

CHAPTER 2: DIAGNOSING AND MANAGING TB INFECTION

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Additional recommendations in this guideline chapter have been adapted from the original work "Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. 2018." This adaptation was not created by WHO. WHO is not responsible for the content or accuracy of this adaptation. The original edition shall be the binding and authentic edition.

SUMMARY OF RECOMMENDATIONS

- Both the tuberculin skin test (TST) and interferon-gamma release assay (IGRA) are acceptable alternatives for the diagnosis of TB infection. Which test is chosen depends on a number of factors.
- Adults who are immunocompromised should be offered testing for TB infection based on an individual risk assessment.
- New healthcare workers who will be in contact with patients or clinical materials should be offered testing for TB infection, if they are arriving from a country with high incidence of TB or if they have not received Bacillus Calmette–Guérin (BCG) vaccination.
- Short-course treatment regimens for TB infection are effective, safe and have higher treatment completion rates compared with longer-course isoniazid monotherapy.
- The regimen of preventive treatment of multidrug-resistant TB (MDR-TB) contacts should be evidence-based, taking account of the drug-resistance profile of the source case.

2.1 Introduction

TB infection (formerly referred to as Latent TB) is a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest TB disease (1).

The primary goal of testing for TB infection is to identify individuals who are at increased risk for the development of TB disease and therefore may benefit from treatment of TB infection to prevent TB disease. If testing for TB infection is performed, there must be an *a priori* commitment to providing tuberculosis preventative treatment (TPT) or active monitoring should TB infection be diagnosed (1, 2).

2.2 Diagnosing TB infection in adults

There is no gold-standard test to confirm the presence or absence of TB infection. Both the TST and IGRA are acceptable alternatives for TB infection diagnosis. Either test can be used for TB infection screening in any of the situations in which testing is indicated, unless specifically contraindicated. Which test is chosen may depend on a number of factors, including:

- Clinical context: TST may be preferable where large numbers of contacts need to be tested.
- Availability: IGRA testing or quantitative reporting of IGRA results may not be available to all clinical settings.
- Cost: IGRA testing may be more costly than TST.
- Staff: TST requires staff trained in its administration, measurement and interpretation (See [Appendix I](#)).
- Follow up: TST requires more than one appointment to obtain a result.
- Contraindications: TST may be contraindicated for some patients (See [Appendix I](#))

Both diagnostic tests may be used sequentially. If either one is negative or borderline, the other test may be used to increase sensitivity if the risk is high for infection, disease progression or for a poor outcome from TB disease, and/or a person has conditions that may reduce the sensitivity of the test (see [Section 22.6, Chapter 22: Tuberculosis](#) of the National Immunisation Advisory Committee guidelines)

When the initial IGRA result is borderline the IGRA may be repeated or a TST used to help arrive at a diagnosis (1).

TST test should only be carried out by those who have received training in its administration, measurement and interpretation.

2.2.1 Close contacts

- If the TST or IGRA is negative and performed within 8 weeks of contact, a second TST or IGRA should be scheduled no sooner than 8 weeks after contact was broken (3).
- If the TST or IGRA test is positive, assess for TB disease (also known as TB disease - see TB disease chapter). If a diagnosis of TB disease is excluded, offer treatment for TB infection.
- If the TST test is positive but a diagnosis of TB disease is excluded, consider an IGRA if more evidence of infection is needed to decide on TB infection treatment. This could be, for example, if the person needs enhanced case management or if there could be adverse events from treatment. Other considerations might include BCG history or non-tuberculous mycobacteria infection.

2.2.2 Adults who are immunocompromised

In adults who are anticipated to be or are currently immunocompromised, do a risk assessment to establish whether testing should be offered, taking into account their:

- Risk of progression to TB disease based on how severely they are immunocompromised and for how long they have been immunocompromised
- Risk factors for TB infection, such as country of birth or recent contact with a case of suspected or confirmed infectious pulmonary or laryngeal TB.

Consider an IGRA alone or an IGRA with a concurrent TST. The risk of a false negative result should be considered among patients who are immunocompromised (4).

If severely immunocompromised (such as those with human immunodeficiency virus (HIV) and CD4 counts of fewer than 200 cells/mm³, or after solid organ or allogeneic stem cell transplant), offer an IGRA with concurrent TST.

- If either test is positive (for TST, this is an induration of greater than 5 mm regardless of BCG history), assess for TB disease.
- If this assessment is negative, offer treatment for TB infection.

2.2.3 Healthcare workers

2.2.3.1 Recommend a TST or IGRA for newly employed healthcare workers who are from a high-incidence country.

- If either test is positive, assess for TB disease; if this assessment is negative, offer them treatment for TB infection.

2.2.3.2 Recommend a TST or IGRA for all other new healthcare workers who will be in contact with patients or clinical materials who have not had BCG vaccination (e.g. they are without a BCG scar, other documentation or a reliable history).

- If either test is positive, assess for TB disease; if this assessment is negative, offer them treatment for TB infection.

2.2.3.3 Recommend a TST or IGRA for new healthcare workers who have had contact with patients in settings where TB is highly prevalent:

- If either test is positive, assess for TB disease; if this assessment is negative, offer them treatment for TB infection.

Healthcare workers who are immunocompromised (see [section 2.2.2](#)) should be screened in the same way as other people who are immunocompromised.

