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Observations on the Protective Effect of BCG Vaccination in a South Indian Rural Population *

J. FRIMODT-MØLLER,[1] JACOB THOMAS [2] & R. PARTHASARATHY [3]

Doubts have been raised on theoretical grounds concerning the effect of BCG in tropical countries, where in most places a large proportion of the population have a naturally acquired tuberculin allergy of low strength and unknown (but almost certainly non-specific) origin. Furthermore, vaccinations in the tropics may be less efficient if the BCG vaccine used has deteriorated from exposure to heat or light. The BCG trial reported here is relevant to these two problems.

A series of epidemiological studies in South India, begun in 1950 and still in progress, included a BCG trial in which half of the tuberculin-negative persons, randomly selected, were vaccinated. In a first report in 1960, preliminary data indicated that the vaccination had conferred no protection against tuberculosis; however, the total number of cases of tuberculosis involved was extremely small. Since then, further follow-up has added a considerable number of cases, and a statistically significant protection from the BCG vaccination is now demonstrated. The number of cases is still too small to show the precise degree of protection.

As this is the first controlled trial on BCG undertaken in an Asiatic population, the present report is of special interest.

INTRODUCTION

In India, BCG vaccination was used for the first time in 1948, when an investigation into the immediate effect of the vaccination was carried out at Madanapalle at the request of the Government of India prior to the introduction of BCG vaccination on a mass scale. At the same time, a tuberculosis survey of the town population by tuberculin tests and X-ray examination was carried out. This was extended to the surrounding villages in 1950. The population surveyed was 53 000, of whom 16 000 lived in the town and 37 000 in about 200 villages within a radius of ten miles. By 1958, the survey population had increased to 61 000—21 000 in the town and 40 000 in the villages.

After the first survey (Round I), another four consecutive surveys (Rounds II-V) were carried out during the years 1951-55 in order to estimate the incidence and changes in the prevalence of tuberculosis. BCG vaccination was given in the first instance to all Mantoux-negative reactors showing indurations of 5 mm or less to 10 tuberculin units (TU), or 4 mm or less to 5 TU. In order to study the protective effect of the vaccination, it was decided from November 1950 to divide the negative reactors at random into two groups, one of which was vaccinated and the other left unvaccinated as a control. As by that time more than half of the survey population had already been examined, only about 9000 persons entered into the BCG trial during Round I; of these about 2100 were vaccinated, 250 were selected for vaccination but were not vaccinated, 2350 were negative non-vaccinated controls, and 4300 had positive reactions. Observations on retests and repeat X-ray examinations up to 1954 have been published as part of a comprehensive report covering the whole survey population (Frimodt-Møller, 1960). No significant difference in the incidence of tuberculosis between the vaccinated and the controls was found, but, as the number of

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[1] Research Director, Madanapalle Tuberculosis Research Unit, South India.

[2] Senior Statistician, Madanapalle Tuberculosis Research Unit.

[3] Senior Medical Officer, Madanapalle Tuberculosis Research Unit.

cases was very small and the observation period only two years, no conclusions could be drawn with regard to the protective effect of the vaccine.

Since 1951, the study population in the BCG trial has increased to about 5100 vaccinated, 700 selected for vaccination but not vaccinated, 5800 unvaccinated controls, and 10 000 initially positive, giving a total of about 21 600. The last admission to the trial was in 1955. The last X-ray survey (Round VI) was in 1957-58, when a coverage of nearly 90% was obtained. The present report deals with fresh cases of tuberculosis found either by X-ray surveys or by symptoms between Round I (1950-51) and Round VI (1957-58), besides cases presenting themselves with symptoms after Round VI and up to the end of June 1963.

TIME-TABLE AND OBSERVATION PERIODS

The first round of tuberculin testing in the villages surrounding Madanapalle took place between May 1950 and August 1951, and the X-ray survey between September 1950 and November 1951 (Round I). The tuberculin testing and X-ray examinations were always done separately, the mobile X-ray unit visiting the villages after the enumeration and tuberculin testing had been finished. This was found to be the simplest and least time-consuming division of labour. There was therefore an interval of some months between the tuberculin tests and the X-ray examinations at each round. The timing of the various operations, as well as the mean interval between admission to the trial and the last examination by mass X-ray in 1957-58 (Round VI) was as follows:

Round	*Initial tuberculin testing*	*X-ray examinations*	*Mean observation period (years)*
I	Nov. 1950-Aug. 1951	Sept. 1950-Nov. 1951	6.9
II	Oct. 1951-Dec. 1952	Nov. 1951-Feb. 1953	5.3
III	Jan. 1953-March 1954	Aug. 1953-July 1954	4.3
IV	April 1954-Jan. 1955	July 1954-Feb. 1955	3.3
V	Feb. 1955-Sept. 1955	June 1955-Sept. 1955	2.4
VI	(not done)	April 1957-June 1958	—

The X-ray examinations in 1955 (Round V) covered only one-third of the villages, as the mobile X-ray unit was used from September 1955 to April 1957 to carry out a sample survey in Andhra Pradesh, Mysore State, and one district in Madras State, in connexion with similar sample surveys carried out at the same time in five zones elsewhere in India (Indian Council of Medical Research, 1959). The sixth round was greatly facilitated by the supply of a second mobile X-ray unit by WHO in 1957.

PROCEDURE OF ANALYSIS

For the purpose of the present analysis, a new set of punch cards was prepared in 1960 based on the whole population present at Rounds IV, V and VI. Further, information about all persons who had been admitted to the BCG trial during Rounds I, II and III but had died or moved away, or whose whereabouts were unknown before Round IV, was also entered in the new set of punch cards. Any cases arising after Round VI were also included. The 1960 set of punch cards was matched against the previous set, and special efforts were made to trace persons present before Round IV but absent in Round IV and later. In order to trace lost persons, special visits were made to the villages and inquiries were made on the spot.

So as to ensure that no case of tuberculosis should be missed owing to possible errors at the initial X-ray reading, the following procedures were adopted.

First, all X-ray films (34 000) taken during the last survey—Round VI (1957-58)—were re-read independently by dividing the material equally between two doctors. They read also the X-ray pictures taken during Round I (1950-51)—about 21 000—so that it would be possible to compare the 1950-51 prevalence with that of 1957-58. As it turned out that the two readers (X and Y) showed considerable individual differences with regard to the number of cases classed as abnormal (Frimodt-Møller, 1962b), the same material was submitted again to an independent assessment by two other doctors (A and B). The films were distributed so that A read one half of the films read by X and Y, and B the other half. Each film was therefore seen by two independent assessors: XA, XB, YA or YB. Thereupon, all the films declared to show pathological changes by any of the four independent readers, or by the original readers from the time of Round VI, were assessed by the senior author (J.F.-M.) He reviewed at the same time any other X-ray films available for any of these cases. In order to ensure that no bias would affect his judgement and reclassification of the cases, new cards were prepared showing only the name of

the case besides the date, roll number and X-ray number of each film taken at any one time of the particular case. All other information regarding previous readings, tuberculin tests, bacteriology, etc., was omitted. The object of this last assessment was, therefore: (*a*) to check that the films for each individual case taken at two or more rounds belonged to the same person; (*b*) to determine which film was the first to show the presence of a lesion; and (*c*) to classify any abnormality in the light of earlier or later developments, as noted by comparing all the available films for each case. The assessor also reviewed X-ray films of all patients who had presented themselves because of symptoms without having had a preliminary mass miniature X-ray.

Secondly, so that no case should be missed owing to filing errors, all cases noted as " X-ray abnormal " at any one time according to the two sets of punch cards, the old and the new, were checked, and any case not yet reassessed by the assessor was submitted to him for review. He reviewed in all about 9000 films, representing an average of three films for each of 2900 persons. Of these 2900, 856 were rejected as being " normal ". Thus, the final assessment covered all cases encountered at any one time, irrespective of whether they were noted before the beginning of the BCG trial or later, had been detected on the first film or on subsequent films, had had bacteriological examinations or not, and irrespective of the result of the initial tuberculin test. As for errors in identifying individuals from round to round, it was gratifying to note that X-ray films of different persons were mistakenly brought together under one name in about 2% of cases only.

X-RAY CLASSIFICATION

The classification of pulmonary pathological changes was made according to the X-ray code designed for the tuberculosis survey conducted in India between 1955 and 1957 (Indian Council of Medical Research, 1959) and described in detail in our previous report (Frimodt-Møller, 1960, p. 104). Each case was classified with regard to (*a*) type of pathology; (*b*) cavity; (*c*) impressions regarding etiology; and (*d*) calcifications. The " new classification " (as shown in Table 19 of the 1960 report) was not used this time. For the present report, all abnormal cases have been tabulated according to the classification under " impressions regarding etiology ". This is the classification commonly used in India at present. The cases were classified under this heading according to the following five categories:

A. Probably non-tuberculous
B. Probably tuberculous but inactive
C. Probably tuberculous, possibly active
D. Probably tuberculous and probably active
E. Undecided

By the term " active " is understood the likelihood of demonstrating tubercle bacilli by ordinary routine methods as used in our laboratory—i.e., by microscopy, and cultures of laryngeal swabs and/or sputum. " Inactive " stands for a slight probability (about 5%), " possibly active " for a small probability (about 10-25%) and " probably active " for a high probability (about 50% or more). This definition is admittedly vague, but experience has shown that the code is workable. As for its merits or demerits, reference may be made to the previous report.

METHOD OF RANDOMIZATION

As it was not considered practicable to give serial numbers to the persons tested and as the use of X-ray numbers for randomization was not feasible since the X-ray photography was done only after the testing, and also as it was not possible to use the year and date of birth (which are unknown entities to the average Indian villager), a system of randomization was devised based upon the random distribution of marked index cards. Before the day's work was begun, a pack of new index cards was divided into two equal groups, of which one half was marked on the back with a cross in ink. Thereafter the cards were shuffled well. All data relating to tuberculin tests were entered on the front of the index card. If a negative tuberculin test was found, the card was turned over and, if the cross was present, vaccination would follow. The system worked well during Round I but not so well during later rounds. At the first follow-up analysis it was seen that the number of unvaccinated controls exceeded the vaccinated at Rounds II-IV, whereas there should have been an equal number of each. In order to find out what had interfered with the randomization, the " presence " or " absence " of the cross indicating selection for vaccination was entered on the new set of punch cards. A random sample of 20% was drawn from all the cards relating to the BCG trial. The relationship of marked and unmarked cards to persons vaccinated or unvaccinated, tuberculin-negative or tuberculin-positive, is shown in Table 1.

The most obvious departure from the intended procedure was the failure to vaccinate a number

TABLE 1

DISTRIBUTION OF A 20% RANDOM SAMPLE OF THE BCG TRIAL MATERIAL ACCORDING TO PRESENCE OR ABSENCE OF CROSS INDICATING SELECTION FOR VACCINATION, RESULTS OF TUBERCULIN TEST, AND WHETHER VACCINATED OR NOT

Round	" Cross present "				" Cross absent "			
	Negative		Positive	Total	Negative		Positive	Total
	Vaccinated	Not vaccinated			Vaccinated	Not vaccinated		
I	403	59	386	848	9	467	422	898
II	162	16	214	392	1	192	353	546
III	274	28	163	465	1	316	303	620
IV	82	25	95	202	1	132	166	299
V	88	30	81	199	—	150	140	290
Total	1 009	158	939	2 106	12	1 257	1 384	2 653

(14%) of tuberculin-negative persons with marked cards. There were also a few (1%) who were vaccinated although they were supposed to remain unvaccinated. This departure from the design has, however, no direct bearing upon the question of whether the cards were marked correctly or not. It merely indicates that some persons refused vaccination or were not done for other reasons. Addition of the vaccinated and unvaccinated " negatives " under the two main headings shows that the " Mantoux negatives " were divided very equally into " cross present " and " cross absent " so far as the first three rounds are concerned. The last two rounds (IV and V) show a clear excess of unmarked over marked cards. Twice the number of marked cards should indicate the number truly randomized. Table 2 shows the extent to which the system operated from round to round.

