Tuberculin Testing in African Children

BY

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In African countries tuberculosis remains one of the major health problems. Tuberculin testing is widely used as a screening test for its detection and B.C.G. vaccination is one of the means for its control. The present investigation was undertaken in order to determine in one area of Rhodesia the extent of B.C.G. vaccination, and also by means of the Heaf Test to compare tuberculosis in the vaccinated and the unvaccinated and the degree to which tuberculin sensitivity as measured by this test and in this partcular population is modified by malnutrition.

Methods

A total of 1,036 children whose ages were from birth to 14 years were observed. These children were those attending schools or well baby clinics in the Wedza district, but were otherwise unselected. Each child was Heaf tested using undiluted P.P.D. and the reaction was inspected three days later. The result was recorded by grade of reaction as originally proposed by Heaf (1951):

Grade 0 = No induration.

Grade 1 = Induration around at least four punctures.

Grade 2 = Coalescence of induration to form a ring.

Grade 3 = As Grade 2 but also with induration within the ring.

Grade 4 = As Grade 3 but also with blistering.

The child's age, sex and weight were recorded and also the presence or absence of a B.C.G. scar. Table I shows the age distribution of the children examined and the numbers at each age who had previously received B.C.G. vaccine. Table II gives the numbers and percentages in each Heaf grade in the vaccinated as compared with the unvaccinated; Columns A and B refer to post-vaccinal Heaf reactions recorded by other observers which will be mentioned during the discussion. Table III gives a breakdown of Table II into the age groups 0-4 years, 5-9 years and 10-14 years. In Table IV in the vaccinated and unvaccinated separately a comparison is made between the nutritional status, the weight of the child being expressed as a percentile on the Boston Growth Charts and the Heaf Grade.

Table I

Total Number of Children at Each Age Showing the Numbers and Percentages Previously Vaccinated with B.C.G.

Age Group	Total No.	B.C.G. Pos.	B.C.G. Pos. % of Total
0-11/12 Mths.	41	0	0
1-1 11/12 Mths.	23	2	8
2-2 11/12 Mths.	34	2	5
3-3 11/12 Mths.	24	1	4
4 Years	23	2	8
5 Years	24	2	8
6 Years	20	4	20
7 Years	118	15	13
8 Years	118	13	11
9 Years	141	32	23
10 Years	140	44	32
11 Years	139	36	26
12 Years	88	26	29
13 Years	81	19	23
14 Years	22	1	5
	1,036	199	11.5

Results and Discussions

Of all children examined, 11.8 per cent. showed evidence of B.C.G. vaccination, a figure which was lower than had been anticipated. Table II shows the Heaf reaction in the vaccinated as compared with the unvaccinated children. In those who had not received B.C.G., 40.5 per cent. showed no sensitivity to tuberculin, while from Table III it will be seen these negative reactors comprise a diminishing percentage with advance in age. In the 0-4 year group 81 per cent. at that age were non-reactors, while of the age group 10-14 years, 21 per cent. were non-reactors. Over the same age ranges the percentage of children reacting at each Heaf grade increased, so that with increase in age there was an increase in tuberculin sensitivity.

However, even in the 10-14 year group 91 per cent. had a Heaf reaction of Grade 2 or less and 71 per cent. a Grade 1 or 0 reaction. This low grade sensitivity to tuberculin has been investigated in many countries by means of differential Mantoux testing in which the response to tuberculin prepared from *Mycobacterium tuberculosis* is compared with the response to tuberculin prepared from a number of different atypical mycobacteria. Ogbuni (1969) carried out such a study in Nigeria using antigens obtained from nine types

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Table II
HEAF REACTIONS IN THE B.C.G. VACCINATED AND UNVACCINATED
(COLUMNS A & B REPORTS OF PREVIOUS INVESTIGATORS)

B.C.G. Positive					B.C.G. Negative	
Grade	No.	%	A	B	No.	%
0	33	16.5	1.1	57	339	40.5
1	93	46.7	77.8	18	334	39.9
2	50	25.1	17.8	22	121	14.4
3	18	9.0	3.3	3	36	4.3
4	5	2.5	0	0	7	0.8

of atypical mycobacteria and was able to demonstrate that low grade reactors to tuberculin derived from *M. tuberculosis* showed a greater degree of sensitivity to one or more tuberculins derived from atypical mycobacteria. There is now general agreement that in persons who have not received B.C.G. vaccine, low grade sensitivity to tuberculin is usually the result of a previous and in most cases a subclinical infection with these atypical mycobacteria.

The degree of tuberculin sensitivity following vaccination with B.C.G. has been studied by many investigators. For comparison with our results the figures obtained by the British B.C.G. Control Centre for 1967 (Irvine, 1969) are shown in Table II Column A and in Column B the results obtained by Carruthers working in Australia (Carruthers, 1969). Both these investigations show that tuberculin sensitivity following B.C.G. vaccination is almost always of low grade. In neither of these series was a Grade 4 reaction recorded and only three per cent. showed a Grade 3 reaction. In our series the B.C.G. vaccinated children showed a similar preponderance of low grade reactors and, as in the case of the unvaccinated group, there was an increase in tuberculin sensitivity with increase in age as shown in Table III.

The reasons for this observed increase in tuberculin sensitivity with increase in age are similar in the two groups; with increasing age there will be an increase in tuberculin sensitivity because of infections with *M. tuberculosis* and atypical mycobacteria. Although B.C.G. vaccination confers an 80 per cent. protection against clinical tuberculosis (British Medical Research Council, 1963), it does not prevent infection which will be manifest by a sharp increase in tuberculin sensitivity (Springett, 1969). Thus when B.C.G. vaccinated persons are infected with *M. tuberculosis* there will be an increase in tuberculin sensitivity both in the 80 per cent. who show no evidence of clinical disease and the 20 per cent. who do. Sensitivity to *M. tuberculosis* and the sensitivity due to B.C.G. are therefore additive and the same applies to allergy to atypical mycobacteria. Thus in a particular child the degree of reactivity to tuberculin may be the result of previous B.C.G. vaccination, infection with *M tuberculosis* and infection with atypical mycobacteria singly or in combination.

