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ORIGINAL ARTICLE

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## The Correlation Between PPD and BCG Vaccination

by

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### Abstract

During the period of October 1975-January 1976 a study on the correlation between induration size of BCG vaccination and Mantoux test using 5 TU PPD-S has been undertaken on 1.100 non-BCG vaccinated children. Good correlation between induration size of BCG vaccination and Mantoux test performed simultaneously were observed, particularly on the third day of examination, with the correlation equation of  $y=4.97+0.69x$ , and a coefficient of correlation = 0.99. Significant differences on the mean size of BCG induration on each Mantoux test group were also observed. The mean size of BCG induration in subjects showing Mantoux test of less than 5mm., 5-9mm., and 10mm. and over were 6.07mm., 12.20mm., and 16.69mm. respectively, while the standard deviation were 2.71mm., 3.65mm., and 4.31mm. respectively. It seems that BCG induration of 8mm. (3rd day) could be taken as an indication for further diagnostic studies in the early case finding of tuberculosis in children, especially in rural areas. However, further study on the correlation of BCG induration and the incidence of tuberculosis is still required.

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### Introduction

Based on a tuberculosis prevalence survey in the areas of Yogyakarta and Malang during the period of 1962-1965, a workshop was held in Ciloto in 1969 which recommended mass BCG vaccination without prior tuberculin Mantoux test on children up to 14 years of age. In children the tuberculin test is very important for establishing the diagnosis of tuberculosis. On the other hand BCG vaccination complicates the interpretation of the tuberculin test (Pagel et al, 1964). Kendig (1972) stated that BCG vaccination generally produces tuberculin induration between 5-9 mm. If the induration exceeds 15 mm., the presence of an active infection of tuberculosis should be suspected. Hasan and Han Sik Liang (1965) found that post-BCG vaccination Mantoux test indurations were between 10-15 mm. in 65% of their subjects, while 35% gave an induration more than 15 mm.

Of considerable interest is the use of BCG as a skin test antigen. There are various ways of carrying out the test. Normal BCG vaccine may be diluted 1/100 with saline solution and the diluted BCG suspension then used instead of PPD for a Mantoux test (Heaf and Rusly, 1968). Hartston (1967) had shown that a satisfactory Heaf multiple puncture test could be carried out using BCG vaccine (undiluted) in place of concentrated PPD solution, while Sula (1962) in Czechoslovakia used killed BCG vaccine for Mantoux test. Iijas Dt.

Batceah (1962) had also used killed BCG vaccine as skin antigen in his study on 200 subjects.

It is of practical interest to prove whether the induration size of BCG vaccination can be used as an additional tool in the correlation between the PPD and the BCG induration size, and the possibility of using BCG induration as an additional tool in the early case-finding of TBC children, especially in the rural areas.

### Material and method

This study was undertaken during the period of October 1975 through January 1976 on 1100 non-BCG vaccinated children (3 months-14 years old) living in the state owned plantation enterprise of PT Perkebunan XIII in the southern part of the Bandung regency. BCG vaccination and PPD Mantoux test were performed simultaneously on the subjects. Freeze dried BCG vaccine (batch + P 235) prepared by PN Bio Farma Bandung, Indonesia, was used in this study. Reconstituted BCG vaccine of 0.1 ml for children of 1 year and older, and 0.05 ml. for children below 1 year, were injected intracutaneously on the upper third of the right upper arm using special syringe and needle for BCG. The induration size was examined on the 3rd and 10th day after vaccination.

Mantoux test using 0.1 ml. 5 TU PPD-S (batch + 44) prepared by PN Bio Farma Bandung, was performed on the volar surface of the left forearm im-

mediately after BCG injection. The reaction was examined on the 3rd day. The BCG vaccination and Mantoux tests were done by 8 qualified para medical personnels and the whole survey was supervised by the authors.

## Results

1. The induration size of Mantoux test on 1100 children is shown in Table 1.

TABLE 1: Age distribution and induration size of the subjects

Age	Number	Mantoux test reaction		
		< 5 mm.	5-9 mm.	≥ 10 mm.
3 mo. — 2 yr.	187	183	2	2
2 — 4 yr.	239	228	2	9
4 — 6 yr.	180	171	4	5
6 — 8 yr.	151	144	2	5
8 — 10 yr.	143	139	—	4
10 — 12 yr.	119	116	—	3
12 — 14 yr.	81	73	—	8
Total	1100	1054	10	36

2. The frequency distribution of BCG induration is shown in Figures 1 and 2. It appeared that the distribution was unimodal and the peak on the third day

was 6-8 followed by 4-6 and 8-10 mm., whereas in the tenth day it has shifted to 0-4 mm.

