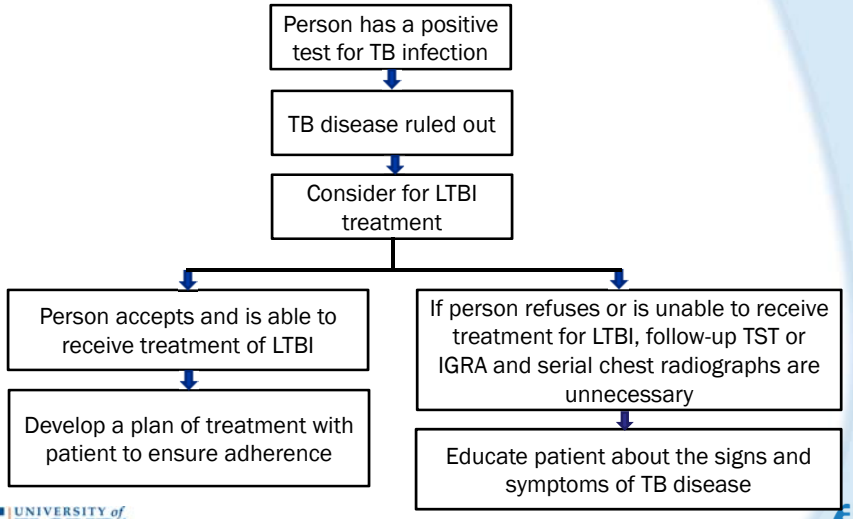
Southeastern National Tuberculosis Center SHARE • LEARN • CURE

EVALUATION OF PERSONS WITH POSITIVE TB TEST RESULTS

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Evaluation of Persons with Positive TB Test Results



UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Close contacts with Negative TB tests results

- Evaluate and treat for LTBI contacts with negative TB test
  - Children under 4 years of age
  - Immunosuppressed persons
  - Any person at high risk of progressing to TB disease once infected
- Always rule out TB disease before treating for LTBI
  - Medical evaluation and chest radiography
- Administer LTBI treatment (window prophylaxis)
- Retest 8-10 weeks after last exposure (to allow for delayed immune response)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI TREATMENT REGIMENS

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Before Initiating Treatment for LTBI

- ✓ Rule out TB disease
  - ✓ history, physical examination, chest radiography
  - ✓ when indicated, bacteriologic studies
- ✓ Determine prior history of treatment for LTBI or TB disease
- ✓ Assess risks and benefits of treatment
- ✓ Determine current and previous drug therapy
- ✓ Recommend HIV testing (opt-out screening)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Treatment Regimens for Latent TB Infection

Drug(s)	Duration	Interval	Minimum Doses
Isoniazid	9 months	Daily	270
		Twice weekly	76
	6 months*	Daily	180
		Twice weekly	52
Isoniazid & Rifapentine	3 months	Once weekly	12
Rifampin	4 mo (adults)	Daily	120
	~~6 mo (children)~~		~~180~~

Note: Rifampin (RIF) & Pyrazinamide (PZA) should not be offered to persons with LTBI. RIF & PZA should continue to be administered in multidrug regimens for treatment of TB disease.

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Treatment Regimens for Latent TB Infection

Drug(s)	Duration	Interval	Min Doses	*Within*
Isoniazid	9 months	Daily	270	12 months
		Twice weekly	76	
	6 months	Daily	180	9 months
		Twice weekly	52	
Isoniazid & Rifapentine	3 months	Once weekly	12	4 months
Rifampin	4 mo (adults)	Daily	120	6 months
	~~6 mo (children)~~		~~180~~	

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens – Isoniazid (INH)

- 9-month regimen of isoniazid (INH) is one of the preferred regimens
  - *THE* preferred regimen for children 2-11 years of age
  - 6-month INH regimen is less effective (drops to 69%) but may be used if unable to complete 9 months
- May be given daily or intermittently (twice weekly)
- Use directly observed therapy (DOT) for intermittent regimen

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens – Isoniazid (INH)

- Doses
  - INH daily for 9 months - 270 doses *within* 12 months
  - INH twice/week for 9 months - 76 doses *within* 12 months
  - INH daily for 6 months - 180 doses within 9 months
  - INH twice/week for 6 months - 52 doses within 9 months

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens – Isoniazid (INH) and Rifapentine (RPT)

- 3-month regimen of INH and RPT is an option equal to 9-month INH regimen for treating LTBI in certain groups, such as otherwise healthy people, 12 years of age and older, who were recently in contact with infectious TB or who had tuberculin skin test conversions or positive blood test for TB*
- Must use directly observed therapy (DOT)