The system of randomization operated quite satisfactorily during the first rounds so far as the negative reactors are concerned, but it evidently did not function properly among the " negatives " in Rounds IV and V and in the " positives " from Round II onwards. The reasons for this apparent breakdown of the system were obscure for a long time. However, further analysis of the material and reference back to the original index cards indicated where the reasons for the discrepancies lay. First, it was found that after Round I the testers departed from the original instructions regarding the marking of cards by postponing the marking until the tuberculin tests had been read. Then they took the cards for the " negatives " alone and divided them into two random groups by shuffling the cards and marking only one half; those whose cards got the cross were vaccinated. In this way, the marking of cards would not include positive reactors. Secondly, by noting the rounds in which the first X-ray was taken of all who had entered the trial, it was found that some had been X-rayed in an earlier round than the one in which they were tested (Appendix Table 1). In such cases, there would already be an index card; sometimes they were marked and randomized and

TABLE 2

PERCENTAGE OF PERSONS COVERED BY THE SYSTEM OF RANDOMIZATION ADOPTED ACCORDING TO RESULT OF THE INITIAL MANTOUX TEST IN THE 20% RANDOM SAMPLE OF THE BCG TRIAL MATERIAL

Round	Negative			Positive		
	Number tested	Randomized [a] No.	%	Number tested	Randomized [a] No.	%
I	938	924	98.5	808	772	95.5
II	371	356	96.0	567	428	75.5
III	619	604	97.6	466	326	70.0
IV	240	214	89.2	261	190	72.8
V	268	236	88.1	221	162	73.3

[a] Equal to twice " Cross present " (see Table 1).

sometimes they were not. As it is not possible now to know from the cards whether such unvaccinated " negatives " belong to the trial as controls or not, they would, if retained, tend to inflate the number of negative controls. It is apparent that the failure to make a special mark on the cards indicating the controls did complicate our analysis in no small measure. Appendix Table 1 shows that the " Mantoux positives " and the unvaccinated " negatives " contain a relatively high percentage of persons who were X-rayed in a round earlier than the one in which they were tested, whereas very few are found among the vaccinated. All persons X-rayed before the round in which they were tested initially have now been excluded from the present analysis and therefore do not appear in the other appendix tables. This appears justified since, after this exclusion, there remain 5808 controls and 5769 selected for vaccination (5069 vaccinated and 700 not done), and the difference between these two figures is not statistically significant. The cases found among those excluded are given in Appendix Table 13.

DEFINITION OF FRESH CASES FOR CALCULATING THE INCIDENCE

For the purpose of calculating the attack rate or incidence per year, cases encountered during the interval between rounds have been referred to the next round together with cases detected on X-ray films taken during that round. All cases showing pathology for the first time on films taken during the same round in which they were tested initially have been excluded as " prevalence " cases. It has already been mentioned that all persons who had been X-rayed earlier than the round in which they were tested (Appendix Table 1) have been excluded from further analysis.

The round in which a case has occurred has been defined as the one in which the first trace of a lesion is visible on an X-ray film, irrespective of when symptoms first occurred or bacilli were demonstrated. The extent and type of pathology, as well as the demonstration of tubercle bacilli, refers to the time of maximal extent of disease—a stage which may occur considerably later than when the lesion first appeared.

MATERIAL

The present report is the first part of a follow-up report on the village population around Madanapalle covering the period 1954-58 subsequent to Round IV; the second part will deal with changes in the prevalence between Round I and Round VI.

As the BCG study population forms a part of the whole village population surveyed and tested, its relation to the latter in terms of the various surveys (rounds) is given in Table 3.

Population surveyed

During Round I, the village population was first tested with 1-10-100 TU. Of 8299 persons tested, 743 who were negative to 1 TU but did not get 10 TU are excluded, leaving 7556; of these, 3324 were vaccinated, 294 were negative but not vaccinated, and 3938 were positive. About half way through Round I, testing with the three dilutions of tuberculin was discontinued in favour of 5 and 100 TU. Up to the time the BCG trial was set up, 2465 were tested with 5-100 TU. Of these, 606 have been excluded from the present analysis since they lived in seven villages in the immediate vicinity of the Union Mission Tuberculosis Sanatorium, where many worked and therefore could have run a higher risk of infection than the rest of the population. This leaves 1859 for analysis. Together with the 7556 tested with 1-10-100 TU, they form a special group of 9415 which was not randomized but in which BCG was offered to all negative reactors. Of these, 479 were not vaccinated. The results obtained in this non-randomized group are discussed later.

After the start of the BCG trial, 9064 persons were tested with 5-100 TU in Round I, but the " negatives " were then divided at random into those to be vaccinated and those to remain unvaccinated. During Round II, 1-10-100 TU were given again in the villages where this schedule was used during Round I, but, this time, also the non-reactors to 10 TU were admitted to the trial according to the same method of randomization as had been started during the second half of Round I; when the tuberculin testing team reached the villages where 5-100 TU had been used previously, 1-10-100 TU doses were stopped and 5-100 TU were again given. The numbers tested in the two groups were 1837 and 4784 respectively. These two groups have been merged for the purpose of the further analysis. From Round III, tests with 1-10-100 TU were discontinued, 5-100 TU remaining the only test doses thereafter. All the tests were done with Danish PPD, batch RT 19-20-21, of which stock solutions were supplied regularly by the Statens Serum-institut, Copenhagen.

TABLE 3

SUMMARY OF SUBDIVISIONS OF 35 490 PERSONS TUBERCULIN-TESTED IN 1950-55 (ROUNDS I-V) AND RESURVEYED IN 1957-58 (ROUND VI) FORMING THE BASIS FOR THE PRESENT ANALYSIS

Initial round of testing	Type of Mantoux test	Vaccinated	Due, but not vaccinated	Controls	Positive reactors	Total
		A. Non-randomized group from Round I				
I	1-10-100 TU	3 324	294	—	3 938	7 556
I	5-100 TU	775	185	—	899	1 859
	Total	4 099	479	—	4 837	9 415
		B. Randomized groups, Rounds I-V				
I	5-100 TU	2 146	253	2 375	4 290	9 064
II	1-10-100 TU [a]	290	50	291	1 206	1 837
	5-100 TU	975	65	1 027	2 717	4 784
III	5-100 TU	1 312	146	1 804	2 396	5 658
IV	5-100 TU	463	139	689	1 264	2 555
V	5-100 TU	372	156	659	990	2 177
	Total	5 558	809	6 845	12 863	26 075
		C. Groups under " B " excluded from the BCG trial (Persons X-rayed before the round of initial Mantoux test)				
I	5-100 TU	—	—	—	—	—
II	1-10-100 TU	40	5	46	306	397
	5-100 TU	298 [b]	19	316	1 032	1 665
III	5-100 TU	43	32	340	663	1 078
IV	5-100 TU	52	31	187	485	755
V	5-100 TU	56	22	148	398	624
	Total	489	109	1 037	2 884	4 519
		D. BCG trial population (Corresponding to Group B minus Group C)				
I	5-100 TU	2 146	253	2 375	4 290	9 064
II	1-10-100 TU	250	45	245	900	1 440
	5-100 TU	677	46	711	1 685	3 119
III	5-100 TU	1 269	114	1 464	1 733	4 580
IV	5-100 TU	411	108	502	779	1 800
V	5-100 TU	316	134	511	592	1 553
	Total	5 069	700	5 808	9 979	21 556

[a] Randomized, vaccinated after 10 TU.

[b] Includes 116 tested in Round I but vaccinated in Round II.

The total number of persons tested after the BCG trial began is 26 075 (Table 3). For the reasons given above, 4519 persons who had been X-rayed at a round earlier than the one in which they had their initial tuberculin test were excluded, leaving the 21 556 who now comprise the BCG study population. These consist of 5069 (23.5%) vaccinated; 700 (3.2%) due for vaccination but not vaccinated; 5808 (26.9%) controls; and 9979 (46.3%) positive reactors.

The group " Due, but not vaccinated " has been included in Appendix Table 3 to show the effect on the composition of the two groups " Vaccinated " and " Controls " with regard to age and sex. As it is mainly elderly people who failed to obtain vaccination, an unequal distribution in the higher age-groups has arisen. The controls include a higher proportion of elderly people than the vaccinated and, since the attack rate of tuberculosis—as will be seen presently—is high among old people, this unbalanced distribution affects the comparison of incidence between the vaccinated and the controls.

The above-mentioned group (" Due, but not vaccinated ") has, however, been excluded from all the other appendix tables.[1] As it is not possible to ensure that every single person due for vaccination is vaccinated, it would have been better if, in the original design of the experiment, provision had been made to use a placebo for the unvaccinated controls, and better still if this had been done in such a way that neither the persons tested nor the staff could know who received the BCG and who the placebo. It would then have been possible to identify a group among the controls corresponding to the " Due, but not vaccinated " among those selected for vaccination.

X-ray coverage

At the time of the different rounds of X-ray examinations, no attention was paid at all to which group the different persons belonged, in fact the staff was unaware of it. The X-ray coverage within each round was therefore very nearly the same for the vaccinated, the controls, and the initially positive (Appendix Table 2). Of the persons admitted to the trial in Rounds I-V, the following percentages were X-rayed at Round VI: 67.8 (I), 57.8 (II), 58.6 (III), 49.3 (IV), and 44.6 (V). The diminishing returns are due to differences in the age and sex composition of the five groups and subsequent differences in losses to each group.

Losses

A statement is given in Appendix Tables 4-8 with regard to the number of persons who died, left the area, or could not be traced, during Rounds I-IV and IV-VI. Again, there is no essential difference between the vaccinated and the controls within each round of entry.

There is no suggestion that the methods of follow-up introduced any factors that could have affected the vaccinated and the controls differently.

RESULTS IN THE NON-RANDOMIZED GROUP FROM ROUND I

The number of tuberculosis cases (Table 4 and Appendix Table 9) in the 1-10-100 TU group after the completion of Round I up to the end of the observation period (June 1963) was 6.3 per 1000 among the vaccinated and 17.0 among the unvaccinated " negatives ". In the 5-100 TU group, the

TABLE 4

NUMBER OF CASES AMONG PERSONS TESTED IN ROUND I (1950-51) IN THE NON-RANDOMIZED GROUP WHERE VACCINATION WAS OFFERED TO ALL WITH NEGATIVE REACTIONS TO EITHER 10 OR 5 TU

Status	Number tested	Number of cases [a]	Cases per 1000
A. 1-10-100 TU group			
Vaccinated	3 324	21 (*9*)	6.3 (*2.7*)
Unvaccinated (negative)	294	5 (*2*)	17.0 (*6.8*)
Positive	3 938	69 (*36*)	17.5 (*9.1*)
B. 5-100 TU group			
Vaccinated	775	4 (*1*)	5.2 (*1.3*)
Unvaccinated (negative)	185	1	5.4
Positive	899	18 (*12*)	20.0 (*13.4*)
C. Both groups			
Vaccinated	4 099	25 (*10*)	6.1 (*2.4*)
Unvaccinated (negative)	479	6 (*2*)	12.5 (*4.2*)
Positive	4 837	87 (*48*)	18.0 (*9.9*)

[a] For distribution according to sex and the round in which the cases were found, see Appendix Table 9.

Note. The italic figures in parentheses indicate bacillary cases.

[1] Among the 700 " Due, but not vaccinated " two cases of tuberculosis were found: (*a*) a female (46 years) tested in Round I and found at Round IV on the first available X-ray photo; and (*b*) a female (16 years) tested in Round II with 1 and 10 TU and detected at Round VI following a normal X-ray photo in Round II itself.

corresponding figures were 5.2 and 5.4. Combining the two groups, the number of cases among the vaccinated was 6.1 per 1000 and among the unvaccinated, 12.5, and, considering only the bacillary cases, 2.4 and 4.2 respectively. These results suggest that there is less chance of developing tuberculosis if vaccinated; however, the observations are few and the two groups are not necessarily comparable as no randomization was done.

RESULTS IN THE BCG STUDY POPULATION

In Table 5, the cases arising among the vaccinated, unvaccinated controls, and positive reactors have been divided into two groups according to whether the X-ray showing the lesion followed after one or more normal films taken at previous rounds or whether it was noted on the first available film. The cases in the former group are more likely to be true fresh cases than those in the latter group, which may have existed even at the time of admission to the trial. Obviously, the longer the interval between admission to the trial and the time of taking the film that showed the lesion, the greater is the probability that the lesion indicates a true primary case. Details of each case found among those initially tuberculin-negative are given in Appendix Table 10, and a summary of the cases found among the positive reactors, in Appendix Table 11; cases considered to be of non-tuberculous origin or with doubtful diagnosis are shown in Appendix Table 12.

