Contacts

Contributors to 2022 updates: **RANDALL R. REVES,** MD, MSc & **MICHELLE K. HAAS,** MD

SUMMARY OF KEY UPDATES (2022)

- Updates from literature and guidelines published since the last edition including recommendations from 2019 ATS/CDC/IDSA/ERS guideline for fluoroquinolone-based LTBI treatment among contacts to MDR-TB.
- Emphasis on treatment of MDR LTBI over clinical monitoring.

Transmission is the major source of drug-resistant TB (DR-TB); evaluation and treatment of contacts to DR-TB are essential.

Challenges: Limited data on LTBI treatment

Pending data from recent randomized clinical trials of treating latent TB infection (LTBI) from DR-TB, clinical treatment decisions are based on data from observational studies and expert opinion. A systematic review conducted in 2017 by Marks SM, et al., identified 21 observational studies that evaluated TB incidence, treatment completion, and adverse effects. The review identified six studies that compared TB incidence among contacts receiving multidrug-resistant- (MDR-) LTBI treatment compared to untreated contacts. Incidence of active TB disease was reduced by 90% in treated contacts. Most patients received fluoroquinolone-containing regimens that were better tolerated than any regimen containing pyrazinamide (PZA). These observational studies informed the latest 2019 American Thoracic Society/Centers for Disease Control and Prevention/European Respiratory Society/Infectious Diseases Society of America (ATS/CDC/ERS/IDSA) treatment recommendations for DR-TB contacts covered in this chapter.

Until more definitive data is available from clinical trials on the safety and effectiveness of second-line drug regimens for LTBI, clinicians caring for patients exposed to MDR-TB will be faced with discussing the risks and benefits of LTBI treatment based on observational data.

Contact identification

Research studies have demonstrated a wide variation in the concentration of infectious particles emitted by patients with smear-positive TB. Until new tools are developed to gauge the risk of infectiousness, public health staff must continue to rely upon sputum AFB smear grade and the results of contact tracing to determine if, and how extensively, transmission has occurred. One of the primary responsibilities of the case manager or disease investigator is to identify, locate, and evaluate contacts. **Identifying contacts of people with MDR-TB is important to detect active TB cases as well as to identify contacts with LTBI who were likely infected by the MDR-TB strain of the index case.**

Results from several studies show that up to 8% of contacts to MDR-TB cases were found to have active TB at the initial evaluation or during follow-up. Of the contacts identified to have active TB, half or more were detected at the initial evaluation, and most of the subsequent incident cases were detected within the first year after the diagnosis of the index case. The majority of culture-confirmed cases among contacts were due to transmission of MDR-TB, but some may have had isolates with other drug-susceptibility patterns.

Contact tracing for DR-TB often requires more resources for communication, e.g., an onsite "TB 101" or additional interactions with the media. Otherwise, in general, the process of performing TB contact tracing is the same whether a case is drug-resistant or not, and includes:

- Review of the index case's medical history and history of present illness with a focus on duration of symptoms, especially cough
- Interview of the index case to identify contacts and/or locations where transmission could have occurred
- Site visit to the locations identified to assess risk of transmission
- Based on the above factors, determine the risk of transmission (see section: ***TB transmission risk assessment***)
- Prioritization and evaluation of initial contacts, considering the risk of infection and risk factors among contacts
- Review of the data on baseline results of initial testing to assess the likelihood that transmission has occurred and whether expanded contact investigation may be indicated
- Provision of treatment for LTBI and follow-up of contacts
- Evaluation of contact tracing outcomes

This assessment of whether transmission of *Mycobacterium (M.) tuberculosis* has occurred due to exposure to MDR-TB is critical. Because many contacts to people with infectious TB might have been exposed previously, it can be challenging to determine whether TB infection among contacts represents recent exposure to a person with DR-TB or previous exposure to a person with drug-susceptible TB. **This determination should be based on the transmission risk assessment findings, the individual contact's TB exposure and LTBI history, and an evaluation of the results of the contact tracing.**