**MMWR*. Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens – Isoniazid (INH) and Rifapentine (RPT)

- Not recommended for
  - children younger than 12 years of age,
  - HIV-infected people taking antiretroviral therapy,
  - pregnant women, or women expecting to be pregnant within the 12-week regimen
- INH and RPT once a week for 3 months - 12 doses *within* 4 months

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens – Rifampin

- Rifampin (RIF) given daily for 4 months is an acceptable alternative when treatment with INH is not feasible (~~6 months for children~~).
- In situations where RIF cannot be used (e.g., HIV-infected persons receiving protease inhibitors), rifabutin may be substituted.
- RIF daily for 4 months - 120 doses *within* 6 months
- ~~RIF daily for 6 months - 180 doses for CHILDREN~~

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Red Book 2015: additional possible regimens for LTBI

- 3 months of daily isoniazid and rifampin, with the isoniazid dosage the same as when used alone and the rifampin dosage of 10 to 15 mg/kg/day (maximum 600mg)
- 2 months of daily rifampin and pyrazinamide when given as part of RIPE (rifampin, isoniazid, pyrazinamide, and ethambutol) therapy for suspected tuberculosis disease (which subsequently is determined to be *M tuberculosis* infection only). The rifampin dose is 10 to 20 mg/kg day, maximum 600 mg; and the pyrazinamide dose is 30 to 40 mg/kg/day, maximum 2 g.

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens for Specific Situations – HIV-Infected Persons

- Consult an expert in managing HIV and TB
- INH daily for 9-mo, *rather than 6-mo*, is optimal: 270 doses *within* 12 months
- RIF is generally contraindicated for persons taking protease inhibitors or delavirdine (Rescriptor®)
- Rifabutin can sometimes be substituted for RIF
  - with dose adjustments
- INH/RPT regimen not recommended for HIV-infected people taking antiretroviral therapy

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens for Specific Situations – Fibrotic Lesions Suggestive of Previous TB

- Should be treated for LTBI if they have
  - A positive TST reaction (at least 5 mm) or IGRA result
  - No symptoms of infectious TB disease, AND
  - No history of treatment for TB disease
- Treat only after active disease is excluded with sputum testing
- Acceptable regimens include
  - 9 months of INH
  - 4 months of RIF (with or without INH); 6 months for children.
  - 3 months of INH and RPT (12-dose regimen)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens for Specific Situations – Multidrug-Resistant (MDR) TB

Contacts of Persons with Multidrug-Resistant TB

- Consider risk for progressing to MDR TB disease before recommending LTBI treatment
- When prescribing treatment for these contacts, consult an MDR TB expert
  - Dual-agent regimen to which the M.tb is susceptible
  - Use of 2nd line antimycobacterial agents (e.g. levofloxacin)
  - Longer duration of treatment
  - Regular follow up is mandatory

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI Treatment Regimens for Specific Situations – Pregnancy and Breastfeeding

- Some experts prefer to delay treatment until after the early postpartum period, unless the pregnant woman is at high risk for progression to TB disease
  - has recent TB infection or HIV infection
- 9 months of INH daily or twice weekly; given with vitamin B6
  - Pregnant women receiving INH should be monitored carefully
- If unable to take INH, consult with TB expert
- Breastfeeding not contraindicated

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI in Transplant Candidates and Recipients

Eur Respir J 2012; 40: 990–1013
DOI: 10.1183/09031936.00000712
Copyright©ERS 2012

REVIEW

The risk of tuberculosis in transplant candidates and recipients: a TBNET consensus statement

Dragos Bumbacea, Sandra M. Arend, Fusun Eyuboglu, Jay A. Fishman, Delia Goletti, Michael G. Ison, Christine E. Jones, Beate Kampmann, Camille N. Kotton, Christoph Lange, Per Ljungman, Heather Milburn, Michele I. Morris, Elmi Muller, Patricia Muñoz, Anoma Nellore, Hans L. Rieder, Urban Sester, Nicole Theodoropoulos, Dirk Wagner and Martina Sester

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

LTBI in Transplant Candidates and Recipients

- Risk assessment in transplant recipients for the development of TB depends on, among other factors, the locally expected underlying prevalence of infection with *M. tuberculosis* in the target population.
- In areas of high prevalence, preventive chemotherapy for all transplant recipients may be justified without immunodiagnostic testing while in areas of medium and low prevalence, preventive chemotherapy should only be offered to candidates with positive *M. tuberculosis*-specific immune responses.
- The diagnosis of TB in transplant recipients can be challenging. Treatment of TB is often difficult due to substantial interactions between anti-TB drugs and immunosuppressive medications

Eur Respir J. 2012 Oct;40(4):990-1013. Epub 2012 Apr 10.
The risk of tuberculosis in transplant candidates and recipients: a TBNET consensus statement

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Completion of Therapy

Completion of therapy is based on the total number of doses administered, not on duration alone.

