

and to 5 TU of PPD. Thus BCG vaccine appears to be more sensitive.

This might be because BCG has a more complete tuberculosis antigen, while PPD may not contain all antigen components synthesized by the bacillus. Moreover, the lipid content of BCG vaccine enhances the antigenicity of the vaccine.

When positive PPD reactions are compared with BCG reactions in correlation with the state of nutrition (tables 2a & 2b): In the undernourished group there was a significant statistical difference, there were 17 (85%) positives for BCG but only 5 (25%) for PPD test. On the other hand in the well-nourished group there was no statistical difference although there were more positive BCG reactions than positive PPD test reactions. ( $P > 0.05$ ). Many studies have found that BCG vaccination can be used as a diagnostic test in tuberculosis and although it has been shown to be more sensitive than the tuberculin test, it is still not sufficiently clear why the BCG test is positive more often than the Mantoux test, especially when malnutrition is present. (Udani et al, 1971). An induration of 6 mm or more in the first week after the BCG test was considered a positive reaction. Other studies indicate that this test is not significantly different from those showing positive reactions after a skin test with 5 TU of PPD. (Choudhry et al, 1974).

The very significant difference in the undernourished group is explained by a

depression of the immunologic system by cellular immunity mechanisms which result in an elevation of cortisol production. (Uetvedt, 1949).

The reaction to the BCG test was not related to the age of the patient; the 26 children with positive BCG reactions occurred randomly in all age groups (table 3) whether 6-10 mm or 10 mm and more of induration size is taken as the criteria for a positive test. This indicates that the BCG test can be used efficiently during infancy for the diagnosis of tuberculosis.

There were no local reactions such as ulceration and regional lymphadenitis/BCG-itis following the BCG test. However Choudhry et al. (1974) found local reactions amounting to ulceration in two patients which healed spontaneously in three weeks.

The relation between PPD and BCG tests and an increase in body temperature was not significant. Only one child (2.9%) developed fever in the patient group. It was sub-febrile and lasted for 1 or 2 days. (table 4). Choudhry et al. (1974) found 2 children (3.0%) who developed fever among children.

The Histogram (Fig. 1) shows the proportion of positive reactions to graded induration size of BCG tests (74.3%) and PPD tests (25.7%). There were more positive reactions to the BCG tests with 10 mm induration or more (31.4%) than to the test with 5 TU of PPD. This was not statistically different but there were more positive BCG reactions

(74.3%) than PPD and statistically there was a significant difference ( $P < 0.01$ ).

The comparison in size of induration following 5 TU of PPD and BCG skin test on 35 patients (Fig. 2) strengthened the findings in this study although there were 3 children with indurations following the 5 TU PPD test larger than those following the BCG test.

### Summary

This study revealed that the BCG test was more sensitive than the 5 TU — PPD test especially in undernourished children as a diagnostic tool for tuberculosis in children.

It may be concluded that BCG is very important whether for prophylactic measures or diagnosis of tuberculosis in children.

TABLE 1: Reaction to BCG and PPD tests

PPD & BCG Reactions	Patient				Control			
	PPD		BCG		PPD		BCG	
	Number	%	Number	%	Number	%	Number	%
Positive	9	25.7	26	74.3	0	0	0	0
Negative	26	74.3	9	25.7	20	100	20	100
Total	35	100	35	100	20	100	20	100

$P < 0.01$

TABLE 2: Correlation between PPD and BCG test reaction and the state of nutrition  
a. Undernourished group

PPD & BCG Reactions	P P D		B C G	
	Number	%	Number	%
Positive	5	25	17	85
Negative	15	75	3	15
Total	20	100	20	100

$P < 0.01$

b. Well-nourished group

PPD & BCG Reactions	P P D		B C G	
	Number	%	Number	%
Positive	4	26.7	9	60
Negative	11	73.3	6	40
T o t a l	15	100	15	100

P > 0.05

TABLE 3: Distribution of BCG reactions in age groups

Age (years)	Number	B C G R e a c t i o n					
		6 mm	%	6-10 mm	%	10 mm	%
1	5	1	2.9	3	8.6	1	2.9
1 — 5	19	6	17.1	8	22.8	5	14.2
5 — 10	8	2	5.7	3	8.6	3	8.6
10	3	0	0.0	1	2.9	2	5.0
T o t a l	35	9	25.7	15	42.9	11	31.4

— 26 positive BCG reactions distributed randomly in all age groups — 9 children showing negative BCG reactions.

