Guideline

Testing, diagnosis and management of TB Infection

Summary Covers recommendations for testing, diagnosis, and management of tuberculosis (TB) infection in NSW. This Guideline includes recommendations for who should be tested, which tests to use, excluding TB disease, patient education and considerations, TB preventive therapy and chest x-ray monitoring.

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NSW Health

Guideline

Testing, diagnosis and management of TB Infection

Guideline Summary

This Guideline covers recommendations for testing, diagnosis, and management of people with tuberculosis infection (TBI) in NSW. Testing and management may be undertaken in Local Health District/Specialty Network TB services/chest clinics, or by a variety of other clinicians including various speciality areas.

Recommendations include who should be tested for TBI, which tests to use, exclusion of disease, patient education, TB preventive therapy (TPT) and chest x-ray monitoring.

Key Principles

TB infection (TBI) testing, diagnosis and management must be provided free of charge to the patient. This includes clinical, laboratory and radiological investigations, and treatment, associated monitoring, and management of any side effects.

TBI testing should be undertaken for people with a high likelihood of being exposed to TB, and for people at high risk for progression to TB disease. TBI may be diagnosed and managed by NSW TB services, and/or specialist services within NSW Health.

Patients should be offered counselling and education on TBI and its management. Individualised approaches are particularly important for people in culturally and linguistically diverse communities and Aboriginal people.

TB contacts with TBI, children less than 5 years of age, and people with immunosuppression should be treated with TPT. All other people diagnosed with TBI should be counselled on its implications and offered TPT.

Revision History

Version	Approved By	Amendment Notes
GL2024_015 November-2024	Deputy Secretary, Population and Public Health & Chief Health Officer	New guideline incorporating: • *Tuberculosis – Minimising the risk of Tuberculosis in patients starting Anti TNF Inhibitors* (GL2008_007), • *Tuberculin Skin Testing* (PD2009_005), and • *Tuberculosis in Children and Adolescents* (GL2005_060).
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1. Background

Tuberculosis (TB) remains a public health issue both globally and locally [1]. TB elimination is central to the World Health Organization's (WHO) End TB Strategy by 2035. TB infection (TBI) (previously referred to as latent TB infection or LTBI) can lie dormant in a person's body for many years before symptomatic manifestation presenting a challenge to achieving TB elimination.

TBI testing and treatment is recommended by the WHO as a core intervention for TB elimination [2]. Programmatic implementation and uptake of TB preventive therapy (TPT, previously referred to as chemoprophylaxis) requires considered and careful implementation starting from the identification of the target population to the completion of TPT.

1.1. About this document

This guideline covers recommendations for testing, diagnosis, and management of TBI. Testing and management may be undertaken in Local Health District/Specialty Network TB services/chest clinics, or by a variety of other clinicians including various speciality areas. This guideline covers:

- Which groups should be tested for TBI (high risk populations)
- TBI tests suitability for different cohorts
- The importance of excluding active TB disease in patients diagnosed with TBI
- Patient education and counselling
- Different TPT regimens available and recommended
- TPT in pregnancy and children
- TPT monitoring, clinical consultation, adverse events and compliance
- Chest radiograph (CXR) monitoring for cases unable to uptake TPT.

1.2. TB infection testing and management free of charge to the patient

All services related to testing, diagnosis, and management of TB infection must be provided at no charge to patients within the NSW public health system. This includes clinical, laboratory and radiological investigations, and treatment, associated monitoring, and management of any side effects.

This policy applies to those eligible and ineligible for Medicare benefits. Further information is provided in NSW Health Policy Directive *Principles for the Management of Tuberculosis New South Wales* (PD2022_007) Section 7.

Occupational screening for TBI may be charged as per NSW Health Policy Directive *Principles for the Management of Tuberculosis New South Wales* (PD2022_007) Section 7.5.

