Public Health Reports

Vol. 66 • NOVEMBER 2, 1951 • *No. 44*

Field Studies on Immunization Against Tuberculosis,

I. Tuberculin Allergy Following BCG Vaccination of School Children in Muscogee County, Georgia

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Early in 1947, the Tuberculosis Control Division of the Public Health Service initiated a series of cooperative studies directed toward an evaluation of the usefulness of BCG vaccination. The site of the first study was Muscogee County, Ga., a county containing Columbus, a city of 75,000, and a surrounding rural area of about 20,000 population. A broad facility for epidemiological research in tuberculosis had already been established in Muscogee County, previously described by Comstock (*1*). The first phase of the BCG inquiry was a control study among school-age children. This report is concerned with the extent of the tuberculin allergy detected in that population 6 months and 3 years after vaccination.

The vaccination program was conducted during April and May 1947. The base population was the entire enrollment of the public and private elementary and high schools of the county—about 16,000 children, mostly between the ages of 6 and 17 years. Parental consent for participation in the program was obtained for slightly more than 80 percent of the children. A first intradermal test of 0.0001 mg. of PPD (5 tuberculin units) was given to these children. Those having reactions with a diameter of 5 mm. or more of palpable induration were eliminated from further testing and the remainder were given the second test of 0.002 mg. PPD (100 tuberculin units). Children not showing reactions of 5 mm. or more of induration to the second test were regarded as eligible for vaccination.

Although detailed characteristics of the tuberculin sensitivity of the total school population in 1947 are to be published separately, certain summary results shown in table 1 bear directly on the findings to be presented in this paper. The frequency of responses to the 5 TU (8 percent in whites and 26 percent in Negroes) was not inconsistent with the general conception of the tuberculosis problem in the

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community, but the 100 TU test produced responses in an unexpectedly large segment (approximately 37 percent in each race). Since 1947, other evidence suggests that many reactions to the larger doses of tuberculin may be "nonspecific" and that Muscogee County lies in an area in which the frequency of these "nonspecific" responses may be especially high (*2*).

It seemed almost incredible that among young children in Muscogee County a level of tuberculous infection could exist as high as that indicated by the combined percentages of the two doses of tuberculin. However, only one course of action appeared appropriate on the basis of procedures then in use in BCG vaccination work: in addition to reactors to the 5 TU test, the large group reacting to the 100 TU test was considered ineligible for vaccination. Thus, only 56 percent of the white and 37 percent of Negro children were eligible for vaccination. These 4,839 children—3,766 white and 1,073 Negro—were principally in the lower school grades, 73 percent were under 12 years of age, and the average age was 9.6 years. This study group was divided by a type of alternation free of individual bias in such a way as to ensure two comparable groups, consisting of 2,498 vaccinated and 2,341 nonvaccinated controls.

Table 1. *Prevaccination tuberculin sensitivity of Muscogee County school children, to 5 and 100 tuberculin units,[1] spring 1947, by race*

Race	Total tested		Reactors[2] to—		Nonreactors to 100 TU	Total reactors to 5 and 100 TU
			5 TU	100 TU		
	Number	Percent	Percentages			
White	7,767	100.0	7.6	36.4	56.0	44.0
Negro	3,495	100.0	25.8	37.6	36.6	63.4

[1] 5 tuberculin units (TU)=0.0001 mg. PPD; 100 tuberculin units (TU)=0.002 mg. PPD.
[2] 5 mm. or more of induration.

About 6 months after vaccination, 70 percent of the vaccinated children were retested with tuberculin through visits to all schools except those in remote rural locations. The nonreactors to 100 TU were revaccinated (8 percent). Because of the short time interval since the prevaccination testing, it was assumed that allergy in the vaccinated group represented only the effect of BCG and that similar tests in the control group were unnecessary.

Early in 1950 the tuberculosis control program in Muscogee County was extended through a mass survey which offered an X-ray film of the chest, a tuberculin test, and vaccination with BCG to the population of the community, including neighboring Russell County, Ala. The tuberculin testing in 1950 was conducted without reference to the results of the 1947 school vaccination program: the nurses read-

ing the test were unaware of which children had participated in the earlier study. Thus, prevaccination tuberculin testing for the 1950 program furnished, as an objective byproduct, observations on the tuberculin sensitivity of the children included in the 1947 study group. Later matching of the records from the two programs provided the data for the present paper on the allergy of those vaccinated and those designated as controls in 1947.

In this connection, it may be mentioned that use of the same type of alternation as in 1947 for selecting vaccinated and controls among the nonreactors excluded the 1947 control group from vaccination in the 1950 program. Members of the 1947 vaccinated group who did not react to 5 TU in 1950 were revaccinated.

Table 2. *Extent of retesting of vaccinated and control groups 6 months and 3 years after vaccination (Muscogee County school children 1947 and 1950)*

Race	Number in BCG study		Extent of retesting							
			Vaccinated group						Control group	
	Vaccinated group	Control group	At 6 months		At 3 years		Both times		At 3 years	
			Number	Percent	Number	Percent	Number	Percent	Number	Percent
White	1,948	1,818	1,327	68.1	1,138	58.4	842	43.2	1,102	60.6
Negro	550	523	391	71.1	308	56.0	236	42.9	277	53.0

Approximately 70 percent of the 1947 study group was reached in the 1950 tuberculosis survey. However, failure to receive a tuberculin test or to report for reading of the test, or conflicting data between the 1947 and 1950 records reduced to 57 percent the group on which data are available for this analysis. Table 2 shows by race the proportions of the vaccinated and control groups on which tuberculin data are available at 6 months and 3 years.

