

Tuberculin Skin Testing

Summary The Tuberculin Skin Testing (TST) Policy Directive has been revised to provide advice to persons undertaking and interpreting TSTs in NSW. The PD was reviewed and approved in April 2008, however this minor addition was necessary to reflect the Australian Immunisation Handbook 9th Edition. Additions to the document 2.2 Contra-indications to TST page 2.

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Distributed to Public Health System, Community Health Centres, Divisions of General Practice, Government Medical Officers, Health Professional Associations and Related Organisations, NSW Ambulance Service, Ministry of Health, Public Health Units, Public Hospitals, Private Hospitals and Day Procedure Centres

Audience Public Health Organisation employees;clinical;nursing

Secretary, NSW Health

This Policy Directive may be varied, withdrawn or replaced at any time. Compliance with this directive is mandatory for NSW Health and is a condition of subsidy for public health organisations.

Tuberculin Skin Testing

This Policy Directive is to be read in conjunction with NSW Health Department Policy Directives:

PD2005_406 Patient Information and Consent to Medical Treatment
PD2007_077 Handling of Medication in New South Wales Public Hospitals
PD2005_208 Bacille Calmette Guerin Vaccination
PD2008_033 Immunisation Services - Authority for Registered Nurses
PD2007_036 Infection Control Policy
GL2005_060 Tuberculosis in Children and Adolescents
PD2008_017 Tuberculosis Contact Tracing
PD2005_072 Preventive Therapy

1. Introduction

The procedures incorporated in this document are required to be complied with.

1.1 Definitions

The tuberculin skin test (TST) is used primarily to identify people infected with *Mycobacterium tuberculosis* (MTB). It is used to identify such people because they have a 5 -10% lifetime risk of developing TB diseaseⁱ. TST should therefore be targeted to those individuals at risk either of acquiring TB infection or of progressing to TB disease, once infected.

Preventive treatment of people infected with MTB reduces their risk of developing TB disease up to 90%ⁱⁱ.

1.2 Composition and Safety

The form of tuberculin used in Australia is purified protein derivative (PPD). PPD consists of bacteria-derived protein without viable organisms and is safe for use in immune compromised persons and in pregnancy.

1.3 Methods of TST Administration

In Australia, tuberculin skin testing is administered by the Mantoux method which involves the intradermal injection of 5 Tuberculin Units (TU) of PPD. Multiple puncture tests are also available to test the cell-mediated response to a variety of antigens including PPD. However, these are not recommended as an alternative to the TST as the dose is less precise and operator variability may be greater.

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2. Indications/Contra-indications regarding TST

2.1 General Indications for TST

TST is routinely recommended for the following persons:

- people identified as close contacts of persons with infectious TB (as defined in Policy Directive PD2008_017 Tuberculosis Contact Tracing)
- health care and other workers in whom surveillance is proposed because of ongoing increased risk of acquiring infection
- people with medical risk factors that increase the likelihood of latent infection progressing to disease
- prior to BCG vaccination in those over 6 months old, and
- in certain clinical situations, to assist in diagnosing or excluding TB disease.

2.2 Contra-indications to TST

TST is best avoided in:

- persons who report any severe adverse reaction following previous TST
- persons previously treated for active TB disease
- persons with documented/known prior positive TST reactions
- persons with a high fever or recent significant infection, eg measles and chicken pox.
- Following recent immunisation with MMR, varicella and yellow fever within the last month as the risk of a false negative TST result is increased. Oral typhoid and oral polio (OPV) vaccines do not necessitate a delay in testing (OPV is no longer used in Australia but may have been received overseas).
- The 9th edition of the Australian Immunisation Handbook does not mention oral rotavirus vaccination in the context of TST tests, but as with other live oral vaccines, there should be no need to modify timing of TST based on administration of this vaccineⁱⁱⁱ.

An undocumented history of a prior positive TST is not an absolute contra-indication to TST because patient recall is often inaccurate.

3. Methods

3.1 Who may administer TST?

- Medical Practitioners
- Registered Nurses employed in an Area Health Service who have the requisite Authority as defined in the NSW Health Department PD2008_033 Immunisation Services – Authority for Registered Nurses. These nurses may undertake TST following NSW Health Department Policies without the written order of a medical practitioner, and
- Registered Nurses who work under the written order of a medical practitioner, as PPD is a schedule 4 drug.

All health professionals performing TST should be appropriately trained to administer and interpret the test results.