TB transmission risk assessment

The risk of TB transmission is contingent on 4 main factors:

1. **Infectiousness of the patient with TB:** Symptoms (particularly cough), sputum smear status, site of TB, presence of cavitary disease
2. **Environment where transmission likely occurred:** Size of room, amount of ventilation, presence of air-disinfection systems
3. **Characteristics of the contact's exposure:** Frequency of contact, use of mask or N95 respirator (or equivalent), proximity, and cumulative duration of the exposure
4. **Host susceptibility:** Very young age and immunocompromise (may or may not be at increased risk of infection, but at increased risk of progression to TB disease if infected)

Indications of transmission include:

- Identification of a secondary case
- High infection rate among contacts, especially among those with low epidemiologic risk (e.g., no prior residence in a TB endemic area)
- Infection in a child less than 5 years of age
- Contacts whose tuberculin skin test (TST) or interferon-gamma release assay (IGRA) results have converted from negative to positive

A "close contact" is described by CDC as:
"A person who had prolonged, frequent, or intense contact with a person with TB while he/she/they were infectious."

According to ATS and CDC, a TST conversion is defined as an increase in induration size by 10 mm or more within a 2-year period. An IGRA conversion is defined as a change from negative to positive within a 2-year period.

Contact TB exposure history

Taking a very thorough TB history from contacts with LTBI will help to assess the likelihood of recent infection and assist in treatment decisions. Unless there is documentation of a prior positive test or concern for a false positive TST (e.g., in a child from a country where bacille Calmette-Guérin [BCG] vaccine is given), a positive result at the time of contact evaluation for DR-TB exposure should generally be considered to represent recent infection.

Include these essential factors in the assessment:

- Prior TST or IGRA history. Taking the time to find documented prior TB testing history is time well spent in a DR-TB contact investigation. Sources of this information include:
  - **Employment or immigration/refugee health record**
  - **Primary care provider medical record**
  - **School health or immunization record**
  - **Military health/immunization records**
  - **Residence or treatment in a facility with TB testing policies:** Corrections, residential drug treatment, hemodialysis, homeless shelters, long term care, psychiatric hospitals, etc.
- History of previous exposure to TB — was the previous exposure to a patient with known drug-susceptibility test (DST) results?
- Was previous testing done with TST or IGRA?
- Was previous treatment for LTBI or active TB disease prescribed and completed? If so, what medications were used?
- Information on the contact's country of birth, year of arrival (if born outside of the U.S.), and travel history is helpful and may give clues to prior exposure potential

Testing for LTBI

LTBI is defined as a positive TST or IGRA without clinical or radiographic evidence of TB disease.

Two commercial IGRAs are available for the diagnosis of LTBI: **QuantiFERON®-TB Gold Plus (QFT-Plus)** and **T-SPOT.TB® (T-SPOT).** None of the tests for TB infection are direct measures of infection but are immunologic assays that measure cell-mediated immunity to protein (PPD for the TST) or more specific peptides (ESAT-6 and CFP-10 for both IGRAs). QFT-Plus replaced the QFT-GIT in 2018, eliminating the peptide TB-7.7 and adding a second antigen tube designed to stimulate both CD4 and CD8 T cells.

Guidance on use of IGRAs continues to evolve. The 2017 ATS/IDSA/CDC diagnostic guidelines recommend IGRA over TST in most people, although TST remains an acceptable option. Numerous studies have demonstrated the following:

- IGRAs appear to perform at least as well as TST in adults, children (including those less than 2 years of age), and immunocompromised populations, having equal or better sensitivity for active TB disease than TST.
- IGRAs have improved specificity over TST, particularly in BCG-vaccinated persons.