Materials and Methods

Tuberculin Testing

In the 1947 prevaccination tests and in the 6 months postvaccination tests, 0.0001 mg. PPD (5 TU) followed by 0.002 mg. PPD (100 TU) was employed, and the reactions were read at 48 hours. Measurement in millimeters of the transverse diameter of erythema and of the palpable induration, and a description of the density of the induration were recorded. The PPD, identified as lot number RT XVIII, was obtained from the Danish State Serum Institute through Dr. Johannes Holm.

Three years after vaccination, only the 5 TU test was used and the European practice of reading at 72 hours was employed. The

reading procedure was the same except that erythema was measured and recorded only in the absence of induration and more careful attention was given to the recording of cases of very small induration. The stock material was Danish PPD, lot RT XIX–XX–XXI, the successor to RT XVIII in the International Tuberculosis Campaign.

Vaccination

BCG vaccine for the program was obtained from Dr. S. R. Rosenthal of the Tice Laboratory, Chicago. Rosenthal's multiple puncture method, 3 rows of 10 punctures each, was applied on the deltoid surface of the left arm. Dr. Rosenthal personally instructed the field teams in methods of handling the vaccine and in using the multiple puncture technique. Five lots of vaccine were used—designated 811K, 811L, 812E, 812L, and 813E by the Tice Laboratory—each stated to contain 15 mg. of BCG organisms per milliliter. Refrigerated air shipments were made weekly to Columbus, and the vaccine was kept cold until opened for use in the schools on the third and fourth days after preparation.

Personnel

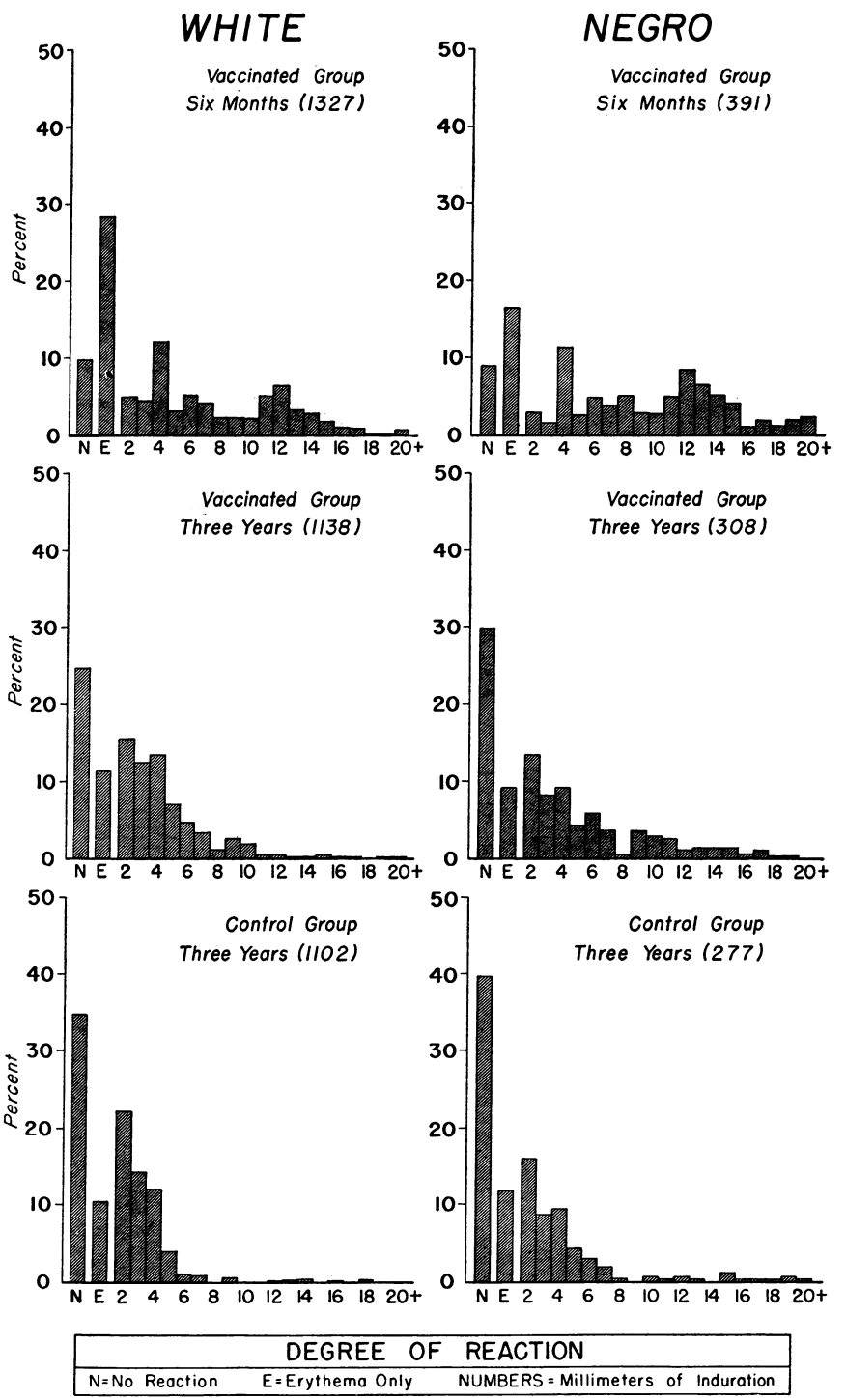
The initial testing and vaccination procedures in 1947 were performed by three Public Health Service teams of a doctor and a nurse. Most of the vaccinations were done by the doctors. Postvaccination observations were performed by Public Health Service nurses especially trained and experienced in tuberculin testing. It is believed that a considerable degree of uniformity was achieved in carrying out the field operations.