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3.2 Procedure for the administration of a TST

3.2.1 Confirm the identity of the patient to be tested

3.2.2 Obtain consent

- Informed consent is required. Verbal consent is sufficient, signed consent forms are not required for minor procedures such as TST administration
- the procedure must be explained to the patient and documented in the patient's medical record see PD2005_406 Patient Information and Consent to Medical Treatment.

3.2.3 For consent to be valid

- The person must have the capacity to give consent, that is the person must be able to understand the implications of having the treatment or procedure
- the consent must be freely given
- the consent must be specifically for the procedure that is being undertaken, and
- the patient must be informed in broad terms of the procedure that is intended.

A person is incapable of giving consent if he/she cannot understand the general nature and effects of the proposed treatment, including implications and possible side effects or:

- is a child is under the age of 14 years, (consent of the parent or legal guardian is necessary) and
- is a school student, without written parental/guardian consent prior to an on-site school screening activity, regardless of age.

Note: while children between the ages of 14 and 16 may give consent, it is prudent to obtain consent of the parent or guardian.

3.2.4 What to do when a person is incapable of giving consent:

The provisions of the Guardianship Act apply to a person who is 16 years or older who is incapable of giving consent to the carrying out of medical or dental treatment.

TST is considered "medical treatment" within the meaning of the Guardianship Act (section 33(1)). TST falls within the meaning of "minor treatment" under the Guardianship Act.

Section 36 of the Guardianship Act provides that for minor medical treatment consent may be given by the "person responsible" for the patient or by the Guardianship Tribunal. The person responsible for the patient is defined under section 33A of the Act.

Consent to undertake TST should be obtained in writing from the person responsible.

Minor treatment may be carried out without any consent if there is no person responsible for the patient, or there is such a person, but that person cannot be contacted or is unable or unwilling to make a decision concerning a request for that

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person's consent for the treatment providing the medical practitioner supervising the carrying out of the TST certifies in writing in the clinical record that:

- the treatment is necessary and undertaking the TST will promote the patient's health and well being, and
- the patient does not object to the carrying out of the TST.

Section 33(3) of the Act provides guidance on the definition of what constitutes a patient objecting to treatment.

Where it is necessary to obtain consent of the Tribunal legislation requires that applications for consent are made in respect of each patient concerned. Prior to granting consent the Tribunal considers the views of the patient, the person proposing the treatment, any person responsible for the patient, and any guardian appointed with respect to the patient's treatment.

4. Pre TST Assessment

Obtain a history or documentation of the following:

- prior TB
- any potential TB exposure
- any previous TST and the result
- BCG vaccination
- medical conditions or treatment that may effect the TST result as outlined in section 10, and
- review the contraindications for TST as outlined in section 2.2.

5. Administration of the TST

5.1 Position

Seat the patient with the left arm resting on a table. Young children should be seated on their attendant's lap with other arm held securely under the attendant's arm. The child's body is held firmly and at the same time the attendant holds the arm on which the test is to be carried out, slightly flexed.

5.2 Site

The anterior aspect of the left forearm at the junction of the upper and middle thirds, using an area away from blood vessels or skin lesions.

5.3 Dose of PPD for adults and children

Five (5) Tuberculin Units (TU) per 0.1ml is the standard dose for the TST.

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5.4 Technique

Use either a single-use insulin syringe with a 29-gauge needle or a 1 mL single-use syringe with 26 or 27 gauge needle. Administer the PPD intradermally with the bevel of the needle uppermost. Inject slowly to produce a pale discrete “bleb” (lump) 5 to 10 mm in diameter. If leakage occurs, repeat the injection at another site at least 5 cm away or in the other forearm.

Repeated TSTs at exactly the same site may result in increased reaction. For this reason the requirement to vary the test site is particularly important in serial or repeated TSTs especially with the 2-step protocol^{iv}.

5.5 Advice to the patient

The patient should be given clear instructions and an information sheet advising of the following:

- not to cover the site with dressings
- not to apply any lotions to the area
- to avoid scratching the site if it becomes itchy
- possibility of skin blistering and/or ulceration following the TST
- when to return for reading of the TST, and
- to contact the clinic if concerned in the interim.

5.6 Infection control

All procedures should follow the current NSW Health Department Policy Directive PD2007_ 036 – Infection Control Policy.

6. Storage of PPD

- PPD should be stored away from light at 2-8 degrees Centigrade. Discard product if exposed to freezing.
- PPD should be administered as soon as possible after drawing up into the syringe and following administration, as the solution can be adversely affected by exposure to light. PPD remaining in a vial may be kept in the refrigerator and used for up to 30 days before discarding, providing care is taken to avoid contamination of the vial^v. It is essential that the date the vial is opened is recorded to ensure disposal occurs within the recommended timeframe.