In an analysis of TST and both IGRAs done in 12,000 individuals at higher risk for TB exposure, either IGRA was superior to TST. This finding was likely related to false-positive TST results because of prior BCG vaccination particularly among immigrant children under 5 years of age for whom the prevalence of positive TST

was 28%, compared with less than 4% for either IGRA. The estimated TST positive predictive value was only 10%. Among all U.S.-born and non-U.S.-born populations, the positive predictive value of either IGRA equaled or was superior to the TST. In conclusion, during baseline screening of high-risk populations, IGRAs have a lower frequency of positive results compared to TST among individuals known or likely to have received prior BCG vaccination, a finding best interpreted as higher specificity rather than lower sensitivity.

Currently, no data exist to determine the optimal timing for performing IGRAs in exposed individuals, but it is reasonable to assume that the tests perform similarly to the TST; i.e., the assumption has been accepted that a test 8-10 weeks after the last exposure is adequate for detection of new TB infection. In general, **test contacts at the time exposure is recognized and again 8-10 weeks following the last exposure.**

As with the TST, a negative IGRA does not rule out early LTBI or even TB disease. This fact is particularly important in subgroups at high-risk for progression to TB disease, such as young children, and adults living with HIV or other medical conditions associated with defects in cell-mediated immunity such as treatment with TNF alpha inhibitors. When the risk of progression is high and the validity of TST and/or IGRA questionable, clinicians may treat in the face of discordant results or in the absence of positive test results.

There appears to be **no value in repeating IGRAs after completion of LTBI therapy** in an attempt to document IGRA reversion.

General principles of evaluating and managing contacts

- Evaluate exposed contacts expeditiously to identify any other cases of TB disease and to prevent further transmission.
- **Rule out TB disease prior to starting any treatment.** Before starting a patient on treatment for LTBI, exclude TB disease to avoid amplification of resistance (by use of an LTBI regimen when active TB disease is present). This evaluation should include a comprehensive symptom screen and a chest radiograph if a positive TB test or respiratory symptoms are present. Patients with other symptoms suggestive of TB (e.g., lymphadenopathy) should undergo a directed diagnostic work up for active TB disease.
    - Children under 5 years of age and persons with HIV infection or significant immunosuppression (e.g., organ transplant, anti-TNF alpha treatment) are routinely evaluated by chest radiography (including a lateral view) even if the TST or IGRA are negative.
    - Some persons with normal chest radiographs should have sputum and other specimens collected if there are clinical signs or symptoms of TB.

- **General principles for treating LTBI are as follows:**
  - Efficacy of any regimen depends on adherence to and completion of therapy.
  - Educate patients on drug resistance, drug side effects, importance of adherence, and TB symptoms.
  - Select the most effective, best-tolerated regimen to which the presumed source case isolate is susceptible and, ideally, for which results of clinical trials have established efficacy.
  - In children under 5 years of age and in close contacts who are living with HIV who have initial negative LTBI tests, **consider window prophylaxis** (i.e., treating for LTBI until there is a reliable negative test result at least 8-10 weeks after last exposure) particularly in the context of documented transmission. See section: ***Window prophylaxis***.
  - Consider the patient's wishes, as there is limited evidence to guide treatment of presumed MDR-LTBI.
- Experts agree that, regardless of the decision to treat or the treatment option selected, it is important to:
  - **Follow those with presumed latent MDR-TB infection at regular intervals for a minimum of 2 years following exposure.** (See sections: ***Follow-up of DR-TB Contacts and No Treatment: Clinical Monitoring***).
  - **Educate patients about the signs and symptoms of TB and encourage patients to return to care if they develop symptoms concerning for TB disease.**

The importance of treating LTBI

- For contacts, overall, there is a **5-10% lifetime risk of developing TB disease** following infection, half of the risk occurring within 1 to 2 years after infection. Among people testing positive for LTBI who were not recently infected, the annual risk (in the absence of other risk factors) is estimated at 0.1%.
- **Treatment of LTBI is widely recommended for individuals at increased risk of developing TB disease,** including, but not limited to, contacts to people with infectious TB, people living with HIV and other immunocompromising conditions, children, and people who have lived previously in TB endemic areas.
- The LTBI treatment options that have well-established efficacy and tolerability profiles are largely for drug-susceptible LTBI. **Given the high morbidity and mortality associated with DR-TB disease, treatment of LTBI thought to be due to infection with DR-TB should be considered** but weigh the risks and benefits of available regimens and their potential toxicities.