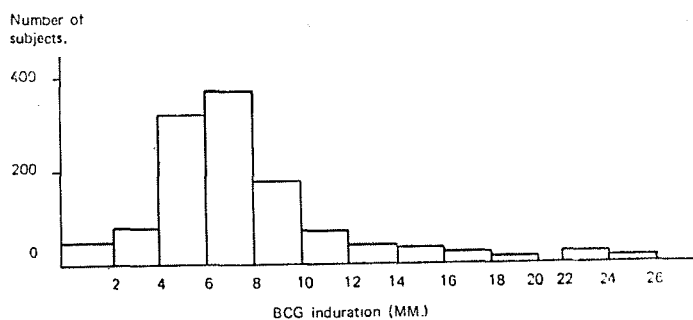


FIG. 1 : Frequency distribution of BCG induration (third day).

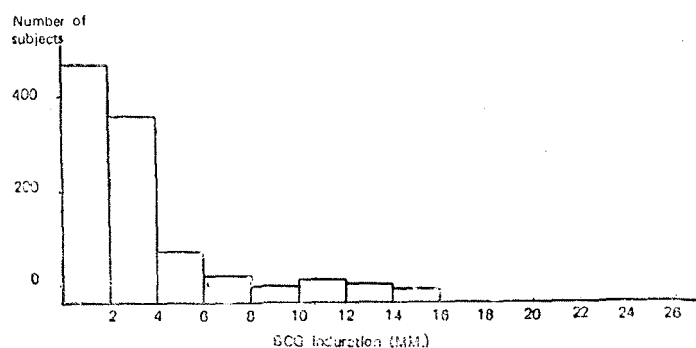


FIG. 2: Frequency distribution of BCG induration (10th day)

3. Statistically, no correlation between BCG induration size and age group was observed in subject with Mantoux test of less than 5 mm., mean BCG induration on the 3rd and 10th day was 6.07 mm. and 2.27 mm. respectively (Table 2).

TABLE 2: Mean size of BCG induration in children with negative Mantoux test

Age	Number	BCG induration			
		3rd day		10th day	
		Mean	S.D.	Mean	S.D.
3 mo. — 2 yr.	123	5.61	1.47	1.37	1.64
2 — 4 yr.	228	5.96	3.11	2.17	2.59
4 — 6 yr.	171	6.34	2.92	2.19	2.25
6 — 8 yr.	144	6.28	2.29	2.11	1.79
8 — 10 yr.	139	6.39	2.54	2.94	2.07
10 — 12 yr.	116	6.38	2.27	2.26	1.96
12 — 14 yr.	73	6.66	2.34	2.64	1.98
<b>Total</b>	<b>1054</b>	<b>6.07</b>	<b>2.71</b>	<b>2.27</b>	<b>1.97</b>

4. Statistically no correlation was observed between the induration size of BCG vaccination and age; the coefficient of correlation was only 0.19 (3rd day). The mean size of BCG induration on the 3rd and 10th day is presented in Table 3.

TABLE 3: Mean size of BCG indurations on different age groups

Age	Number	B C G i n d u r a t i o n			
		3rd day		10th day	
		Mean	S.D.	Mean	S.D.
3 mo. — 2 yr.	187	5.29	2.79	1.42	1.75
2 — 4 yr.	239	6.44	2.79	2.56	3.11
4 — 6 yr.	180	6.79	3.62	2.71	3.22
6 — 8 yr.	151	6.73	3.23	2.57	2.78
8 — 10 yr.	143	7.16	2.91	3.26	2.80
10 — 12 yr.	119	6.74	3.16	2.53	2.58
12 — 14 yr.	81	7.66	3.26	3.74	3.92

5. There were statistically significant differences in the BCG induration size between subjects with Mantoux test reaction of less than 5 mm., 5-9 mm. and 10 mm. and over (Tables 4 and 5).

