



Administration and Interpretation of PPD Test

PPD Testi Uygulaması ve Yorumu

Bengisu Menentoğlu¹(iD), Ceren Şimşek¹(iD), Nevin Hatipoğlu¹(iD)

¹ Clinic of Pediatrics, SBU Bakırköy Dr Sadi Konuk Training and Research Hospital, İstanbul, Turkey

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Introduction and General Information

Tuberculosis (TB) is a devastating infectious disease caused by *Mycobacterium tuberculosis* and most frequently affects the lungs. In children, direct detection of the organism in diagnosis is challenging and at a low rate. Therefore, tests depending on the host's response to the infection is important in the diagnosis of tuberculosis in children. Two screening tests are used in the diagnosis of TB: 1-Tuberculin skin test (TST), 2- Interferon-gamma release test (IGRT).

The oldest tuberculosis screening test most widely used in the diagnosis of tuberculosis is the practice of intracutaneous injection of purified protein derivative (PPD) known as tuberculin. PPD contains antigenic components isolated through protein precipitation from tuberculosis bacilli culture filter. PPD-S is accepted as the international standard, and PPDs produced equivalently are used for tests.

TST is a method showing the cellular immune response of a previously infected individual with *M. tuberculosis*. TST does not differentiate latent infection from active tuberculosis disease and is used more to evaluate the presence of latent TB infection. Principally, it is used for the contact screening of people in close contact with tuberculosis. In addition, it is used as part of tests targeted at high risk groups for TB such as healthcare workers working in high risk areas for TB and residents and employees of penitentiaries.

The most reliable method in the administration of tuberculin test is the intracutaneous test known as "Mantoux". It should be done and read by a physician or a healthcare worker trained in the procedure at a healthcare center with appropriate equipment.

Equipment required for the procedure (Figure 1)

- Well-lit table and chair
- Refrigerator with automated temperature monitoring system
- PPD solution
- Single use syringe with a thickness of 27 gauge and 1 mL measurement divisions.
- Disposal cup for sharp medical objects resistant to puncture
- A transparent ruler with millimeters
- Ball-point pen
- Gloves
- Gauze, cotton
- Patient form and PPD result card to record the result

Pre-procedure Preparation

PPD test can be administered to outpatients and inpatients. The family and the child are informed on the procedure, and consent is received. It should be explained to the

Correspondence Address / Yazışma Adresi

Nevin Hatipoğlu

SBÜ Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi,
Çocuk Sağlığı ve Hastalıkları Kliniği,
İstanbul-Türkiye

E-mail: naydin9@mynet.com

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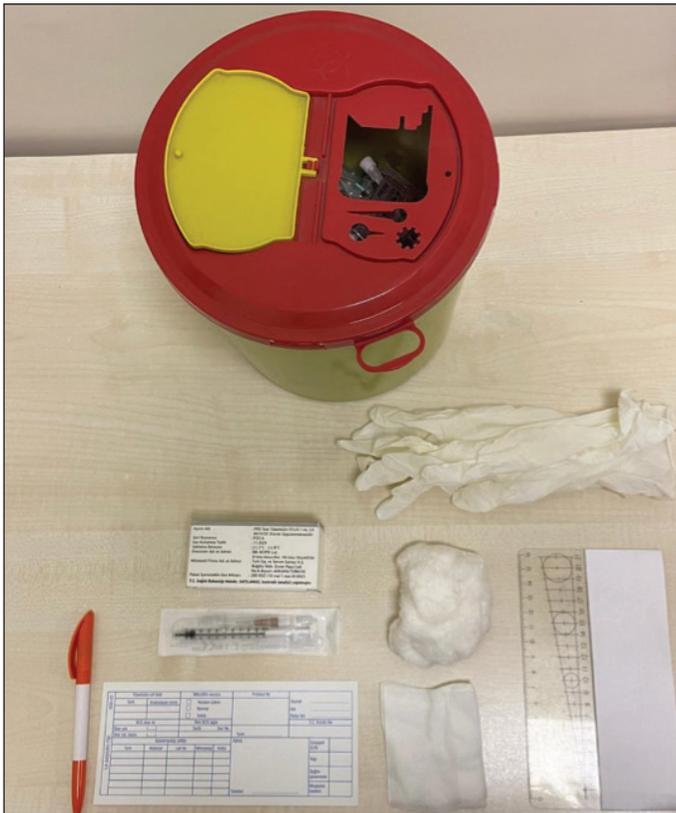


Figure 1. Equipment used during PPD test.

family that the procedure will not take long but the child will feel pain for a short period of time on his/her arm. It is preferably administered into the inner surface of the left forearm far from veins and without scar tissue, irritation and open wound. The forearm is placed on a well-lit, fixed and plain surface with the palm facing upward. During the procedure, the elbow of the patient should be slightly bent and held steady without moving the arm. If both arms cannot be used for the test, it can be administered at the back of the shoulder.

