Technical Instructions for Panel Physicians

Lisa Armitige, MD, PhD

June 16, 2022

TB in Children and Pregnant Women: For Clinicians, by Clinicians
Webcast Series Part 1 of 6
June 16, 2022

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Lisa Armitige, MD, PhD has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity

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Assistant Medical Director
Heartland National TB Center

WEBCAST SERIES
TB in Children and Pregnant Women:
For Clinicians, by Clinicians
Thursday, June 16, 2022

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Objectives

- Describe the CDC TB Technical Instructions (TI) for TB updates.
- Explain the application of TIs for TB screening.
- Explain the application of the TIs for Directly Observed Therapy.
- Describe the guidelines for clearance for travel.
- Discuss the impact on US TB care after implementation of the TIs.

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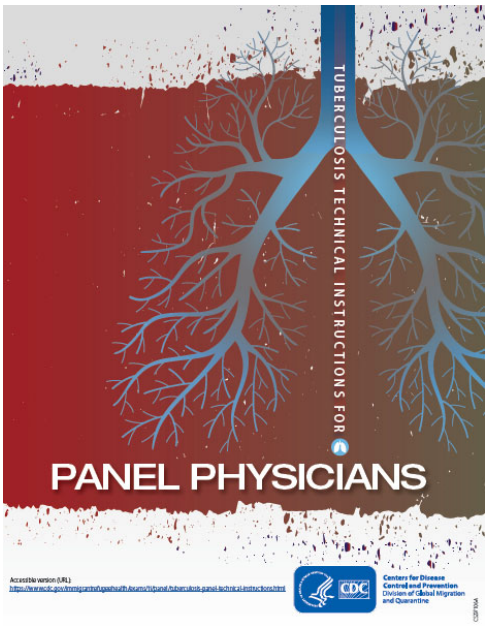

Accessible version (URL): https://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-panel-technical-instructions.html

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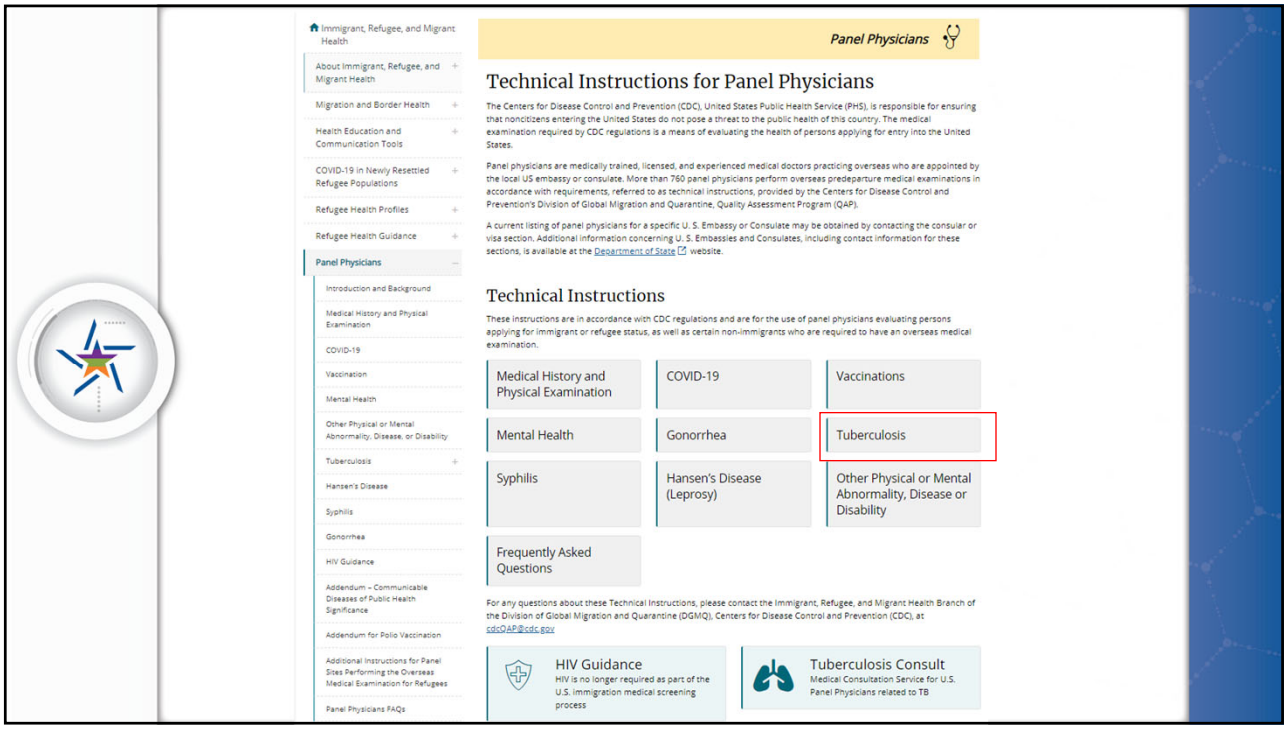

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Medical Screening Overseas

- The Centers for Disease Control and Prevention (CDC), United States Public Health Service (PHS), is responsible for ensuring that noncitizens entering the United States do not pose a threat to the public health of this country.
- The medical examination required by CDC regulations is a means of evaluating the health of persons applying for entry into the United States.