Selecting a treatment regimen for contacts to drug-resistant TB

Variables to consider

- Drug-susceptibility pattern of the *M.tuberculosis* isolate of the presumed source case
- Infectiousness of the source DR-TB case and closeness and intensity of DR-TB exposure
- Contact's likelihood of prior exposure to drug-susceptible TB, which can be evaluated by:
  - Place of birth and history of foreign residence or travel
  - History of prior TB disease or exposures to TB disease
  - TST/IGRA history. Note: Interpret TB testing history cautiously – prior positive TST during routine screening in younger immigrants may have been false-positive TST due to BCG cross-reaction. IGRA testing of such contacts is recommended because some may have negative IGRA results at baseline and be candidates for 8-week post-exposure testing. For those with a positive baseline IGRA, one cannot distinguish between those previously infected or more recently infected with DR-TB.
- Likelihood that the contact will progress to TB disease, including factors such as:
  - **Immunosuppression** (HIV, steroids, tumor necrosis factor [TNF] alpha agents, other immune-suppressing drugs)
  - **Age** (less than 5 years of age; even higher probability of progression among children less than 1 year of age)
  - **Documented TST** or **IGRA conversion**
  - **Diabetes, renal failure,** and **certain other medical conditions**
- Tolerability and toxicity of potential anti-TB drugs for treatment of LTBI

In 2019, ATS/CDC/ERS/IDSA updated recommendations for treatment of DR-TB contacts:

- For patients exposed to DR-TB, either a fluoroquinolone* for 6-12 months alone or with a second active drug (based on source-case isolate DST results) versus observation alone, avoiding PZA due to toxicity
- For patients exposed to fluoroquinolone-resistant TB, treatment with ethambutol (EMB) plus PZA could be considered if documented source-case susceptibility

Due to inadequate data, no recommendations for the use of any other drugs were given in the 2019 guidelines.

*Levofloxacin (LFX) may be preferred for children due to availability of an oral suspension. See **Chapter 6, *Pediatrics,*** for dosing information.

- Seek expert consultation in the selection of a treatment regimen for MDR-LTBI.

- Treatment of MDR-LTBI was estimated to be cost effective with both fluoroquinolone alone or fluoroquinolone with EMB being most cost-saving compared with no treatment, and more cost-saving than a fluoroquinolone with PZA.
- Consider the well-documented toxicity of PZA-containing regimens, and the poor tolerability of most of the second-line anti-TB drugs. Recommendations are based on expert opinion, and the **risk versus benefit must be evaluated.**
- For isoniazid- (INH-) monoresistant LTBI, rifampin (RIF) can be offered and is preferred over the use of a fluoroquinolone.
- A large observational study published in 2020 from Peru by Huang et al., found that that INH was as effective in preventing TB among contacts aged 19 years or younger exposed to household members with MDR-TB as those with INH-susceptible TB. INH was not effective against INH-monoresistant LTBI and a plausible mechanism for this intriguing finding is unclear. Nevertheless, this study raises the question of whether 6-9 months of INH might be effective against MDR LTBI.
- Other regimens such as RIF, INH plus rifapentine (RPT) or INH may be considered for patients likely to have been infected by a drug-susceptible case before exposure to the drug-resistant case, especially when the drug resistant exposure is brief or questionable and the prior positive test is well-documented and untreated.
- A 2014 observational study by Bamrah, et al., showed a treatment completion rate of 89% and no secondary MDR-TB cases among contacts treated with a fluoroquinolone as monotherapy or combined with EMB or ethionamide (ETA) in an MDR-TB outbreak in Micronesia. Of 15 contacts not treated, 3 developed TB disease (20%).
- Many providers treat children for DR-LTBI, although efficacy data from randomized controlled trials are lacking. In general, DR-LTBI regimens are better tolerated in children than adults. Fluoroquinolone monotherapy is sometimes used, especially in older children. See **Chapter 6, *Pediatrics,*** for more information on treating DR-LTBI in children.
- No treatment with clinical monitoring may be appropriate. (See section, ***No treatment: Clinical monitoring.***)

