Diagnosing TB infection

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Learning Objectives

After completing this training, participants will be able to:

1. conduct TB risk assessment screening to identify individuals at risk for latent TB infection and disease progression, to inform appropriate use in clinical practice

2. describe the diagnostic tests for latent TB infection including rationale for test selection and interpretation of results, to inform appropriate use in clinical practice

3. describe the impact of BCG vaccination on TB testing, to inform appropriate interpretations of results for clinical decision making

Polling question #1

TB Infection is:

A. Not a treatable Infection

B. Transmissible to others

C. Absence of active TB but positive TB testing (TST or IGRA)

D. Requires hospitalization

TB Infection (TBI) Definition

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

- is a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB.   - WHO definition

TB Infection vs TB Disease

TB Infection

- Asymptomatic; feels well
- Non-infectious
- Usually has a positive TB test
- Normal Chest x-ray
- Negative AFB Smears/AFB cultures

TB Disease

- Symptomatic; feels sick
- May be infectious to others
- Usually has a positive TB Test
- Abnormal chest x-ray or imaging
- Positive AFB smears/AFB cultures

Trends in Tuberculosis, 2022

Key Findings

The rate of decline in the United States remains too slow to achieve TB elimination in this century.

>80% of U.S. TB cases are attributed to reactivation of LTBI

Timely detection and treatment of TB and LTBI among persons at risk are needed to achieve TB elimination in the United States.

Source: Tuberculosis — United States, 2022
https://www.cdc.gov/mmwr/volumes/72/wr/mm7212a1.htm?s_cid=mm7212a1_w#F1_down

FIGURE. Tuberculosis disease cases* and incidence,† by patient U.S. birth origin status§,¶ — National Tuberculosis Surveillance System, United States, 2012–2022
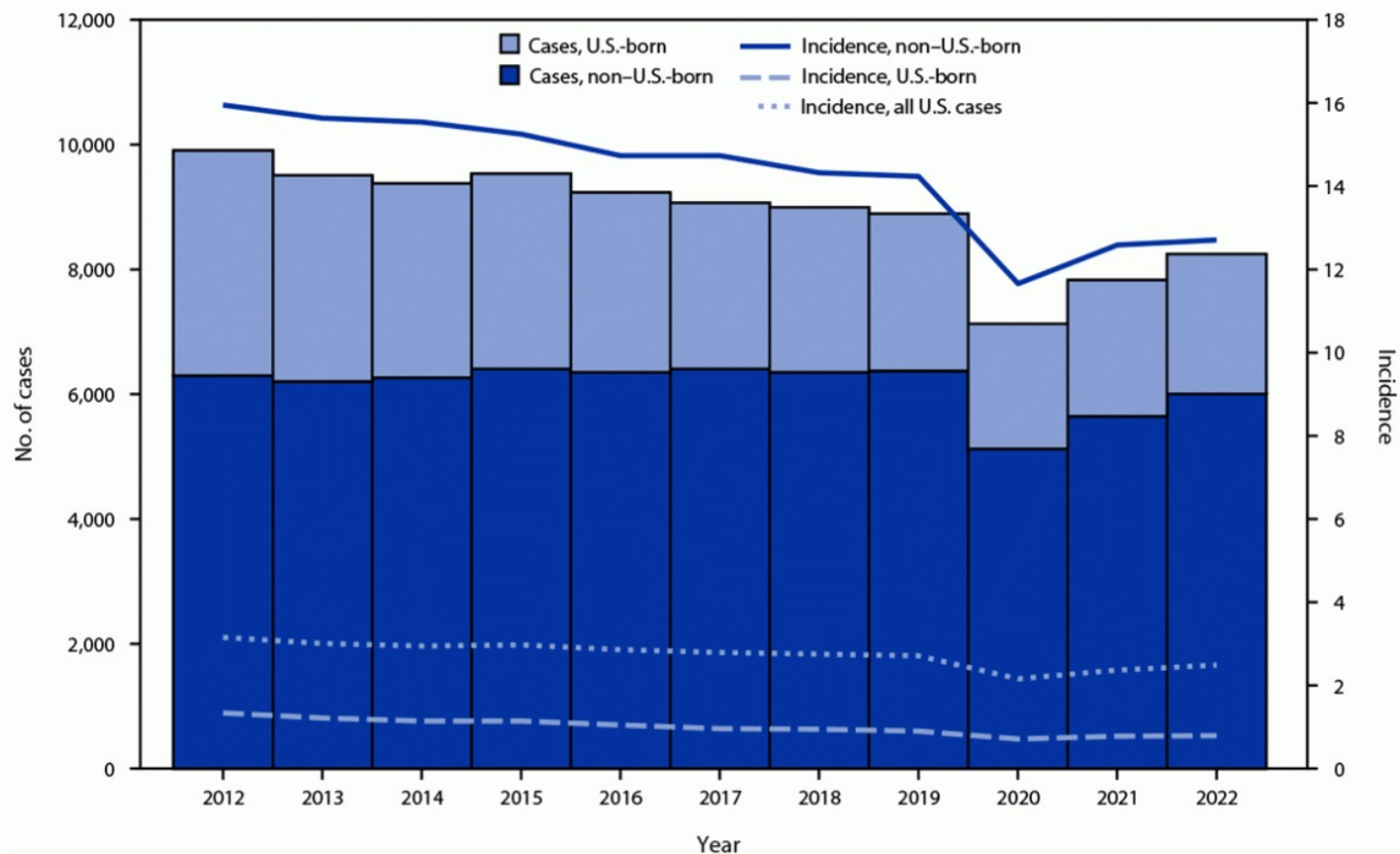
Persons at Risk for Developing TB Disease
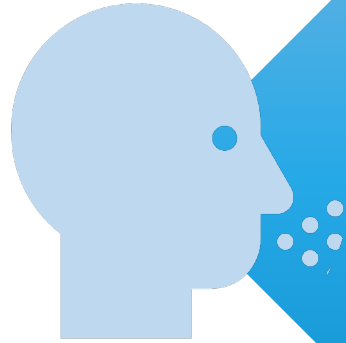
increased likelihood of exposure to persons with TB disease