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Panel Physician (Definition)

- Medically trained, licensed and experienced medical doctor practicing overseas who is appointed by the local U.S. Embassy or Consulate
- There are 760 panel physicians who perform overseas pre-departure medical exams in accordance with the technical instructions provided by the CDC and DGMQ Quality Assessment Program (QAP).
- These medical professionals receive U.S. immigration-focused training in order to provide examinations as required by the Centers for Disease Control and Prevention (CDC) and U.S. Citizenship and Immigration Services.

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Overview of TB TIs for Panel Physicians

- Based on the understanding that the medical screening for TB is an essential component of the medical evaluation
- The emphasis for the pre-immigration medical evaluation is on infectiousness (disease of lung parenchyma, pleura, larynx, intrathoracic lymph nodes).
- Extrapulmonary tuberculosis and latent tuberculosis infection (LTBI) are not included in the definition of tuberculosis disease for the purposes of these Technical Instructions.
- These instructions define the specific responsibilities of panel physicians in terms of testing and treatment of tuberculosis disease among applicants overseas for purposes of US immigration medical eligibility only.

https://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/technical-instructions-panel-physicians.html

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Background and Outcome

- Each year, approximately, **450,000 immigrants and 70,000 refugees** enter the US after being screened at a panel site
- Technical Instructions from 1991 only required a CXR for ≥ 15 years of age. Later analysis showed this to be 34% sensitive at detecting active disease prior to immigration
- Approximately 1,100 cases of TB were diagnosed during 2012 on their overseas exam. About 60% of those were smear negative/culture positive cases. Of those cases, 14 were MDR
- Successful implementation of this screening program: savings in excess of $15 million yearly

Posey, D.. . . Cetron, M. (2014). Implementation of New TB Screening Requirements for U.S. - Bound Immigrants and Refugees - 2007-2014. Morbidity and Mortality Weekly Report (MMWR), 63(11), 234-236. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6311a3.htm?s_cid=mm6311a3_w

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More Facts!

- Retrospective study from records of 122 patients with active TB disease diagnosed at *Clinico Medica Internacional* from 2009 – 2012
- All cases confirmed by culture
  - 80% were smear negative and 20% smear positive
- 8 out of 10 cases would have been missed if sputum smear was the only diagnostic tool in these patients with abnormal chest X-rays. (Almost everyone is asymptomatic at their immigration exam)

Roberto Assael, MD, Joaquin Cervantes, MD, Gerardo Barrera, MD. *Smears and cultures for diagnosis of pulmonary tuberculosis in an asymptomatic immigrant population*. Clinica Medica Internacional, 2013. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3783499/

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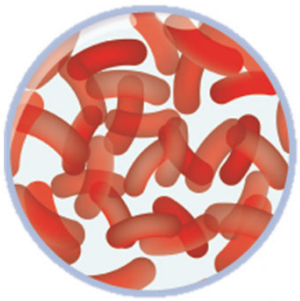
TB Screening

- Complete screening exam includes:
  - Medical history
  - Physical examination
  - IGRA (when required)
  - Sputum for AFB smear and culture testing for *Mycobacterium tuberculosis* (when required)
  - HIV is no longer part of the US medical screening process



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Medical History

- Focused on risk factors for TB disease
  - History of TB disease or current illness suggestive of TB disease
  - Prior diagnostic evaluation suggestive of TB disease
  - This can look different in children
- Inquiry about family or household contact to someone with TB disease
- History of BCG vaccination
- If history of TB disease but now with normal CXR, no current signs or symptoms and no known HIV: "**No TB Classification**"

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Physical Exam

- Height, weight, temperature, heart rate, blood pressure
- Pulmonary examination
- Inspection and palpation of lymph nodes
- Inspection for scars of scrofula or prior chest surgery