Various conditions may cause a depression of sensitivity to tuberculin. These include the effects of malnutrition which has been studied by Har-

Table III
HEAF REACTIONS ACCORDING TO AGE IN THE B.C.G. VACCINATED AS COMPARED WITH THE UNVACCINATED

B.C.G. POSITIVE

Age Group	Grade 0		Grade 1		Grade 2		Grade 3		Grade 4		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	
0-4	2	28.0	5	71.0	—	—	—	—	—	—	7
5-9	16	24.6	25	38.0	16	24.6	7	10.7	2	1.5	66
10-14	15	11.9	63	50.0	34	26.9	11	8.0	3	2.3	126
Total	33		93		50		18		5		199

B.C.G. NEGATIVE

Age Group	Grade 0		Grade 1		Grade 2		Grade 3		Grade 4		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	
0-4	112	81.1	23	13.8	3	2.1	—	—	—	—	138
5-9	155	43.6	136	38.3	48	13.5	14	3.9	2	0.5	355
10-14	72	20.9	175	50.8	70	20.0	22	6.5	5	1.4	344
Total	339		334		121		36		7		837

land and Brown (1965) and Harland (1965). These observers studied children up to the age of three years and reported a reduction in the size of induration occurring in response to Mantoux testing in previously B.C.G. vaccinated children who showed no evidence of malnutrition other than that they were below 80 per cent. of their expected weights. Table IV shows the grade of Heaf reaction correlated with the nutritional state, the children being grouped into those below the third percentile, from the third to twenty-fifth percentile to the fiftieth percentile and above the fiftieth percentile. In the previously vaccinated group there are no differences between the percentages in each group who show a strong (Grade 3 or 4 reaction) to Heaf testing. However, in those who had not received B.C.G. vaccination there is a progression from the children below the third percentile, three per cent. of whom had a Heaf reaction of Grades 3 or 4, to seven per cent. in those over the fiftieth percentile who showed this degree of sensitivity. This finding, however, does not reach the level of statistical significance as it did in the series reported by Harland and Brown. These latter observers, however, showed that the reduction in tuberculin sensitivity in malnourished children was not absolute, but could be overcome by increasing the intradermal dose of tuberculin from 2 T.U. to 20 T.U. Heaf testing is known to be of about the same degree of sensitivity as this higher dosage of tuberculin used in the intradermal test, so that a maximal reaction would be expected to occur in children in our series and thus the effect of malnutrition would not be apparent.

In a particular child the observed degree of sensitivity to tuberculin is the result of those factors which bring about tuberculin sensitisation on the one hand, and on the other hand those factors which are capable of causing a depression of response. Tuberculin sensitivity may result from B.C.G. vaccination, infection with *M. tuberculosis* and also atypical mycobacteria either singly or in any combination. Factors which depress tuberculin sensitivity include malnutrition, recent infection with measles and to a lesser extent poliomyelitis and chicken pox, hypothyroidism, Hodgkin's disease and sarcoidosis, treatment with glucocorticosteroids and overwhelming tuberculous infection. It also suggested that non-specific anergy may exist since occasionally known cases of tuberculosis other than those with the above-mentioned complications may show a failure to react to tuberculin (Rosenberg and Gottlieb, 1968).

Summary

In 1,036 children Heaf testing was carried out and the result related to age, nutritional status and the presence or absence of previous B.C.G. vac-

Table IV
Heaf Reaction Related to Nutritional Status
B.C.G. NEGATIVE

Nutritional Status	Grade 0		Grade 1		Grade 2		Grade 3		Grade 4		Total	Grade 3 & 4 Combined	
	No.	%	No.	%	No.	%	No.	%	No.	%	Number	No.	%
3%	94	44.0	77	36.0	34	16.0	6	2.0	1	0.4	212	7	3.0
3-25%	87	42.0	78	38.0	31	15.0	7	3.0	1	0.4	204	8	3.0
25-50%	82	38.0	95	44.0	25	11.0	10	4.0	3	1.3	215	13	6.0
50+%	76	36.0	84	40.0	31	15.0	13	6.0	2	0.9	206	15	7.0
Total	339	40.5	334	39.9	121	14.4	36	4.3	7	0.8	837	43	5.0

B.C.G. POSITIVE

Nutritional Status	Grade 0		Grade 1		Grade 2		Grade 3		Grade 4		Total	Grade 3 & 4 Combined	
	No.	%	No.	%	No.	%	No.	%	No.	%	Number	No.	%
3%	6	10.0	34	57.0	13	22.0	4	6.0	2	3.0	59	6	10.0
3-25%	6	11.0	25	49.0	14	27.0	6	11.0	0	0.0	51	6	11.0
25-50%	11	28.0	12	30.0	10	25.0	3	7.0	3	7.0	39	6	15.0
50+%	10	20.0	22	44.0	13	26.0	5	10.0	0	0.0	50	5	10.0
Total	33	16.5	93	46.7	50	25.1	18	9.0	5	2.5	199	23	11.0

cination. The observed pattern of tuberculin sensitivity is described, compared with the reports of previous investigations and discussed in the light of factors known to promote and depress tuberculin sensitivity. The Heaf test when recorded by grade of reaction and related to those factors known to induce or diminish tuberculin sensitivity remains a valuable diagnostic investigation both in children who have received B.C.G. vaccine and in the unvaccinated.

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