Table 1 lists suggestions for regimens that are fluoroquinolone-based, due to the significant activity of LFX or moxifloxacin (MFX) for TB disease and lower anticipated toxicity. Other second-line drugs for LTBI treatment may be less acceptable due to toxicity. The actual regimen chosen will depend on the individual clinical scenario; consultation with an expert in drug-resistant TB is recommended.

TABLE 1. **Specific treatment options dependent on susceptibility of source case isolate**

Resistance pattern	LTBI treatment options
INH (RIF-susceptible)	RIF 4 months (adults and children)
INH and RIF, with or without resistance to EMB and/or PZA	Fluoroquinolone or Fluoroquinolone + second drug 6-12 months • EMB if susceptible • Other second-line drug based on resistance pattern (seek expert consultation)
INH, RIF, fluoroquinolones, with or without EMB and/or PZA	Expert consultation recommended Options may include: • No treatment, clinical monitoring* • Other two-drug combinations may be considered but there are no data on risk versus benefit*

* See section: ***No treatment: Clinical monitoring***

**EMB + PZA is an option when EMB and PZA are susceptible. This regimen is a recommended option in ATS/CDC/ERS/IDSA 2019 guidelines. Use of PZA in LTBI treatment regimens has been associated with high rates of adverse events especially when combined with a fluoroquinolone. There is limited data on adverse events or efficacy of this regimen. Consider expert consultation.

Choosing DR-LTBI treatment

LFX or MFX monotherapy

- Better tolerated than 2-drug combination, and therefore more likely to complete regimen.
- Demonstrated bactericidal activity against *M. tuberculosis.*
- Limited observational data on efficacy in preventing progression to TB disease.
- Due to the potential risk of tendon rupture (a few case reports), advise patients to report any joint symptoms. One observational study of Medicare data (fluoroquinolones not used for TB treatment) showed an increased risk for LFX but not MFX.
- Use of fluoroquinolones for pediatric MDR-LTBI has been well-tolerated, despite concerns for potential arthropathy seen in animal studies. 2019 guidance suggests LFX preferred in pediatrics due to availability of suspension formulation. See **Chapter 6, *Pediatrics***.
- Consider the risks versus benefits regarding the use of fluoroquinolones in pregnant or breastfeeding women. (See **Chapter 7, *Co-morbidities and Special Situations,*** for more information.)
- Consider use in TST or IGRA converters and those with newly documented positive TST or IGRA, but who may have intermediate exposure to index case (exposure to MDR-TB was less certain)

LFX or MFX and a second drug (EMB preferable) to which isolate is likely to be susceptible (e.g., EMB, ethionamide [ETA], para-aminosalicylate [PAS], cycloserine [CS])

- Frequently poorly tolerated due to increased side effect profile.
- Side effects may deter patient from completing this regimen. Potential toxicity must be balanced against benefits. See section: ***LFX or MFX monotherapy*** for additional caveats regarding use of fluoroquinolones
- Limited observational data on efficacy in preventing progression to TB disease.
- Published experience in Texas, New York City, Orange County, California, and Geneva, Switzerland indicates **high risk for hepatitis and/or intolerance to a fluoroquinolone and PZA combination, and it should generally be avoided.**

Three clinical trials are evaluating additional regimens to treat DR-LTBI; all three trials are evaluating a six-month regimen and following-up for incident TB disease for 18–30 months.