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IGRAs

- Applicants ages 2 through 14 years of age in countries with TB disease incidence of ≥ 20/100,000 must have an IGRA
  - No mention of one over the other (QFT or T spot)
- Exceptions to required testing
  - Written documentation of a **prior positive** IGRA (prior positive TST must still have an IGRA) with date, type, result in standard units and interpretation, testing physician information
  - Documented **previous TB disease**
- An **indeterminate should be documented as such** (no requirement for retesting by panel physician, CXR or B2 classification). Applicant should be advised to have it repeated in the US on arrival
- TST can only be substituted if an IGRA is not available in that country or in children < 2 y/o

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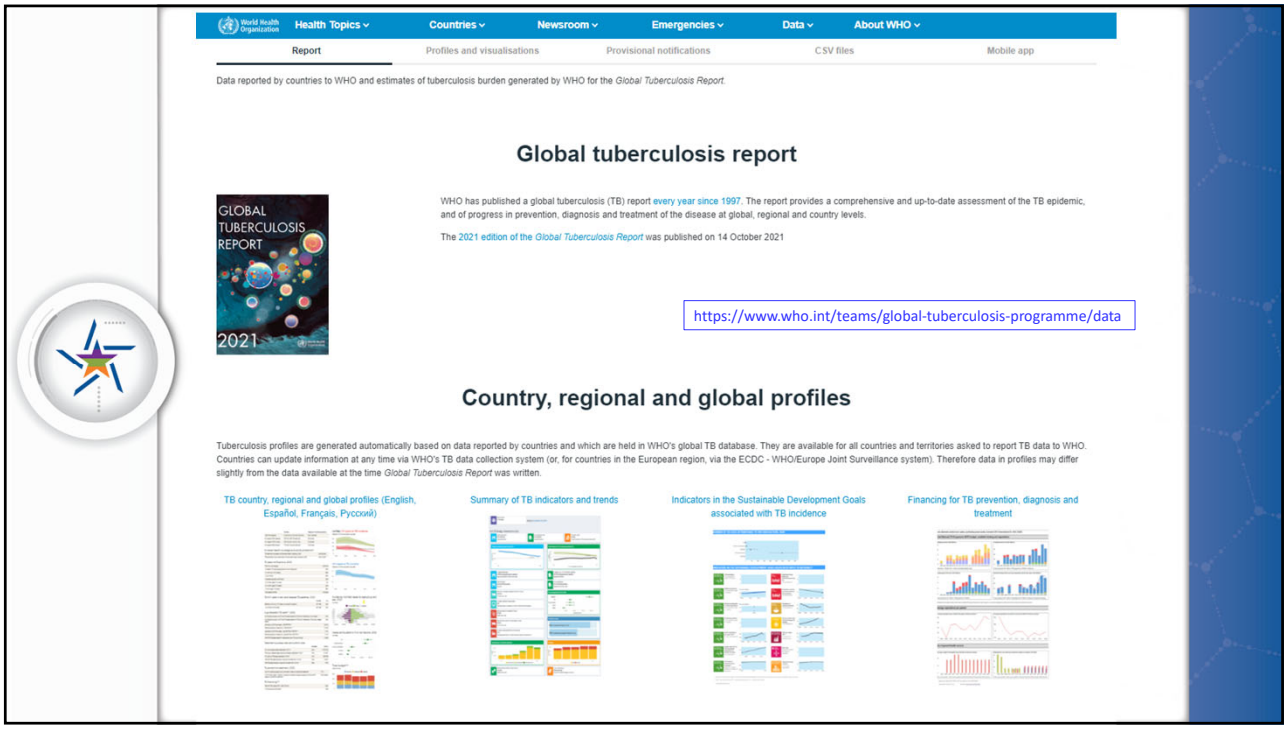
Health Topics
Countries
Newsroom
Emergencies
Data
About WHO
Report
Profiles and visualisations
Provisional notifications
CSV files
Mobile app
Data reported by countries to WHO and estimates of tuberculosis burden generated by WHO for the Global Tuberculosis Report.
Global tuberculosis report
GLOBAL TUBERCULOSIS REPORT 2021
WHO has published a global tuberculosis (TB) report every year since 1997. The report provides a comprehensive and up-to-date assessment of the TB epidemic, and of progress in prevention, diagnosis and treatment of the disease at global, regional and country levels.
The 2021 edition of the Global Tuberculosis Report was published on 14 October 2021
https://www.who.int/teams/global-tuberculosis-programme/data
Country, regional and global profiles
Tuberculosis profiles are generated automatically based on data reported by countries and which are held in WHO's global TB database. They are available for all countries and territories asked to report TB data to WHO. Countries can update information at any time via WHO's TB data collection system (or, for countries in the European region, via the ECDC - WHO/Europe Joint Surveillance system). Therefore data in profiles may differ slightly from the data available at the time Global Tuberculosis Report was written.
TB country, regional and global profiles (English, Español, Français, Русский)
Summary of TB indicators and trends
Indicators in the Sustainable Development Goals associated with TB incidence
Financing for TB prevention, diagnosis and treatment

