

TUBERCULIN PPD

(From **Human** Strains of *M. tuberculosis*)

ACTIONS

TUBERCULIN PPD contains soluble growth products derived from the tubercle bacillus. When administered intradermally, either by injection or by means of a puncture device, a hypersensitivity reaction, manifesting as induration and erythema, will appear in sensitive individuals. A positive reaction is an indication that the patient has had, at some time, a tuberculous infection. A positive test does not indicate the presence of an active infection, but indicates that further evaluation should be done.

INDICATIONS

Used in skin testing as an aid in the diagnosis of tuberculosis.

WARNINGS

Tuberculin should not be administered to known tuberculin-positive reactors because of the severity of reactions (eg vesiculation, ulceration or necrosis) that may occur at the test site in very highly sensitive individuals.

Avoid injecting tuberculin subcutaneously. If this occurs, no local reaction develops, but a general febrile reaction and/or acute inflammation around old tuberculous lesions may occur in highly sensitive individuals.

PRECAUTIONS

As with any biological product, adrenaline should be immediately available in case an anaphylactoid or acute hypersensitivity reaction occurs. Tuberculin testing should be done with caution in persons with active tuberculosis. However, activation of quiescent lesions are rare.

It should be noted that reactivity to tuberculin may be depressed or suppressed for as long as four weeks by viral infections, live virus vaccines, (eg measles, polio, rubella and mumps), or by the administration of corticosteroids. Malnutrition may also have a similar effect. When of diagnostic importance, a negative test should be accepted as proof that hypersensitivity is absent only after normal reactivity to nonspecific irritants has been demonstrated.

A child who is known to have been exposed to a tuberculous adult must not be adjudged free from infection until he has a negative tuberculin reaction at least ten weeks after contact with the tuberculous person has ceased.

A positive tuberculin reaction does not necessarily signify the presence of active disease. Further diagnostic procedures should be carried out before a diagnosis of tuberculosis is made.

ADVERSE REACTIONS

In highly sensitive individuals, strong positive reactions including vesiculation, ulceration, or necrosis may occur at the test site. Cold packs or topical steroid preparations may be employed for symptomatic relief of the associated pain, pruritus, and discomfort. Minimal bleeding may be experienced at a puncture site. This occurs infrequently and does not affect

interpretation of the test. Strongly positive test reactions may result in scarring at the test site.

FOR USE IN MANTOUX TEST AND HEAF TESTS

TUBERCULIN PPD (Purified Protein Derivative) is used for the Tuberculin test. The tests most commonly used in Australia are the Mantoux test and the Heaf test.

TUBERCULIN PPD conforms to the requirements of the British Pharmacopoeia. Its potency is expressed in terms of the International Tuberculin Unit (IU). One unit (1 IU) is equivalent to 0.1 mL of TUBERCULIN PPD at a strength of 0.0002 mg/mL.

MODE OF ISSUE

TUBERCULIN PPD (Human) for the Mantoux test is available as the following solutions:

100 IU	(0.002 mg) per mL	1 mL size
100 IU	(0.002 mg) per mL	10 mL size
1000 IU	(0.02 mg) per mL	1 mL size

(The solutions contain 0.005% v/v Tween 80 as a stabilizer and 0.5% w/v phenol as a preservative).

TUBERCULIN PPD (Human) for the Heaf Test is issued as a concentrated solution at a strength of 2 mg per mL. The material contains 50% v/v glycerol to facilitate application on the skin, and 0.5% w/v phenol as a preservative.

THE MANTOUX TEST (USING TUBERCULIN PPD)

Inject intradermally 0.1 mL of a solution* containing 100 IU per mL (i.e 10 IU per dose of 0.1 mL) into the ventral surface of the upper part of the forearm. The resultant reaction is normally read at 72 hours but could be read from 48 hours to the fifth day. The characteristic reaction consists of a circular area of induration which may or may not be accompanied or surrounded by erythema. The reaction commences within 24 hours and reaches a maximum size in 48 to 72 hours. It then gradually subsides although it usually remains visible for several days. Rarely, vesiculation or even local necrosis may occur, sometimes accompanied with lymphangitis or regional adenitis. When reading the reaction, it is the oedema or induration that is important and can usually be detected more easily by the finger than the eye. The diameter of the area of induration or oedema should be measured in millimetres and recorded. Any vesiculation or necrosis should also be recorded. Erythema without oedema or induration should be disregarded.

The National Tuberculosis Advisory Council (Canberra) suggested the following degrees of reaction to the 10 IU dose Mantoux Test:

Negative	- less than 5 mm diameter
Weak positive	- 5 to 9 mm diameter
Intermediate positive	- 10 to 14 mm diameter
Strong positive	- 15 mm diameter or more with vesiculation

Important: A separate syringe should be kept for tuberculin testing and should not be used for any other purpose.

THE HEAF TEST

This test is performed by puncturing the skin of the ventral surface of the forearm through a smear of the preparation TUBERCULIN PPD for the Heaf test.

The needles of the Heaf gun are set at either 1 or 2 mm, the former depth being used for infants and young children. The instrument is sterilised by dipping the end plate and needles into a small petri dish filled with alcohol to a depth of about 7 mm, then withdrawing and flaming gently, the alcohol being allowed burn until the flame goes out. The end of the gun is then allowed to cool and, at the same time, is kept protected from contamination until use.

A suitable position on the forearm is sterilised with spirit which is allowed to dry. Using a platinum loop or glass rod, a small amount of the Heaf test tuberculin is applied to the forearm over an area of about 1 cm². The glass rod or platinum loop is then sterilised by flaming. The end plate of the Heaf gun is then pressed gently but firmly over the area, and the needles released while the skin is held taut. The procedure is painless. The results may be read at any time after 72 hours up to 7 days.

No accurate measurements are made, the degrees of reaction being determined qualitatively according to the following definitions:

Negative	-	No reaction or puncture marks only, with or without a small amount of congealed blood.
Grade i	-	A palpable papule at 4 to 6 of the puncture sites.
Grade ii	-	A ring of induration.
Grade iii	-	A solid weal of induration.
Grade iv	-	Vesiculation.

NON-SPECIFIC REACTIVITY

As many of the weak positive reactions could be non-specific, simultaneous comparative testing with tuberculins from atypical mycobacteria should be carried out in such cases. PPD tuberculins from certain atypical mycobacteria are available from these Laboratories as special products.

STORAGE

All PPD tuberculins should be stored, protected from light, at 2°C to 8°C. Unused material should be discarded.

***NOTE:** Different strengths are used in different countries for the Mantoux test. In Australia, 10 International Units per dose of 0.1 mL is usually used for routine purposes when there is no reason to suspect active tuberculosis. If the test is doubtful or negative, 100 IU may then be injected. Recent contacts of sputum-positive cases, or those giving a history or having symptoms suggestive of tuberculosis infection, should first be tested with 1 IU. This may be obtained by mixing 0.1 mL of a solution containing 100 IU per mL with 0.9 mL Sodium chloride Injection BP immediately prior to use. 0.1 mL of this dilution contains 1 IU. This solution should not be stored and the residue discarded.

Oct 2002