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Management of Patient Who Missed Doses

- Extend or re-start treatment if interruptions were frequent or prolonged enough to preclude completion
- When treatment has been interrupted for more than 2 months, patient should be examined to rule out TB disease
- DO*p*T may be recommended as needed

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

MONITORING DRUG TREATMENT

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Clinical Monitoring

Educate patient to report signs and symptoms of adverse drug reactions:

- Fever
- Headache
- Rash
- Anorexia, nausea, vomiting, or abdominal pain in right upper quadrant (hepatotoxicity)
- Fatigue or weakness
- Dark urine
- Persistent numbness in hands/feet (peripheral neuropathy)

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Clinical Monitoring

Monthly visits should include a brief physical exam and a review of:

- Rationale for treatment
- Adherence with therapy
- Symptoms of adverse drug reactions
- Plans for continued treatment

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Clinical Monitoring

INH hepatotoxicity is defined in the guidelines of the American Thoracic Society as an increase in ALT > 3 times ULN with symptoms of hepatitis and/or jaundice, or ALT > 5 times ULN without symptoms.

- Incidence of clinical hepatitis in persons taking INH is lower than previously thought (as low as 0.1%)
- Hepatitis risk increases with age
  - Uncommon in persons < 20 years old
  - Nearly 2% in persons 50 to 64 years old
- Risk increases with underlying liver disease or heavy alcohol consumption

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Clinical Monitoring

Original Article

Hepatotoxicity in Children Receiving Isoniazid Therapy for Latent Tuberculosis Infection

Shiow-Huey Chang,[1] Payam Nahid[2] and Sarah R. Eitzman[3]
[1]Public Health Department, Santa Clara County, San Jose, California; [2]Division of Pulmonary and Critical Care, University of California San Francisco, San Francisco General Hospital, California; and [3]Department of Pediatrics, Santa Clara Valley Medical Center, San Jose, California

Hepatotoxicity seen in 13 (1.1%) of 1235 children <18y old who completed 9-mo INH (0.8% of 1582 who started INH)

- 8 girls (62%), 9 Hispanics (69%)
- 11 of 13 had symptoms & signs (2 asymptomatic ALT >5xULN)
- 3 developed hepatotoxicity ≥ 6mo after INH start
- ALT dropped to normal in ALL patients after stopping INH

Conclusions. In children who have latent tuberculosis infection, isoniazid hepatotoxicity has low frequency and typically is reversible when isoniazid is stopped. Evidence of late drug-induced liver injury indicates the importance of monitoring symptoms and serum transaminases throughout isoniazid therapy.

J Pediatr Infect Dis Society. 2014;3(3):221-227

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Baseline Laboratory Monitoring

Baseline liver function tests (e.g., AST, ALT, and bilirubin) are not necessary except for patients with risk factors:

- ❑ HIV infection
- ❑ History of liver disease
- ❑ Regular alcohol use
- ❑ Pregnancy or in early postpartum period

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Repeat Laboratory Monitoring

- ✓ Abnormal baseline results
- ✓ High risk for adverse reactions
- ✓ Symptoms of adverse reaction
  - ✓ Nausea; RUQ pain
- ✓ Liver enlargement or tenderness during examination
- ✓ Current or recent pregnancy

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Laboratory Monitoring

- Asymptomatic elevation of hepatic enzymes
  - seen in 10%-20% of people taking INH
  - Levels usually return to normal after completion of therapy
- Discontinue treatment if transminase level is
  - ≥ 3x ULN if patient has symptoms of hepatotoxicity
  - ≥ 5x ULN if patient is asymptomatic

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Meeting the Challenge of TB Prevention

For every patient:

- ✓ Assess TB risk factors
- ✓ If risk is present, perform TST or IGRA
- ✓ If TST or IGRA is positive, rule out TB disease
- ✓ If TB disease is ruled out, initiate treatment for LTBI
- ✓ If treatment is initiated, ensure completion

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Additional Resources

- Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection *MMWR* 2000; 49 (No. RR-6) http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm
- Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w
- CDC TB Website - http://www.cdc.gov/tb
- Latent Tuberculosis Infection: A Guide for Primary Health Care Providers http://www.cdc.gov/tb/publications/LTBI/default.htm

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

INSTRUCTIONAL CASES

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 1

- 7-year-old Hispanic male
- Moved to U.S. from Bolivia 4 years ago
- Received BCG vaccine at age 1 year
- Known contact of infectious TB case
- TST = 5 mm of induration
- No symptoms of TB disease
- Normal CXR, CBC, AST, and bilirubin

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Questions

1. What are this patient's risk factors for TB infection or disease?
2. What is the appropriate management for this patient?