7. Adverse reactions

Adverse reactions to TSTs are rare. They include:

- vaso-vagal reactions
- immediate flare with a local rash
- blistering and/or ulceration at the site of the injection
- lymphangitis and
- serious or life-threatening hypersensitivity reactions. These are extremely rare (0.08 reactions per million doses of PPD)^{vi}

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Although the risk of anaphylaxis is very low, adrenaline (and information re its dosage and administration) must be available when TST is being undertaken^{vii}.

8. Pregnancy

There is no evidence that TST poses any risk in pregnancy and/or when breastfeeding an infant^{viii} or that tuberculin reactions are influenced by pregnancy^{ix}.

9. Reading

The tuberculin skin test should be read 48 to 72 hours after the injection, by measuring the diameter of **induration** across the transverse axis of the forearm.

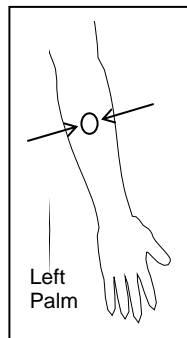
Only the induration should be measured, not the erythema (redness).

Record the TST results in millimetres (mm) of induration, not as **positive** or **negative**. A tuberculin skin test with no induration should be recorded as **0 mm**.

The tuberculin skin test is to be read by the “pen technique”.

Slowly draw a line with a ballpoint pen from a point 2 to 3 cms away from the margin of the skin test reaction, towards its centre. Maintain skin tension by exerting slight traction in the opposite direction of the pen movement.

When the ballpoint reaches the margin of the indurated area you will feel definite resistance, lift the pen. Repeat the procedure from the opposite side of the reaction. Measure the distance between opposing lines with a ruler.



9.1 Documentation

Document in the patient’s medical record:

- the date the TST was administered
- the dose of PPD administered
- the batch number and expiry date of the PPD
- BCG vaccination history, including age or ages at vaccination
- the presence or absence of BCG scars
- date the TST was measured
- size in mm of the transverse diameter of induration
- presence of vesiculation and
- signature of the person administering the TST and reading the result.

10. Interpretation of TST results

The TST result should be interpreted in light of factors that increase the probability that the patient has been infected with TB. These include:

- recent high risk (close) contact with persons with infectious TB,
- residence in countries with high prevalence of TB (>50 cases/100,000 persons),
- persons with chest x-ray evidence of past, untreated TB,
- prior or current residence in high-risk congregate settings (eg. prisons, homeless shelters, alcohol rehabilitation and drug treatment centres),
- prior vaccination with BCG,
- intravenous drug use,
- health care workers, and
- exposure to mycobacteria other than TB (MOTT).

The TST result may be decreased by:

- immune suppressive therapy, malignancy and HIV/AIDS^x
- acute viral or bacterial infections, including 5-17% of persons with active TB^{xi}
- infancy, advanced age^{xii}, renal failure^{xiii} or significant malnutrition^{xiv}, and
- recent (within 4 weeks) live virus vaccinations^{xv}.

Note that technical factors also influence the TST induration size. Such factors include:

- variation in the storage, handling and dosage of PPD used and
- errors in administration or reading.

10.1 Prior vaccination with BCG

Most people vaccinated with BCG will develop, within 2 months, a TST reaction which will then wane variably over time. TST following BCG vaccination is not recommended to assess the effectiveness of BCG.

BCG vaccination given in infancy is unlikely to affect TST interpretation in adults^{xvi}. Where BCG has been given in the last 5 years or more than one BCG has been administered the interpretation of TST results needs to be undertaken by a physician with experience in TB medicine^{xvii}.

TST reactions > 20mm are rarely due to BCG alone^{xviii}.

10.2 Evidence of TST conversion

Where serial tests are done a TST conversion is defined as an increase in the diameter of TST induration of $\geq 10\text{mm}$, between consecutive readings^{xix}. This increase usually occurs in 4 – 8 weeks following exposure to TB^{xx}.

TST conversion indicates recent TB infection. Occasionally false positive conversions may occur due to the TST booster phenomenon. The 2-step TST may assist in distinguishing true conversions from the booster phenomenon see section 11, see section 11 – Two-step TST and the Booster Phenomenon.

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10.3 The size of the TST induration

The interpretation of TST reactions to identify those requiring assessment for preventive therapy is based on: (a) the probability that the TST represents recent infection and (b) the risk of progression to active disease if there is infection with MTB.

Note that all children < 4 years of age who have had close contact with a case of infectious TB should receive preventive therapy irrespective of TST response, until the second TST (3 months later) proves negative (See GL2005_060 TB in Children and Adolescents).