A summary of the findings as shown in Table 5 is given in Table 6. The number of cases showing lesions after a previous normal film are 6 and 20 in the vaccinated and control group, respectively; those in which the lesion was seen on the first available

TABLE 5

DISTRIBUTION OF CASES IN THE BCG TRIAL ACCORDING TO ROUNDS OF INITIAL TESTING AND ROUNDS WHEN LESIONS FIRST OCCURRED

Round of initial tuberculin test	Group	Number	Cases													
			One or more normal films preceding the lesion							Lesion seen on first film						Total
			II	III	IV	V	VI	After VI	Total	II	III	IV	V	VI	After VI	
I	Vaccinated	2 146	1 (1)	—	—	—	1	2 (1)	4 (2)	1	1	—	—	—	—	2
	Controls	2 375	1 (1)	1	2 (1)	—	4 (1)	4 (4)	12 (7)	3	—	1 (1)	—	2	—	6 (1)
	Positive	4 290	7 (4)	7 (3)	2 (2)	—	23 (10)	8 (7)	47 (26)	19 (5)	5 (1)	2	1 (1)	8 (2)	—	35 (9)
II	Vaccinated	927		—	—	—	—	—	—		—	—	—	—	—	—
	Controls	956		—	—	—	4 (2)	—	4 (2)		—	—	—	—	—	—
	Positive	2 585			1	—	15 (7)	4 (4)	20 (11)		4 (3)	1	3 (2)	6 (3)	1 (1)	15 (9)
III	Vaccinated	1 269			1	—	—	1 (1)	2 (1)			2	—	1	—	3
	Controls	1 464			—	—	2	2 (2)	4 (2)			—	—	—	1 [a]	1
	Positive	1 733			1 (1)	—	4 (2)	2 (2)	7 (5)			3	1	9 (3)	—	13 (3)
IV	Vaccinated	411				—	—	—	—				—	—	—	—
	Controls	502				—	—	—	—				—	1	—	1
	Positive	779				—	1	1 (1)	2 (1)				2	7 (4)	—	9 (4)
V	Vaccinated	316					—	—	—					—	—	—
	Controls	511					—	—	—					1	—	1
	Positive	592					—	1 (1)	1 (1)					—	—	—

[a] A case of cervical adenitis.

Note. The italic figures in parentheses indicate bacillary cases.

TABLE 6
TOTAL NUMBER OF CASES FOUND IN THE BCG TRIAL

Group	Number	Lesions noted subsequent to a normal X-ray	Lesions seen on first available film	Total	Cases per 1000
Vaccinated	5 069	6 (*3*)	5	11 (*3*)	2.17 (*0.59*)
Controls	5 808	20 (*11*)	9 (*1*)	29 (*12*)	4.99 (*2.07*)
Positive	9 979	77 (*44*)	72 (*25*)	149 (*69*)	14.93 (*6.91*)

Note. The italic figures in parentheses indicate bacillary cases.

film are 5 and 9, respectively, giving a total of 11 and 29 (with bacilli: 3 and 12).

The observation of 11 and 29 cases among the vaccinated and controls, respectively, corresponds to rates of 2.17 and 4.99 cases per 1000, respectively, the difference being statistically significant ($P<5\%$). It corresponds to a reduction of 56% of cases in the vaccinated as compared with the controls. Considering the bacillary cases only, the rate of 0.59 in the vaccinated is significantly lower than the rate of 2.07 in the controls ($P<5\%$).

Omitting the cases that occurred after Round VI, the annual incidence for the vaccinated is 0.34 per 1000; for the controls is 0.86; and for the " positives " is 2.88 (Table 7). The difference in incidence between the vaccinated and the controls corresponds to a reduction of 60%. This difference also is statistically significant ($P<5\%$). As for the bacillary cases, the difference between the annual rates of 0.04 and 0.23 does not attain statistical significance at the 5% level of probability.

Before Round IV, the annual incidence rates among the vaccinated and the controls were 0.55 and 0.66, respectively. This corresponds to a reduction of only 18%. Compared with the rates for the period Rounds I-VI, these findings suggest that in a small body of material the effect of the vaccination may not be demonstrable before some years have passed.

In the period after Round VI (Table 8), there were 3 cases among the vaccinated and 7 among the controls. This gives crude rates of 0.84 and 1.74 per 1000, respectively, corresponding to a reduction of 51%. As these cases entered the trial 4-7 years earlier, the findings would suggest that the effect of the vaccination may be apparent beyond the first four years.

TABLE 7
INCIDENCE OF TUBERCULOSIS BETWEEN ROUNDS I AND VI

Group	Person-years of observation	Number of cases	Annual rate per 1000
Period covering Rounds I-IV			
Vaccinated	10 967	6 (*1*)	0.55 (*0.09*)
Controls	12 004	8 (*3*)	0.66 (*0.25*)
Positive	22 403	52 (*19*)	2.32 (*0.85*)
Whole period: Rounds I-VI			
Vaccinated	23 248	8 (*1*)	0.34 (*0.04*)
Controls	25 645	22 (*6*)	0.86 (*0.23*)
Positive	45 846	132 (*53*)	2.88 (*1.16*)

Note. The italic figures in parentheses indicate bacillary cases.

TABLE 8
CASES SEEN AFTER ROUND VI

Group	Number present at Round VI	Number of cases	Cases per 1000
Vaccinated	3 575	3 (*2*)	0.84 (*0.56*)
Controls	4 029	7 (*6*)	1.74 (*1.49*)
Positive	6 662	17 (*16*)	2.55 (*2.40*)

Note. The italic figures in parentheses indicate bacillary cases.

INCIDENCE RELATED TO SEX

Although the number of cases is not large enough to allow a very detailed analysis with regard to sex and age, Table 9 shows certain trends that may be important.

TABLE 9

CASES FOUND AMONG VACCINATED AND CONTROLS, ACCORDING TO AGE, SEX, AND CATEGORY [a]

Age-group (years)	Males						Females					
	Vaccinated			Controls			Vaccinated			Controls		
	B	C	D	B	C	D	B	C	D	B	C	D
0-4	—	1	—	—	—	—	—	—	—	—	2	—
4-14	1	—	—	2	—	—	—	—	—	1	1 [b]	2 (2)
15-24	1	—	—	2	—	—	—	—	—	—	—	2 (2)
25-34	1	1	—	1	—	1 (1)	1	—	2 (2)	3 (1)	—	2 (1)
35-44	—	1	—	—	2 (1)	1 (1)	—	—	—	—	2 (1)	—
45-54	—	1	—	1	—	—	—	—	—	1	—	—
55+	—	—	1 (1)	1	—	2 (2)	—	—	—	—	—	—
Total	8 (1)			13 (5)			3 (2)			16 (7)		

[a] For definition of categories B, C and D, see text, page 547.
[b] A case of cervical adenitis.
Note. The italic figures in parentheses indicate bacillary cases.

It is noteworthy that there is only a relatively small difference in the number of cases among the vaccinated and unvaccinated males, whereas there is a striking difference in the females (significant at the 1% level). The distribution of cases among the males suggests perhaps that the vaccinated include fewer advanced cases than the controls. Comparing the distribution among controls alone, there appears to be a different pattern between males and females with regard to the age-groups yielding the more advanced types of disease. In males, it is mainly the older groups that are affected, whereas in females, it is the younger groups. This may perhaps reflect a basically different epidemiological pattern between the two sexes.

INCIDENCE IN MALES AND FEMALES RELATED TO THE FOLLOW-UP PERIOD

If the material is divided into cases observed up to Round IV only and those observed up to Round VI, the findings from the first period are inconclusive, there being 6 vaccinated and 4 control cases among the males, and 0 vaccinated and 4 controls among the females (Table 10). The second period (Rounds I-VI) shows 7 cases among the vaccinated and 11 among the controls in males, and 1 and 11, respectively, in the females. The latter difference is highly significant. The numbers observed after Round VI are too small to allow any conclusions to be drawn with regard to either sex, there being 1 vaccinated and 2 control cases among the males and 2 and 5, respectively, among the females (see Appendix Table 10). This suggests again that the protective effect of the vaccination should not be judged from observations during the period immediately following admission to the trial unless the material is large; it becomes apparent only after there has been time enough for a sufficient number of persons to become infected and for the lesions to develop sufficiently to be demonstrable.

So far in this analysis the estimate of the incidence has been based upon all the cases observed after the completion of the round in which the cases had been tested initially and admitted to the trial. This means that possibly some of the cases included could have had lesions in their lungs at the time of testing but were missed because no X-ray had been taken at that time; or it may be that the cases had already been infected with tubercle bacilli but were still in the pre-allergic phase at the time of testing and therefore did not react to tuberculin; or the tuberculin test may have been erroneously read as negative. Such types of case are less likely to be included if we deal only with those arising after another round had been completed.

Of the 7 vaccinated males and 1 vaccinated female found between Rounds I and VI (Table 10), 5 males

TABLE 10

INCIDENCE IN MALES AND FEMALES ACCORDING TO PERIOD OF FOLLOW-UP

Group	Rounds I-IV			Rounds I-VI		
	Person-years of observation	Number of cases	Annual rate per 1000	Person-years of observation	Number of cases	Annual rate per 1000
			Males			
Vaccinated	5 299	6 (*1*)	1.13	11 324	7 (*1*)	0.62
Controls	5 944	4 (*2*)	0.67	12 700	11 (*3*)	0.87
Positive	10 719	37 (*11*)	3.45	22 007	91 (*34*)	4.13
			Females			
Vaccinated	5 668	—	—	11 924	1	0.08
Controls	6 060	4 (*1*)	0.66	12 946	11 (*3*)	0.85
Positive	11 684	15 (*8*)	1.29	23 839	41 (*19*)	1.72

Note. The italic figures in parentheses indicate bacillary cases.

were found during the period following immediately after the round in which they were admitted to the trial. Similarly, among the controls, 3 males and 2 females, and, among the " positives ", 26 males and 10 females, were also found just after their admission to the trial. Omitting these, Table 11 shows the cases found after the completion of a second round following that in which they were tested initially.

It is very interesting that, after exclusion of the cases mentioned above, the males also show a marked although not statistically significant difference in incidence between the vaccinated and the controls: 2 cases among the vaccinated and 8 among the controls. The difference in the females is again striking: 1 case among the vaccinated and 9 among the controls ($P < 5\%$). Adding the males and the females together, there are 3 cases among the vaccinated and 17 among the controls, which corresponds to annual incidence rates of 0.13 and 0.66 per 1000, respectively—a difference that is statistically highly significant ($P < 1\%$).

Taking into account also the cases found from 1958 to 1963—i.e., after Round VI (Table 12)—the incidence among males was 3 cases among the vaccinated and 10 among the controls, or 1.2 and 3.4 per 1000, respectively; for the females, it was 3 and 14 cases, or 1.1 and 4.9 per 1000, respectively. This suggests that the vaccine may be as effective among males as among females, and that the failure to show any significant difference between vaccinated

TABLE 11

INCIDENCE AFTER EXCLUSION OF CASES FOUND IN THE ROUND FOLLOWING THAT OF ADMISSION TO THE TRIAL

Group	Males			Females			Both sexes		
	Person-years of observation	Number of cases	Annual rate per 1000	Person-years of observation	Number of cases	Annual rate per 1000	Person-years of observation	Number of cases	Annual rate per 1000
Vaccinated	11 324	2	0.18	11 924	1	0.084	23 248	3	0.13
Controls	12 700	8 (*3*)	0.63 (*0.24*)	12 946	9 (*2*)	0.69 (*0.15*)	25 645	17 (*5*)	0.66 (*0.19*)
Positive	22 007	65 (*26*)	2.95 (*1.18*)	23 839	31 (*14*)	1.30 (*0.59*)	45 846	96 (*40*)	2.09 (*0.87*)

Note. The italic figures in parentheses indicate bacillary cases.

TABLE 12

TOTAL NUMBER OF CASES INCLUDING THOSE FOUND AFTER ROUND VI, BUT EXCLUDING THOSE FOUND IN THE ROUND FOLLOWING THAT OF ADMISSION TO THE TRIAL

Group	Males			Females			Both sexes		
	Number of persons	Number of cases	Cases per 1000	Number of persons	Number of cases	Cases per 1000	Number of persons	Number of cases	Cases per 1000
Vaccinated	2 446	3	1.23	2 623	3 (*2*)	1.14	5 069	6 (*2*)	1.18
Controls	2 920	10 (*5*)	3.42	2 888	14 (*6*)	4.85	5 808	24 (*11*)	4.13
Positive	4 835	75 (*36*)	15.51	5 144	38 (*20*)	7.39	9 979	113 (*56*)	11.32

Note. The italic figures in parentheses indicate bacillary cases.

and controls in males when the total material was considered could be due to an admixture with cases that should have been eliminated by the initial tuberculin test.