Results

Post vaccination allergy is usually reported simply in terms of the frequency of tuberculin conversions, that is, the percent reacting to the same tuberculin test or tests used to select persons for vaccination. Such summarization is clearly inadequate, as recent reports from the international counterpart of this office, the Tuberculosis Research Office of the World Health Organization have shown (*3*). Figure 1 and appendix table 1, therefore, present in detail the Muscogee County data, showing the reactions to the 5 TU test in the vaccinated group at 6 months and 3 years, and in the control group at 3 years. In addition, the extent of low grade allergy to this test possessed by each group before vaccination is given in the appendix table.

Tuberculin Allergy in the Vaccinated

As shown in the chart, the sizes of the 5 TU postvaccination reactions at 6 months are spread rather broadly over the scale from no reaction at all to those measuring 20 mm. or more of induration. At 3 years the reactions tended to be much smaller, with very few as



Distributions of the vaccinated and control groups by degree of reaction to 5 tuberculin units for tests at 6 months and at 3 years (appendix table 1).

large as 10 mm. and many measuring only 2 to 4 mm. in diameter. These numerous small indurated reactions at the 3-year observation may reflect the special care taken then to note and record them, and a considerable proportion of the "erythema only" observations in the 6-month data may represent small indurations not noted at that time. As summarized in table 3, it is clear that the degree of tuberculin sensitivity of the vaccinated apparently never reached a high level and that it declined very markedly.

Table 3. *Sensitivity to 5 tuberculin units (0.0001 mg. PPD) among vaccinated persons and nonvaccinated control persons at specified periods, by race (Muscogee County school children, 1947 and 1950)*

Degree of reaction	White					Negro				
	Vaccinated group			Control group		Vaccinated group			Control group	
	Tuberculin tested at					Tuberculin tested at				
	Origin	6 months	3 years	Origin	3 years	Origin	6 months	3 years	Origin	3 years
Percentage										
No reaction	83.7	9.7	24.5	83.8	34.3	85.5	9.0	29.9	81.7	39.7
Erythema only or induration less than 5 mm.	16.3	49.4	52.9	16.2	58.6	14.5	32.0	39.6	18.3	45.5
Induration 5–9 mm.	-------	16.8	18.9	-------	6.3	-------	19.2	17.9	-------	9.4
Induration 10 mm. or more	-------	24.0	3.7	-------	.8	-------	39.9	12.7	-------	5.4
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Induration 5 mm. or more	-------	40.8	22.6	-------	7.1	-------	59.1	30.5	-------	14.8
Any reaction	16.3	90.3	75.5	16.2	65.7	14.5	91.0	70.1	18.3	60.3
Number tested	[1] 1,948	1,327	1,138	[1] 1,818	1,102	550	391	308	[1] 523	277

[1] Includes unknown (nonreactors to 100 TU); percentages are based upon total known.

Six months after vaccination, when nearly the optimum degree of allergy might be expected, 90 percent of the white children showed some reaction to the 5 TU test, but more than half of these reactions were either of "erythema only" or induration less than 5 mm. in diameter. Only 41 percent had reactions of 5 mm. or more of induration. By the end of 3 years the percent having some reaction was 75, with only 23 percent with 5 mm. or more of induration. Before vaccination 16 percent had shown some reaction, mostly of erythema only.

Tuberculin Allergy in the Controls

While the results in the vaccinated group were unexpected because of the low level of allergy revealed, the findings among the controls were surprising because of the remarkable degree of sensitivity acquired in 3 years: among unvaccinated children, nonreactors 3 years previously to 100 TU and not subject to unusual conditions of tuber-

culous exposure, 66 percent showed some reaction to 5 TU. Though most of these responses were small, 7 percent of the group showed reactions of 5 mm. or more of induration. On the whole, the allergy of the control group was quite similar to that for the vaccinated.

Correlation of Allergy at 6 Months and 3 Years in the Vaccinated

Although the decline of allergy in the vaccinated is apparent from a comparison of the 6-month and 3-year distribution of the reactions, additional details on the nature of the change may be obtained by examining the reactions of the children retested at both 6 months and 3 years. The correlation of the tuberculin responses at the two periods is shown in appendix table 2 for each race and is presented in percentage form in table 4 for the white group.