PPD solution must be preserved in a light-proof brown glass bottle (Figure 2), and when not used, it must be kept in a refrigerator at +2 and +8°C with automated monitoring of the temperature (Figure 3). Once opened, the PPD solution can be used for 1 month, and bottles exceeding this duration must be disposed of. It should not be allowed for syringes filled with PPD solution to be used after the 20th minute, and the unused full syringes must be disposed after 20 minutes. Exposure to room temperature and light can make the skin test antigen less effective. If the syringes have been filled previously and the liquid containing tuberculin is kept in the syringe, the proteins can stick to the wall of the syringe and make the test ineffective.

The test is not performed in cases that show severe systemic allergic reaction and anaphylactic shock or in cases of blisters, ulcerations and necrosis formation on the administration area.

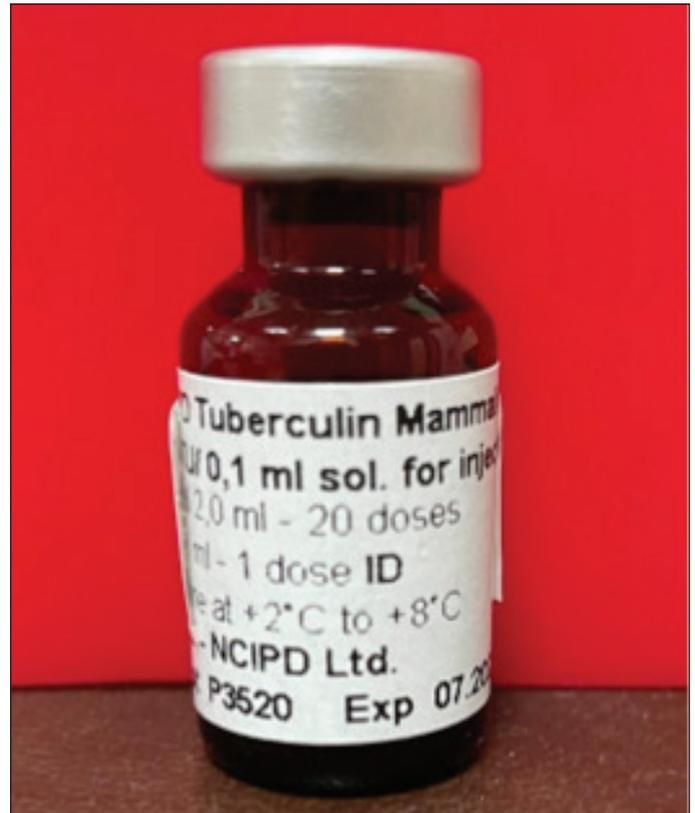


Figure 2. PPD solution must be kept in a brown light-proof glass bottle.

The procedure (Figure 4)

PPD test is a two-phase procedure, and the patient must be in the healthcare institution for both procedures:

First Phase (PPD administration): The test is administered to the patients by a trained healthcare worker.

Second Phase (PPD reading): After a specific period of time (at the 48th or 72nd hour), the change on the skin of the test area is evaluated.

Prior to drawing the PPD solution, which is kept in the refrigerator when not used, to the injection syringe, the vial is wiped by an alcohol-soaked cotton. 0.1 mL of the solution is drawn into the injection syringe with a needle of 27 gauge thickness. In order to guarantee the right volume, more than a one-tenth of 1 milliliter is drawn into the injection syringe, and the needle is taken out of the bottle. While the syringe is held at an upright position, the piston is slightly retracted, the syringe is slightly hit to gather all air bubbles and pushed forward. This way, the air bubbles and the extra liquid in the syringe is drawn out, and exactly one-tenth of the tuberculin solution is left in the syringe.