INCIDENCE RELATED TO AGE

Taking into account that vaccination was not done in elderly persons to the extent required by the random selection and that the numbers in each age-group of vaccinated and controls are not everywhere the same, the latter often exceeding the former, the number of observed cases among the vaccinated was compared with the numbers among the controls after adjusting for difference in numbers at risk (Table 13). This leads to a further reduction in the difference between the vaccinated and controls in the males, the vaccinated showing 8 cases against 9.22 among the controls. In the females, there were 3 observed cases among the vaccinated compared with the adjusted 14.3 among the controls. This apparent difference in efficacy in males and females

TABLE 13

NUMBER OF CASES OBSERVED AMONG THE VACCINATED AND THE CONTROLS, COMPARED WITH THE NUMBER EXPECTED AMONG THE CONTROLS AFTER ADJUSTMENT FOR DIFFERENCES IN NUMBERS WITHIN AGE-GROUPS

Age-group (years)	Males					Females				
	Controls			Vaccinated		Controls			Vaccinated	
	Number	Cases [a]		Number	Cases [a]	Number	Cases [a]		Number	Cases [a]
		Obs.	Adj.		Obs.		Obs.	Adj.		Obs.
0-4	1 061	0	0	954	1	1 018	2	1.76	898	—
5-14	1 109	2	1.72	954	1	863	4	3.88	837	—
15-24	282	2	1.53	216	1	396	2	2.17	429	—
25-34	191	2	1.36	130	2	322	5	4.42	285	3
35-44	96	3	3.25	104	1	146	2	1.60	117	—
45-54	84	1	0.80	67	1	89	1	0.47	42	—
55+	85	3	0.56	16	1	48	—	—	12	—
Not recorded	12	—	—	5	—	6	—	—	3	—
Total	2 920	13	9.22	2 446	8	2 888	16	14.30	2 623	3

[a] Obs. = observed number; Adj. = number after adjustment.

is not quite significant (the probability is between 5% and 10%) and it therefore seems reasonable to combine the results for both sexes. The total of 11 observed cases among the vaccinated against the adjusted 23.5 among the controls is still statistically significant at the 5% level (the result in females, taken separately, is of course strikingly significant).

A summary of the results in males and females is given in the tabulation below.

Broad age-group (years)	*Controls (adjusted) Number*	*Vaccinated*	
		Number	*Percentage of controls*
0-14	7.36	2	27.1
15-34	9.48	6	63.2
35 +	6.68	3	44.0
All ages	23.52	11	46.8

If one studies the effect within age-groups, the figures in the tabulation suggest that vaccination may be useful not only in the younger age-groups but also in the older ones. If confirmed on a larger body of material this would be important because it would mean that vaccination should not be limited to the young but should be extended to all ages. The present observations indicate that even after the age of 35 the chances of acquiring a fresh primary infection leading to the development of radiologically and clinically demonstrable tuberculosis are still quite high, and, as nearly one-third of all fresh cases occur after that age, the importance of this age-group should not be overlooked.

TABLE 14

CASES FOUND IN THE BCG TRIAL ACCORDING TO RADIOLOGICAL TYPE AND EXTENT, CAVITATION, AND CATEGORY, AT MAXIMAL DISEASE

Disease status	Vaccinated (11 cases)	Controls (28 cases [a])	Positive (149 cases)
Extent and type of lesion:			
Slight, parenchymal	1	4	17
Moderate, parenchymal	3	6 (*2*)	38 (*5*)
Extensive, parenchymal	3 (*3*)	12 (*10*)	81 (*62*)
Hilar adenitis	1	3	2
Pleural scar	1	—	3
Pleural effusion	2	3	8 (*2*)
Cavitation :			
Nil	8	16 (*1*)	66 (*4*)
Doubtful	—	2 (*2*)	21 (*10*)
Present	3 (*3*)	10 (*9*)	62 (*55*)
Category :			
B. Probably inactive	4	12 (*1*)	51 (*3*)
C. Possibly active	4	6 (*2*)	38 (*13*)
D. Probably active	3 (*3*)	10 (*9*)	60 (*53*)

[a] In addition, one case of cervical adenitis.
Note. The italic figures in parentheses indicate bacillary cases.

INCIDENCE RELATED TO TYPE OF LESION

As for the type and extent of the disease, there were no obvious differences between the groups: vaccinated, controls and "positives" (Table 14). It would seem that, once a case of disease has developed, the further clinical course is independent of the person's original status in respect of vaccination.

EFFECT OF VACCINATION IN REDUCING THE TOTAL INCIDENCE

The value of a potent BCG vaccine in a tuberculosis control programme depends not only upon its ability to prevent the development of potential cases of tuberculosis, but also upon the relative distribution of non-infected persons and infected persons as well as upon the degree of exposure to infection. The larger the proportion of the non-infected and the smaller that of the infected, the greater is the area in which the vaccine can function. However, in such situations the chances of infection are usually small. On the other hand, there may be situations in which the proportion of non-infected persons is so small compared with that of the infected that the effect of the vaccine, though this may be highly potent, will be very limited. Between these two rather extreme situations, there may be found a certain quantitative relation between the non-infected and the infected which could be called the ideal, or the optimal, for the vaccine to exert its fullest protective effect. It is likely also that the situation will change in the same population as time goes on—for example, the total effect of the vaccine may be small to begin with, but will increase later on by a reduction in the number of infected persons and an increase in the number of non-infected.

By doubling the number of cases found among the controls and adding the new number to the cases arising from the positive reactors, we have an

TABLE 15

ESTIMATE OF THE RELATIVE CONTRIBUTION TOWARDS THE CASE-LOAD BY TUBERCULIN-NEGATIVE AND TUBERCULIN-POSITIVE REACTORS IN THE POPULATION ACCORDING TO PERIOD OF FOLLOW-UP

Tuberculin reaction	Rounds I-IV		Rounds IV-VI		After Round VI		Total	
	No.	%	No.	%	No.	%	No.	%
				Males				
Negative	8	17.8	14	20.6	4	28.6	26	20.5
Positive	37	82.2	54	79.4	10	71.4	101	79.5
Total	45	100.0	68	100.0	14	100.0	127	100.0
				Females				
Negative	8	34.8	14	35.0	10	58.8	32	40.0
Positive	15	65.2	26	65.0	7	41.2	48	60.0
Total	23	100.0	40	100.0	17	100.0	80	100.0
				Both sexes				
Negative	16	23.5	28	25.9	14	45.1	58	28.0
Positive	52	77.5	80	74.1	17	54.1	149	72.0
Total	68	100.0	108	100.0	31	100.0	207	100.0

estimate of the total number of cases that would have occurred if vaccination had not been done. This follows the design of the present experiment, in which just half the " negatives " were vaccinated and the other half remained unvaccinated. Table 15 shows that in males only about 20% of the fresh cases develop from the " negatives ", while 80% develop from the " positives ". Obviously, vaccination given to all the " negatives " can at the most affect 20% of the potential cases—at least within the span of time here observed. The corresponding proportions of cases among the females would be 40% from the " negatives " and 60% from the " positives ".

Comparing the situation from period to period (Table 15), the data indicate that the proportion of cases coming from the negative group assumes a greater significance as time goes by. Between Rounds I and IV, the percentage of cases (males plus females) among the " negatives " was 23; in the next period, it was 26; and, after Round VI, it was 45. The same trend is observable in both sexes: in the males, the proportion increases from 18% to 29%; in the females, from 35% to 59%. Evidently, the chances of ascertaining the possible effect of BCG are greater the longer the period of observation, provided, of course, that there is no waning of the induced immunity.

The effect of vaccination in reducing the total incidence in the present study population, if all tuberculin "negatives" had been vaccinated, could be estimated by doubling the number of cases found among the vaccinated, adding the new number to that arising from the " positives ", and comparing it with the number that would have occurred had none been vaccinated.

Considering first males plus females (Table 16), without any vaccination there would have been 207 cases throughout the whole period of observation. Had all the " negatives " been vaccinated, there would have been 171, i.e., 83%; so the total reduction would be 17%. In this calculation, the material of the first period (Rounds I-IV) has been included, and that is the period in which the incidence in vaccinated and controls showed very little difference. The reduction in this period would amount to as little as 6%, and only the females would have contributed to it. In the second period

TABLE 16
ESTIMATED NUMBER OF CASES IN THE POPULATION WITH AND WITHOUT VACCINATION OF ALL TUBERCULIN-NEGATIVE REACTORS

	Rounds I-IV		Rounds IV-VI		After Round VI		Total	
	No.	%	No.	%	No.	%	No.	%
Males								
If vaccination done	49	100.0	56	82.3	12	85.8	117	92.3
If vaccination not done	45		68		14		127	
Females								
If vaccination done	15	65.2	28	70.0	11	64.7	54	67.5
If vaccination not done	23		40		17		80	
Both sexes								
If vaccination done	64	94.1	84	77.7	23	74.2	171	82.6
If vaccination not done	68		108		31		207	

(Rounds IV-VI) the estimated reduction caused by vaccination would be 18% for the males and 30% for the females; in the third period (after Round VI), the figures would be 14% and 35%, respectively. Considering the total experience in males, vaccination would reduce the incidence from 127 to 117 cases, i.e., by only 8%; whereas, in the females, the incidence would be reduced from 80 to 54—a reduction of 32.5%.

COMPARISON OF THE RESULTS AS GIVEN IN THE PREVIOUS AND THE PRESENT REPORTS

The first report dealt with persons tested and allocated to the trial in Round I. The cases found at Rounds II-IV were: 9 vaccinated and 7 controls. According to the present analysis, the number of cases found in the same group and during the same period were: 3 vaccinated and 8 controls (Table 5). Evidently, some of the cases noted as incidence cases in the first report have now been excluded, and others not noted at the time of the first analysis have been included. The reasons for the difference have been examined.

There could be 3 ways in which differences could have arisen. First, as the last assessment was carried out entirely independently of the first, it could have happened that a case was classified differently at the two assessments owing to different interpretations of the radiological character of the lesions. Secondly, an X-ray photograph taken during Round VI could have provided new information on the character of lesions seen at earlier rounds, leading to a modified or changed diagnosis at the present assessment. Thirdly, as the whole material was re-punched for the purpose of the present analysis, certain regroupings could have occurred in the course of the statistical processing.

The cases included in the previous report show the following status at the present assessment: of the 9 vaccinated cases, 3 have been confirmed as tuberculosis cases. One of these, according to the first report, was found at Round II, but this time has been classified as belonging to Round I and therefore excluded. Another 6 cases have also been excluded: 2 classified as non-tuberculous on the basis of the original X-ray pictures, and 4 X-rayed in Round VI, now classified as either non-tuberculous (3) or doubtful (1). Of the 7 cases found among the unvaccinated controls, according to the first report, 4 have now been confirmed as tuberculous. One of these is now excluded as not belonging to the trial study population since the patient was tested in Round I just before the trial began. Another 3 cases are now excluded because, when X-rayed in Round VI, the patients were classified as either non-tuberculous (1) or doubtful (2).

Included in the present report, but not in the first, are the following cases: 1 vaccinated case (male, 61 years, normal at Round I, pleurisy at Round II followed by extensive parenchymal pulmonary tuberculosis, sputum-positive) that by mistake was not

given a punch card at the previous analysis, and 5 control cases, all detected by X-ray examination in Round VI and, by inspection of their earlier films, traced back to Round II (2 cases), Round III (1 case) and Round IV (2 cases) respectively, although, when these films were read originally, they were considered to be normal.

The 3 vaccinated cases included in the present report consist, therefore, of 2 cases reported earlier plus 1 new one, and the 8 control cases, of 3 reported earlier plus 5 new ones. Therefore, of a total of 22 cases (16 reported earlier and 6 new), 8 were diagnosed as tuberculous at both assessments, while 14 were diagnosed as tuberculous at one of the two assessments. In 12 of these 14 cases, the change of diagnosis was due to new information obtained at the X-ray examination in Round VI; in the remaining two, it was due to a difference in interpretation of the same X-ray pictures at the two assessments. Of the 8 cases diagnosed as tuberculous at both assessments, 5 (2 vaccinated and 3 controls) are included in both reports while 3 are included in either one or the other owing to different classification at the statistical processing. Two cases (1 vaccinated and 1 control) present in the first report are now excluded, and 1 vaccinated case omitted in the first report is now included.

It is unavoidable in investigations dealing with X-ray readings that a proportion of pulmonary abnormalities will be interpreted differently by different readers or by the same reader at different times. It is, therefore, not surprising that in the present material there are also a number of cases which have given rise to different interpretations from time to time. The chief requirement in an investigation of the present type is that the whole material should be subjected to the same kind of " treatment " at all stages from beginning to end, so that no bias is introduced that could affect the unhindered flow of observations whether they relate to the vaccinated, the controls or the initially Mantoux-positive reactors. With the limitations described earlier, this principle has been adhered to throughout the present investigation.

DISCUSSION

Certain pertinent questions need to be discussed:

(*a*) Does the present investigation show that BCG vaccination is able to prevent tuberculosis in Indians ?

(*b*) If so, to what extent ?

(*c*) How can the present findings be reconciled with those previously reported from Madanapalle ?

(*d*) Are the present results consonant with those obtained by the BCG trials in the United Kingdom and the United States of America ?