1.3. Key definitions

Acid fast bacilli (AFB)	A rod-shaped bacterium which can be seen on microscopic examination of a stained clinical specimen using Ziehl-Neelsen technique or fluorescent microscopy.
Countries with a high incidence of TB	Countries with a TB incidence ≥40 cases per 100,000 population per year. A list of high incidence countries is located on the NSW Health website at: https://www.health.nsw.gov.au/Infectious/tuberculosis/Pages/high-incidence-countries.aspx
Interferon Gamma Release Assay (IGRA)	An in-vitro TB screening technique that uses whole blood to measure immune responsiveness when exposed to TB antigens to identify people likely to be infected with *M. tuberculosis.*
Polymerase Chain Reaction (PCR)	A molecular amplification of DNA sequences specific to *Mycobacterium tuberculosis* to allow for rapid detection and identification in a clinical specimen or bacterial isolate.
QuantiFERON TB Gold Plus (QFT-Plus®)	The brand name of the available IGRA test in NSW.
Tuberculosis disease (TB)	Disease (illness), also referred to as TB disease caused by the *Mycobacterium tuberculosis complex* bacilli.
TB infection (TBI)	*M. tuberculosis* infection without disease; previously referred to as latent TB infection.
TB screening	Performing relevant clinical assessment (including symptom screening, medical history regarding previous TB infection, immunosuppressive conditions and TB-exposure risk) and tests to exclude TB disease and TB infection. Tests used for detecting TB infection include the TST and/or IGRA, while tests for TB disease include a chest CXR and sputum sampling for acid fast bacilli (AFB), polymerase chain reaction (PCR) and mycobacterial culture.

TB test conversion	A change from a negative TB test result to a positive test result after a recent exposure to a known case with TB disease, with sufficient time since last exposure to the index case to ensure that any immune response to recent infection can develop and be detected in the second test. Where the TST is employed, a change of 10mm from baseline reading defines a conversion. Where IGRA is employed, change in test results from negative to positive need to be interpreted by an experienced TB clinician to determine true conversion.
TB clinical review	Assessment by an experienced clinician (usually at a local chest clinic/TB service) to diagnose or exclude TB disease in a person who has confirmed TB infection, and/or abnormal CXR and/or symptoms suggestive of TB disease.
TB preventive therapy (TPT) **Also known as chemoprophylaxis**	A course of TB-specific medications to prevent progression of TB infection to TB disease.
Tuberculin skin test (TST) – also known as Mantoux test	A skin test (in-vivo) which measures cell mediated immune responsiveness to Tuberculin purified protein derivative (PPD) to identify people likely to be infected with *M. tuberculosis.*
Window TB Preventive Therapy (TPT)	A course of TB-specific medications provided to people at risk of rapid progression of TBI to TB disease following close contact with an infectious TB case that have a negative TST or IGRA baseline screening until follow-up screening at 8-12 weeks following last exposure is undertaken.

2. Who Should be Tested for TB Infection?

Health services should test the following for TB infection (TBI):

- People with high likelihood of having been exposed to TB (and therefore who have an increased risk of TBI, and
- People at high risk for progression to tuberculosis (TB) disease.

Table 1. Indications, responsibility and timing of TBI testing

Reason for testing	Who should be tested	Responsibility for testing	When to test
People with high likelihood of exposure to TB	Close contacts of people with confirmed pulmonary TB	TB services	Within 2 weeks, and 8-12 weeks post TB exposure[1]
	Workers and students in healthcare, aged care or disability care	General practitioners Immigration service providers	At the time of commencement with the LHD[2] Immigration medical examination
	Migrants from TB high incidence countries	TB services General practitioners Immigration service providers (for permanent migrants)	When referred to TB services as per usual migrant referral processes
People at high risk for progression to TB disease	Immunocompromised people (as per the below identified groups - see section 2.1)	Managing specialist physician General practitioners	Upon diagnosis of condition Prior to commencement of immunosuppressive medications Consideration of rescreening for potential re-exposure, such as travel to high incidence counties