TABLE 4: Mean size of BCG induration on the 3rd day reading

Mantoux test reaction	Number	B C G i n d u r a t i o n s i z e (m m)		
		Mean	S.D.	S.E.
< 5 MM.	1054	6.07	2.71	1.16
5 — 9 MM.	10	12.20	3.65	1.34
≥ 10 MM.	36	16.69	4.31	

TABLE 5: Mean size of BCG induration of the 10th day reading

Mantoux test reaction	Number	B C G i n d u r a t i o n s i z e (m m)		
		Mean	S.D.	S.E.
< 5 MM.	1054	2.27	1.97	1.11
5 — 9 MM.	10	9.50	3.50	1.28
≥ 10 MM.	36	12.30	3.86	

6. Statistically, there was correlation between Mantoux test reaction and the induration size of BCG vaccinations. The equation line and the coefficient of correlation on the 3rd and 10th day rea-

ding were respectively  $y = 4.97 + 0.69x$ ,  $r = 0.99$  and  $y' = 1.36 + 0.66x'$ ,  $r' = 0.63$  (Tables 6 and 7 and Figures 3 and 4).

TABLE 6 : Correlation table of PPD and induration (3rd day).

B C G (m m)	0-4	5-9	10-14	15-19	20-24	Total
P P D (m m)						
0 — 4	255	688	102	9	0	1054
5 — 9	0	2	4	4	0	10
10 — 14	0	1	5	5	2	13
15 — 19	0	0	4	7	2	13
20 — 24	0	0	0	1	9	10
Total	225	691	155	26	13	1100

TABLE 7 : Correlation table of PPD Mantoux test and BCG induration (10th day).

B C G (m m)	0-4	5-9	10-14	15-19	20-24	Total
P P D (m m)						
0 — 4	935	99	20	0	—	1054
5 — 9	1	3	5	1	0	10
10 — 14	2	1	8	2	0	13
15 — 19	0	2	8	2	1	13
20 — 24	0	1	4	5	0	10
Total	938	106	45	10	1	1100

BCG Induration (MM.)

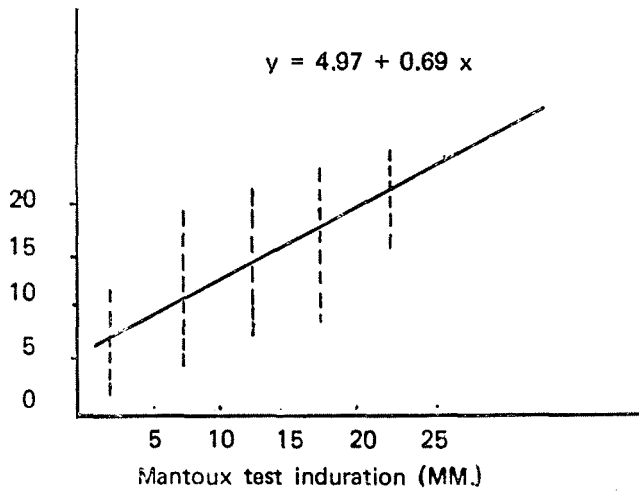


FIGURE 3: Correlation between BCG and PPD Mantoux test indurations (5rd day).

BCG induration (MM.)

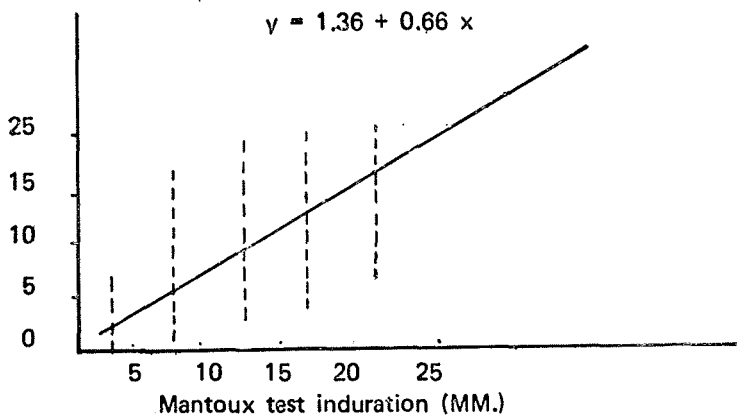


FIGURE 4: Correlation between BCG and PPD Mantoux test indurations (10th day).

7. The cumulative chart of BCG (3rd day) in each Mantoux test reaction induration and frequency distribution are presented in Figure 5 and Table 8.

TABLE 8 : Frequency distribution of BCG induration on Mantoux test group (3rd day).