Question (*a*) must be answered in the affirmative. Although the number of cases observed is not large, the incidence among the vaccinated is so much lower than among the non-vaccinated controls that it is unlikely to have resulted merely from sampling variations. As the two groups are very similar and have been observed equally closely, there does not seem to be any factor other than the BCG vaccination itself to account for the difference in incidence. Therefore, it may be concluded that the vaccination has been able to prevent the development of tuberculosis in a certain number of cases.

As for the degree of protection, this question is more difficult to answer. Considering the cases found between Rounds I and VI (Table 7) the difference between the annual incidence of 0.34 per 1000 among the vaccinated and 0.86 among the controls corresponds to a reduction of 60% attributable to the vaccination. This figure is not necessarily identical with the true protection offered by the vaccination, which could have been found if our material had been much larger. However, an estimate can be made as to the range within which the true figure must lie, by working out the fiducial limits based upon the present sample. At a confidence level of 95%, these are 14.3% and 84.1%. This is obviously a very wide range, so it is only possible to say that the true degree of protection is likely to be between 14% and 84%. If we include also the cases found after Round VI (Table 6), the rate of 2.17 per 1000 in the vaccinated corresponds to a reduction of 56.5% of the rate of 4.99 in the controls. The fiducial limits are now 16.3% and 79.9%, which again does not allow a very precise estimate of the true degree of protection. Even if we assume that the cases arising shortly after the time of initial tuberculin testing and vaccination could have been infected before the testing, and therefore consider only the cases that developed later (Table 12), which represented a rate of 1.18 per 1000 in the vaccinated and 4.13 in the controls, corresponding to a reduction of 71.4%, the fiducial limits are 35.5% and 90.3%, which again gives a very wide margin. It must be concluded, therefore, that the present findings point to substantial protection, but

that the true degree of protection may be considerably lower or considerably higher.

With regard to the question of how the present findings can be reconciled with the previous findings at Madanapalle, it is now quite clear that the results obtained previously were inconclusive because the material was too small and the observation period too short. This was already anticipated and mentioned in the first report, and later stressed by Ranganathan (1962). However, at the time when the first report was written, it was not so obvious, so the author suggested a number of other factors that could have interfered with the effect of the vaccination. Some of these points have been taken up for further study since the last report.

The observation that the postvaccination allergy appeared to be very low was a point of major concern in the first report. Retests carried out 1-4 years after the initial tests showed indurations with a mean size of only 5.5-7 mm in the vaccinated and 3.5-4.8 mm in the controls; thus neither the level of tuberculin sensitivity obtained nor the difference observed between the sensitivity in the vaccinated and the controls was very impressive. The possibility that this may have been due to damage to the vaccine in transit between the production centre in Madras and Madanapalle has been examined.

A group of children was vaccinated in 1960 with two batches of BCG vaccine, one of which had been transported from Madras to Madanapalle in the ordinary way by train, with the vaccine placed in a heat-insulated box containing ice-filled tins, while the other had been sent up by car from Madras with the vaccine kept in a vacuum flask filled with ice. The two batches of vaccine produced the same level of postvaccination allergy (Frimodt-Møller, 1962a).

It has been found also that the reason for the apparently low postvaccination allergy obtained at Madanapalle as compared with that found by others elsewhere (WHO Tuberculosis Research Office, 1955a, 1955b, 1957; Bhushan, 1960) is due to the difference in standards of reading the size of indurations. Comparative readings of tests in children in 1960 at Madanapalle showed that the readers there consistently recorded reactions 4-8 mm smaller than those recorded by a WHO/TRO-trained nurse who had been exclusively engaged in tuberculin testing for a number of years (Frimodt-Møller, 1962a).

In 1961, retests with tuberculin were carried out in a high school at Vayalpad, where a large proportion of children had been vaccinated by the Madanapalle field team as far back as 1950-55, i.e., up to 11 years earlier. Other children at the same school from villages outside our study area had been vaccinated 4 years earlier by the Mass Vaccination Campaign team of the Andhra State Government. The indurations in the non-vaccinated children in both groups showed a bimodal distribution, with the strong reactions having a mode at about 17 mm and separated clearly, at the level of about 10 mm, from a group of weak reactions with a mode of about 3 mm. In the vaccinated children, the indurations formed a broad normal distribution with a mode at about 10-12 mm. The vaccinated children possessed a tuberculin skin sensitivity which was less than that found in the non-vaccinated children with strong reactions, but higher than that found in the non-vaccinated children with small reactions, the latter presumably corresponding to a non-specific allergy. Even if allowance is made for the possible effect of superinfection with virulent bacilli, it is quite evident that the majority of the children vaccinated 11 years earlier, as also those vaccinated 4 years earlier, presented an allergy that could be attributed only to the vaccination (Frimodt-Møller, Parthasarathy & Benjamin, 1962).

These observations suggest that it is not correct that the postvaccination allergy obtained in the children vaccinated at Madanapalle during the years 1950-55 was unusually low, as was suggested in the previous report. Had the readings been done by specially trained personnel, the mean indurations in the vaccinated would very likely have been 4-8 mm higher, i.e., about 12-14 mm. Further, the allergy obtained in children vaccinated 11 years earlier was comparable to that obtained in the children vaccinated only 4 years earlier by the Mass Vaccination Campaign team.

A study of the allergy obtained in the vaccinated at Madanapalle with that found in persons vaccinated elsewhere in India and in other countries in the South-East Asia region shows very much the same pattern (Frimodt-Møller, 1962a). The mean indurations in vaccinated children usually occupy, according to size, a position midway between that of the " naturally positive " and that of the non-infected. The level of allergy produced by the BCG vaccine is not as high as that found in the " positives ", but it is clearly higher than the allergy in the " negatives " even if these possess a low degree of allergy attributable to infection with non-pathogenic mycobacteria. Assuming that the degree of immunity induced by BCG is related to the degree of allergy induced, it is

reasonable to expect that BCG vaccination should confer a measurable degree of immunity against tuberculosis even if the allergy is not as strong as that found among " naturally positives ".

All these observations may be summed up by concluding that the allergy produced by the BCG vaccine at Madanapalle has been substantial and not inferior to that found elsewhere in this region, and that the level of tuberculin sensitivity can be maintained for more than ten years. It is therefore reasonable that the present investigation should also now show the presence of immunity.

As for the suggestion made in the previous report —that the development of a low-grade, non-specific allergy in the unvaccinated controls, due to infection with non-pathogenic acid-fast mycobacteria, might also have produced a certain degree of immunity which might have competed with that produced by the BCG in the vaccinated—it is possible that this factor may be less significant than was previously thought. As a large proportion of the vaccinated and the controls were also tested with a high dose of tuberculin (100 TU) at the time of the initial test, this point is now being analysed and will be reported on separately.

On the question of how the results in the Madanapalle trial compare with those of the American and British trials, it may be recalled that, in the former, the average annual incidence at Puerto Rico was 0.30 per 1000 in the vaccinated and 0.43 in the controls, giving a percentage reduction of 30.9% in tuberculosis incidence among the vaccinated; and, in the Muscogee-Russell trial, annual incidence rates of 0.14 and 0.22 per 1000, respectively, with a reduction of 35.9% in tuberculosis cases among the vaccinated (Palmer, Shaw & Comstock, 1958). The British trial showed an annual incidence of 0.40 per 1000 in the vaccinated and of 1.91 in the controls, which gives a reduction of 79% attributable to vaccination. The Madanapalle findings, which show a reduction of 56-60% attributable to vaccination, therefore fall midway between the findings of the other two trials. In view of the wide range of the fiducial limits pertaining to the Madanapalle findings as discussed above, our results are compatible with those obtained in both the American and the British trials; in other words, the true effect of vaccination at Madanapalle may be theoretically as high as that found in the British trials and as low as that found in the American trials, and yet, if only the cases arising after the initial period of 1-1½ years are considered, the Madanapalle results appear closer to the British than to the American results. Only a larger body of material or a longer period of observation, or both, would permit of determining more precisely the true level of protection afforded by vaccination, and its relationship to findings elsewhere.

With regard to the incidence among persons already infected with tubercle bacilli at the time of the first testing, i.e., the " naturally positive ", and to the incidence among the tuberculin-negative, the present findings confirm those of the American trials (Palmer, Shaw & Comstock, 1958). At Madanapalle, also, the great majority of cases (70-80%) observed during the first ten years arose among the " naturally positive ", and only 20-30% among the initially " negative ". This must necessarily be so, as the former had already been infected and the latter not yet. In time, however, the initially tuberculin-positive reactors will represent a decreasing, and the initially " negative reactors " an increasing, share of the fresh cases, and, if the initially negative have been vaccinated, the effect of the vaccination will become progressively greater. This, however, presupposes that the effect of the vaccine does not wane.

The observation made here, that BCG appears to offer protection in the age-groups above 35 years, confirms that made in the previous report: namely, that quite a high proportion of the population at Madanapalle remains uninfected with tubercle bacilli until late in life. Therefore, there would appear to be a need for extending vaccination also to adults in middle life, at least when BCG is first introduced into such a community. If provision is made for periodic vaccination of children, so that the whole population can be covered progressively, it may suffice to vaccinate the children only.

SUMMARY

From 1950 to 1955, a population of 40 000 living in nearly 200 villages around Madanapalle, South India, was surveyed five times (Rounds I-V) by tuberculin tests and mass miniature X-ray examinations. A preliminary report, published in 1960, on the early results of BCG vaccination among persons tested in Round I showed no

difference in the incidence of tuberculosis between the vaccinated and the non-vaccinated; however, the material was small and the period of observation short. The present paper is a follow-up report, covering a larger material and a much longer period of observation. From 1950 to 1955 (Rounds I-V) a total of 21 556 persons were tested with tuberculin: 11 577 of these were found to be non-reactors (having indurations of 4 mm or less to Mantoux tests with 5TU, or 5 mm or less to 10 TU) and 9979 to be reactors. The non-reactors (" negatives ") were divided at random into two groups: one of 5769 persons, selected for BCG vaccination, and the other of 5808 persons, selected as unvaccinated " controls ". Of the former group, 5069 were vaccinated and 700 were not.

During the period 1957-58, an X-ray examination (Round VI) was made of almost the whole village population (nearly 90% of all persons aged 5 years or more). The cases of tuberculosis found either by the X-ray survey or because of symptoms were: 8 vaccinated (1 bacillary case), 22 controls (6 bacillary) and 132 reactors (" positives ") (53 bacillary), giving the following annual incidence rates per 1000: vaccinated 0.34, controls 0.86 and reactors 2.88, and, for the bacillary cases, 0.04, 0.23 and 1.16, respectively. The difference between the vaccinated and the controls corresponds to a reduction of 60.0% attributable to vaccination, the 95% fiducial limits being 14.3% and 84.1%.

In the period following Round VI and up to the end of June 1963, another 27 cases were found because of symptoms: 3 vaccinated (2 bacillary), 7 controls (6 bacillary) and 17 reactors (16 bacillary). When these are added to the cases found up to 1957-58, the total numbers become: 11 vaccinated (3 bacillary), 29 controls (12 bacillary) and 149 reactors (69 bacillary). The corresponding rates per 1000 are 2.17, 4.99 and 14.93, respectively, and, for the bacillary cases, 0.59, 2.07 and 6.91, respectively. The reduction in the rate, attributable to vaccination, is 56.5% (for the bacillary cases, 71.4%) with the fiducial limits of 16.3% and 79.9% (for the bacillary cases, 12.1% and 94.9%).

There were 46 cases (15 bacillary) that occurred shortly after the persons' entry into the trial: 5 vaccinated (1 bacillary), 5 controls (1 bacillary) and 36 reactors (13 bacillary). It is possible that some of these were due to infections that had taken place before the initial tuberculin tests. The remaining 143 cases were most likely to be due to infections that took place after the first tuberculin test. The distribution of these cases was as follows: 6 vaccinated (2 bacillary), 24 controls (11 bacillary) and 113 reactors (56 bacillary). The corresponding rates per 1000 are 1.18, 4.13 and 11.32, and, for the bacillary cases, 0.39, 1.89 and 5.61. The reduction in tuberculosis cases attributable to vaccination is 71.4% (for the bacillary cases, 79.2%) with the fiducial limits 35.5% and 90.3% (for the bacillary cases, 25.6% and 98.1%).

It is concluded that vaccination has produced a significant reduction in the number of tuberculosis cases. The degree of protection may be about 56-60%, but owing to the limited material no precise estimate can be given.

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RÉSUMÉ

De 1950-1955, une enquête de dépistage de la tuberculose a été effectuée dans environ 200 villages (soit auprès de 40 000 habitants) dans les environs de Madanapalle, Inde méridionale. A cet effet, la population a été passée en revue cinq fois (tour I-V) et soumise à des tests tuberculiniques et à la radiographie de masse sur microfilms. Un rapport préliminaire, en 1960, sur les premiers résultats de la vaccination au BCG parmi les personnes examinées lors du tour I, indiquait qu'il n'y avait pas de différence dans l'incidence de la tuberculose chez les vaccinés et les non-vaccinés; toutefois, le matériel était peu abondant et la période d'observation brève. Le pré-

sent article représente un rapport comportant un matériel plus étendu et une période d'observation plus longue. De 1950-1955 (tours I-V), 21 556 de ces habitants ont subi des épreuves tuberculiniques, à la suite desquelles 11 577 ont été reconnues comme négatives — non réacteurs — (ayant des indurations de 4 mm ou moins au Mantoux 5 UT et de 5 mm ou moins au Mantoux 10 UT); 9979 étaient positifs-réacteurs. Les sujets négatifs ont été divisés, au hasard, en deux groupes: l'un, de 5769 personnes, a été choisi pour être vacciné par le BCG, l'autre, de 5808 personnes, servait de témoin, non vacciné. 5069 personnes du premier groupe furent vaccinées, 700 ne le furent pas.

En 1957-58, des radiographies sur microfilms (tour VI) furent effectuées sur l'ensemble de la population des villages (90% des habitants ayant 5 ans et plus). Les cas de tuberculose dépistés soit à la suite de la radiographie soit à la vue des symptômes étaient de: 8 vaccinés (1 bacillaire), 22 témoins (6 bacillaires) et 132 positifs à la tuberculine, ce qui donne une incidence annuelle, pour 1000 habitants, de: 0,34 chez les vaccinés; 0,86 chez les témoins; 2,88 chez les positifs; pour les bacillaires: 0,04, 0,23, et 1,16 respectivement. La différence entre vaccinés et témoins correspond à une diminution de 60,0%, attribuable à la vaccination (les limites de sécurité étant 14,3% et 84,1%).

Dans la période qui suivit cet examen et jusqu'en juin 1963, on découvrit, d'après les symptômes, 27 autres cas soit 3 vaccinés (2 bacillaires), 7 témoins (6 bacillaires) et 17 positifs (16 bacillaires). En ajoutant ces chiffres aux précédents, on obtient le nombre de cas suivant: 11 vaccinés (3 bacillaires), 29 témoins (12 bacillaires), et 149 positifs (69 bacillaires). Les taux correspondants, pour 1000 habitants, sont: 2,17, 4,99, et 14,93 respectivement; pour les bacillaires: 0,59, 2,07, et 6,91. La réduction du taux d'infection, imputable à la vaccination, est de 56,5% (pour les cas bacillaires, 71,4%), avec des limites de sécurité de 16,3 et 79,9% (pour les bacillaires 12,1 et 94,9%).

Il y eut 46 cas qui se manifestèrent peu après leur admission à l'enquête: 5 vaccinés (1 bacillaire), 5 témoins (1 bacillaire) et 36 positifs (13 bacillaires). Il est possible que certains d'entre eux résultent d'infections contractées avant les tests tuberculiniques initiaux. Les autres sont probablement des primo-infections qui se sont produites après le premier test. Ils se répartissaient comme suit: 6 vaccinés (2 bacillaires), 24 témoins (11 bacillaires), 113 positifs (56 bacillaires). Les taux correspondants, pour 1000 habitants, sont: 1,18, 4,13, et 11,32 respectivement; pour les bacillaires, 0,39, 1,89 et 5,61. La diminution du nombre de cas de tuberculose attribuable à la vaccination est de 71,4% (pour les bacillaires 79,2%) avec des limites de sécurité de 35,5% et 90,3% (pour les bacillaires 25,6% et 98,1%).

On peut conclure de ces chiffres que la vaccination a produit une diminution significative du nombre des cas de tuberculose. Le degré de protection peut être évalué à 56-60%, mais le nombre de cas étant restreint, on ne peut donner de proportions plus précises.

REFERENCES

Bhushan, K. (1960) *Indian J. med. Res.*, **48**, 407

Frimodt-Møller, J. (1960) *Bull. Wld Hlth Org.*, **22**, 61

Frimodt-Møller, J. (1962a) *Bull. Wld Hlth Org.*, **25**, 875

Frimodt-Møller, J. (1962b) *Indian J. Tuberc.*, **9**, 187

Frimodt-Møller, J., Parthasarathy, R. & Benjamin, P. (1962) *Indian J. Tuberc.*, **9**, 192

Great Britain, Medical Research Council (1956) *Brit. med. J.*, **1**, 413

Great Britain, Medical Research Council (1959) *Brit. med. J.*, **2**, 379

Great Britain, Medical Research Council (1963) *Brit. med. J.*, **1**, 973

Indian Council of Medical Research (1959) *Tuberculosis in India. A sample survey 1955-1958*, New Delhi (*Special Research Series*, No. 34)

Palmer, C. E., Shaw, L. W. & Comstock, G. W. (1958) *Amer. Rev. Tuberc.*, **77**, 877

Ranganathan, K. S. (1962) *Bull. Wld Hlth Org.*, **25**, 871

WHO Tuberculosis Research Office (1955a) *Bull. Wld Hlth Org.*, **12**, 63

WHO Tuberculosis Research Office (1955b) *Bull. Wld Hlth Org.*, **12**, 101

WHO Tuberculosis Research Office (1957) *Bull. Wld Hlth Org.*, **17**, 203

APPENDIX TABLE 1

VACCINATED, UNVACCINATED (NEGATIVE), AND POSITIVE REACTORS DISTRIBUTED ACCORDING TO ROUND OF ENTRY INTO THE BCG TRIAL AND SHOWING THE NUMBER OF PERSONS X-RAYED FOR THE FIRST TIME AT EACH ROUND REGARDLESS OF WHEN FIRST TESTED

Entry into BCG trial	Group	Sex	Number tested	Round of first X-ray						
				I	II	III	IV	V	VI	Total
Round I	Vaccinated	M	1 026	628	127	65	35	—	91	946
		F	1 120	680	151	68	31	—	94	1 024
	Unvaccinated	M	1 156	674	167	78	40	—	104	1 063
		F	1 219	725	160	59	32	—	117	1 093
	Positive	M	2 059	1 479	251	79	32	—	92	1 933
		F	2 231	1 555	252	77	20	—	151	2 055
Round II	*1-10-100 TU :*									
	Vaccinated	M	144	*18*	59	10	5	4	25	121
		F	146	*22*	63	14	5	8	23	135
	Unvaccinated	M	154	*25*	49	16	6	6	23	125
		F	137	*21*	47	14	7	3	15	107
	Positive	M	631	*209*	257	41	5	8	38	558
		F	575	*97*	266	53	8	11	54	489
	5-100 TU :									
	Vaccinated	M	408	*73*	108	39	26	—	92	338
		F	451	*109*	87	43	26	—	114	379
	Unvaccinated	M	540	*158*	109	41	32	—	115	455
		F	487	*158*	62	44	28	—	109	401
	Positive	M	1 430	*613*	318	96	57	—	179	1 263
		F	1 287	*419*	281	80	63	—	232	1 075
Round III	Vaccinated	M	630	*8*	*13*	121	41	16	262	461
		F	682	*11*	*11*	144	25	21	278	490
	Unvaccinated	M	948	*106*	*94*	172	51	14	278	715
		F	856	*79*	*61*	146	39	18	303	646
	Positive	M	1 278	*266*	*153*	353	69	14	191	1 046
		F	1 118	*127*	*117*	324	56	10	234	868
Round IV	Vaccinated	M	220	*2*	*3*	*22*	25	4	78	134
		F	243	*1*	*3*	*21*	26	9	93	153
	Unvaccinated	M	356	*28*	*31*	*44*	38	9	104	254
		F	333	*36*	*19*	*29*	33	11	104	232
	Positive	M	693	*130*	*52*	*116*	95	14	136	543
		F	571	*71*	*42*	*74*	83	16	134	420
Round V	Vaccinated	M	195	*2*	*3*	*9*	*24*	5	74	117
		F	177	*3*	—	*6*	*9*	14	62	94
	Unvaccinated	M	337	*18*	*12*	*27*	*28*	13	90	188
		F	322	*16*	*13*	*16*	*18*	18	94	175
	Positive	M	551	*88*	*44*	*69*	*67*	56	99	423
		F	439	*32*	*25*	*30*	*43*	60	123	313

Notes. The figures in italics refer to groups that were excluded from the trial owing to incomplete randomization and are not included in the following appendix tables.

APPENDIX TABLE 2
COVERAGE BY X-RAY, AT EACH ROUND, OF PERSONS IN THE BCG TRIAL

Entry into BCG trial	Group	Sex	Number of persons	Number X-rayed in each round					
				I	II	III	IV	V	VI
Round I	Vaccinated	M	1 026	628	460	402	383	—	751
		F	1 120	680	481	436	308	—	695
	Controls	M	1 156	674	527	449	384	—	823
		F	1 219	725	536	440	319	—	791
	Positive	M	2 059	1 479	1 024	799	632	—	1 432
		F	2 231	1 555	997	785	527	—	1 484
Round II	*1-10-100 TU:*								
	Vaccinated	M	126	—	59	38	30	25	68
		F	124	—	63	46	32	39	81
	Controls	M	129	—	48	38	26	27	64
		F	116	—	47	37	30	29	57
	Positive	M	422	—	258	151	107	103	199
		F	478	—	265	181	109	117	252
	5-100 TU:								
	Vaccinated	M	335	—	108	87	75	—	208
		F	342	—	87	81	75	—	217
	Controls	M	382	—	109	86	90	—	238
		F	329	—	62	70	61	—	207
	Positive	M	817	—	318	233	182	—	482
		F	868	—	281	187	162	—	510
Round III	Vaccinated	M	609	—	—	121	96	44	381
		F	660	—	—	144	75	38	419
	Controls	M	748	—	—	172	132	43	438
		F	716	—	—	146	98	52	436
	Positive	M	859	—	—	353	215	66	450
		F	874	—	—	324	160	46	491
Round IV	Vaccinated	M	193	—	—	—	24	7	89
		F	218	—	—	—	25	14	110
	Controls	M	253	—	—	—	39	15	128
		F	249	—	—	—	33	18	137
	Positive	M	395	—	—	—	95	30	190
		F	384	—	—	—	83	27	181
Round V	Vaccinated	M	157	—	—	—	—	5	78
		F	159	—	—	—	—	14	69
	Controls	M	252	—	—	—	—	13	100
		F	259	—	—	—	—	18	104
	Positive	M	283	—	—	—	—	56	123
		F	309	—	—	—	—	60	159

APPENDIX TABLE 3

DISTRIBUTION OF PERSONS ADMITTED TO THE BCG TRIAL IN EACH OF THE FIVE ROUNDS ACCORDING TO SEX AND AGE, AND WHETHER "VACCINATED", "DUE FOR VACCINATION, BUT NOT VACCINATED", "UNVACCINATED CONTROLS" OR "POSITIVE"

Age-group (years)	Males				Females			
	Vaccinated	Due, but not vaccinated	Controls	Positive reactors	Vaccinated	Due, but not vaccinated	Controls	Positive reactors
Round I								
0-4	150	17	184	73	140	13	161	66
5-14	515	36	516	329	482	30	485	340
15-24	134	7	165	273	191	10	194	324
25-34	89	8	117	397	185	24	203	580
35-44	80	6	64	408	87	13	103	439
45-54	46	9	57	303	30	26	54	328
55+	11	36	53	276	5	18	19	153
Not recorded	1	—	—	—	—	—	—	1
Total	1 026	119	1 156	2 059	1 120	134	1 219	2 231
Round II[a]								
0-4	193	15	186	180	179	17	204	205
5-14	202	20	221	262	157	12	125	212
15-24	37	1	43	195	78	7	50	277
25-34	12	4	26	191	35	5	37	246
35-44	10	1	13	155	11	6	14	152
45-54	6	1	5	116	2	—	6	134
55+	1	—	16	138	4	2	9	119
Not recorded	—	—	1	2	—	—	—	1
Total	461	42	511	1 239	466	49	445	1 346
Round III								
0-4	381	21	385	102	361	26	374	108
5-14	159	19	235	162	120	19	159	132
15-24	26	4	48	108	105	7	82	207
25-34	20	3	30	177	47	6	47	185
35-44	9	3	14	124	14	1	19	90
45-54	10	1	17	90	8	1	19	81
55+	2	1	11	88	2	2	12	65
Not recorded	2	—	8	8	3	—	4	6
Total	609	52	748	859	660	62	716	874
Round IV								
0-4	128	20	143	53	128	39	132	40
5-14	44	5	78	83	48	11	55	66
15-24	8	2	10	61	27	10	31	103
25-34	5	2	9	73	10	4	19	81
35-44	4	3	4	54	3	2	3	40
45-54	1	1	4	33	1	2	4	24
55+	1	2	2	32	1	3	3	29
Not recorded	2	2	3	6	—	—	2	1
Total	193	37	253	395	218	71	249	384
Round V								
0-4	102	45	163	27	90	43	147	39
5-14	34	10	59	55	30	10	39	46
15-24	11	1	16	44	28	9	39	101
25-34	4	4	9	69	8	4	16	54
35-44	1	—	1	35	2	2	7	26
45-54	4	2	1	25	1	1	6	20
55+	1	2	3	28	—	1	5	22
Not recorded	—	—	—	—	—	—	—	1
Total	157	64	252	283	159	70	259	309
Grand total (Rounds I-V)	2 446	314	2 920	4 835	2 623	386	2 888	5 144

[a] The two groups 1-10-100 TU and 5-100 TU shown in Appendix Table 2 have been merged.