Table 4. *Tuberculin sensitivity observed 3 years after vaccination among vaccinated persons subdivided according to their degree of reaction at 6 months, 5 tuberculin units used in both tests; sensitivity in control group at 3 years shown for comparison (Muscogee County white school children, 1947 and 1950)*

Degree of reaction at 6 months	Total		Degree of reaction at 3 years					
	Number	Percent	No reaction	Erythema only or induration < 5 mm.	Induration 5–9 mm.	Induration 10 mm. or more	Induration 5 mm. or more	Any reaction
			Percentages					
No reaction	78	100.0	42.3	51.3	6.4	0.0	6.4	57.7
Erythema only or induration less than 5 mm	406	100.0	32.0	58.1	8.4	1.5	9.9	68.0
Induration 5–9 mm	145	100.0	17.9	57.2	22.1	2.8	24.8	82.1
Induration 10 mm. or more	213	100.0	11.7	43.7	33.8	10.8	44.6	88.3
Total vaccinated	842	100.0	25.4	53.7	17.0	3.9	20.9	74.6
Total control group	1,102	100.0	34.3	58.6	6.3	0.8	7.1	65.7

There is a clear cut correlation between the responses at 3 years and those at 6 months. The percent with 5 mm. or more induration at 3 years ranges from 6 percent for those with no reaction at 6 months to 45 percent for those who showed 10 mm. or more induration at 6 months.

The loss of allergy, however, is quite apparent and it is most extreme among those who had the largest reactions at 6 months. Reactions at 3 years were equal to or greater than their 6 month counterparts in only 11 percent of the reactions measuring 10 mm. or more, 25 percent of the reactions of 5–9 mm. induration, and 68 percent of the reactions of small induration or erythema only. While not explicitly shown, only 37 percent of the persons who might be regarded as "reactors" (5 mm. or more of induration) at 6 months showed that much allergy at 3 years.

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An important finding from table 4 is that both the vaccinated who showed no reaction and those who showed very little response at 6 months had virtually the same degree of allergy at 3 years as the control group.

Allergy Among Those Revaccinated at 6 Months

Of special interest are 68 children included in the 3-year tests who were among the 119 white children revaccinated at 6 months when they failed to show reactions of at least 5 mm. to 100 TU. This group showed much less sensitivity at 3 years than those who had not been revaccinated. They had, in fact, about the same sensitivity as the control group; 68 percent showed some reaction and only 10 percent showed reactions of 5 mm. or more of induration.

Summary and Discussion

The results presented in this paper must be judged in the light of two important, basic, and very general considerations. First, the fundamental relationship between allergy to tuberculin and immunity to tuberculosis is still a highly controversial matter. It follows, therefore, that there is no scientific basis for judging the immunological significance of BCG induced tuberculin allergy, whether it be sensitivity to a low or to a high dose of tuberculin. Second, purely empirical criteria of tuberculin sensitivity are still being used in all practical BCG programs both for selecting eligibles for vaccination and for measuring the effect of vaccination. Substantial modification of these criteria since the beginning of the Muscogee County program in 1947 obviously has important implications with respect to the interpretation of the findings reported here.

Although there was not unanimity of opinion, eligibility for BCG vaccination up until 1948 had generally been based on failure to react to 100 to 250 TU, and acceptable postvaccination allergy had been the acquisition of sufficient allergy to react to one or the other of these fairly large doses of tuberculin. During the last few years, along with increasing evidence of the "nonspecific" character of reactions to the larger doses of tuberculin, there has been a reduction in the doses used in practical BCG work. In 1950, at its 5th session, the Expert Committee on Tuberculosis of the World Health Organization recommended that a single 5 TU dose be used in mass campaigns to select candidates for vaccination (*4*). The same year Holm, Technical Director of the International Tuberculosis Campaign, says in his second annual report: "One should not be satisfied with the vaccination unless there is a high degree of allergy, which means a typical tuberculin reaction to a small dose of tuberculin (e. g. 5 TU)" (*5*).

It is not likely that all workers in the field of BCG vaccination would agree with the recommendations of the WHO Expert Committee

or with Holm's view that satisfactory postvaccination allergy should be a typical reaction to 5 TU. With respect to the latter, it is evident from the available reports on postvaccination allergy that such a high degree of tuberculin sensitivity has rarely been obtained in BCG programs in the past. On the other hand, information from the Tuberculosis Research Office of the World Health Organization indicates that such results can be obtained: almost 100 percent of several thousand Danish children have reactions larger than 5 mm. of induration to the 5 TU dose both 10 weeks and 1 year after vaccination with Danish vaccine given by the intradermal method (*6*).

It is against this background that the postvaccination tuberculin sensitivity in the Muscogee County program must be examined. The school children vaccinated in 1947 were selected according to the then current criterion that they not react to 100 TU. Post vaccination testing in 1950 was done according to a new criterion—5 TU—the one actually used in expanding the Muscogee County program and to revaccinate those who had been vaccinated in 1947. The results are clear: most of the children vaccinated in 1947 failed to show the level of tuberculin sensitivity required. Only 41 percent of the white children had reactions measuring 5 mm. or more of induration 6 months after vaccination and this percentage dropped to 23 by the end of 3 years. Even this finding must be tempered by the fact that 7 percent of a comparable group of unvaccinated controls also attained that degree of allergy at 3 years. Fairly similar results were obtained on the Negro children in the community and, taking both white and Negro children together, about 75 percent of the persons vaccinated in 1947 were revaccinated in 1950.

In terms of postvaccination tuberculin allergy the 1947 BCG vaccination program in Muscogee County cannot be regarded as fulfilling current criteria widely used throughout the world. Only time and study of the development of tuberculosis in vaccinated and unvaccinated control groups can be expected to show both the protective value of BCG and its relation to tuberculin allergy.