TABLE 4: The influence of PPD and BCG tests on body temperature

Temperature	P a t i e n t		C o n t r o l		T o t a l	
	Number	%	Number	%	Number	%
Increase *)	1	2.9	3	15.0	4	7.3
No increase	34	97.1	17	85.0	51	92.7
T o t a l	35	100.0	20	100.0	55	100.0

P < 0.01

\*) The temperature was sub-febrile and lasted for 1 or 2 days

FIG. 1: Histogram showing the proportion of positive reactions in PPD and BCG tests

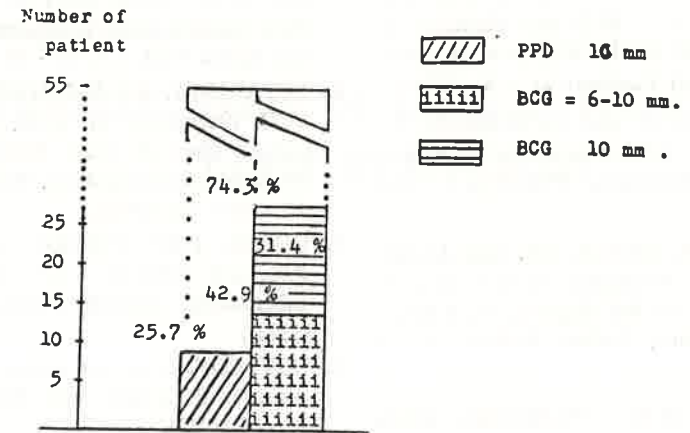
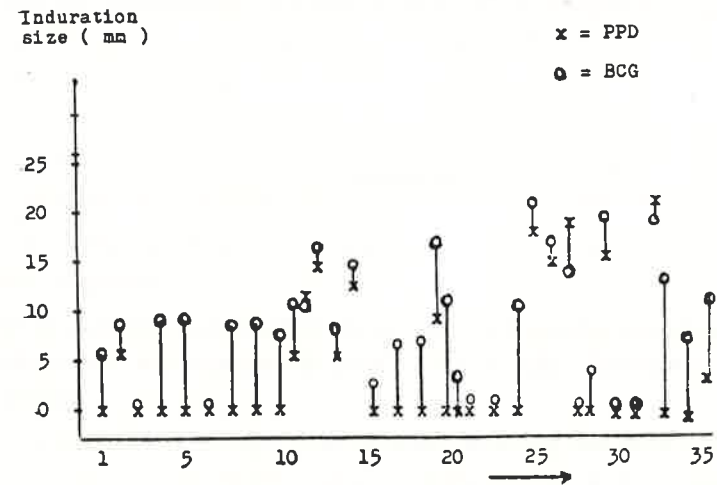


FIG. 2: Comparison of induration size following 5 TU PPD and BCG skin tests done on 35 patients



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ORIGINAL ARTICLE

BCG as Diagnostic Test for Primary Tuberculosis in Children

by

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Abstract

*BCG and PPD Mantoux Intradermal Test were done simultaneously on 35 children suffering from primary tuberculosis hospitalized in the Department of Child Health, School of Medicine, Gajah Mada University, Yogyakarta, Indonesia, during the period of June 1980 to November 1980.*

*This study revealed that :*

- *The BCG test was almost three times (74.3%) more sensitive than the PPD Mantoux Intradermal test in children suffering from primary tuberculosis.*
- *In under-nourished children with tuberculosis, the BCG test was even more sensitive (85.0% : 25.0%) and this difference was statistically significant ( $P < 0.01$ )*

*There was a high frequency of false negative tuberculine reaction (74.3%) and accelerated BCG reaction (74.3%) in primary tuberculosis. It is suggested that BCG test be used as a diagnostic test as well as prophylactic in tuberculosis children who have had a BCG vaccination.*

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## Introduction

Mass BCG vaccination in Indonesia has been done before without prior tuberculin testing. It is now being done as one of the programs of the Indonesian Department of Health, namely PPI. (Expanded Program on Immunization).

In Indonesia tuberculosis, like in other developing countries, is still one of the major causes of morbidity and mortality. So in the tuberculosis eradication program, the aspect of therapy is not less important than the aspect of prophylaxis. For this reason an accurate, reliable and easily available tool is needed for early diagnosis and treatment.