clinical conditions that increase their risk of progressing from LTBI to TB disease

Polling question #2

Which of these options is a risk for TB exposure?

A. 2-year-old child

B. Elementary school cafeteria worker

C. Women living a women's shelter for last 4 months

D. All of the above

TB Exposure Risks

Persons at risk for exposure to persons with TB disease include:

- Close contacts to person with infectious TB

- Persons who have immigrated from areas of the world with high rates of TB

- Persons who work or reside with people who are at high risk for TB in facilities or institutions such as hospitals, homeless shelters, correctional facilities, nursing homes, and residential homes for those with HIV

Fig. 2.1.2 Estimated TB incidence in 2021, for countries with at least 100 000 incident cases
The eight countries that rank first to eighth in terms of numbers of cases, and that accounted for two thirds of global cases in 2021, are labelled.

Number of incident cases

100 000
500 000
1 000 000
2 000 000

China
Bangladesh
Philippines
Pakistan
India
Nigeria
Indonesia
Democratic Republic of the Congo
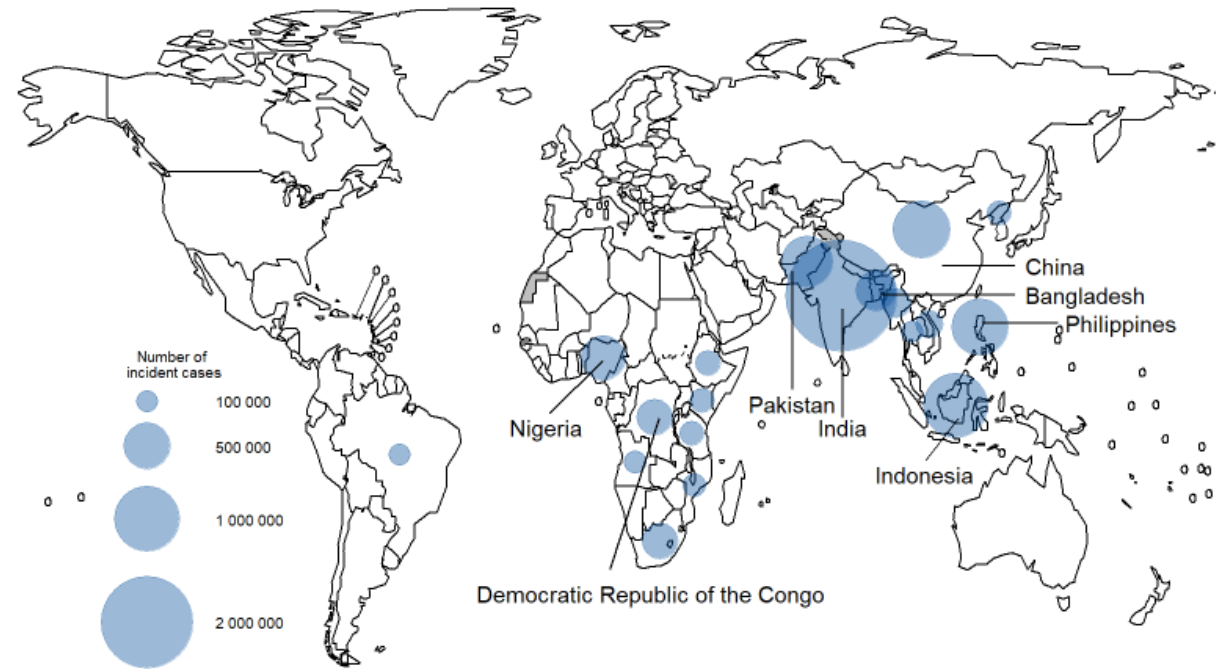
Source: WHO Global TB Report 2022 https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022/tb-disease-burden/2-1-tb-incidence