[1] As per NSW Health Guideline *Tuberculosis Contact Investigations* (GL2019_003)

[2] As per NSW Policy Directive *Occupational Assessment, Screening and Vaccination Against Specified Infectious Diseases* (PD2024_015)

2.1. People at high risk for progression to TB disease

- Immunocompromised people, including:
  - Patients with human immunodeficiency virus (HIV)
  - Patients initiating treatment with tumour necrosis factor-alpha (TNF-α) and Janus Kinase (JAK) inhibitors
  - Patients who have had or preparing for a solid organ or haematological transplant
  - Patients taking the equivalent of >15mg/ day of prednisolone (or equivalent) for 1 month or longer [3]
- People with specific comorbidities, including:
  - Patients on renal dialysis
  - Patients with silicosis

- Patients with diabetes (especially those with sub-optimal control).

- People with other identified risk factors, including:
  - Prisoners, homeless people and people who use illicit drugs
  - People who engage in the harmful use of alcohol
  - Tobacco smokers
  - People who are severely malnourished.

3. Testing for TB Infection

The tuberculin skin test (TST or Mantoux test) and TB interferon gamma-release assay (IGRA) are both suitable for TBI testing [2, 4]. A comparison between the tests is shown in Table 2.

Table 2. Comparison between TST and IGRA tests

	TST	IGRA
Visits required	2 visits separated by 48-72 hours	1 visit
Procedure	Intradermal injection	Phlebotomy (4x1ml blood tubes)
Interpretation	Observer human dependant	Internal machine controlled
Infrastructure	Tuberculin requires cold chain	Requires specialised laboratory equipment
For patients with BCG	Can cause false positive	No influence on result
Specificity	Non-tuberculous mycobacteria can produce a false positive [5]	More specific, though false positives can occur by: • some non-tuberculous mycobacteria can produce a false positive (such as *Mycobacterium kansasii, M. szulgai or M. marinum)* [6] • Rheumatoid arthritis with positive anti-citrullinated protein antibodies (ACPA) (13% false positive rate) [7]

Both tests measure the immune response to *Mycobacterium tuberculosis* (MTB). People with recent contact to a person with TB disease should be tested at baseline (within 2 weeks following most recent exposure) and 8-12 weeks after the date of most recent exposure [8]. People who have previously had TB disease or have tested positive in the past should not be re-tested.

The following should be considered when selecting an appropriate test:

- Both tests are contraindicated within 4 weeks of live parenteral vaccines such as measles, mumps, rubella (MMR), varicella, zoster and yellow fever [9]
- Both tests do not differentiate between TB disease and TBI, thus active disease must be excluded (see Section 4)

- Both tests may have poor sensitivity in patients who are immunocompromised, and clinical correlation in such patients is important
- If a person has had a bacille Calmette-Guérin (BCG) vaccination, IGRA testing should be the preferred test.

Children <5 years of age who test negative should be considered for and referred for BCG vaccination if there is concern of ongoing TB exposure risk.

3.1. TST interpretation

TST administration and reading must be performed by appropriately trained health care professionals in accordance with the *Poisons and Therapeutic Goods Regulation 2008* (NSW), and the Authorised Registered Nurse/Midwife Vaccination Standards where applicable.

A comprehensive TB risk assessment is required to interpret TST results (Table 3).

Table 3. TST induration diameter which indicative of infection with MTB in varying clinical settings

>5mm	>10mm[#]	>15mm[#]
Recent high risk (close) contacts of persons with infectious TB	People born or resident (>3 months) in countries with high prevalence of TB (>40 cases / 100,000)	People >5 years of age without any identified risk factors
People with HIV infection	Children <5 years of age without any identified risk factors	Health Care Workers with BCG vaccination in the past 10 years
People with organ transplants or immune suppressive therapy equivalent to prednisone >15mg/day for >1 month	People who live or spend time in high-risk congregate settings (such as prisons, homeless shelters, alcohol rehabilitation and drug treatment centres	
People with CXR evidence of past untreated TB	Health care workers without BCG vaccination in the past 10 years	
	People who inject drugs	
	People with certain medical conditions, such as diabetes; silicosis; some malignancies (head, neck, lung and haematological); chronic renal failure; gastrectomy or jejunal bypass; malnutrition or low body weight (>10% below ideal body weight) [10]	