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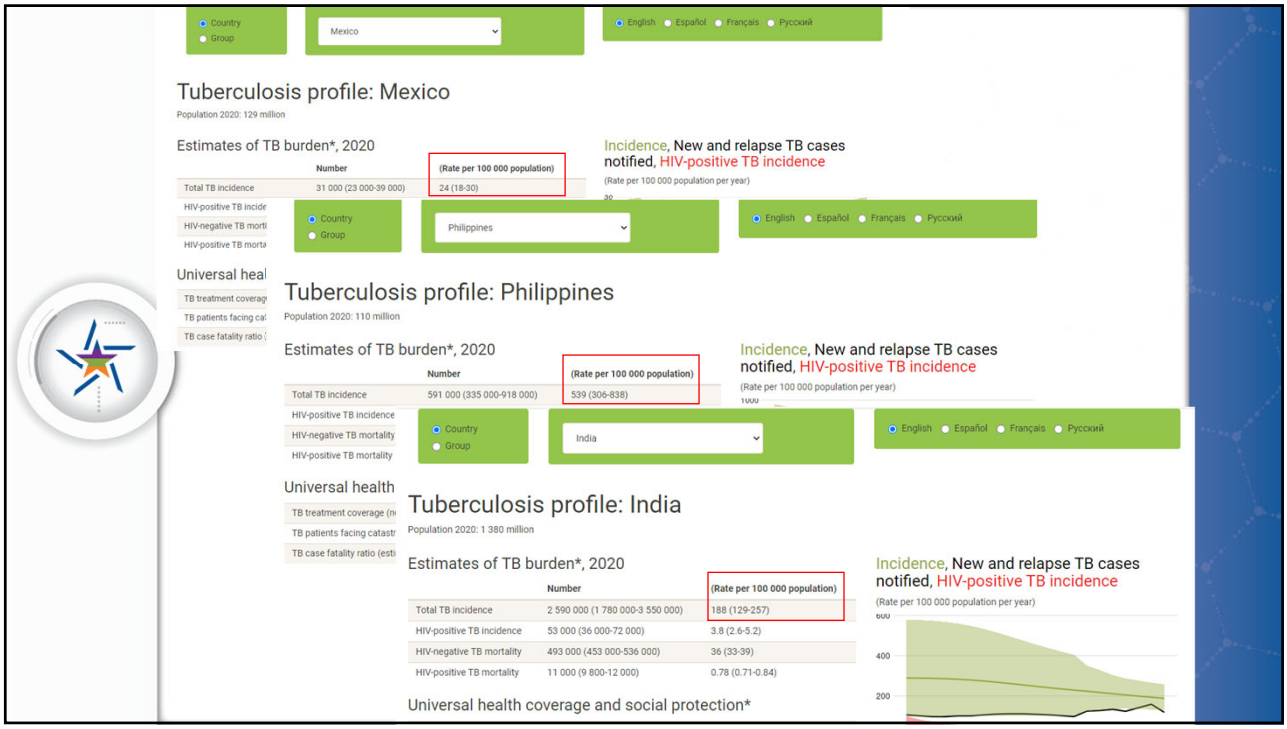
Country
Group
Mexico
English
Español
Français
Русский
Tuberculosis profile: Mexico
Population 2020: 129 million
Estimates of TB burden*, 2020
Number
(Rate per 100 000 population)
Total TB incidence
31 000 (23 000-39 000)
24 (18-30)
Incidence, New and relapse TB cases notified, HIV-positive TB incidence
(Rate per 100 000 population per year)
Philippines
Universal heal
Tuberculosis profile: Philippines
Population 2020: 110 million
Estimates of TB burden*, 2020
Total TB incidence
591 000 (335 000-918 000)
539 (306-838)
HIV-positive TB incidence
HIV-negative TB mortality
HIV-positive TB mortality
India
Universal health
Tuberculosis profile: India
Population 2020: 1 380 million
Estimates of TB burden*, 2020
Total TB incidence
2 590 000 (1 780 000-3 550 000)
188 (129-257)
HIV-positive TB incidence
53 000 (36 000-72 000)
3.8 (2.6-5.2)
HIV-negative TB mortality
493 000 (453 000-536 000)
36 (33-39)
HIV-positive TB mortality
11 000 (9 800-12 000)
0.78 (0.71-0.84)
Universal health coverage and social protection*