Polling question #3

Which group is at higher risk for progression from TB Infection to TB Disease?

A. 18-year-old volunteer with new positive TB test

B. 4-month-old exposed to grandfather with TB

C. 1st year nursing student

D. Patient starting treatment for Crohns with untreated TBI

Risk for Progression to Disease <u>after infection</u>
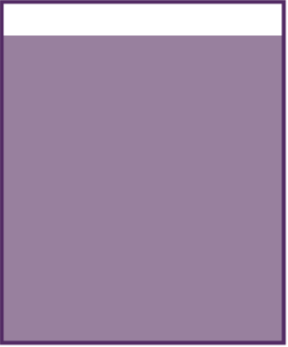
Persons who have been Recently Infected with TB Bacteria

- Children less than 5 years of age who have a positive TB test
- Groups with high rates of TB transmission, such as homeless persons, injection drug users, and persons with HIV infection
- Recent converters (first 2 years after conversion)

Persons with Medical Conditions that Weaken the Immune System

- Babies and young children often have weak immune systems.
- HIV infection
- Substance abuse
- Silicosis
- Diabetes mellitus
- Severe kidney disease
- Low body weight
- Organ transplants

- Head and neck cancer
- Medical treatments such as corticosteroids or organ transplant
- Specialized treatment such as TNF-α antagonists for rheumatoid arthritis or Crohn's disease

Risk of Developing TB Disease

TB infection and no risk factors (about 10% over a lifetime)	TB infection and diabetes (about 30% over a lifetime)	TB infection and HIV infection (a very large risk over a lifetime)
For people with TB infection and no risk factors, the risk is about 5% in the first 2 years after infection and about 10% over a lifetime.	For people with TB infection and diabetes, the risk is 3 times greater, or about 30% over a lifetime.	For people with TB infection and HIV infection (not on HIV treatment), the risk is about 7% to 10% PER YEAR, a very large risk over a lifetime.

What is our role in TB Elimination

Screening for Latent Tuberculosis Infection in Adults
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE In the US, tuberculosis remains an important preventable disease, including active tuberculosis, which may be infectious, and latent tuberculosis infection (LTBI), which is asymptomatic and not infectious but can later progress to active disease. The precise prevalence rate of LTBI in the US is difficult to determine; however, estimated prevalence is about 5.0%, or up to 13 million persons. Incidence of tuberculosis varies by geography and living accommodations, suggesting an association with social determinants of health.

OBJECTIVE To update its 2016 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a systematic review on LTBI screening and treatment in asymptomatic adults seen in primary care, as well as the accuracy of LTBI screening tests.

POPULATION Asymptomatic adults 18 years or older at increased risk for tuberculosis.

EVIDENCE ASSESSMENT The USPSTF concludes with moderate certainty that there is a moderate net benefit in preventing active tuberculosis disease by screening for LTBI in persons at increased risk for tuberculosis infection.

RECOMMENDATION The USPSTF recommends screening for LTBI in populations at increased risk. (B recommendation)

← Editorial page 1457
+ Multimedia
← Related article page 1495 and JAMA Patient Page page 1526
+ Supplemental content
+ Related article at jamanetworkopen.com

Author/Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

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Summary of Recommendation

Population	Recommendation	Grade
Asymptomatic adults at increased risk of latent tuberculosis infection (LTBI)	The USPSTF recommends screening for LTBI in populations at increased risk. See the Assessment of Risk section for additional information on adults at increased risk.	B

See the Summary of Recommendation figure.