[#] BCG vaccination given in infancy is less likely to affect TST interpretation in adults. However, where BCG vaccination is recent (within 5 years) or where there have been 2 or more BCG vaccinations, the above stratification may need to be modified and TST results should be interpreted individually by physicians experienced in TB medicine.

3.2. TB IGRA

In NSW, the current available IGRA test kit is QuantiFERON –TB Gold Plus® (QFT-Plus). The interpretation of QFT-Plus results is shown in Figure 1.

Figure 1. Interpretation of QFT-Plus results [6]

Nil (IU/ml)	TB1 minus Nil (IU/ml)	TB2 minus Nil (IU/ml)	Mitogen minus Nil (IU/ml)*	QFT-Plus result	Report/ interpretation
≤8.0	≥0.35 and ≥0.25% of Nil	Any	Any	Positive#	*M. tuberculosis* infection likely
	Any	≥0.35 and ≥0.25% of Nil			
	<0.35 or ≥0.35 and <0.25% of Nil	<0.35 or ≥0.35 and <0.25% of Nil	≥0.5	Negative	*M. tuberculosis* infection NOT likely
	<0.35 or ≥0.35 and <0.25% of Nil	<0.35 or ≥0.35 and <0.25% of Nil	<0.5	Indeterminate#	Likelihood of *M. tuberculosis* infection cannot be determined
>8.0	Any				

* Responses to the Mitogen positive control (and occasionally TB Antigen) can be outside the range of the microplate reader. This has no impact on test results. Values >10 IU/ml are reported by the QFT-Plus software as >10 IU/ml

Where *M. tuberculosis* infection is not suspected, initially positive results can be confirmed by retesting the original plasma samples in duplicate in the QFT-Plus ELISA. If repeat testing of one or both replicates is positive, the test result is considered positive.

Clinical considerations for the use of IGRA include:

- Whilst the IGRA is a highly specific test [4], false negatives can occur in people with TB disease (usually with advanced disease) [11]. A TB specific symptom and risk assessment should be undertaken when testing for TB disease.
- Where there is an indeterminate result from insufficient mitogen response in immune suppressed patients, a TST is recommended.
- Where an indeterminate result arises from incorrect blood draw or handling of the blood tubes following collection, the test should be repeated.
- Reversions (where once someone tested positive and later test negative) can occur, particularly around the 0.35 IU/mL cut-off. However, with a paucity of literature on this topic, seek expert advice before retesting.

4. Excluding TB Disease

TB disease must be excluded in people who test positive with TST or IGRA prior to commencing TB preventive therapy (TPT). TPT in the setting of active disease can lead to undertreatment and risks the emergence of drug resistance.

Testing and assessment for TB disease includes:

- Symptom screen for cough, fever, weight loss and/or night sweats; and additionally in children failure to thrive, reduced playfulness and/or lethargy [12]
- Physical examination for palpable lymphadenopathy or other signs of extrapulmonary TB disease
- Chest radiograph (CXR) (and/or chest computed tomography (CT))
- Sputum specimen collection, ideally three early morning sputum samples, and/or bronchoscopy if indicated.

If there are any concerns regarding the possibility of TB disease, please refer to the local TB service/chest clinic for specialist advice.

4.1. Considerations for pregnancy

A risk assessment must be undertaken prior to CXR during pregnancy. Pregnancy is not an absolute contra-indication for CXR. Additional measures, including a lead shield, can be used to protect the fetus.