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HIV

- No longer part of the panel physician screening process
- Panel physicians may advise applicants about HIV testing if the panel physician feels it is indicated
- Patients must consent to HIV testing. Consent should include:
  - Applicants understand they do not have to be tested
  - Applicants understand if tested, they do not have to be tested by the panel physician
  - Applicants understand HIV results will need to be included in their paperwork if these results are known
- All HIV infected applicants must provide sputum for smear/culture regardless of CXR or IGRA result

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Chest Radiography

- < 10 years of age, AP or PA and lateral
- > 10 years of age, PA
- Must be interpreted by a radiologist AND reviewed by the panel physician
- Women who are pregnant may postpone until after pregnancy but must have one before immigration, must consent for imaging and must be provided a lead apron
- Must be digital radiography

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INTERIM UPDATE

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG COMMITTEE OPINION

Number 723 • October 2017 (Replaces Committee Opinion Number 656, February 2016)

Table 3. Fetal Radiation Doses Associated With Common Radiologic Examinations ⇦

Type of Examination	Fetal Dose* (mGy)
Very low-dose examinations (<0.1 mGy)	
Cervical spine radiography (anteroposterior and lateral views)	<0.001
Head or neck CT	0.001–0.01
Radiography of any extremity	<0.001
Mammography (two views)	0.001–0.01
Chest radiography (two views)	0.0005–0.01

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Sputum Collection

- Must have at least 3 specimens
- Early morning fasting, must be directly observed, 5-10 ml each, at least 24 hours apart, can be induced
- Applicants unable to produce sputum must have alternate collection method (gastric aspirates may be used for all ages, so can bronchoscopy)
- Sputum samples should be submitted for microscopy for AFB, culture for mycobacteria and drug susceptibility testing for positive cultures

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Culture Yield

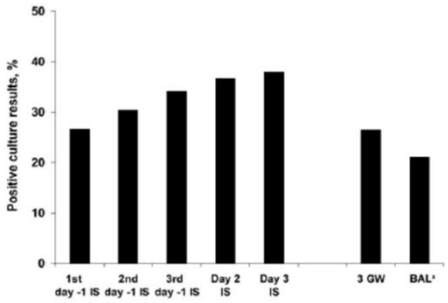

Figure 2. Proportion of subjects with cultures positive for *Mycobacterium tuberculosis*, by diagnostic technique, for 79 subjects with results for all 5 sputum samples obtained by induction with nebulized hypertonic saline (IS) and all 3 gastric washing (GW) specimens. Cumulative proportions are shown for the 5 IS samples. $P = .25$, by paired binomial probability test comparing diagnostic yield of all 5 IS samples versus 3 day 1 IS samples. *Bronchoalveolar lavage (BAL) culture results were available for 19 subjects.

Brown et al Clin Iinfect Dis 2007(44):1415

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Culture and Drug Susceptibility Testing

- Solid and liquid cultures must be performed and cultured a minimum of 6 weeks (liquid) and 8 weeks (solid), if positive, must be identified to the level of *M. tuberculosis* complex
- Positive cultures must have DST to at least INH, rifampin, EMB, PZA, Streptomycin
- Rifampin resistant cultures must have second line testing to at least ethionamide, fluoroquinolone, amikacin, capreomycin, PAS
- Panel physicians can use Xpert MTB/RIF, Xpert MTB/RIF Ultra or tests such as Hain GenoType MTBDRplus only if they have regulatory approval in that country

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ORIGINAL RESEARCH

Multidrug-Resistant Tuberculosis in U.S.-Bound Immigrants and Refugees

Yecai Liu[1], Drew L. Posey[1], Quanhe Yang[2], Michelle S. Weinberg[1], Susan A. Maloney[3], Lauren A. Lambert[4], Luis S. Ortega[1], Nina Marano[1], Martin S. Cetron[1], and Christina R. Phares[1]

[1]Division of Global Migration and Quarantine, [2]Division for Heart Disease and Stroke Prevention, [3]Division of Global HIV and TB, and [4]Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, Georgia

- Culture-based overseas TB screening in U.S.-bound immigrants and refugees prevented 24.4 MDR-TB cases per year from arriving in the United States, 18.2 cases more than smear-based overseas TB screening.
- Conclusion: Culture-based overseas TB screening in U.S.- bound immigrants and refugees substantially reduced the importation of MDR-TB into the United States.