The skin area to be used for tuberculin administration is not wiped with any antiseptics. The administrator holds the skin between the thumb and index finger tight so as to provide better and easier penetration of the needle into the skin.



Figure 3. PPD solution (marked in blue frame) must be kept in a refrigerator whose temperature is monitored (between +2 and +8°C).



Figure 4. Intradermal administration technique of the PPD test.

The needle tip is penetrated into the skin held at 5-15° with the needle bevel facing upward. The needle tip is pressed forward for 3 mm, and the obliquity of the needle should be seen right under the skin. A rather hard resistance will be felt once the tuberculin is injected into the skin. Upon injecting the solution intracutaneously, a wheal 6 to 10 mm in diameter should be produced on the injection area. The needle is withdrawn without massaging or pressing the site. Afterwards, the used syringe must be immediately disposed of in the specified cup resistant to puncture. It is not unusual to have a drop of blood on the injection site even if the needle is placed correctly. In this case, the blood is softly wiped with a gauze or cotton.

There is no need to wrap the area with a special bandage. It should be explained that there might be slight itchiness and swelling and these are all normal reactions that do not require treatment and will heal in a week. The patient should be told not to scratch the area, to keep it clean and dry and not to put cream, lotion or sticky bandage on it. Moreover, it should also be noted that bathing the area with water is not harmful but it should not be scratched or rubbed.

Allergic reaction can be seen with tuberculin, and adrenalin must be kept available during the procedure.

If the PPD skin test could not be done technically correct, a second test dosage can be administered at least 5 cm away

Since PPD test is time-sensitive, tests read late may reveal less skin reaction size and would be incorrect to evaluate. In order to prevent this, the test is recommended to be performed again if the reaction is not read on time. Nonetheless, in order to avoid booster effect with the first test, the second should be preferably performed within the 7 days after the first test. Moreover, the area of the second test should be another place of the body, like the other arm.

Bulla, vesicle and similar reactions can be observed on the test area, but additional treatment is not required. Painkillers can be taken if necessary for this condition that heals spontaneously. It should be remembered that reliable reading of the PPD skin test requires lots of practice and compliance to steps of administration.

Discussion

The benefit of PPD skin test is that it enables rapid identification of the presence of TB infection and thus its diagnosis. PPD test is a simple and cheap skin test. Even if TB infection is not active, the detection of latent TB decreases the risk of progression to active TB.

Rigidity within the 48-72 hours in the area where PPD has been placed demonstrates delayed-type hypersensitivity reaction and infection with *M. tuberculosis*. T cells that have already become sensitive with previous infection accumulate in the test area and release lymphokine. Induration occurs with vasodilatation, edema, fibrine storage developing in this area and the clustering of other inflammatory cells. Presence of erythema without induration is considered negative.

An induration of 0-4 mm shows negative reaction. There are some factors decreasing response to tuberculin test (Table 1). PPD test can be found negative if bacillus is taken recently and thus the infection is still in the incubation period. In addition, tuberculin reaction may not occur at times in advanced and untreated tuberculosis. Furthermore, tuberculin reaction is found negative during immunosuppressant treatment and measles and varicella vaccination and insufficient nutrition. Live measles vaccine generates a temporary anergia (non-response) lasting for 2-3 weeks, like in the measles disease. Other viral vaccines can also suppress skin reaction. In infants under the age of 6 months and especially in those under 3 months, a sufficient regional inflammatory response for a positive skin test may not generate even if the child has been infected with tuberculosis bacillus. Induration 15 mm and larger in diameter demonstrates tuberculosis infection (Table 2). This limit is valid for every age in our country. A measurement 5-15 mm in diameter is suspected reaction. This reaction can be seen as a result of BCG vaccination; however, the probability of tuberculosis infection and atypical mycobacteria infection should also be considered.

from the first, original spot. The area of the procedure can be circled with a ball-point pen so that the family or the child can easily notice the test area. The procedure is recorded with information on date and hour of the test, injection area and location, and tuberculin lot number. PPD solution is put in the refrigerator since room temperature can cause deterioration in its activity.

Post-procedure Evaluation (Figure 5)

Interpretation and evaluation of the skin test should be done 48-72 hours later. Therefore, reading appointment should be given when the hospital is open for outpatients, and the patient must be asked to come back. Another PPD appointment is required for the patients who do not show up within the 72 hours.