In its broad implications, the Muscogee County vaccination program must be recognized as one carried out in an area in which a very large proportion of the school age population shows reactions to the higher doses of tuberculin. The significance of that fact cannot be judged at the present time. Nevertheless, after 3 years the unvaccinated control group of children showed a distribution of reactions to the 5 TU test that must be regarded as reflecting the acquisition of a substantial amount of low grade tuberculin allergy, which would undoubtedly have been more clearly brought out had 100 TU postvaccination tests been given. Thus both the vaccinated and control children were subjected for 3 years to whatever factor is responsible in the locality for the remarkably high prevalence of high dose tuberculin sensitivity.

Speculations as to the effect of superimposing this factor upon BCG induced allergy might include an hypothesis that the allergy of the vaccinated would be increased—a type of "booster dose" effect. Quite the opposite effect might also be postulated, that the factor producing high dose allergy tends to reduce BCG allergy, a type of desensitization. It is of more than academic interest that in the paper which follows in this issue, the authors find it acceptable to postulate just such a desensitizing effect in order to explain differences in naturally acquired tuberculin sensitivity occurring in certain populations in India.

From the viewpoint of obtaining sound scientific knowledge on the production of tuberculin allergy by BCG vaccination, the present study brings out the tremendous importance of having equivalent observations on a comparable control group of unvaccinated persons. In the absence of the controls, it is almost certain that most of the reactions in the vaccinated would have been attributed to BCG. An entirely different conclusion is quite admissible: that there was very little residual effect of BCG after 3 years, for BCG cannot be considered as essential in producing the major part of the allergy observed.

ACKNOWLEDGMENTS

Any undertaking of this magnitude involves the cooperation and contribution of many public health administrators and research workers. The project was given approval and support by the County Health Commissioner, Dr. J. A. Thrash, and by the Director of the Division of Tuberculosis Control of the Georgia State Health Department, Dr. H. C. Schenck. Both the 1947 and 1950 field programs were accomplished under the general guidance of Dr. George W. Comstock, Tuberculosis Control Officer for Muscogee County. The field operations were under the direction of Dr. Leroy E. Bates in 1947 and under Dr. Harold S. Barrett in 1950. The nursing activities in the large 1950 survey were under the direction of Helen Gertz. The statistical processing of the data collected has been accomplished under the direction of Teresa E. Roache. This report has been prepared with the guidance and assistance of Shirley H. Ferebee and Dr. Carroll E. Palmer.

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(*5*) General Introduction to Field Operations. Prepared by International Tuberculosis Campaign Headquarters. Second Annual Report of the International Tuberculosis Campaign, Copenhagen, 1950, p. 123.

(*6*) Personal communication from Carroll E. Palmer.

Appendix table 1. *Distributions of the vaccinated and control groups by degree of reaction to 5 tuberculin units (0.0001 mg. PPD) for tests at origin, at 6 months and at 3 years after vaccination, by number and percent, for each race (Muscogee County school children, 1947 and 1950)*

Degree of reaction to 5 tuberculin units	Number of persons					Percentages				
	Vaccinated group			Control group		Vaccinated group			Control group	
	Tuberculin tested at					Tuberculin tested at				
	Origin	6 months	3 years	Origin	3 years	Origin	6 months	3 years	Origin	3 years
	WHITE									
No reaction	1,621	129	279	1,513	378	83.7	9.7	24.5	83.8	34.3
Erythema only	240	376	128	222	113	12.4	28.3	11.3	12.3	10.3
Induration (mm.)										
2	40	63	178	41	244	2.1	4.8	15.6	2.3	22.2
3	27	58	143	19	157	1.4	4.4	12.6	1.1	14.2
4	8	159	153	11	132	.4	12.0	13.4	0.6	12.0
5		42	81		44		3.2	7.1		4.0
6		68	53		11		5.1	4.7		1.0
7		55	38		9		4.1	3.3		.8
8		29	14		-------		2.2	1.2		-------
9		29	29		5		2.2	2.5		.5
10		28	20		-------		2.1	1.8		-------
11		68	4		-------		5.1	.4		-------
12		85	4		1		6.4	.4		.1
13		43	2		2		3.2	.2		.2
14		36	2		3		2.7	.2		.3
15		23	4		-------		1.7	.4		-------
16		12	2		1		.9	.2		.1
17		11	2		-------		.8	.2		-------
18		3	-------		2		.2	-------		.2
19		2	1		-------		.2	.1		-------
20		3	-------		-------		.2	-------		-------
21		1	-------		-------		.1	-------		-------
22		-------	1		-------		-------	.1		-------
23		1	-------		-------		.1	-------		-------
24		-------	-------		-------		-------	-------		-------
25		2	-------		-------		.2	-------		-------
31		1	-------		-------		.1	-------		-------
Total	[1] 1,948	1,327	1,138	[1] 1,818	1,102	100.0	100.0	100.0	100.0	100.0
	NEGRO									
No reaction	470	35	92	425	110	85.5	9.0	29.9	81.7	39.7
Erythema only	52	64	28	57	32	9.5	16.4	9.1	11.0	11.6
Induration (mm.)										
2	17	11	41	19	44	3.1	2.8	13.3	3.7	15.9
3	6	6	25	10	24	1.1	1.5	8.1	1.9	8.7
4	5	44	28	9	26	.9	11.3	9.1	1.7	9.4
5		10	13		12		2.6	4.2		4.3
6		19	18		8		4.9	5.8		2.9
7		15	11		5		3.8	3.6		1.8
8		20	2		1		5.1	.6		.4
9		11	11		-------		2.8	3.6		-------
10		11	9		2		2.8	2.9		.7
11		20	8		1		5.1	2.6		.4
12		33	3		2		8.4	1.0		.7
13		25	4		1		6.4	1.3		.4
14		20	4		-------		5.1	1.3		-------
15		16	4		3		4.1	1.3		1.1
16		4	2		1		1.0	.6		.4
17		7	3		1		1.8	1.0		.4
18		4	1		1		1.0	.3		.4
19		7	1		2		1.8	.3		.7
20		4	-------		-------		1.0	-------		-------
21		2	-------		1		.5	-------		.4
22		1	-------		-------		.2	-------		-------
26		2	-------		-------		.5	-------		-------
Total	550	391	308	[1] 523	277	100.0	100.0	100.0	100.0	100.0

[1] Including unknown (nonreactors to 100 TU); percentages are based upon total known.

Appendix table 2. *Correlation of degree of reaction to 5 tuberculin units 3 years after vaccination with degree of reaction 6 months after vaccination (Muscogee County school children, 1947 and 1950)*

Degree of reaction at 6 months	Total	Degree of reaction at 3 years						
		No reaction	Erythema only	Induration, in millimeters				
				2–4	5–7	8–9	10–14	15 or more
	WHITE							
No reaction	78	33	6	34	5			
Erythema only	228	83	33	90	15	2	4	1
Induration (mm.):								
2–4	178	47	27	86	15	2		1
5–7	104	20	8	49	20	5	1	1
8–9	41	6	5	21	5	2	1	1
10–14	171	23	18	62	40	20	7	1
15 or more	42	2	4	9	7	5	11	4
Total	842	214	101	351	107	36	24	9
	NEGRO							
No reaction	22	5	4	9	1	1	2	
Erythema only	34	17	3	9	3			2
Induration (mm.):								
2–4	37	15	6	13			1	2
5–7	28	8	4	10	6			
8–9	17	7	1	6	3			
10–14	67	15	6	21	9	4	9	3
15 or more	31	4	1	3	6	4	9	4
Total	236	71	25	71	28	9	21	11

Erratum

In the article "Body Mechanisms in Progressive Tuberculosis," by Howard Payne, M.D., Public Health Reports, vol. 66, no. 40, October 5, 1951, references to "agglutination" in the last paragraph on page 1266 should have been "percipitation."

Research Contributions of BCG Vaccination Programs,

II. Tuberculin Sensitivity at Different Altitudes of Residence

By LeRoy E. Bates, M.D., Thøger Busk, Cand. Act., and Carroll E. Palmer, M.D.*

For many decades, the tuberculin test has enjoyed a respectability shared by few other medical tests. Most of this respect has been justified by the test's usefulness in the diagnosis of clinical cases, its contribution to epidemiological knowledge, its value in the construction of control programs, and more recently, its integration into the vast international BCG vaccination campaigns of prevention. On the basis of such extensive application it might seem obvious that the tuberculin test is so firmly grounded on facts that even the most careful scientific scrutiny will not destroy its basic principles.

As the applications of the test widen, however, evidence occasionally appears which challenges the traditional theories regarding the test. Up to the present time, thorough investigation of these threats has contributed to our understanding of the tuberculin test and has further reinforced its fundamental principles. An outstanding illustration occurred in recent years. The reliability of the test was seriously questioned when it was proved that pulmonary calcification commonly accepted as evidence of healed tuberculosis was found in many persons who failed to react to tuberculin. The subsequent finding that most of these cases react to histoplasmin was followed by strong epidemiological, clinical, and pathological evidence that infection with the fungus *Histoplasma capsulatum*, as well as tuberculosis, is an important cause of pulmonary calcification.

At the present time one of the most persistent threats to traditional tuberculin test theory concerns the specificity and stability of tuberculin reactions to high doses (100–250 TU) among persons negative to low doses (1–5 TU). In the first place, the prevalence of high dose reactors does not appear to be associated with other evidence of tuberculosis—neither morbidity, mortality, nor the frequency of low dose reactors (which has been uniformly interpreted as representing true tuberculous infection within communities). Second, high dose reactions often differ in appearance from low dose reactions: they are pale, soft, diffuse, and, in general, less intense reactions. Third, the

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size of high dose reactions is reported to vary considerably in short periods of time, more so than the size of reactions to low doses of tuberculin. And finally, the prevalence of high dose reactors, though apparently unassociated with other indications of tuberculous infection, is surprisingly related to geographic factors. A large body of evidence from studies of student nurses (*1*) and school children (*2*) in widely separated areas of the United States points to this relationship.

The accumulating evidence of uncertainties in the interpretation of high dose reactions has rather serious implications. To explain this devious behavior of high dose reactions, we must do one of two things. We must sharpen our concepts of the relationship between tuberculin sensitivity and the microbiology of the tubercle bacillus, the mechanics of infection, and the physiological processes of the body that relate to allergy production; or, we must postulate the existence of an infecting agent which produces low-grade sensitivity to tuberculin, and is extremely prevalent in some areas and rare in other areas.

It is interesting that a problem so fundamentally related to tuberculin testing should appear after more than five decades of continuous application of the test, but it is not astonishing. Visualization of this problem depended on techniques and opportunities which have been at hand for only a few years. Since the problem involved a quantitative comparison of tuberculin test results in different areas, it depended on the development of standardized tuberculin products and techniques skillfully and uniformly applied by experienced personnel. It awaited, as well, the creation of research agencies with national and even international scope and the integration of research with broad national and international tuberculosis control programs.