2.3 Managing TB infection

Be aware that certain groups of people with TB infection are at increased risk of going on to develop TB disease, including people who:

- Are living with HIV
- have recently acquired TB infection (5).
- are having treatment with anti-tumour necrosis factor-alpha or other biologic agents
- are younger than 5 years (please see upcoming Paediatric TB Chapter for more information)
- have excessive alcohol intake
- are injecting drug users
- have had solid organ transplantation
- have a haematological malignancy
- are having chemotherapy

- have had a jejunioileal bypass
- have diabetes
- have chronic kidney disease or receive haemodialysis
- have had a gastrectomy
- have silicosis.

For people, including those living with HIV, with evidence of TB infection offer one of the following drug treatments (summarised in [Table 2.1](#))^{*}:

- 4 months of daily rifampicin
- 3 months of daily isoniazid (with pyridoxine) and rifampicin
- 3 months of once weekly isoniazid (with pyridoxine) plus rifapentine[†]

Alternatives:

- 6 months of daily isoniazid (with pyridoxine)
- 9 months of daily isoniazid (with pyridoxine)

^{*} Unless they are a contact of multi-drug or extensively resistant TB

[†] Currently not available in Ireland

Table 2.1: Summary of Recommended Treatment Regimens for TB Infection in Adults (6)

Regimen	Duration	Dose	Frequency	Common Adverse Effects
Rifampicin	4months (120 doses)	10mg/kg Maximum: 600mg	Daily	Rash, drug interactions
Isoniazid and rifampicin	3months (90 doses)	Isoniazid: 5mg/kg Maximum: 300mg Rifampicin: 10mg/kg Maximum: 600mg (rifampicin and isoniazid combination tablets may be an option)	Daily	Hepatotoxicity, peripheral neuropathy, drug interaction
Rifapentine* and isoniazid	3months (12 doses)	Isoniazid: 15mg/kg Maximum: 900mg Rifapentine: 10-14.0 kg: 300mg 14.1-25.0 kg: 450mg 25.1-32.0 kg: 600mg 32.1-49.9 kg: 750mg ≥50.0 kg: 900mg Maximum: 900mg	Once weekly	Flu-like reactions, drug interactions
Alternative Regimens				
Isoniazid	6 months (180 doses)	5mg/kg Maximum: 300mg	Daily	Hepatotoxicity, peripheral neuropathy
Isoniazid	9 months (270 doses)	5mg/kg Maximum: 300mg	Daily	Hepatotoxicity, peripheral neuropathy

* Rifapentine not licensed in Ireland www.hpra.ie (correct as of 21 May 24)

Short-course treatment regimens as above are effective, safe and have higher treatment completion rates compared with longer-course isoniazid monotherapy (7).

Shorter rifampicin treatment regimens have a lower risk of hepatotoxicity compared with longer-course isoniazid monotherapy.

Although effective, 6 or 9 months of isoniazid have higher toxicity risk and lower treatment completion rates compared with most short-course treatment regimens (7).

The risks and potential benefits of each treatment regimen should be clearly explained. In discussion with the patient, a suitable regimen should be selected, if they wish to proceed with preventive treatment. Drug treatments should only be offered if hepatotoxicity is not a concern.

Clinicians should choose the appropriate treatment regimen based on drug-susceptibility results for the source case (if known), co-existing medical conditions and potential for drug-drug interactions. If a person also has severe liver disease, a specialist multidisciplinary team with experience of managing TB and liver disease should be worked with.

2.3.1 Baseline testing

There is insufficient evidence to support testing of baseline liver function. It is, however, strongly encouraged, where feasible, for individuals with the following risk factors: history of liver disease, regular use of alcohol, chronic liver disease, HIV infection, age > 35 years, pregnancy or in the immediate postpartum period (within 3 months of delivery). For individuals with abnormal baseline test results, sound clinical judgement is required to ensure that the benefit of TB preventive treatment outweighs the risks, and they should be tested routinely at subsequent visits. Appropriate laboratory testing should also be performed for patients who become symptomatic while on treatment (e.g. liver function tests for those with symptoms of hepatotoxicity). Offer testing for HIV, hepatitis B and hepatitis C before starting treatment for TB infection.

2.3.2 Monitoring

Individuals receiving treatment for TB infection should be monitored routinely at monthly visits to health care providers, who should explain the disease process and the rationale of the treatment and emphasize the importance of completing it. Patients receiving treatment should be advised to contact their health care provider at any time if they become aware of symptoms such as anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-coloured urine, pale stools or jaundice. If a health care provider cannot be consulted at

the onset of such symptoms, the patient should stop treatment immediately and record date and time the treatment was stopped.

2.3.3 Adherence

All people having treatment for TB infection should have an assessment of potential barriers to adherence or treatment completion. Ensure people having treatment for TB infection who also have social risk factors, such as misusing alcohol or drugs or being homeless, are linked to support services. They should also have an assessment of social needs and stability, including potential barriers to adherence or treatment completion (this will be elaborated on in the upcoming National TB Guidelines Chapter on adherence, treatment completion and follow up).

People with TB infection who, for whatever reason, do not commence or complete treatment should be advised of the risks and symptoms of TB and, on the basis of an individual risk assessment, considered for follow up with serial chest radiography.[‡]

2.4 Managing TB infection in contacts of multi drug-resistant TB (MDR-TB)

The regimen of preventive treatment of MDR-TB contacts should be evidence-based, taking account of the drug-resistance profile of the source case. Later-generation fluoroquinolones (e.g. levofloxacin and moxifloxacin) are considered to be important components of a preventive treatment regimen unless the strain of the source case is resistant to them (2).

[‡] Note: Only applies to contact tracing and does not apply to health care work screening or pre-biologics.

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