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 1

Discussion of risk factors

- Patient is a contact of an infectious TB case
- Recent immigrant to the US from a country with a high prevalence of TB
- If the patient had not been a contact, the recent immigration (within 5 years) would have made him a candidate for targeted TB testing, but the 5-mm reaction would not be considered positive

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 1

Discussion of risk factors

- Persons who immigrate from TB-endemic countries have increased rates of TB
- Rates of TB approach those of their countries of origin for 5 years after arrival in the U.S.
- These increased rates most likely result from recent *M. tuberculosis* infection in their native country

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 1

Discussion of management

- As a contact of an active TB case, 5 mm of induration is considered positive
- This patient should be treated for LTBI immediately

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 2

- 12-year-old Asian female
- Moved to U.S. from Philippines > 5 years ago
- Plans to volunteer at a long term care facility
- TST result negative (0 mm) 1 year ago
- TST prior to volunteering = 26 mm of induration
- CXR normal
- No symptoms of TB disease
- No known contact with a TB patient

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Questions

1. What are this patient's risk factors for TB infection or disease?
2. What is the appropriate management for this patient?

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Case 2

Discussion of risk factors and management

- Patient's TST converted from negative to positive (within a 2-year period)
  - TST conversion increases risk for progressing from LTBI to TB disease
- Foreign-born status is less of a risk factor
  - i.e., she immigrated more than 5 years ago
- Patient is a recent converter and, as such, is a candidate for treatment of LTBI with INH

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Case 2

Discussion of management

- Patient's TST conversion indicates failure to identify this person as high risk for recent exposure to TB
- Patient may have had extended travel to her country of origin or other high-prevalence parts of the world

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Case 3

- 16-year-old Asian male
- Moved to U.S. from China < 5 years ago
- Received BCG vaccine in China as an infant
- QFT-GIT result = Positive
- CXR normal
- No symptoms of TB disease
- Known contact with a TB patient

UF UNIVERSITY of FLORIDA The Foundation for The Gator Nation

Southeastern National Tuberculosis Center SHARE • LEARN • CURE

Questions

1. What are this patient's risk factors for TB infection or disease?
2. What is the appropriate management for this patient?

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Case 3

Discussion of risk factors

- Positive IGRA result suggests that *M. tuberculosis* infection is likely
  - result is not affected by prior BCG vaccination
- Recent immigrant to the US from a country with a high prevalence of TB
- Foreign-born status is a risk factor
  - i.e., he immigrated < 5 years ago
- Known contact with a TB patient

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Case 3

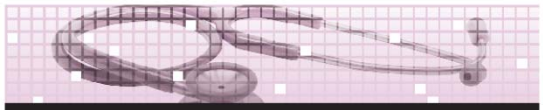
Discussion of management

- Patient recently immigrated from a TB endemic country
  - positive QFT-GIT result may be indicative of LTBI
- Contact with a TB patient could have been source of infection
- Should be treated for LTBI

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

Southeastern National Tuberculosis Center
SHARE • LEARN • CURE

Questions?



ADVANCED CONCEPTS IN PEDIATRIC TUBERCULOSIS

WEBINAR SERIES

In this 8-part series of modules, the Pediatric ID Board Certifying Examination Content related to TB is presented by expert speakers via case-based, interactive live webinars. The series goes beyond basic TB concepts while following the pediatric ID guidelines and is intended for a diverse audience, including pediatric ID fellows and faculty as well as other clinicians who diagnose and treat TB in children.

Advanced Concepts in Pediatric Tuberculosis series topics include:

- Introduction, Mycobacteriology, Pathogenesis and Epidemiology with Ana Alvarez - August 14, 2014
- Latent TB Infection with Nizar Maraqa - September 11, 2014
- Diagnosis: Old and New Diagnostic Tools & Challenges with Entesar Husain - October 9, 2014
- Clinical Manifestations and Work Up with Amina Ahmed - November 13, 2014
- TB and HIV with Ayesha Mirza - January 8, 2015
- Treatment of TB, including MDR with Jeffrey Starke - February 12, 2015
- Pharmacotherapeutics of TB Drugs with Charles Peloquin - March 12, 2015
- Infection Control, Source Case and Contact Investigation with Ana Alvarez - April 9, 2015

OBJECTIVES

Participants who complete this series will be able to recognize, evaluate and manage Mycobacterium tuberculosis infections in children.

REGISTRATION & COURSE DETAILS

- Register online for each live event: http://sntc.medicine.ufl.edu/Training.aspx
- Completion of a post-test evaluation is required to receive continuing education credit
- These webinars will be recorded and available on our website in the future.

QUESTIONS?

Contact the Southeastern National Tuberculosis Center (SNTC) by email at **sntc@medicine.ufl.edu** or call **352-273-7682** (toll free at **888-265-7682**).

Southeastern National Tuberculosis Center

UF UNIVERSITY of FLORIDA

UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation