adequate and that it is almost impossible to get a concentration that will produce glandular complications so common with higher doses of intradermal vaccine. Practical reasons for preferring a dosage of 83 mg./ml. have already been mentioned.

Modification of Guns and Needles.—This is a factor which has received very little attention in previous reports. First attempts at multiple-puncture vaccination (Rosenthal, 1939; Rosenthal and Neiman, 1941) by means of 20 to 30 tangential pricks from a single needle were followed by use of Birkhaug's instrument (Birkhaug, 1947), of which the Heaf (1951) multiple-puncture apparatus would seem to be a simple modification. The present Rosenthal technique (Rosenthal, 1957) utilizes a disk with 36 points and does not depend on any spring pressure. At the moment we are interested in the question of the physical factors involved in firing the gun, and this will be discussed in a later paper; it is quite evident, however, that the technique of multiple-puncture vaccination must be as meticulous as that for the intradermal method even though it calls for less basic skill.

Comparison with Results of Intradermal Inoculation.—Previous reports on the relative efficiency of intradermal and multiple-puncture vaccination have been conflicting. Rosenthal (1939) and Rosenthal and Neiman (1941) consider that multiple puncture vaccination is as effective as intradermal and indeed offers more complete protection against tuberculosis. Ejlersen (1953) takes the opposite view. In the present series the aim has been to improve the technique of multiple-puncture vaccination so that it is, as nearly as possible, as effective as the intradermal vaccination with freeze-dried vaccine.

Summary

A total of 2,221 newborn infants have been inoculated with British freeze-dried B.C.G. vaccine by multiple-puncture vaccination between March, 1959, and April, 1960.

Details of technique are described and significant factors discussed.

The results of multiple-puncture vaccination are compared with those of intradermal vaccination.

It is suggested that, using the British freeze-dried vaccine, optimal results are obtained by firing 20 needles to a depth of 2 mm. through a vaccine concentration of 83 mg./ml. It is hoped that by further improvement in technique the efficiency of multiple-puncture vaccination may be raised to the standard produced by intradermal vaccination.

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OBSERVATIONS ON VACCINATING SCHOOLCHILDREN WITH DANISH FRESH B.C.G.

BY

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In 1954 eight medical officers of health in the Oxford Region adopted a uniform procedure for the testing and B.C.G. vaccination of their schoolchildren. The scheme was in full operation by 1955. In that year, however, the P.P.D. issued for routine Mantoux testing was sub-standard. The findings have therefore been analysed from 1956 onward. The overall conversion rates for that year have already been published (Irvine, 1958). In this report the conversion rates and the local reactions to vaccination are studied in greater detail.

Material and Method

The analysis is based on 8,990 routine B.C.G. vaccinations of 13-year-old schoolchildren in the Oxford Region during the school year 1956-57. Mantoux 10 T.U. tests were given for the pre- and post-vaccination tests in 5,390 children and Heaf multiple-puncture tests in 3,600. The standard preparations of P.P.D. issued by the Ministry of Health were used for each test. Both Mantoux and Heaf tests were read at 2 to 4 days; the criterion of a minimum positive reaction for the Mantoux was an area of induration whose diameter was 6 mm., and for the Heaf test induration at four punctures. Non-reactors were vaccinated intracutaneously by some 50 school medical officers with 0.1 ml. of Danish fresh vaccine (0.75 mg./ml.), using about 40 different batches. The post-vaccination test was carried out between 6 and 19 weeks after vaccination. The local reaction to vaccination was inspected at the time of the post-vaccination test, and the diameter in millimetres of the indurated papule was measured with callipers; all Mantoux reactions were also measured with callipers. Where a vaccination or Mantoux reaction was not circular, the measurement recorded was the mean of the largest and the smallest diameter. None of the children was in contact with known open tuberculosis at the time of vaccination.

Results

Hertzberg (1948) found that sex had no influence on the size of the vaccination reaction or the conversion rate. An initial analysis of the present data provided similar results, and this factor has accordingly been ignored in the study.

Conversion Rate.—This has been analysed according to the number of weeks elapsing since vaccination. The

TABLE I.—Analysis of Local Reactions to B.C.G. Vaccination

Series	Weeks after Vaccination:		6	7	8	9	10		11	12		13	14	15		16	17	18	19	All		Total Vaccinations	Conversion Rate (%)	
	Converters (+):	Non-converters (-):					+	-		+	-			+	-					+	-			
Mantoux 10 T.U.	Local reaction to vaccination (mean diameter of papule in mm.)	0 1- 6- 11- 16+	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	44 543 4,158 581 64	61.4 90.4 97.8 98.6 100.0
	*Mean diameter (mm.)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5,390	96.8	
	Standard error of mean (mm.)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	8.54	—	
	Standard deviation (mm.)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	0.04	—	
	Conversion rate (%)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2.66 96.8	—	
Heaf	Local reaction to vaccination (mean diameter of papule in mm.)	0 1- 6- 11- 16+	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	— — — — —	103 977 2,203 274 43	35.0 99.4 98.8 98.9 97.7	
	*Mean diameter (mm.)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	3,600	97.7	
	Standard error of mean (mm.)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	7.47	—	
	Standard deviation (mm.)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	0.05	—	
	Conversion rate (%)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	3.15 97.7	—	

* Means, standard errors, and standard deviations were calculated on the actual diameter of the vaccination reaction.

results are summarized in Table I. The post-vaccination tests for the Mantoux series fall by chance between 7 and 18 weeks after vaccination and for the Heaf series between 6 and 19 weeks. The overall conversion rate for the Mantoux series was 96.8%, the weekly conversion rate ranging between 93.7 and 100%. Within this period there was no indication that the conversion rate was affected by the length of time between vaccination and post-vaccination testing. The overall conversion rate for the Heaf series was 97.7%. There was little difference, therefore, between the Heaf and Mantoux tests in this respect. The weekly conversion rate ranged between 93.7 and 100%; from 6 to 11 weeks the rate increased slightly, thereafter the range being between 99 and 100%.

Local Reaction to Vaccination.—An analysis has been made at weekly intervals to determine whether there was any alteration in the diameter of the vaccination papule during the period under observation (Table I). In the Mantoux series the vaccination papule had an overall mean diameter of 8.5 mm. The weekly mean diameter from 7 to 18 weeks ranged between 7.6 and 9.2 mm., which indicated that there was little change in the diameter of the vaccination reaction during the period of observation. In the Heaf series the findings were similar. The overall mean diameter was 7.5 and the weekly mean diameter from 6 to 19 weeks ranged between 5.7 and 8.7 mm.—a range of 3 mm. There was a slight tendency for the range to be larger from 6 to 14 weeks, but from 12 to 19 weeks it was less than 2 mm.

Relationship between Local Reaction to Vaccination and Conversion Rate.—Inspection of the local reaction to vaccination is a simpler procedure than giving and reading a post-vaccination tuberculin test. An analysis has therefore been made to determine whether there was any relationship between the vaccination reaction and the conversion rate. In the Mantoux series, 5,346 children had vaccination reactions ranging from 1 to 40 mm. in diameter; of these, 153 (2.9%) failed to convert, giving a conversion rate of 97.1%. In addition, there were 44 children who had no vaccination reaction; of these, 17 (38.6%) failed to convert, giving a conversion rate of 61.4%. In the Heaf series, 3,497 children had vaccination reactions ranging from 1 to 32 mm. in diameter; of these, only 15 (0.4%) failed to convert, giving a conversion rate of 99.6%. In addition, there were 103 children who had no vaccination reaction; of these, 67 (65%) failed to convert, giving a conversion rate of only 35%. In both the Mantoux and the Heaf series failure to convert was uncommon among children with a recognizable local reaction to vaccination. In

children with no local vaccination reaction, failure to react is comparatively frequent. This association is more evident with the Heaf test. The Mantoux series was further analysed to determine whether the diameter of the vaccination reaction bore any relationship to the diameter of the Mantoux reaction. Table II shows that the vaccination and Mantoux reactions increased uniformly. This is in accordance with the findings of Hertzberg (1948).

TABLE II.—Mean Diameter of Post-vaccination Mantoux Reaction for Different Diameters of Vaccination Reaction

Local Reaction to Vaccination (Mean Diameter of Papule in mm.)	Mantoux 10 T.U. P.P.D. Reaction			No. of Children*
	Mean Diameter (mm.)	Standard Error of Mean	Standard Deviation	
1-2	8.2	0.66	1.64	6
2-3	9.8	0.53	2.55	23
3-4	9.7	0.25	2.45	99
4-5	10.1	0.16	2.94	354
5-6	11.0	0.11	3.26	838
6-7	11.2	0.11	3.28	926
7-8	11.8	0.10	3.19	1,023
8-9	12.6	0.14	3.51	596
9-10	12.7	0.14	3.40	618
10-11	12.7	0.27	3.48	168
11-12	13.1	0.26	3.85	215
12-13	13.2	0.49	3.24	43
13-14	13.8	0.41	3.69	82
14-15	14.5	0.52	4.14	64
15-16	13.5	0.29	2.31	63

* Excludes children whose Mantoux reaction was not read or not reported.

Discussion

The findings described above relate to the diameter of the vaccination reaction and the conversion rate at different intervals after vaccination. Approximately 9,000 children were concerned, each of whom was examined once only at intervals after vaccination ranging from 6 to 19 weeks. The vaccination lesions and tuberculin reactions have been analysed according to the period after vaccination at which the examinations were made. The analysis is therefore a number of cross-sections at different time intervals and not a serial investigation of conversion rates.

In the Mantoux series no change was observed in the conversion rate between 7 and 18 weeks after vaccination. In the Heaf series an increase in the conversion rate was noted in children tested after 11 weeks as compared with those tested between 6 and 11 weeks after vaccination. However, 96 of the children tested between 6 and 11 weeks had no vaccination reaction. If all children with no vaccination reaction are excluded from the analysis, the overall conversion rate for the Heaf series becomes 99.6% and shows no upward or downward trend. These findings suggest that the conversion rate to a Mantoux or Heaf test is not greatly affected by the time elapsing since vaccination within a range 6 to 19 weeks.

Similarly, the diameter of the vaccination papule remains constant from 6 to 19 weeks, the mean varying only within the narrow range of 3 mm. Thus valid comparisons may be made between the vaccination reaction and the conversion rate to a Mantoux 10 T.U. carried out between 7 and 18 weeks, or to a Heaf test carried out between 11 and 19 weeks.

The relationship demonstrated between the local reaction to vaccination and the conversion rate in the Heaf series is striking; only 0.4% of children with vaccination reactions failed to convert. Similarly, the association found between the diameter of the vaccination papule and of the Mantoux reaction is marked. It must, however, be borne in mind that this relationship

has been shown only for Danish fresh vaccine, a vaccine whose potency and effectiveness has already been demonstrated (Medical Research Council, 1959). As the proportion of dead organisms is increased in a vaccine, the conversion rate declines more rapidly than the associated decrease in the diameter of the local reaction (Edwards, Palmer, and Magnus, 1953). Thus in vaccines of known potency the vaccination reaction is a useful guide to the likelihood of tuberculin conversion having been achieved. This relationship may not hold good for vaccines of inferior potency. Provided that Danish fresh vaccine maintains its past standards, it seems reasonable to suggest that, where evidence of successful vaccination is required, inspection of the vaccination site at or after 11 weeks could replace conversion testing. A test would then only be required for those vaccinations that have no local reaction.

Summary and Conclusion

In the Oxford Region 8,990 13-year-old schoolchildren were vaccinated with Danish fresh B.C.G. during the school year 1956-7; in 5,390 children the pre- and post-vaccination test was a Mantoux 10 T.U. P.P.D. and in 3,600 the Heaf multiple-puncture test was used. An analysis of the conversion rate and of the size of the local reaction to vaccination was made according to the interval in weeks (6-19) after vaccination.

In the Mantoux series the conversion rate between 7 and 18 weeks after vaccination remained within the range 93.7 to 100% and showed no tendency to decline or increase. In the Heaf series the conversion rate rose from 94.1% at six weeks to between 99 and 100% from 11 to 19 weeks; this increase in the conversion rate with the Heaf test was probably not due to the interval from vaccination.

The average diameter of the local reaction to vaccination did not vary by more than 3 mm. in either series over the period of observation.

In the Heaf series the conversion rate of those who had no local reaction was 35%; in those who had a local reaction, however small, the conversion rate was 99.6%. In the Mantoux series it was found that the diameter of the Mantoux reaction had a direct relationship to the diameter of the vaccination papule.

The presence of any local reaction to intracutaneous vaccination with Danish fresh vaccine may be regarded as an indication of successful vaccination. Only persons with no local reaction to vaccination require a conversion test.

The figures for this paper are taken from the special records kept by the eight local health authorities in the Oxford Region who now form the B.C.G. Control Centre: Berkshire, Gloucestershire, Northamptonshire, Oxfordshire, and Wiltshire County Councils, and Northampton, Oxford, and Reading County Borough Councils; we thank all the medical officers of health and school medical officers concerned. We are particularly grateful to Dr. T. M. Pollock and Dr. I. Sutherland, of the Medical Research Council, who read and criticized the original draft of this paper. We also thank the staff of the records and statistics department of the Oxford Regional Hospital Board for their co-operation. One of us (K.N.I.) is indebted to the Medical Research Council for grants towards this research.

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