BCG induration (MM)	Mantoux reaction			Total
	< 5 MM.	5-9 MM	≥ 10 MM	
0 — 1	52	—	—	52
2 — 3	86	—	—	86
4 — 5	296	1	—	297
6 — 7	347	—	—	347
8 — 9	162	1	1	164
10 — 11	73	1	5	79
12 — 13	24	2	3	29
14 — 15	12	3	4	19
16 — 17	2	2	7	11
18 — 19	—	—	3	3
20 — 21	—	—	8	8
22 — 23	—	—	4	4
24 — 25	—	—	1	1
Total	1054	10	36	1100

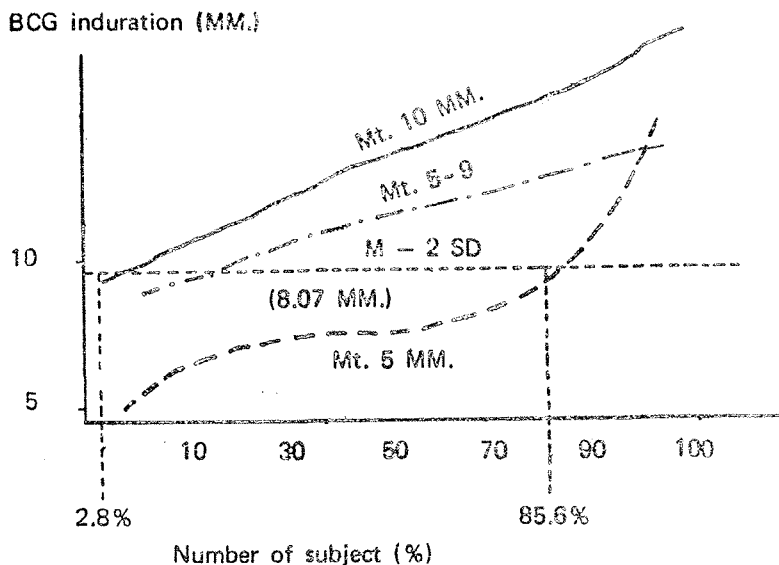


FIGURE 5 : The cumulative chart of BCG induration in each group of Mantoux reaction.



### Discussion

It is believed that the immunity to tuberculosis is established concurrently with the development of tuberculin allergy. The tuberculin test measures the tuberculin allergy, while the BCG test measures the antibacterial allergy (Sula, 1962). The correlation between the mean size of tuberculin test reaction and that of BCG vaccination scar has been studied by Howitz and Bunch-Christensen (1972). Sutarjo and Ibrahim in 1971 and 1973 found no difference statistically in the mean size of post BCG vaccination tuberculin reaction and BCG scar by decreasing the dosage of BCG vaccine (from 0.1 ml. down to 0.05 ml. in primary school children, and from 0.05 ml. to 0.025 ml. in infants).

BCG vaccine as skin antigen has been used by many authors. Collins (1965) studied the accelerated reaction to multiple puncture concurrently. He found that there was a correlation between those persons who gave a positive Heaf test and those who showed an accelerated BCG reaction. Hartston (1967), using BCG vaccine in place of PPD solution, found that there was a good correlation between a positive reaction in this test and concurrently performed Mantoux test with 10 TU of PPD. However, a proportion of subjects in both studies has been found who gave a positive BCG test and negative Mantoux reaction. Good correlation between the induration size of BCG vaccination and

Mantoux reaction was observed in our study.

The coefficient of correlation on the 3rd day was 0.99, while on the 10th day it was only 0.63. It was generally accepted that Mantoux reaction of  $\geq 10$  mm. indicated the presence of tuberculous infection. Watts (1974) suggested BCG induration on the 3rd day of  $\geq 10$  mm. as indicated for further diagnostic studies of tuberculosis. The mean induration size of BCG vaccination on subjects with Mantoux reaction of less than 5 mm., 5-9 mm., and  $\geq 10$  mm. was respectively 6.07, 12.2, and 16.69 mm. on the 3rd day reading, while on the 10th day reading it was respectively 2.27 mm., 9.5 mm. and 12.3 mm.

There were statistically significant differences in the mean BCG induration size between the 3 groups. The number of subjects with negative Mantoux reaction showing induration size of BCG vaccination of more than 8.07 mm. ( $16.7 - 2$  SD) was 14.5%, while those with positive Mantoux reaction ( $\geq 10$  mm.) showing induration size of BCG vaccination of less than 8.07 mm. showed only 2.78% (3rd day reading), as seen in Figure 5 and Table 8. It seems that BCG induration of  $\geq 8$  mm. (3rd day) could be taken as an indication for further investigation in the early case-finding of tuberculosis in children, especially in rural areas. However, further study still needs to be undertaken. A study on the correlation between the induration size of BCG vaccination and

the incidence of tuberculosis on these subjects is already under way.

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