Readers' Forum

Interpretation of Mantoux Test

Q. *What are the recommended dimensions of positive Mantoux test for clinical and epidemiological uses?*

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***A**. The Manoutx Test*

Tuberculin test in which the antigen is injected intradermally is called Mantoux test. The "old tuberculin" is no longer used for this purpose; instead, a more standardized product called PPD-S (purified protein derivative, prepared according to the method described by Siebert, from *Mycobactenum tuberculosis)* is used. PPD of non-tuberculosis *(i.e.,* atypical) mycobacteria are identified by a letter other than S. PPD-A is from *M. avium;* PPD-G from Gause strain of schotochromogen; PPD-B from the non-photochromogen Battey bacilli; PPD-F from the rapid grower M. *fortuitum* and PPD-Y from the yellow photochromogen M. *kanasasii.*

The strength of the test dose of PPD-S is denoted in tuberculin units (TU). For the sake of standardization of reading and interpretation of results, 5 TU of PPD-S contained in 0.1 ml, is used almost universally. It is to be injected strictly intradermally, using 28 or 26 gauge needle and tuberculin syringe from which 0.05 ml or 0.1 ml can be delivered accurately. The volar aspect of the forearm is the preferred site of test.

The Test Result

The test result must be read no earlier than 48 and no later than 72 hours from injection. It must be read in good light and the transverse and longitudinal diameters of induration measured in millimeters with the help of a suitable ruler (scale). If the two diameters do not agree, the greater diameter is used for interpretation.

A measurable induration of 2-4 mm or more (for practical purposes 5 mm or more), is indicative of the presence of cell mediated immunity (CMI) of the *delayed hypersensitivity* type. Technically, this means that the person has had prior sensitization with mycobacterial antigen, either of *M. tuberculosis* or of another cross reacting mycobacterium. In other words a result of 5 mm and above of induration is positive for CMI, strictly from immunological view point. This test result must be further interpreted to discern what it might mean.

Interpretation of Negative Mantoux Test

The absence of CMI to tuberculin may be due to the lack of previous sensitization, or due to a false negative result for various reasons, or due to anergy because of immune suppression. Most children with negative result have not been infected with *M. tuberculosis. A* small proportion of otherwise normal children with *M. tuberculosis* infection remain PPD negative for unknown reasons. From the time of infection to the development of CMI there is a window period of some 2 to 6 weeks, when the Mantoux test would be negative. In this situation, a chest radiograph may show the

pneumonitis of primary complex and yet the test may be negative. A repeat test after a couple of weeks will usually be positive. In malnourished children with tuberculosis and in severe and disseminated disease including miliary or meningeal disease the test may be often negative. One of the reasons for energy may be HIV infection.

Interpretation of Positive Mantoux Test

I recommend to those seriously interested in this subject to read a paper published in Indian Journal of Medical Research in 1971 on skin sensitivity survey to six mycobacterial antigens in a sample population of children and adults(l). In our communities, tuberculin sensitivity may be due to infection with *M. tuberculosis,* with atypical mycobacteria, *M. bovis* in the form of BCG, or any combination of these. Since the test antigen is PPD-S, true tubeculin sensitivity induration tends to be larger than that to BCG which in turn tends to be larger than that to atypicals. For practical purposes we classify PPD reactions as large and small(l). In Vellore region, the diameter that separates the two, is by actual survey, 8 mm. In other regions in India the cut-off may be 10 mm or even 12-14 mm(2). In general, in those not given BCG, locally defined large reactions are taken to indicate tuberculin sensitivity and smaller reactions (in Vellore 7 mm and less) are taken to indicate cross reaction to atypicals. The most popular cut-off is 10 mm and above. It is unlikely that BCG-induced reaction will be more than 10 mm five years after inoculation. Upto five years after BCG, the interpretation of PPD-S response is difficult; but if the reaction is some 14 or 15 mm and above, it is quite likely to be due to M. *tuberculosis* sensitisation. In places where atypicals are rare, and BCG is not given, induration of 5 mm and above is clear evidence for tuberculin sensitivity. For these reasons my recommendation is to quote always the actual diameter of induration rather than 'positive' or 'negative' when the test result is reported. Thereafter, at the stage of interpretation we may use the terms positive or negative, but positive always accompanied by the qualifier meaning: 'tuberculin sensitive' or 'BCG sensitised' or 'false positive' or 'non-specific reaction'.

Clinical and Epidemiological Uses **of Mantoux Test**

In asymptomatic children without BCG immunization, and in children more than 5 years after giving BCG, a reaction of 10 mm or more is to be taken to mean past infection with *M. tuberculosis.* In symptomatic children with BCG scar, a reaction of less than 14 mm may be attributed to immunization for upto 5 years after giving BCG. In such children, 15 mm or more reaction may be due to infection with *M. tuberculosis.* In children below 3 years of age with tuberculin sensitivity and in persons in whom recent (within 3 years) conversion from negative to positive reaction has been documented, preventive therapy with Isoniazid and Rifampicin is recommended for 6 months(3).

In children with suspected tuberculosis disease (TB), tuberculin reaction (10 mm or more in unimmunized; 15 mm or more in immunized, but upto 5 years; 10 mm or more beyond 5 years after BCG) is additional evidence in support of the diagnosis. However, a negative test or a small (less than 10 mm) reaction does not exclude TB or *M. tuberculosis* infection.

In a family in which any person has TB, all other members should be tested, classified, and followed up. Children below 3 years with large reaction and recent converters must be given preventive therapy(3).

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