- In Vietnam the V-QUIN trial is comparing LFX versus placebo among all MDR-TB contacts (ACTRN12616000215426, 2016).
- The TB CHAMP trial in South Africa compares LFX versus placebo among children under 5 years (ISRCTN-ISRCTN92634082, 2019).
- The PHOENIx trial (at ACTG sites) is comparing delamanid (DLM) versus INH for all contacts of MDR-TB (NCT03568383, 2018).

Mouse model data indicates that bedaquiline (BDQ) monotherapy is efficacious for LTBI but this has never been studied in human trials.

No treatment: Clinical monitoring

- This may be a reasonable alternative to treatment, particularly when the source resistance pattern limits options to toxic combinations, given the limited data on efficacy of treatment regimens for MDR-LTBI and side effects.
- **Evaluate with clinical exam, symptom review every 3 to 6 months for 2 years** (with chest radiographs and/or sputum collection every 6 months or as clinically indicated).
- Educate the patient about symptoms of TB disease.

Clinical monitoring without treatment, especially when there is evidence of significant transmission, is not advised when the contact is:

- Living with HIV or otherwise significantly immunocompromised
- Under 5 years of age
- Someone with a documented recent conversion or otherwise at high risk for progression to TB disease

Duration of therapy

- National guidelines recommend treatment of MDR-LTBI for 6 to 12 months. There are rare exceptions such as INH-monoresistant infection in which 4 months of RIF could be offered. Note: Most published experience with fluoroquinolones, either as mono-therapy or in combination, has been for 12 months.
- Lower-risk individuals should receive at least 6 months of treatment. Some experts recommend 9 months of therapy for children and others if it is tolerated.
- 12 months of treatment should be considered for people living with HIV, and other individuals with medical risk factors.
- Patient preference may help guide duration between 6 and 12 months.

Adherence and monitoring

- If local resources permit, consider directly observed therapy (DOT) for treatment of contacts with presumed MDR-LTBI especially those at higher risk for progression and nonadherence. Adherence enhancers, such as video-observed DOT, incentives, and enablers can also be considered.
- Individuals receiving treatment for DR-LTBI should be monitored closely and supported through side effects.
- Side effects should be treated symptomatically and with great encouragement and support as few alternate treatment options are available.
- Arthralgias and myalgias are common in patients receiving fluoroquinolones for prolonged periods of time. Expert opinion suggests that giving patients short drug holidays or a switch of fluoroquinolone may decrease these symptoms and allow for treatment completion.
- For patients starting LFX, a baseline assessment of renal function to guide dosing is important. MFX should be used cautiously in patients with liver disease, expert consultation is recommended.
- For patients at risk for QT prolongation (e.g., underlying cardiac arrhythmias, structural heart disease, treated with other medications that prolong the QT interval) consider performing a baseline ECG as well as a follow-up ECG at least 2-4 weeks into therapy. The optimal frequency of ECG monitoring in patients on fluoroquinolones is not well-studied and consultation with an expert is recommended. There is evidence to suggest LFX is less QT-prolonging than MFX and many experts will choose LFX over MFX for patients at higher risk.

Children under 5 years of age are at increased risk of developing active TB if infected and deserve aggressive evaluation and treatment if exposed to an individual with TB.

Window prophylaxis

Window prophylaxis is the practice of treating a patient who has been exposed to a person with infectious/pulmonary TB but has no current evidence of TB disease or infection.