Although laboratory facilities for finding tubercle bacilli are advanced, its detection in children is very difficult. (Rahayu, N.N., 1975; Yati et al., 1976).

Tuberculin test is one of the important tests to diagnose primary tuberculosis but there are many conditions causing false negative tuberculin reactions such as: anemia, severe infection, malnutrition, malignancy, the use of immunosuppressive drugs. Malnutrition is still a problem in Indonesia, and 15.0% of all pre-school children are suspected suffering from moderate to severe malnutrition.

## Material and Methods

This study was done during the period of June 1980 through November 1980 on 35 children aged 3 months to 14 years suffering from primary tuberculosis admitted to the Child Health Depart-

ment, School of Medicine, Gajah Mada University, Yogyakarta. Twenty other children of the same age and state of nutrition were being used as a control group.

The diagnosis of tuberculosis in these patients was made on the basis of history, clinical symptoms, laboratory findings and radiological evidence.

BCG and PPD Mantoux Intradermal Tests were simultaneously done on the subjects. Freeze dried BCG vaccine (batch + P 235) prepared by P.N. Bio Farma Bandung, Indonesia, was used in this study.

Reconstituted BCG vaccine, 0.05 ml for children under the age of 1, and 0.10 ml for children age 1 and over, was injected intracutaneously in the deltoid region of the upper right arm.

The widest transverse diameter of the induration was measured during the first week after the injection, and 6 mm or more was considered to be a positive BCG reaction.

The PPD Mantoux Intradermal test using 0.10 ml 5TU of PPD-S (batch + 44) prepared by P.N. Bio Farma, Bandung was done intracutaneously on the volar surface of the left forearm immediately after the BCG injection. The reaction was examined between 48 and 72 hours thereafter and considered to be positive if the induration was 10 mm or more.

During these tests antihistamine and corticosteroid/immunosuppressive therapy were avoided.

## Results

Positive BCG & PPD reactions in patients and controls are shown in table 1; there were 26 patients with positive BCG reactions and 9 patients with positive PPD reactions but there were no positive reactions among the controls.

The correlation between the status of nutrition and positive reaction to either BCG or PPD is shown in tables 2a and 2b.

There were 5 children with positive tuberculin reactions and 17 with positive BCG reaction ( $P < 0.01$ ) in the undernourished group. In the well-nourished group there were 4 children with positive PPD reactions and 9 children with positive BCG reactions ( $P > 0.05$ ).

The distribution of BCG reactions in different age groups can be seen in table 3; 26 positive BCG reactions were distributed randomly in any age group.

There were no local reactions such as ulceration and regional lymphadenitis following BCG tests. One child in the patient group and three control children developed fever, just sub-febrile, for 1 or 2 days (Table 4).

Figure 1: The Histogram shows the proportion of positive reactions to graded induration size of BCG tests (74.3%) and PPD tests (25.7%).

Figure 2 shows a comparison in size of induration following 5 TU of PPD and BCG skin tests on each child.

## Discussion

Immunity to tuberculosis is established concurrently with the development of tuberculin allergy. BCG vaccine as a skin antigen has been cited by many authors. (Friedmann, 1952; Udani et al., 1971; Lothe et al., 1973; Choudhry et al., 1974).

The tuberculin test measures tuberculin allergy, while the BCG test measures bacterial allergy.

Our study confirms earlier claims that BCG skin tests are more sensitive for detecting tuberculin allergy irrespective of whether 6 or 10 mm of induration is taken as being a positive reaction.

Sutarjo and Ibrahim (1971; 1973) found no statistical difference in the mean size of post BCG vaccination tuberculin reactions and BCG vaccination scars by decreasing dosage of BCG vaccine. However an other research indicates that the response to tuberculin test increases with a rise in the dosage (strength) of PPD.

This study shows a statistical difference of  $P < 0.01$  in BCG and PPD test reactions (table 1). Of 35 BCG vaccinated patients there were 26 (74.3%) with positive reactions and only 9 (25.7%) with positive PPD reactions. Our findings are not greatly different from Lothe's (Lothe et al, 1973). However Choudhry et al. (1974) found that there was a very significant statistical difference between reactions to BCG and to 1 TU of PPD test but there was no difference between reactions to BCG