Background of Present Study

The investigation presented here was suggested by information in reports from the Joint Enterprise [1] BCG vaccination teams working in India. Unusually high proportions of persons were reported to be reacting strongly to the second (higher) dose of tuberculin. Because a similar very disturbing situation with respect to high dose reactors had previously been observed in Louisiana, in contrast to certain other areas in the United States, the Tuberculosis Research Office of the World Health Organization recognized an opportunity to pursue this problem of geographic variations in tuberculin sensitivity on a much wider basis.

An experienced BCG research team composed of a doctor, nurse, and statistician was assigned the task of collecting precise, quantitative information on tuberculin sensitivity in various places in India. An

[1] A cooperative enterprise between Scandinavian Relief Organizations and UNICEF with technical assistance from WHO.

area around the Indian town of Darjeeling was selected as the locale of one investigation. A portion of the findings of the investigation in this area is reported here since it demonstrates remarkable differences in tuberculin sensitivity at different altitudes of residence. The nature of these differences indicates that the problem of varying patterns of tuberculin sensitivity is broader than originally supposed and invites serious thought and continued investigation.

Location of Study

Darjeeling is an Indian town situated high in the Himalayan foothills about 300 miles north of Calcutta. It is within a few air miles of the borders of Nepal, Bhutan, and Tibet and lies at the end of a mountain ridge which drops away precipitously from the town in three directions. From the valley beds at 1,000 feet to the crest of the ridge at 7,000 feet the mountain side is dotted with tea plantations. Laborers and their families on nine of these tea gardens were tuberculin tested and vaccinated with BCG.

The map shown in figure 1 gives the altitude curves for the region and shows the positions of eight of the nine tea gardens chosen for testing. The ninth garden, Ambootia, lies about 15 air miles to the south. The gardens, belonging to two tea companies are listed in table 1, along with their altitudes based on the level at which the majority of the workers live. Although their altitudes differ widely eight of them lie almost entirely within a circle having a radius of only 3 air miles.

Population Chosen for Study

The population chosen for testing was composed of tea-garden workers and their families. About one-third of the total population in each tea company was tested. In one company, persons from 0 to 20 years of age were selected for study; in the other, persons from 5 to 25 years of age were selected. In general, male and female children work from the age of 12; consequently nearly half the population are workers. The population and the number tested in each garden are given in table 1. The age distribution is given in table 2. The number of males and females was approximately equal.

As far as is known, tests were given to practically everyone in the age groups chosen for testing, and about 90 percent of the tests were completed (table 1).

The majority of the tea laborers are Nepalese people of Mongolian race. They are small in stature and work hard from a very young age. Their faiths vary. About 13 percent are Buddhists; a very few are Christians or Moslems. The rest, the major portion, are Hindus who, however, apparently do not adhere so strictly to vegetarianism as do the Hindus in other parts of India.

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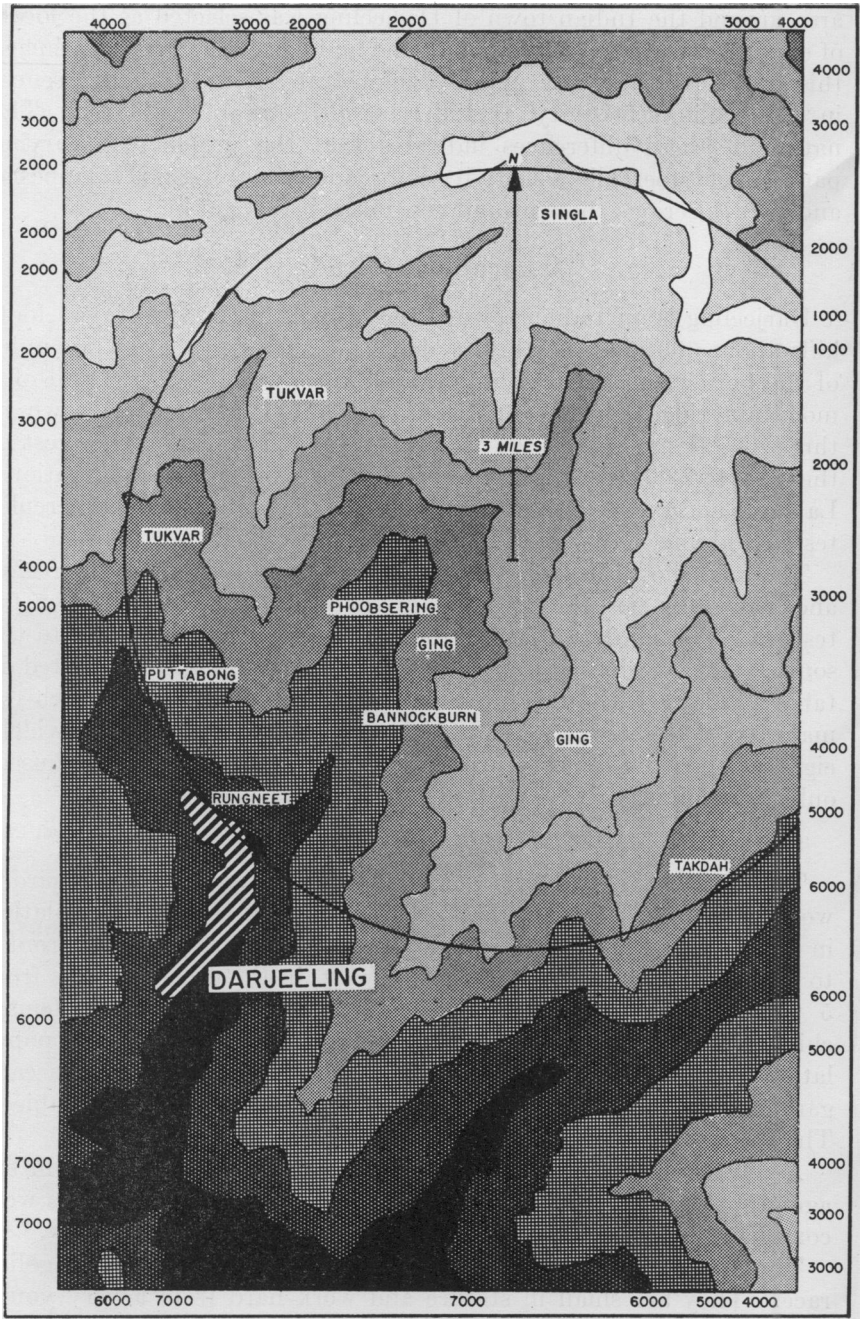