APPENDIX TABLE 4

PERSONS TESTED IN ROUND I, ACCORDING TO SEX AND AGE, WHO SUBSEQUENTLY DIED (D), LEFT THE AREA (L) OR WERE UNTRACEABLE (U)

Age-group (years)	Number at Round I	Rounds I-IV			Number present at Round IV	Rounds IV-VI			Number present at Round VI
		D	L	U		D	L	U	
Vaccinated: males									
0-4	150	9	5	6	130	1	9	8	112
5-14	515	7	32	16	460	4	20	18	418
15-24	134	3	9	4	118	2	10	2	104
25-34	89	—	9	1	79	2	5	2	70
35-44	80	1	5	2	72	2	4	1	65
45-54	46	2	1	—	43	4	2	—	37
55 +	11	2	—	—	9	2	—	—	7
	1	—	—	1	—	—	—	—	—
	1 026	24	61	30	911	17	50	31	813
Vaccinated: females									
0-4	140	4	11	7	118	3	5	3	107
5-14	482	7	44	13	418	6	99	27	286
15-24	191	7	21	5	158	5	27	2	124
25-34	185	8	16	4	157	2	10	8	137
35-44	87	3	5	3	76	4	2	1	69
45-54	30	1	2	—	27	2	2	—	23
55 +	5	—	—	—	5	2	—	—	3
	1 120	30	99	32	959	24	145	41	749
Total	2 146	54	160	62	1 870	41	195	72	1 562
Controls: males									
0-4	184	9	12	2	161	4	7	5	145
5-14	516	8	48	16	444	4	24	25	391
15-24	165	3	10	4	148	1	15	6	126
25-34	117	—	10	2	105	1	9	6	89
35-44	64	1	6	4	53	—	3	1	49
45-54	57	6	5	1	45	3	1	—	41
55 +	53	6	3	1	43	5	2	1	35
	1 156	33	94	30	999	18	61	44	876
Controls: females									
0-4	161	5	8	3	145	5	9	1	130
5-14	485	4	42	11	429	3	109	17	299
15-24	194	5	25	3	161	4	26	5	126
25-34	203	2	14	2	185	3	12	5	165
35-44	103	1	4	—	98	5	2	6	85
45-54	54	4	2	—	48	2	2	—	44
55 +	19	2	—	—	17	1	5	—	11
	1 219	23	95	19	1 082	23	165	34	860
Total	2 375	56	189	49	2 081	41	226	78	1 736
Positive reactors: males									
0-4	73	3	2	—	68	3	5	1	59
5-14	329	2	36	16	275	2	26	13	234
15-24	273	4	19	12	238	4	16	6	212
25-34	397	6	22	11	358	4	21	13	320
35-44	408	11	26	8	363	6	14	7	336
45-54	303	18	17	6	262	18	9	8	227
55 +	276	33	12	4	227	33	10	6	178
	2 059	77	134	57	1 791	70	101	54	1 566
Positive reactors: females									
0-4	66	7	6	1	52	2	3	2	45
5-14	340	2	24	6	308	5	76	15	212
15-24	324	3	32	11	278	5	41	9	223
25-34	580	10	36	9	525	12	39	7	467
35-44	439	16	28	9	386	9	22	7	348
45-54	328	13	20	3	292	30	12	7	243
55 +	153	19	7	5	122	15	5	4	98
Not recorded	1								
	2 231	70	154	44	1 963	78	198	51	1 636
Total	4 290	147	288	101	3 754	148	299	105	3 202

APPENDIX TABLE 5

PERSONS TESTED IN ROUND II, ACCORDING TO SEX AND AGE, WHO SUBSEQUENTLY DIED (D), LEFT THE AREA (L), OR WERE UNTRACEABLE (U) (1-10-100 TU AND 5-100 TU GROUPS COMBINED)

Age-group (years)	Number at at Round II	Rounds II-IV			Number present at Round IV	Rounds IV-VI			Number present at Round VI
		D	L	U		D	L	U	
Vaccinated: males									
0-4	193	13	11	8	161	7	12	2	140
5-14	202	1	25	23	153	1	10	26	116
15-24	37	1	7	2	27	—	4	3	20
25-34	12	—	—	1	11	—	1	—	10
35-44	10	—	—	1	9	—	—	—	9
45-54	6	—	—	1	5	1	—	—	4
55 +	1	—	—	—	1	—	—	—	1
	461	15	43	36	367	9	27	31	300
Vaccinated: females									
0-4	179	7	9	6	157	2	9	4	142
5-14	157	2	15	9	131	4	22	13	92
15-24	78	3	11	1	63	2	14	3	44
25-34	35	1	3	2	29	1	3	1	24
35-44	11	—	3	—	8	1	1	—	6
45-54	2	—	—	—	2	—	1	—	1
55 +	4	—	—	—	4	1	—	—	3
	466	13	41	18	394	11	50	21	312
Total	927	28	84	54	761	20	77	52	612
Controls: males									
0-4	186	5	11	3	167	7	17	9	134
5-14	221	5	29	28	159	3	15	18	123
15-24	43	—	8	4	31	—	2	2	27
25-34	26	—	3	1	22	—	2	3	17
35-44	13	1	1	2	9	—	1	—	8
45-54	5	1	1	—	3	1	—	—	2
55 +	16	2	—	—	14	2	1	—	11
	1		1						
	511	14	54	38	405	13	38	32	322
Controls: females									
0-4	204	13	13	6	172	5	12	6	149
5-14	125	1	17	10	97	—	18	7	72
15-24	50	1	14	2	33	—	7	4	22
25-34	37	1	5	2	29	—	5	—	24
35-44	14	—	5	—	9	—	—	—	9
45-54	6	—	—	—	6	1	1	—	4
55 +	9	—	3	—	6	—	1	1	4
	445	16	57	20	352	6	44	18	284
Total	956	30	111	58	757	19	82	50	606
Positive reactors: males									
0-4	180	6	7	7	160	3	14	9	134
5-14	262	2	35	30	195	4	16	32	143
15-24	195	2	42	10	141	1	14	16	110
25-34	191	—	36	9	146	1	17	7	121
35-44	155	5	25	5	120	4	12	8	96
45-54	116	4	15	8	89	5	6	3	75
55 +	138	13	11	9	105	15	5	7	78
	2		2						
	1 239	32	173	78	956	33	84	82	757
Positive reactors: females									
0-4	205	11	14	10	170	4	12	7	147
5-14	212	3	31	5	173	4	41	13	115
15-24	277	1	46	10	220	13	38	5	164
25-34	246	5	24	14	203	4	29	5	165
35-44	152	2	22	10	118	4	14	6	94
45-54	134	4	11	2	117	10	13	4	90
55 +	119	11	5	3	100	14	13	8	65
	1			1					
	1 346	37	153	55	1 101	53	160	48	840
Total	2 585	69	326	133	2 057	86	244	130	1 597

APPENDIX TABLE 6

PERSONS TESTED IN ROUND III, ACCORDING TO SEX AND AGE, WHO SUBSEQUENTLY DIED (D), LEFT THE AREA (L), OR WERE UNTRACEABLE (U)

Age-group (years)	Number at Round III	Rounds III-IV			Number present at Round IV	Rounds IV-V			Number present at Round VI
		D	L	U		D	L	U	
Vaccinated: males									
0-4	381	11	9	3	358	22	28	15	293
5-14	159	1	17	15	126	1	7	31	87
15-24	26	—	2	—	24	1	2	2	19
25-34	20	—	2	—	18	1	1	5	11
35-44	9	—	—	1	8	—	1	—	7
45-54	10	—	—	—	10	1	—	2	7
55 +	2	—	—	—	2	1	—	—	1
	2	—	—	1	1	—	—	1	—
	609	12	30	20	547	27	39	56	425
Vaccinated: females									
0-4	361	14	16	2	329	21	29	10	269
5-14	120	1	6	3	110	4	20	12	74
15-24	105	—	9	1	95	1	21	6	67
25-34	47	—	4	1	42	4	8	2	28
35-44	14	—	3	—	11	1	2	—	8
45-54	8	—	—	—	8	1	—	—	7
55 +	2	—	—	—	2	2	—	—	—
	3	—	—	1	2	—	2	—	—
	660	15	38	8	599	34	82	30	453
Total	1 269	27	68	28	1 146	61	121	86	878
Controls: males									
0-4	385	22	21	3	339	17	24	10	288
5-14	235	1	11	39	184	3	24	31	126
15-24	48	—	3	4	41	1	9	4	27
25-34	30	—	2	—	28	2	5	2	19
35-44	14	—	1	—	13	1	—	—	12
45-54	17	—	3	1	13	3	1	—	9
55 +	11	1	3	1	6	1	—	—	5
	8	—	2	4	2	—	1	—	1
	748	24	46	52	626	28	64	47	487
Controls: females									
0-4	374	19	8	5	342	17	30	10	285
5-14	159	1	19	11	128	1	21	5	101
15-24	82	—	3	5	74	2	21	8	43
25-34	47	—	3	1	43	2	10	2	29
35-44	19	—	3	1	15	1	2	2	10
45-54	19	1	2	—	16	1	3	1	11
55 +	12	—	1	—	11	2	—	—	9
	4	—	—	3	1	—	—	1	—
	716	21	39	26	630	26	87	29	488
Total	1 464	45	85	78	1 256	54	151	76	975
Positive reactors: males									
0-4	102	3	5	—	94	4	12	5	73
5-14	162	—	15	21	126	—	22	27	77
15-24	108	1	12	10	85	—	20	5	60
25-34	177	1	16	4	156	4	51	5	96
35-44	124	2	6	—	116	4	20	6	86
45-54	90	3	7	—	80	12	16	—	52
55 +	88	4	4	3	77	14	5	2	56
	8	—	—	5	3	—	1	1	1
	859	14	65	43	737	38	147	51	501
Positive reactors: females									
0-4	108	8	2	1	97	7	12	5	73
5-14	132	2	13	8	109	2	24	9	74
15-24	207	1	15	2	189	5	43	10	131
25-34	185	—	15	3	167	1	32	13	121
35-44	90	2	9	1	78	4	7	4	63
45-54	81	3	7	2	69	2	10	7	50
55 +	65	2	1	2	60	8	8	5	39
	6	—	1	5	—	—	—	—	—
	874	18	63	24	769	29	136	53	551
Total	1 733	32	128	67	1 506	67	283	104	1 052

APPENDIX TABLE 7

PERSONS TESTED IN ROUND IV, ACCORDING TO SEX, WHO SUBSEQUENTLY DIED (D), LEFT THE AREA (L), OR WERE UNTRACEABLE (U)

Group	Sex	Number at Round IV	Rounds IV-VI			Number present at Round VI
			D	L	U	
Vaccinated	M	193	14	32	23	124
	F	218	7	44	18	149
Controls	M	253	14	44	37	158
	F	249	14	47	19	169
Positive reactors	M	395	18	95	44	238
	F	384	22	110	33	219

APPENDIX TABLE 8

PERSONS TESTED IN ROUND V, ACCORDING TO SEX, WHO SUBSEQUENTLY DIED (D), LEFT THE AREA (L), OR WERE UNTRACEABLE (U)

Group	Sex	Number at Round V	Rounds V-VI			Number present at Round VI
			D	L	U	
Vaccinated	M	157	2	14	13	128
	F	159	4	15	16	124
Controls	M	252	5	19	30	198
	F	259	4	36	32	187
Positive reactors	M	283	6	57	62	158
	F	309	6	72	35	196

APPENDIX TABLE 9 [a]

DISTRIBUTION OF CASES (CATEGORIES B, C AND D [b]) FOUND AMONG PERSONS TESTED WITH 1-10-100 TU AND 5-100 TU IN ROUND I BEFORE THE SETTING UP OF THE BCG TRIAL

Group	Sex	Number tested	Round						Total
			II	III	IV	V	VI	After VI	
1-10-100 TU tests									
Vaccinated	M	1 738	2 (*1*)	1	1	1	3 (*1*)	1	9 (*2*)
	F	1 586	—	2 (*1*)	1 (*1*)	1 (*1*)	4 (*1*)	4 (*3*)	12 (*7*)
Negative, not vaccinated	M	141	—	1 (*1*)	—	—	1	—	2 (*1*)
	F	153	—	2 (*1*)	—	—	1	—	3 (*1*)
Positive	M	2 141	10 (*3*)	4 (*1*)	6 (*3*)	1	12 (*6*)	8 (*6*)	41 (*19*)
	F	1 797	6 (*5*)	5 (*3*)	1 (*1*)	4 (*2*)	11 (*6*)	1	28 (*17*)
5-100 TU tests									
Vaccinated	M	382	—	—	—	—	—	1	1
	F	393	1	—	—	1 (*1*)	1	—	3 (*1*)
Negative, not vaccinated	M	83	—	—	—	—	—	—	—
	F	102	1	—	—	—	—	—	1
Positive	M	450	7 (*4*)	—	2 (*1*)	—	1 (*1*)	1 (*1*)	11 (*7*)
	F	449	1 (*1*)	2 (*1*)	—	—	1	3 (*3*)	7 (*5*)

[a] See also Table 4, page 551.