Pathway to Benefit

To achieve the benefit of screening, it is important that persons who screen positive for LTBI receive follow-up and treatment.

Testing for TBI

Polling question #4

Which statement is true?

A. A TB skin test is the only test available to test for TB disease

B. IGRA can be used to test for TB infection

C. CDC recommends TB blood testing only

D. TB testing can detect transmission immediately after exposure

TB SKIN TEST

TB BLOOD TEST

Testing methods

- There are two testing methods available for the detection of *M. tuberculosis* infection in the United States:
  - Mantoux tuberculin skin test (TST)
  - Interferon-gamma release assays (IGRA)
    - T-Spot or
    - QuantiFERON Gold Plus

- These tests do not exclude LTBI or TB disease

- Decisions about medical and public health management should include other information, and not rely only on TST or IGRA results

TB Skin Test (TST)

Advantages

- Easy to perform
- Low cost
- Observation (reading) reflects an immune response
- Foundation of well controlled studies
- Well established definitions of TST conversion

Disadvantages

- Trained person to place and interpret test
- Variability in interpretation, reading may be subjective
- 2 visits necessary
- Need 2 tests for baseline for serial testing
- False positives/negative

Table 7. Criteria for tuberculin positivity, by risk group

Reaction ≥5 mm of induration	Reaction ≥10 mm of induration	Reaction ≥15 mm of induration
Human immunodeficiency virus (HIV)-positive persons	Recent immigrants (i.e., within the last 5 yr) from high prevalence countries	Persons with no risk factors for TB
Recent contacts of tuberculosis (TB) case patients	Injection drug users	
Fibrotic changes on chest radiograph consistent with prior TB	Residents and employees[†] of the following high-risk congregate settings: prisons and jails, nursing homes and other long-term facilities for the elderly, hospitals and other health care facilities, residential facilities for patients with acquired immunodeficiency syndrome (AIDS), and homeless shelters	
Patients with organ transplants and other immunosuppressed patients (receiving the equivalent of ≥15 mg/d of prednisone for 1 mo or more)*	Mycobacteriology laboratory personnel	
	Persons with the following clinical conditions that place them at high risk: silicosis, diabetes mellitus, chronic renal failure, some hemato-logic disorders (e.g., leukemias and lymphomas), other specific malignancies (e.g., carcinoma of the head or neck and lung), weight loss of ≥10% of ideal body weight, gastrectomy, and jejunoileal bypass	
	Children younger than 4 yr of age or infants, children, and adolescents exposed to adults at high-risk	

Source: Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000; 49(No. RR6)

*Risk of TB in patients treated with corticosteroids increases with higher dose and longer duration.

† For persons who are otherwise at low risk and are tested at the start of employment, a reaction of ≥15 mm induration is considered positive.

SOURCE: Adapted from Centers for Disease Control and Prevention. Screening for tuberculosis and tuberculosis infection in high-risk populations: recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR 1995;44(No. RR-11):19–34.

TST Performance - BCG

- Bacille Calmette-Guerin (BCG)
  - A vaccination given usually shortly after birth

- Impact of BCG vaccination on TST result is strongly associated with age when BCG vaccinated:
  - Greatest when BCG given after 1 year of age
  - BCG in infancy has little effect on TST ≥10 years after vaccination

- BCG World Atlas
  - http://www.bcgatlas.org/index.php

Image credit: WHO

Source: Farhat M, Greenaway C, Pai M, Menzies D.(2006) *IJTLD*.10(11):1192-1204

Handout

The Online TST/IGRA Interpreter × +

The Online TST/IGRA Interpreter
Version 3.0

The following tool estimates the risk of active tuberculosis for an individual with a tuberculin skin test reaction of ≥5mm, based on his/her clinical profile. It is intended for adults tested with standard tuberculin (5 TU PPDS, or 2 TU RT-23) and/or a commercial Interferon Gamma release assay (IGRA). For more details about the algorithm used, go to the About page. The current version of the algorithm contains modifications of the original version, which was detailed in a paper by Menzies, et al. (2008). For further information see references, or contact dick.menzies@mcgill.ca

Please select the best response for each field:

TST Size:
5-9 mm ▼

IGRA Result:
IGRA Not Done ▼

Age:
32 ▼

Age at immigration (if person immigrated to a low TB incidence country):
13 ▼

Country of birth:
Philippines ▼

BCG status: Vaccinated age ≥ 2 years ▼
For more info, visit: BCG World Atlas.