Table 1. TST induration diameter which should be considered indicative of infection with MTB in various clinical settings

$\geq 5\text{mm}$	$\geq 10\text{mm}^\#$	$\geq 15\text{mm}^\#$
Recent high risk (close) contacts of persons with infectious TB	Persons born or resident (for greater than 3 months) in countries with high prevalence of TB (>100 cases / 100,000)	People > 4 years of age without any identified risk factors
Persons with HIV infection	Children < 4 years of age without any identified risk factors	Health Care Workers with BCG vaccination in the past 10 years
Persons with organ transplants or immune suppressive therapy equivalent to prednisone >15mg/day for >1 month	Persons who live or spend time in high risk congregate settings (eg prisons, homeless shelters, alcohol rehabilitation and drug treatment centres)	
Persons with CXR evidence of past untreated TB	Health care workers without prior BCG vaccination in the past 10 years	
	Intravenous drug users	
	Persons on prednisone equivalent to $\geq 15\text{mg/day}$ or for $\geq 1\text{month}$ or those with certain medical conditions eg 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) ^{xxi}	

BCG vaccination is unlikely to affect TST interpretation in adults, if given in infancy. However, where BCG 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.

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10.4 TST positive persons

The recommended management for persons identified as TST positive is either preventive therapy or chest x-ray follow up as per Policy Directive PD2005_072 Preventive Therapy.

If preventive therapy is not given, the person is to be counselled about the future risk of TB and to seek medical care if symptoms develop. Chest x-ray follow up is required in three to four months and then annually for two years. The risk of developing tuberculosis is highest within the first two years.

11. Two-step TST and the Booster Phenomenon

In some people previously exposed to *Mycobacteria* the ability to mount an immunological response to mycobacterial antigens wanes over time. These individuals may not initially react to a TST, but the TST may boost immunological memory for the mycobacterial antigens. If this does occur, a repeat TST shortly after the initial one will produce a much larger TST response (a boosted response). The initial TST result is therefore falsely negative and the second result should be considered the true result. However, this boosting phenomenon may be misinterpreted as a TST conversion.

The TST boosted response is maximal 1-5 weeks after the first TST, but can persist for 1-2 years^{xxii}. A 2-step TST is designed to avoid false negative baseline TSTs, so a subsequent positive TST is not misinterpreted as a TST conversion. The second TST of the 2-step procedure should be done 1-5 weeks after the initial negative TST. The results of the second TST should be taken as the baseline for future assessment of TST conversion.

The 2-step TST is ideally suited to the situation of health worker screening where it is expected that there will be repeat testing at future regular intervals, and it is desirable to identify booster phenomena so as not to confuse the results with genuine TST conversion in health care workers. The 2-step TST is not routinely recommended in contact tracing.

12. Alternative/in vitro tests

Interferon- γ -release-assays such as the QuantiFERON tests (Cellestis Limited, Carnegie, Melbourne), are assays that detect cell mediated immune (CMI) responses to TB specific proteins that are secreted by the *M.tuberculosis* organism. These CMI responses are demonstrated to be both specific for *M.tuberculosis* infection and have less cross-reactivity with BCG and most non-tuberculosis mycobacteria.

The QuantiFERON – TB Gold® assay has been evaluated for use with immune competent healthy adults. A result of greater than 0.35IU/ml of interferon to the specific antigens indicates TB infection.

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The assay has not been evaluated for use within children aged < 12 years, infants, pregnant women, immunocompromised individuals (HIV positive individuals), or people with certain clinical conditions predisposing immunosuppression (i.e. diabetes, silicosis, cancers, organ transplants), or those taking immunosuppressive medication. Studies are currently underway to assess the performance of QuantiFERON – TB Gold® within these groups.

The US Center for Disease Control and Prevention state in the Morbidity and Mortality Weekly Report of 16 December 2005/54/No.RR-15, that the QuantiFERON – TB Gold® assay may be used in certain circumstances to diagnose LTBI. However, the National Tuberculosis Advisory Committee is currently evaluating the results of international studies to determine the recommendations for use of QuantiFERON – TB Gold® in Australia. The TST continues to be the recommended methodology for diagnosing LTBI and QuantiFERON – TB Gold® is not recommended for assessment of LTBI^{xxiii}.

Persons referred to NSW TB Prevention and Control Services for evaluation of LTBI following screening with QuantiFERON – TB Gold® must have their results assessed in conjunction with other clinical and laboratory information to determine the risk of TB infection and/or active TB. It is not considered necessary to undertake a TST in this group of people.

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