5. Patient Education and Considerations

Patients should be offered counselling and health education on management of TB Infection (TBI). Components of education, tailored to the patient's needs include:

- Testing and management free of charge to the patient in NSW Health facilities
- Information on TB and the difference between TB disease and TBI
- Individual risk of progression to TB disease
- Information on TB preventive therapy (TPT), including efficacy and potential adverse effects
- Reporting of nausea, vomiting, jaundice or confusion if on TPT to the treating clinician as soon as possible
- Purpose of chest radiograph (CXR) monitoring, if used in lieu of TPT.

People with TBI should be informed of their lifelong risk of TB disease. Whilst the risk is greatly decreased with the uptake of TPT, it is still present [13]. Individuals should be instructed to seek healthcare if they develop symptoms of TB disease.

5.1. Culturally and linguistically diverse people

Individual approaches may be required to support culturally and linguistically diverse people, including working with health workers from the relevant cultural background.

Information on TB disease and TBI is available in multiple languages on the NSW Health Tuberculosis fact sheets and patient information in other languages webpage. An accredited or certified interpreter must be engaged whenever language could potentially pose a barrier to effective care, including ensuring patient understanding of the TBI and treatment. Refer to

the NSW Health Policy Directive *Interpreters - Standard Procedures for Working with Health Care Interpreters* (PD2017_044).

5.2. Aboriginal people

TBI management is to be tailored to meet the unique and local needs of Aboriginal individuals, families, and communities based on the principles outlined in the NSW Aboriginal Health Plan 2024-2034 [14]. This may involve working with local Aboriginal community-controlled health services (ACCHSs) and ensuring integrated planning and service delivery with Aboriginal people.

Aboriginal health workers, Aboriginal health practitioners and Aboriginal liaison officers within the Local Health Districts and Specialty Networks can assist in determining culturally safe approaches to care.

6. Tuberculosis Preventive Therapy

Tuberculosis preventive therapy (TPT) is proven to be effective and can halt progression to active disease by up to 90% [15, 16]. TPT does not increase the development of drug resistance, provided that TB disease has been excluded before the initiation of therapy [2] .

The drug susceptibility profile of the index case (if known) should be considered when deciding on a TPT regimen. If the drug susceptibility profile is not known, a regimen should be chosen for a presumptive first line susceptibility profile, unless epidemiological information suggests otherwise.

All regimens can be self-administered, with appropriate follow-up and support. Directly observed therapy (DOT) is not routinely advised unless necessary due to individual patient circumstances.

6.1. Who should be treated for TB infection?

TB contacts with TB infection (TBI), children less than 5 years of age, and people with immunosuppression should be treated with TPT.

All people diagnosed with TBI should be counselled on its implications and offered TPT.

People commencing immunosuppressive therapy should be treated for TBI prior to, or for at least one month prior to the commencement of immunosuppressive therapy where possible.

6.2. Window TB Preventive Therapy

Children less than 5 years old, or highly immunosuppressed patients who are close contacts of a smear positive pulmonary TB case should be prescribed TPT to prevent rapid progression to TB disease following a negative baseline screening (known as window TPT, previously known as window chemoprophylaxis) [8]. Window TPT should be continued if testing positive and should be ceased if testing negative for TBI on follow-up screening 8-12 weeks following the last exposure.

6.3. TB Preventive Therapy Regimens

There are multiple options for TPT available (Table 4). TPT regimens selection should consider:

- age
- risk of hepatotoxicity
- drug-drug interactions
- comorbidities
- pregnancy
- drug susceptibility of the likely source case
- drug availability
- pill burden and length of treatment.

The World Health Organization (WHO) recommend TB Programs transition to shorter rifamycin-containing regimens given the better safety profile and improved rates of TPT completion [17]. Rifamycin (a group of antibiotics including rifampicin and rifapentine) regimens may reduce the efficacy of the oral contraceptive pill and should be taken into consideration when counselling patients [18].

Consideration should be given to palatable paediatric formulations and tolerability of medications to optimise adherence to treatment.