Ann Am Thorac Soc Vol 19, No 6, pp 943–951, June 2022

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Applicants from Low Incidence Countries

- < 20 cases per 100,000 population
- < 15 years of age
  - Physical examination and history
  - Those with signs or symptoms suggesting TB disease should have an IGRA, a CXR and provide three sputum specimens
- >15 years of age
  - Medical history, physical examination, CXR
  - Those with signs or symptoms suggesting TB disease or known HIV must provide sputum for AFB smear/culture

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Applicants from High Incidence Countries < 2 years of age

- > 20 cases per 100,000 population
- Physical examination and history
- Those with signs or symptoms of active TB disease or known HIV must have:
  - An IGRA or TST
  - A CXR
  - Must provide three 'sputum' specimens for AFB smear/culture

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Applicants from High Incidence Countries 2–14 years of age

- **IGRA must be performed if available in the country of screening** (TST should be used only if IGRA not available)
- If the IGRA is positive, if there are signs or symptoms of active TB disease or if there is known HIV infection, the applicant must have a CXR
- Those with a CXR suggesting active TB disease, signs or symptoms of active TB disease or known HIV must provide three 'sputum' specimens for AFB smear/culture

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THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

US Postarrival Evaluation of Immigrant and Refugee Children with Latent Tuberculosis Infection Diagnosed Overseas, 2007-2019

Zanju Wang, MPH[1], Drew L. Posey, MD[1], Richard J. Brostrom, MD[2], Sapna Bamrah Morris, MD[2], Nina Marano, DVM[1], and Christina R. Phares, PhD[1]

(J Pediatr 2022;-:1-9).

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Algorithm for TB Screening (2–14-year-olds)

Figure1a: Tuberculosis screening for applicants 2 - 14 years of age in low TB burden countries*

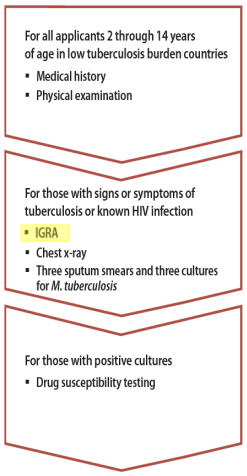
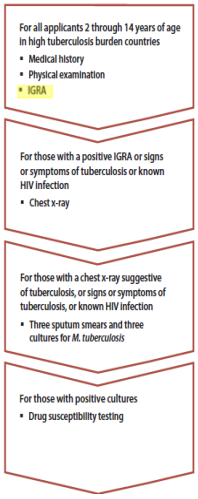


Figure 2a: Tuberculosis screening for applicants 2 - 14 years of age in high TB burden countries*



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Applicants from High-Risk Countries ≥ 15 years of age

- CXR
- Those with a CXR suggesting active TB disease, signs or symptoms of active TB disease or known HIV must provide three sputum specimens for AFB smear/culture

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Algorithm for TB Screening (≥ 15 years old)

Figure1b: Tuberculosis screening for applicants 15 years of age or older in low TB burden countries*

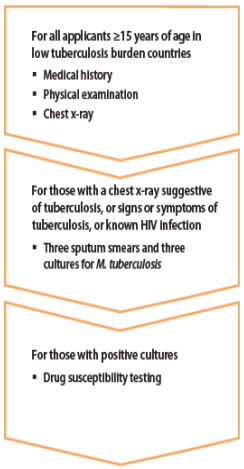
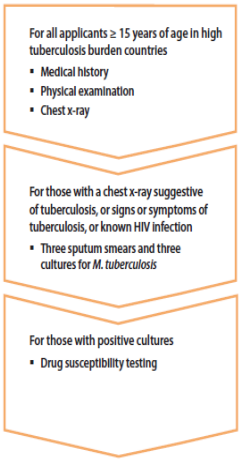


Figure 2b: Tuberculosis screening for applicants 15 years of age or older in high TB burden countries*



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TB Classifications and Travel Clearance

- **No TB Classification**
  - No HIV, no current findings to suggest active TB, negative IGRA, normal CXR.
  - Travel clearance valid for 6 months
- **Class A TB Disease**
  - Tuberculosis disease, includes extrapulmonary TB, CXR suggestive of TB disease (regardless of smear/culture)
  - Not cleared for travel until after treatment
  - Can request a waiver
- **Class B0 TB, Pulmonary**
  - Diagnosed with active TB by panel physician or presented to the Panel Physician on treatment who successfully completed treatment by DOT under supervision of panel physician
  - Travel clearance valid for 3 months from final culture

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TB Classifications and Travel Clearance

- **Class B1 TB, Pulmonary**
  - Signs or symptoms, physical exam or CXR suggest disease but smears/cultures negative and the applicant is not diagnosed with TB
  - Patients diagnosed with TB disease who refuse DOT by a panel physician and are returning after treatment and a 1 year wait
  - Travel clearance valid for 3 months from final culture
- **Class B1 TB, Extrapulmonary**
  - Extrapulmonary TB with a normal CXR and negative sputum smears/cultures
  - Travel clearance valid for 3 months from final culture
- **Class B2 TB, LTBI Evaluation**
  - Positive IGRA or TST, otherwise negative evaluation
  - All tests (if there were more than one) must be documented
  - If they are a contact to someone with active TB, they will get a B3 classification as well
  - Travel clearance valid for 6 months from final culture