- It can take weeks to months for the immune system to recognize a TB infection (and to produce a positive TST or IGRA test); therefore, **window prophylaxis** can potentially abort an early infection or prevent rapid progression from early TB infection to TB disease in vulnerable hosts.
- **Window prophylaxis for DR-TB should be considered in consultation with TB experts for the following two groups: children under 5 years of age, and people with HIV or other significant immunocompromise (e.g., organ transplant recipients, people treated with anti-TNF alpha medications, or other immunosuppressive medications).**
- Before window prophylaxis are initiated, contacts should be screened by history, physical exam, symptom review, and chest radiograph to rule out TB disease
- **Contacts are typically treated for 8 to 10 weeks from the end of risk of transmission, and then the TST or IGRA is repeated.** If the test has become positive, treatment for LTBI is continued to complete a full course. If the test remains negative, window prophylaxis is stopped.
- In patients who are immunocompromised or in infants less than 6 months of age, consider empiric treatment for LTBI even if follow-up testing is negative because the sensitivity of TST/IGRA is reduced in immunosuppressed patients.
- In the rare event that an infant or child with a negative IGRA or TST cannot be removed from ongoing exposure to a case of DR-TB and window treatment is not possible, the BCG vaccine might be considered. BCG may be challenging to obtain in the U.S. (See ***Resources*** at the end of this chapter for more information.)

Follow-up of DR-TB contacts

- It is essential to carefully educate contacts with DR-LTBI who have not received treatment and those finishing DR-LTBI treatment about the signs and symptoms of TB, stressing the need for prompt medical evaluation if symptoms occur.
- **Given the limited efficacy data on MDR-LTBI treatment, some experts recommend evaluation/symptom review every 3-6 months for 2 years, even for contacts who** have completed treatment. Chest radiographs and sputum testing should be done every 6 months or as clinically indicated. Special emphasis should be placed on high-risk contacts: people with HIV and other immunocompromised individuals; children under 5 years of age; and persons with documented TST/IGRA conversion.

SUMMARY

- Identification and evaluation of individuals who have been exposed to persons with TB caused by drug-resistant *M. tuberculosis* are critical activities to prevent ongoing transmission of drug-resistant organisms and to minimize health risks to exposed persons.
- Particular attention should be paid to evaluation of exposed persons who, if infected, have a high risk of developing active TB: children less than 5 years of age, persons with HIV infection, and persons with immunocompromising conditions or those on immunosuppressants.
- IGRAs may be used instead of TST in contact tracing, and IGRAs are especially preferred in non-US born persons who have a history of BCG vaccination, even if previously TST-positive.
- Careful contact tracing is required to determine likely timing of infection and appropriateness of treating for drug-susceptible LTBI or DR-LTBI.
- The drug resistance profile of the index patient should be taken into account when determining possible regimens for treating LTBI in contacts.
- There are limited data on efficacy of regimens for MDR-LTBI and MDR window prophylaxis. Seek expert consultation when selecting regimens.
- In select situations, clinical monitoring without treatment may be an appropriate option, but treatment of LTBI should be strongly considered in most circumstances, and particularly for patients at highest risk for progression to active TB disease.
- Given the lack of data on efficacy and the documented poor tolerability/toxicity of 2-drug regimens (especially regimens that include PZA), most contacts to fluoroquinolone-susceptible MDR-TB should receive fluoroquinolone monotherapy after active TB is excluded.
- High-risk contacts with MDR-LTBI, regardless of treatment, should be monitored for 2 years for evidence of progression to active TB disease.

Resources

Contact Investigation

Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR 2005; 54 (No. RR-15, 1-37).
www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm
Accessed September 28, 2022.

Instructions for BCG application

https://www.merck.com/product/usa/pi_circulars/b/bcg/bcg_pi.pdf
Accessed September 28, 2022.

Information about how to obtain BCG

BCG can be ordered from any wholesaler that distributes Merck vaccines. You may also contact Merck (800-672-6372) directly to determine if the product is available as shortages may occur. It is important to clarify your request for BCG vaccine for percutaneous use (not the BCG live for intravesical administration for bladder cancer).

The BCG World Atlas

An interactive website providing detailed information on current and past BCG policies and practices for over 180 countries. A useful resource to assist clinicians with interpretation of TB diagnostics.
http://www.bcgatlas.org
Accessed September 28, 2022.

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