Table 4. TPT regimens [2, 19]

Regimen	Drug/Dose	Frequency	Duration	Additional information
4R	Rifampicin 10 mg/kg up to 600 mg • child <14 years and >50kg: 600 mg; • child <14 years and <50kg: 15 mg/kg up to 450 mg	Daily	4 months	Suitable for contacts where index case is resistant to isoniazid but not rifampicin Better tolerated and safer than 3HR or 6-9H Rifamycin regimens may reduce the efficacy of the oral contraceptive pill
3HP*	Rifapentine • adult and child ≥12 years and >50 kg: 900 mg, • adult and child ≥12 years and 32.1 to 50.0 kg: 750 mg, • child age 2-11 years: ○ 10 to 14 kg: 300 mg ○ 14.1 to 25 kg: 450 mg; ○ 25.1 to 32 kg: 600 mg; ○ 32.1 to 50 kg: 750 mg; ○ > 50 kg: 900 mg PLUS Isoniazid 15 mg/kg up to 900 mg (child age-11 years: 25 mg/kg up to 900 mg)	Weekly	12 weeks	Rifapentine not recommended for children <2 years Rifamycin regimens may reduce the efficacy of the oral contraceptive pill Requires TGA Special Access Scheme (SAS) . Fixed dose combination tablets may be available through local TB services/chest clinics
3HR*	Rifampicin 10 mg/kg up to 600 mg • child <14 years and >50kg: 600 mg; • child <14 years and <50kg: 15 mg/kg up to 450 mg PLUS Isoniazid (adult and child) 10 mg/kg up to 300 mg	Daily	3 months	Rifamycin regimens may reduce the efficacy of the oral contraceptive pill Convenient, safe, and high rates of completion compared to 6H* Paediatric, water dispersible fixed dose combination tablets may be available through local TB services/chest clinics or Westmead Children's Hospital Pharmacy Department. TGA SAS required for fixed dose combination tablets.
6-9H*	Isoniazid (adult and child) 10 mg/kg up to 300 mg	Daily	6-9 months	Suitable for contacts where index case is rifampicin mono-resistant Fewer drug-drug interactions (especially for patients with HIV or post-transplant patients)

Regimen	Drug/Dose	Frequency	Duration	Additional information
6Lfx/Mfx^	Levofloxacin (adult: 10-15 mg/kg, children < 27kg: 15-20 mg/kg) OR Moxifloxacin (adult: 400mg; children >27kg 400mg)	Daily	6 months	Suitable for contacts where the index case is resistant to isoniazid and rifampicin, but susceptible to fluoroquinolones. Levofloxacin requires TGA SAS . Levofloxacin strongly preferred in children.

^In high-risk and household contacts of patients with multidrug-resistant TB (MDR-TB), the following TPT may be considered based on an individualised risk assessment and sound clinical justification (especially in children less than 5 years of age) [20-22]. Symptomatic observation and chest X-ray (CXR) monitoring for TB disease is recommended for 2 years after MDR-TB exposure, regardless of TPT uptake.
*Pyridoxine (vitamin B6) when taking INH-containing regimens should be considered for individuals at risk of peripheral neuropathy.

1HP regimen (one month of isoniazid and rifapentine daily) is not currently recommended in NSW. Whilst the 1HP regimen (one month of isoniazid and rifapentine daily) has been shown to be noninferior to self-administered 9H in a large randomised controlled trial (RCT) in HIV patients in Africa [23], and WHO has recommended the use of this regimen regardless of HIV status [2], the applicability of this regimen in low-burden settings and HIV-negative people is still unknown though clinical trials are being undertaken [24].

6.3.1. Pregnancy and breastfeeding

Rifapentine should not be used during pregnancy until further evidence on dosing and safety are available.

Rifampicin is a category C drug. It should be used in pregnant women and women of childbearing potential only if the potential benefit justifies the potential risk to the foetus.