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TB Classifications and Travel Clearance

- **Class B3 TB, Contact Evaluation**
  - Recent contact of a known TB disease case, regardless of IGRA or TST result
  - IGRA or TST result must be documented
  - Information about the source case must be provided
  - Travel clearance valid for 6 months from final culture
- **TB Classification Pending**
  - Any studies deemed necessary must reach a conclusion about the presence or absence of TB disease

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TB Classifications and Travel Clearance

- Applicants can be Class B1 and Class B3 OR Class B2 and Class B3
- Applicants with sputum smear positive for AFB cannot be cleared and should be started on treatment for TB disease
  - If the cultures finalize negative, the panel physician should use their judgment to decide if treatment should be continued
  - If the cultures grow NTM, the panel physician should use their judgement to determine if treatment should be continued
- Applicants with negative smears and positive cultures cannot be cleared and should be treated for active disease.

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TB Classifications and Travel Clearance

- For applicants with extrapulmonary TB (except for laryngeal/pleural/ IT LNs/lung parenchyma):
  - With a CXR suggesting TB disease should be treated for TB disease regardless of smear/culture results
  - With a normal CXR, negative sputum smears/cultures, can be cleared for travel (Class B1 TB)
  - Should be considered for treatment (must be DOT) if not traveling in the next 3 months
- Applicants with a single contaminated sputum specimen can be cleared to travel but if there are 2 or more contaminated specimens, 3 more specimens should be collected and resulted.

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TB Classifications and Travel Clearance

- Applicants diagnosed with active TB who refuse DOT are not cleared for travel. They must repeat the medical screening 1 year after the 'non-sanctioned' treatment. If the exam is negative, they can be cleared to travel with Class B1 TB, Pulmonary classification.
- Applicants ages < 10 years who require sputum analysis can travel as soon as the **smears** result negative (unless they have cavities, extensive disease/forceful cough, contact with MDR case). Document as Class B1 TB, Pulmonary, document the cultures are pending and email DGMQ the results when available.

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TB Treatment

- Must be based on US treatment guidelines and must use quality assured drugs
- Must be by DOT (which must be provided by panel physician, or they must identify an in-country treatment program)
- Panel physician must report applicants who refuse treatment by the panel physician.
- Applicants with rifampin resistance must be reported to DGMQ within 1 week of receipt of the DST report. The panel physician must request consultation with a Center of Excellence (COE).
- If the panel physician does not treat a patient with rifampin resistance, they must follow their treatment and alert DGMQ if it does not meet US treatment requirements.

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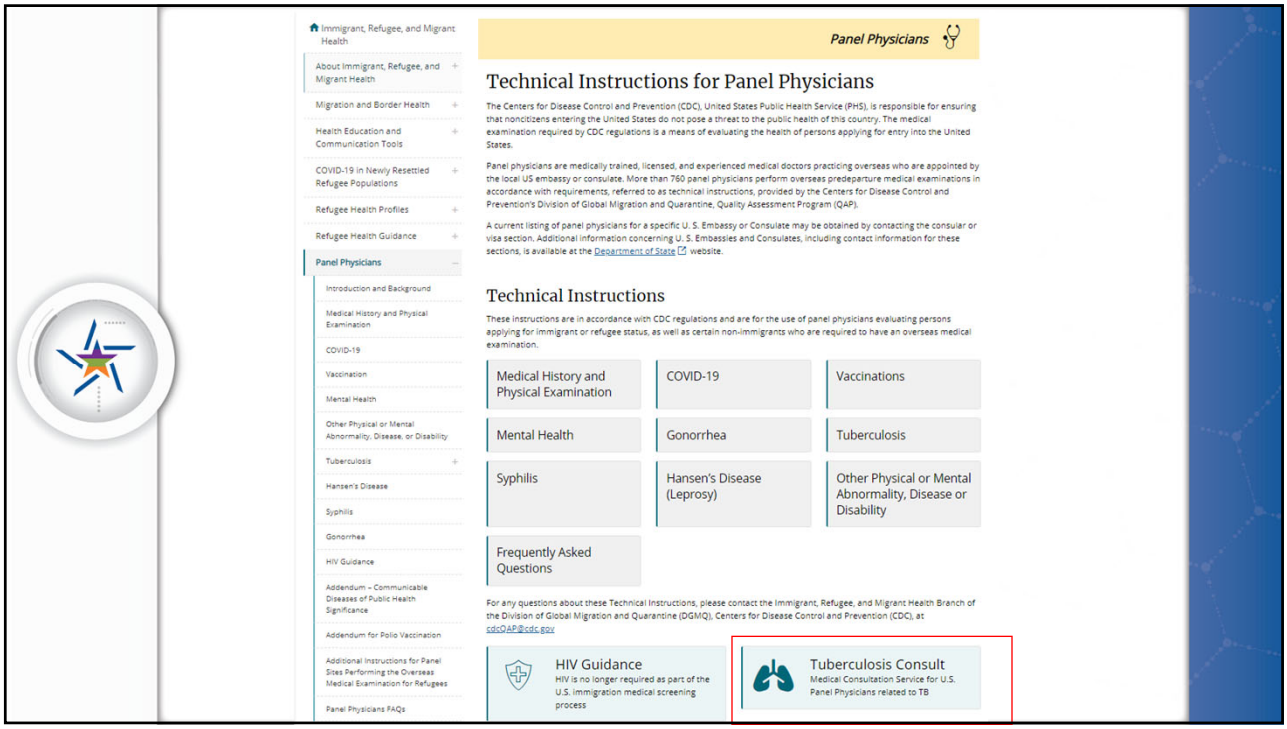