[b] For definition of categories B, C and D, see text, page 547.

Note. The italic figures in parentheses indicate bacillary cases.

APPENDIX TABLE 10

NOTES ON THE INCIDENCE CASES FOUND IN THE BCG TRIAL AMONG (*a*) THE VACCINATED AND (*b*) THE CONTROLS

Round of admission to trial	Sex	Age when tested (years)	Round when pathology first appeared	No. of normal X-rays preceding first abnormal X-ray	Type of lesion (at maximal disease) or extent of lung lesion	Cavity	Category [a]	Bacteriology [b]
				(*a*) Vaccinated				
I	M	61	II	1	Extensive	Present	D	+ TB
I	M	35	II	0	Pleural effusion	Nil	C	Negative
I	M	3	III	0	Moderate	Nil	C	Negative
I	M	9	VI	1	Moderate	Nil	B	Not examined
I	F	26	After VI	1	Extensive	Present	D	+ TB
I	M	31	After VI	2	Pleural scar	Nil	B	Negative
III	M	45	IV	1	Pleural effusion	Nil	C	Negative
III	M	23	IV	0	Moderate	Nil	B	Not examined
III	M	34	IV	0	Pleural effusion	Nil	C	Negative
III	F	30	VI	0	Slight	Nil	B	Negative
III	F	30	After VI	1	Extensive	Present	D	+ TB
				(*b*) Controls				
I	F	36	II	1	Extensive	Doubtful	C	+ TB
I	M	24	II	0	Pleural effusion	Nil	B	Negative
I	M	46	II	0	Moderate	Nil	B	Negative
I	F	41	II	0	Extensive	Nil	C	Not examined
I	F	31	III	2	Slight	Nil	B	Not examined
I	M	60	IV	2	Extensive	Doubtful	D	+ TB
I	M	41	IV	0	Moderate	Present	C	+ TB
I	F	4	IV	2	Moderate	Nil	C	Not examined
I	F	26	VI	1	Extensive	Nil	B	+ TB
I	F	26	VI	1	Extensive	Present	D	Negative
I	F	51	VI	4	Slight	Nil	B	Negative
I	M	6	VI	2	Moderate	Nil	B	Negative
I	M	61	VI	0	Moderate	Nil	B	Not examined
I	F	7	VI	0	Hilar adenitis	Nil	B	Not examined
I	F	7	After VI	1	Extensive	Present	D	+ TB
I	M	36	After VI	2	Extensive	Present	D	+ TB
I	F	21	After VI	3	Extensive	Present	D	+ TB
I	M	31	After VI	2	Extensive	Present	D	+ TB
II	M	11	VI	2	Hilar adenitis	Nil	B	Not examined
II	F	27	VI	1	Slight	Nil	B	Not examined
II	F	22	VI	4	Extensive	Present	D	+ TB
II	M	59	VI	1	Extensive	Present	D	+ TB
III	M	40	VI	1	Pleural effusion	Nil	C	Negative
III	M	28	VI	3	Slight	Nil	B	Negative
III	F	12	After VI	2	Extensive	Present	D	+ TB
III	F	28	After VI	2	Moderate	Present	D	+ TB
III	F	9	After VI	—	Normal–cervical adenitis	—	—	Negative
IV	F	2	VI	0	Hilar adenitis	Nil	C	Not examined
V	M	19	VI	0	Pleural effusion	Nil	B	Not examined

[a] For definition of categories B, C, and D, see text, page 547.

[b] + TB = positive for tubercle bacilli.

APPENDIX TABLE 11

DISTRIBUTION OF INCIDENCE CASES (CATEGORIES B, C AND D [a]) AMONG POSITIVE REACTORS IN THE BCG TRIAL ACCORDING TO ROUND OF ENTRY, AGE, SEX AND PERIOD WHEN LESION FIRST APPEARED

Round of entry	Age-group (years)	Males									Females								
		Round I-IV			Round IV-VI			After Round VI			Round I-IV			Round IV-VI			After Round VI		
		B	C	D	B	C	D	B	C	D	B	C	D	B	C	D	B	C	D
I	0-4	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	5-14	—	—	—	—	—	—	1 (1)	—	—	—	1	—	—	1 (1)	—	1	—	1 (1)
	15-24	—	2	1 (1)	2	—	—	—	—	—	—	—	2 (2)	—	—	2 (2)	—	—	—
	25-34	1	—	2 (2)	1	2 (2)	3 (3)	—	—	2 (2)	—	—	—	1	1	1 (1)	—	—	—
	35-44	2	3	1 (1)	3	2 (1)	2 (2)	—	1 (1)	—	1	1 (1)	2 (2)	1	—	1	—	—	1 (1)
	45-54	4	2	1	4	—	—	—	1 (1)	—	1	—	1 (1)	—	1	—	—	—	—
	55 +	3	2 (1)	4 (3)	2 (1)	1	1	—	—	—	3	1 (1)	—	—	—	—	—	—	—
	Total	10	10 (1)	9 (7)	12 (1)	5 (3)	6 (5)	1 (1)	2 (2)	2 (2)	5	3 (2)	5 (5)	2	3 (1)	4 (3)	1	—	2 (2)
II	0-4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	5-14	—	—	—	—	—	—	—	—	2 (2)	—	—	—	—	—	—	—	—	—
	15-24	—	—	—	—	1	1 (1)	—	—	—	—	—	—	—	—	3 (3)	—	—	—
	25-34	—	—	1 (1)	3	—	1 (1)	—	—	—	—	—	—	—	1	2 (1)	—	—	—
	35-44	1	—	—	—	1 (1)	2 (2)	—	—	—	—	—	—	—	—	1 (1)	—	—	—
	45-54	1	—	—	1	1	2 (2)	—	—	2 (2)	—	1	—	—	—	—	—	—	—
	55 +	—	—	1 (1)	—	2	1	—	—	1 (1)	—	—	1 (1)	1	—	—	—	—	—
	Total	2	—	2 (2)	4	5 (1)	7 (6)	—	—	5 (5)	—	1	1 (1)	1	1	6 (5)	—	—	—
III	0-4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	5-14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	15-24	—	—	—	1	—	2 (2)	—	—	—	—	—	—	—	—	—	—	1 (1)	—
	25-34	—	—	—	—	—	1 (1)	—	—	—	—	—	—	—	1	—	—	—	1 (1)
	35-44	1 (1)	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	45-54	1	—	—	—	—	—	—	—	—	—	—	—	—	1	1 (1)	—	—	—
	55 +	1	—	1	3	1	1 (1)	—	—	—	—	—	—	1	—	—	—	—	—
	Total	3 (1)	—	1	5	1	4 (4)	—	—	—	—	—	—	1	2	1 (1)	—	1 (1)	1 (1)
IV	0-4				—	—	—	—	—	—				—	—	—	—	—	—
	5-14				—	—	—	—	—	—				—	—	—	—	—	—
	15-24				—	—	—	—	—	—				—	2	—	—	—	1 (1)
	25-34				—	—	1 (1)	—	—	—				—	—	—	—	—	—
	35-44				1	—	1 (1)	—	—	—				—	—	1 (1)	—	—	—
	45-54				1	—	—	—	—	—				—	—	—	—	—	—
	55 +				—	1 (1)	—	—	—	—				1	1	—	—	—	—
	Total				2	1 (1)	2 (2)	—	—	—				1	3	1 (1)	—	—	1 (1)
V	0-4				—	—	—	—	—	—				—	—	—	—	—	—
	5-14				—	—	—	—	—	—				—	—	—	—	—	—
	15-24				—	—	—	—	—	—				—	—	—	—	—	1 (1)
	25-34				—	—	—	—	—	—				—	—	—	—	—	—
	35-44				—	—	—	—	—	—				—	—	—	—	—	—
	45-54				—	—	—	—	—	—				—	—	—	—	—	—
	55 +				—	—	—	—	—	—				—	—	—	—	—	—
	Total				—	—	—	—	—	—				—	—	—	—	—	1 (1)

[a] For definition of categories, see text, page 547.

Note. The italic figures in parentheses indicate bacillary cases.

APPENDIX TABLE 12

LIST OF CASES EXCLUDED FROM THE ANALYSIS AS THE ETIOLOGY WAS CONSIDERED TO BE NON-TUBERCULOUS (A) OR TOO UNCERTAIN FOR CLASSIFICATION (E), ALL ROUNDS COMBINED

Age-group (years)	Vaccinated			Controls			Positive		
	Number	A	E	Number	A	E	Number	A	E
Males									
0-4	954	7	—	1 061	3	1	435	3	2
5-14	954	2	1 [a]	1 109	2	—	891	4	—
15-24	216	2	—	282	1	—	681	8	1
25-34	130	—	—	191	1	2	907	5	—
35-44	104	3	—	96	1	1	776	11	4
45-54	67	2	1	84	1	—	567	14	3
55 +	16	—	—	85	4	1	562	12 [b]	4
Not recorded	5	—	—	12	—	—	16	—	—
Total	2 446	16	2	2 920	13	5	4 835	57	14
Females									
0-4	898	2	1	1 018	1	2	458	2	—
5-14	837	1	2	863	2	1	796	1	—
15-24	429	3	—	396	—	2	1 012	6	2
25-34	285	2	2	322	4	—	1 146	10	4
35-44	117	2	—	146	4	—	747	13	3
45-54	42	—	—	89	2	—	587	14	3
55 +	12	—	—	48	1	1	388	4	3
Not recorded	3	—	—	6	—	—	10	—	—
Total	2 623	10	5	2 888	14	6	5 144	50	15

[a] *Boy, 5 years :* BCG-vaccinated 1952. First miniature X-ray 1954: lesion with cavity right lower lobe. Admitted for observation: microscopy of sputum positive for acid-fast bacilli on first two days, but culture contaminated. Thereafter 15 cultures in all (12 sputum, 2 laryngeal swab, and one gastric lavage) and one guinea-pig inoculation of sputum, all negative. Bronchial washing also negative. No treatment given. Discharged after 6½ months. Another routine X-ray 1957 (Round VI) showed lesion unchanged. 1960: boy known to be healthy.

[b] *Including one man, 75 years :* Mantoux-positive 1953. Routine X-ray 1955: tumour, upper zone, left lung. Another routine X-ray 1957 (Round VI): lesion unchanged. Routine bacteriological examination 1958: growth of tubercle bacilli by culture. Admitted for observation: 8 microscopies and 5 cultures negative. Diagnosis: hydatid cyst. X-rayed 1960: lesion unchanged.

APPENDIX TABLE 13

CASES FOUND AMONG THE VACCINATED, THE UNVACCINATED AND THE POSITIVE REACTORS IN THE GROUP OF PERSONS TESTED IN ROUNDS II-V BUT EXCLUDED FROM THE BCG TRIAL BECAUSE THEY HAD BEEN X-RAYED BEFORE THE ROUND IN WHICH THEY WERE FIRST TESTED

Group	Number of persons	Number of cases	
		Rounds I-VI	After Round VI
Vaccinated	489	0	1 (*1*)
Unvaccinated	1 037	1 (*1*)	1 (*1*)
Positive	2 884	23 (*11*)	8 (*4*)

Note. The italic figures in parentheses indicate bacillary cases.