Isoniazid use in pregnancy may be associated with higher risks of liver failure, and close monitoring is therefore required [25]. Pyridoxine (vitamin B6) should be prescribed when taking isoniazid-containing regimens whilst breastfeeding.

6.4. Retreatment

If people previously treated with TPT for TBI are re-exposed to a case of TB, testing for TBI should not be repeated. In immune-competent adults, there is evidence that a first episode of TBI provides approximately 79% protection against development of disease following re-exposure [26]. However, a second course of TPT should be considered for people who have been exposed to TB following previous TPT, particularly if they had recent close contact with TB, or are at high risk for progression to disease, including:

- children less than 5 years of age
- people living with HIV
- immune suppressed individuals
- other individuals of concern with comorbidities, or significant social issues [27].

For people with known exposure to MDR-TB, TPT retreatment with a fluoroquinolone-based regimen should be considered if previous course of TPT was isoniazid and/or rifamycin-based.

7. TB Preventive Therapy Monitoring

All patients should be followed-up throughout TB preventive therapy (TPT) to support the patient with adherence, promptly identify and manage adverse events and monitor for signs or symptoms of TB disease.

7.1. Baseline tests

Baseline tests are required for some patients.

7.1.1. Liver function tests

TPT regimens confer a small risk of hepatoxicity. Baseline liver function tests (LFTs) and ongoing monitoring for drug-induced liver injury from TPT are required for patients who are or have:

- age over 35 years
- history of liver disease, including viral hepatitis
- harmful alcohol intake
- pregnant, and up to 3 months postpartum
- immunocompromised, including people living with HIV
- on statin therapy, and/or
- unable to reliably report symptoms of hepatotoxicity (such as, people with cognitive deficits).

TPT with rifampicin and/or isoniazid can be commenced if liver enzymes are less than 3 times the upper limit of normal (ULN). For people with abnormal baseline test results, the benefits and risks of TPT must be considered before proceeding with TPT.

7.1.2. Electrocardiogram (ECG)

For fluoroquinolone (FQ) containing TPT in adults, a baseline electrocardiogram (ECG) should be performed to ensure the QTc interval is not prolonged (relative contraindication). This is not necessary for children less than 18 years of age unless symptomatic or high-risk concerns are present.

7.1.3. Pregnancy testing

Pregnancy testing should be considered for women of child-bearing age.

7.2. Monitoring throughout treatment

All patients on TPT should be monitored clinically at regular intervals for adverse events. TPT regimens are generally safe and well tolerated, and most adverse reactions are minor and occasional. Common adverse events are covered in section 7.3.

Specific attention must be paid to hepatic dysfunction to prevent drug-induced liver injury.

7.2.1. Liver function tests

LFTs whilst on TPT should be undertaken when:

- as soon as possible for patients reporting nausea, vomiting, jaundice or confusion
- one month after commencement of TPT if baseline LFTs were undertaken and patient is asymptomatic
- regularly (at least once a month) for patients with abnormal LFTs at baseline or throughout treatment.

If LFTs at one month into treatment are normal and the patient is asymptomatic, LFTs should be attended at the discretion of the treating physician.

Where clinical symptoms are indicative of hepatitis or acute liver failure, TPT should be withheld until LFT results are available and a clinic review can be undertaken.

Where there is an increase in transaminases to 5 times or greater the upper limit of normal (ULN) when asymptomatic, or up to 3 times ULN in the presence of symptoms of hepatotoxicity, TPT should be withheld and a review undertaken.

7.2.2. Electrocardiogram (ECG)

Adult patients receiving fluoroquinolones (moxifloxacin or levofloxacin) should have regular electrocardiogram (ECG) monitoring due to potential for QT-prolongation.

ECGs should be repeated one month after commencement of treatment. Ongoing monitoring is dependent on individual patient characteristics, inclusive of:

- baseline and one month ECG results
- presence of additional comorbidities (particularly cardiovascular impairments)
- when patients also take other QT-prolonging medications.

Treating clinicians should consider referring to a cardiologist for patients of concern.