Recent contact with active TB: Close Contact ▼

Please select all the conditions that currently apply to the pa
(If none of these conditions apply, please leave boxes unchecked

☐ AIDS

☐ Abnormal chest x-ray: granuloma

Sidebar tabs: Calculator | About | Disclaimer | References | Links

Results

Printable version

Below are the results for a patient with a TST reaction of **5-9 mm**, who is **32** years old, born in **Philippines**, **immigrated at age 13**, whose BCG status is **Vaccinated age ≥ 2 years**, and who has had **Close Contact** with active TB.

The likelihood that this is a true positive test (PPV) is: **74.72%**

The risk of development of active tuberculosis disease for the next 2 years is estimated to be: **3.74%**

The annual risk of development of active tuberculosis disease after 2 years is estimated to be: **0.07%**.

The cumulative risk of active tuberculosis disease, up to the age of 80, is: **7.17%**

If treated with INH, the probability of clinically significant drug-induced hepatitis is **0.3%**, and the associated probability of hospitalization related to drug-induced hepatitis is **0.1%**.

Refresh

IGRA

Advantages

- BCG-vaccinated population
- Screening hard to reach populations
  - One patient visit
- 2-step testing not required
- Results can be available in 24 hours

Disadvantages

- Requires blood draw
- Requires access to lab
- Indeterminate rate may be higher in practice than in studies
- Errors in collecting and transporting blood, or in interpreting assays can decrease accuracy of IGRAs

Recommendations for TBI testing

ATS/IDSA/CDC Clinical Practice Guidelines: Diagnosis of TB in Adults and Children

- **Recommend IGRA** rather than TST in 5 years of older who
  - Are **likely to be infected** with mycobacterium tuberculosis
  - Have a **low or intermediate** risk of disease progression
  - LTBI testing is warranted (risk assessment)
  - Have a history of **BCG vaccination**
  - Or are unlikely to return for TST read
- TST is acceptable alternative when limitations exist
  - IGRA not available, too costly, too burdensome
- **Recommend TST or IGRA** in likely infected, **high risk** of progression.

Recommendations for TBI testing

- Recommend that persons at **low risk** for TB infection and disease progression **NOT** be tested for TB infection.
  - Suggest **IGRA instead of TST**
    - TST acceptable when limitations exist for performing IGRA
  - Suggest second test (TST or IGRA) if initial test is positive
- Healthy children over 5 years old TST over IGRA
  - Yield to IGRA preference for BCG