The evaluation must be made visually at the 48th or 72nd hour (96th hour in special cases) under good light. Not redness (erythema) along the forearm, but thickening of the skin (rigidity, induration) must be measured. Rigidity may not always be visible, and palpation with fingertips must be done to understand its presence. Points of origin of induration can be detected with a ballpoint pen (pen-ball method). Marking should be made from the widest edges of the induration. The diameter of the indurated area should be measured across the forearm perpendicular to the long axis. If margins are irregular, the longest diameter should be marked and measured. The starting and ending points of the induration are millimetrically measured with a transparent ruler, and the result is recorded in millimeters. If the distance in mm scale is between a value of two lines, it is more appropriate to accept the shorter measurement as test result. It is correct to note "0 mm" not "negative" in the absence of induration.



Figure 5. The reading technique of PPD test by marking the starting point of the exanthema with a ball-point pen.

Table 1. Factors decreasing response to tuberculin test

Factor	Disease or Condition
Factors related to the individual being tested	<ul style="list-style-type: none"> Infections <ul style="list-style-type: none"> Viral (measles, mumps, varicella, HIV) Bacteria (typhoid, typhus, brucella, pertussis, prevalent TB, TB pleurisy) Fungal (South America blastomycosis) Live virus vaccines (measles, mumps, polio, varicella) Metabolic disorders (chronic renal deficiency) Low proteins (serious low protein levels, afibrinogenemia) Diseases affecting lymphoid organs (Hodgkin's disease, lymphoma, chronic leukemia, sarcoidosis) Drugs (corticosteroids and many other immunosuppressive drugs) Age (newborns, elderly patients with "decreased" sensitivity) Stress (surgical, burns, mental diseases, graft versus host reactions)
Factors related to the tuberculin used	<ul style="list-style-type: none"> Inappropriate storage (exposure to light and heat) Inappropriate dilution Chemical denaturation Contamination Ahesion (partially controlled adding Tween 80)
Factors related to method of administration	<ul style="list-style-type: none"> Injecting very few antigens Subcutaneous injection Late administration after drawing to the injector Close injection to other skin tests
Factors related to reading and evaluation	<ul style="list-style-type: none"> Inexperienced reader Conscious or unconscious mistakes Mistakes in records

Table 2. Evaluation criteria of tuberculin skin test (TST) in our country.

BCG Vaccination Status	Induration Diameter	Interpretation
In patients with BCG vaccination	0-5 mm*	Accepted negative.
	6-14 mm*	Could be related to BCG vaccination or non-tuberculous mycobacteria
	15 mm and over	Accepted positive.
In patients without BCG vaccination	0-5 mm*	Accepted negative.
	6-9 mm*	Could be related to non-tuberculous mycobacteria
	10 mm ve üzeri	Accepted positive.
In immunosuppressed persons**		5 mm and over is accepted positive.

BCG: Bacille Calmette-Guerin vaccination, TDM: Non-tuberculous mycobacteria.

* Since it is possible in adults for the immune response to diminish in intensity, the test is repeated within 1-4 weeks in persons with a TST response of 1-14 mm with BCG vaccination and 1-9 mm without BCG vaccination, and the value is evaluated according to the table. This practice referred to as the booster effect is not used in the examination of people in contact.

** Immunosuppressed persons are those with HIV positivity, AIDS, chronic renal failure, high dose corticosteroid patients (high dose is considered as daily steroid doses equivalent to 15 mg and higher prednisone doses for 2-4 weeks) and other conditions requiring immunosuppressive treatment, and those with reticuloendothelial system malignancy.

Provided that BCG vaccination has not been administered in between, at least 6 mm increase in TST in the last two years and becoming positive or a single 10 mm increase in TST is defined as TST conversion, and PPD test is considered positive.

Repeated tuberculin tests do not affect active or latent tuberculosis infection process. IGRT is preferred in individuals who has received Bacille Calmette-Guerin (BCG) vaccination rather than the tuberculin test. However, the possibility of uncertain results in children aged under 5 years and in immunosuppressed patients is high, and meticulous evaluation should be made. It is recommended in developed countries that IGRT

be performed in individuals aged 5 and over and tuberculin skin test as an alternative. In children under the age of 5 years, vice versa is recommended. If IGRT is to be performed in a patient in whom PPD test has already been done, then it should be carried out within the following three days of PPD test.

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