7.3. Common adverse drug reactions

Common adverse events of the key drug classes are listed below.

7.3.1. Isoniazid

Common adverse effects, including hyper-sensitivity reactions, that have been associated with isoniazid TPT include:

- symptomatic or asymptomatic elevation of serum liver enzymes

- peripheral neuropathy
- neutropenia
- flu-like symptoms
- pruritis with or without rash
- gastro-intestinal intolerance (nausea, vomiting, diarrhoea).

7.3.2. Rifamycins (rifampicin and rifapentine)

Common adverse events include:

- flu-like symptoms
- cutaneous reactions
- hypersensitivity reactions
- gastro-intestinal intolerance (nausea, vomiting, diarrhoea)
- hepatotoxicity.

7.3.3. Fluoroquinolones (levofloxacin and moxifloxacin)

Common adverse events include:

- headache or dizziness
- pain or swelling in the muscle or joints
- loss of appetite
- itchy skin or rash
- gastro-intestinal intolerance (nausea, vomiting, diarrhoea).

7.4. Monitoring treatment adherence

Treatment completion is defined as 80% of prescribed doses taken within 133% of the scheduled duration of the chosen TPT regimen (Table 4) [2]. Given the absence of a reliable test that can ascertain infection clearance, maximizing adherence is important.

Table 4. TPT completion by regimen^ [2]

Regimen	Total duration	Expected number of doses	80% of recommended doses (days)	Extended time for treatment completion (days)
4R (daily)	4 months	120	96	150
3HP (weekly)	12 weeks	12	11*	120
3HR (daily)	3 months	84	68	120
6H/9H (daily)	6/9 months	182/273	146/218	239/363

*90% of recommended number of doses

^ WHO do not currently provide a treatment completion definition for 6Lfx/Mfx

Patients that do not complete TPT should be counselled to ascertain the reasons surrounding non-compliance with attempts to circumvent the potentially identified barriers. If patients fail to complete TPT with 3 different attempts, further attempts should not be undertaken. Reasons for non-completion of TPT should be recorded.

Interventions to enhance adherence and completion of TPT should be tailored to the specific needs of risk groups, be culturally safe and in the preferred language of the individual.

7.5. Evaluation

Patients should be evaluated at the end of TPT with the following:

- Clinical review to assess for symptoms of TB disease
- Chest radiograph (CXR) to exclude early TB disease
- Documentation of course of treatment/self-reported adherence or other outcome
- Provision of documentation outlining the treatment provided.

8. Chest X-Ray Monitoring

Chest radiograph (CXR) monitoring can be used where TB preventive therapy (TPT) is not suitable. CXR monitoring does not decrease the risk of TB reactivation – it is useful only in early detection of TB disease. CXR monitoring can occur over a 2-year period – 6 months after the exposure date, then 12 months after the exposure date, then 24 months after the exposure date (6, 12, 24 CXR monitoring).

Increased frequency of CXR monitoring may be considered where there are concerns for risk of rapid progression to TB disease, and where TPT was not considered appropriate or not agreed to by the patient.

9. Program Monitoring

For quality assurance, clinics and/or practitioners testing for TBI and providing TB preventive therapy (TPT) should monitor uptake and completion of TPT. Indicators are provided in Table 5. Reasons for non-completion of TPT are to be recorded.

Table 5: TBI indicators

Indicator	Definition
Proportion patients with TBI commenced on TPT	The number of patients commenced on preventive treatment, divided by the number of patients diagnosed with TBI
Proportion of patients completed TPT	The number of contacts that completed preventive treatment, divided by the number of patients commenced on preventive treatment

Indicator	Definition
Proportion of patients commenced on CXR monitoring	The number of patients commenced on CXR monitoring, divided by the number of patients diagnosed with TBI
Proportion of patients completed CXR monitoring	Number of contacts that completed CXR monitoring, divided by the number of contacts commenced on CXR surveillance

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