☐ **No**

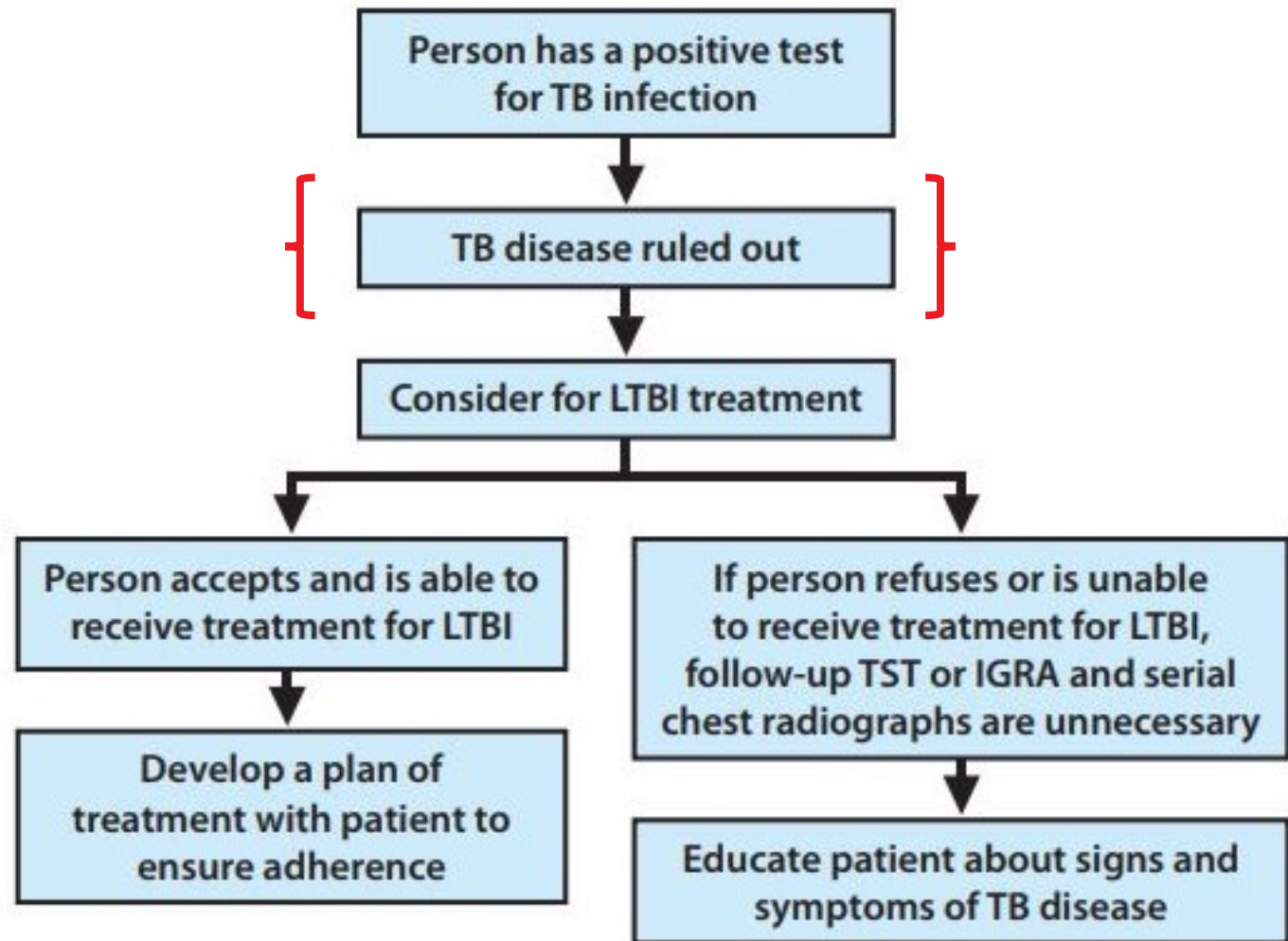| **TB testing is recommended if <u>any</u> of the 3 boxes below are checked** |
|---|
| ☐ **One or more sign(s) or symptom(s) of TB disease**
  • TB symptoms include prolonged cough, coughing up blood, fever, night sweats, weight loss, or excessive fatigue. |
| ☐ **Birth, travel, or residence** in a country with an elevated TB rate for at least 1 month
  • Includes countries <u>other than</u> the United States, Canada, Australia, New Zealand, or Western and North European countries.
  • Interferon gamma release assay (IGRA) is preferred over tuberculin skin test (TST) for non-US-born persons. |
| ☐ **Close contact** to someone with infectious TB disease during lifetime |
| **Treat for LTBI if TB test result is positive and active TB disease is ruled out** |

Who to test

CA Adult TB Risk Assessment

Polling question #5

Who would be considered low risk and SHOULD NOT be tested?

A. New elementary school teacher

B. Contact to a TB case

C. 18-year-old homeless shelter volunteer

D. Person newly immigrating from India

Evaluation of persons with Positive TB tests

Evaluation of Persons with Positive TB Test Results

Person has a positive test for TB infection
↓
TB disease ruled out
↓
Consider for LTBI treatment
↓ (branches)

Left branch:
Person accepts and is able to receive treatment for LTBI
↓
Develop a plan of treatment with patient to ensure adherence

Right branch:
If person refuses or is unable to receive treatment for LTBI, follow-up TST or IGRA and serial chest radiographs are unnecessary
↓
Educate patient about signs and symptoms of TB disease

Why is it important to rule out active TB prior to LTBI Treatment

- because failure to do so may result in
  - inadequate treatment of active TB disease and/or
  - development of drug resistance

Resources

CDC : Latent TB Infection info:
https://www.cdc.gov/tb/topic/treatment/decideltbi.htm

NTCA: Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations
http://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/#.YKKQPahKhhE

Centers of Excellence:
Curry International Tuberculosis Center (CITC)

Global Tuberculosis Institute at Rutgers, The State University of New Jersey (GTBI)

Mayo Clinic Center for Tuberculosis (MCCT)

Southeastern National Tuberculosis Center (SNTC)

BCG Atlas:
http://www.bcgatlas.org/

TST/IGRA online interpreter site:
http://tstin3d.com/

Break

- 20-20-20

The rule says that for every 20 minutes spent looking at a screen, a person should look at something 20 feet away for 20 seconds.