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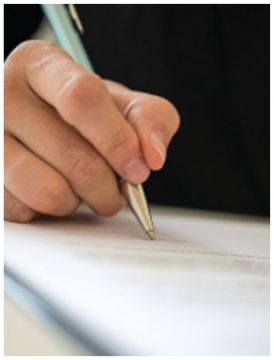
Waivers for Class A Patients with TB Disease

- A provision allows applicants undergoing pulmonary or laryngeal tuberculosis treatment to petition for a Class A waiver.
- Panel physician should provide all available medical information to the CDC (with a summary) and the Department of Homeland Security will make a determination



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TB Treatment Monitoring

- Again, must be based on US treatment guidelines
- Culture positive/rifampin sensitive:
  - 2 sputum specimens must be collected monthly for smear/culture during treatment until 2 consecutive cultures are negative
  - 2 sputum specimens must be collected for smear/culture at the end of therapy
- Culture positive/rifampin resistant:
  - 2 sputum specimens must be collected monthly during treatment
  - 2 sputum specimens must be collected for smear/culture at the end of therapy
- No drug susceptibility results (culture negative or contamination):
  - 1 sputum specimen must be collected monthly for smear/culture and at the end of therapy

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Contacts of TB Cases

- A contact is a person who has shared airspace with a person with smear or culture positive TB disease for a prolonged period (days/weeks, not minutes/hours)
- Applicants who are contacts must be evaluated for TB disease by the panel physician and receive an IGRA (or TST)
- If IGRA negative (TST < 5 mm), CXR normal (if indicated), no clinical symptoms of TB, no known HIV may travel immediately
  - **Class B3 TB Contact Evaluation**, if travelling < 8 weeks after break in contact (BIC)
  - If not travelling immediately, **and no treatment instituted**, repeat IGRA every 3 months until departure (if ongoing exposure) or until ≥ 8 weeks after BIC
  - If screening test negative ≥ 8 weeks after BIC, no B3 designation

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Contacts of TB Cases

- If IGRA positive (TST ≥ 5 mm), must have further evaluation (exam, CXR, symptom screen)
  - if any is positive, must provide sputum, and if diagnosed with TB must be treated
  - If sputum negative smear/culture, Class B1, pulmonary and Class B3
  - If all evaluation is negative, Class B2, LTBI evaluation and B3 (can be cleared immediately) but if no treatment and no immediate travel, must be reevaluated every 3 months until departure
- Children < 4 years of age and applicants with impaired immunity who are contacts to a known TB case
  - Preventative therapy should be initiated overseas (after TB disease has been ruled out by evaluation)
  - Should start DOPT regardless of result of the screening test (treatment can stop if IGRA/TST is negative after ≥ 8 weeks)
  - If applicant does not complete DOPT, may be cleared for travel while on preventative therapy as Class B3, Contact Evaluation, should receive a 30-day supply of medications and instructions on how to take them

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Documentation

1. CXR findings and images
2. IGRA results
3. Sputum AFB smear results
4. Cultures for mycobacteria
5. Drug susceptibility test results
6. DOT regimen
7. Clinical Course

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Conclusions

- The Technical Instructions are a key factor for success of TB elimination among immigrants screened overseas
- Panel Physicians play a vital role in the care of these patients
- The care provided by panel physicians is based on US guidelines and are compliant with the CDC and ATS standards for the diagnosis and treatment of TB

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THANK YOU
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