Figure 1. Topographic map showing the location and elevation of eight of the nine tea gardens where tuberculin tests were given, Darjeeling, 1949–50.

Table 1. *Extent of tuberculin testing in tea gardens grouped by altitude, Darjeeling, 1949–50*

Garden [1]	Altitude above sea level (feet)	Population [2]	Persons 0–24 years		
			Tested with 1 TU	Testing completed [3]	Percent testing completed
Low altitude					
Singla	2,000	1,553	499	395	79
Ging, lower	2,600	1,366	399	394	99
Amboottia	3,000	1,911	597	554	93
Tukvar, lower	3,300	1,019	325	286	88
Total		5,849	1,820	1,629	90
Middle altitude					
Bannockburn	4,500	909	347	333	96
Tukvar, upper	4,600	1,710	545	513	94
Ging, upper	4,800	726	212	204	96
Takdah	5,000	1,641	508	458	90
Total		4,986	1,612	1,508	94
High altitude					
Phoobsering	5,500	993	307	268	87
Puttabong	5,500	913	374	309	83
Rungneet	6,500	513	185	150	81
Total		2,419	866	727	84
Total for all gardens		13,254	4,298	3,864	90

[1] Puttabong, Tukvar, and Singla tea gardens belong to 1 tea company while the 6 other tea gardens belong to a second tea company.
[2] Based on census taken within 6 months of testing. Division of population on upper and lower parts of Tukvar and Ging is estimated.
[3] 10 and/or 100 TU tests were given if required and all reactions were read within 4 days.

Frequently four to six persons live in a hut 10 x 20 feet which is usually built directly on the ground with walls of plank or of bamboo plastered with earth. They have roofs of thatch or of corrugated iron sheeting. The huts are dark and poorly ventilated and very often their small windows are deliberately covered by the occupants. During the very heavy rains that occur in the monsoon seasons, the houses afford but moderate protection.

Table 2. *Number of persons tested with 1, 10, and 100 TU, by age and altitude of residence, Darjeeling, 1949–50*

Age in years	1 TU			10 TU			100 TU		
	Altitude								
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Reactions read:									
0–4	160	171	109	138	160	98	125	157	90
5–9	328	329	166	254	264	136	208	249	122
10–14	520	547	224	369	382	155	233	319	127
15–19	487	356	205	322	206	109	147	141	98
20–24	226	163	77	96	79	36	34	40	28
Total	1,721	1,566	781	1,179	1,091	534	747	906	465
Reactions not read	99	46	85	36	42	24	56	16	30
Total tested	1,820	1,612	866	1,215	1,133	558	803	922	495

The majority of the tea laborers go barefooted most of their lives. Hookworm and respiratory ailments are common. Malaria is said to be frequent at the low altitude, but rare above 3,500 to 4,000 feet. In the six gardens belonging to one of the tea companies, the crude death and birth rates for the year 1948 were 2 and 4 percent, respectively.

Materials and Methods

The work of the team was carried out in accordance with a protocol carefully prepared in advance. In addition, all necessary supplies were new and carefully cleansed, packed, and sterilized in the headquarters office in Copenhagen.

The tuberculin used for testing was part of a lot of purified protein derivative (No. RT XIX–XX–XXI) prepared by the State Serum Institute at Copenhagen. Three different doses were given as follows: the 1 unit test (0. 00002 mg.) was given to all persons in the study group. The 10 unit test (0.0002 mg.) was given only to those persons who had reactions of less than 6 millimeters of induration to the 1 TU test. The 100 unit test (0.002 mg.) was given only to persons who had reactions of less than 6 millimeters of induration to the 10 TU test. The dilutions of tuberculin were carefully prepared in the field from a concentrated stock solution using pipettes. In no instance were the dilutions used longer than 16 days after preparation.

The tuberculin tests were given intradermally in the upper half of the volar surface of the forearm. One-tenth of a cubic centimeter of diluted tuberculin was carefully measured from a tuberculin syringe for each injection. Only reactions which were read at 3 or 4 days are used in this study. The widest transverse diameter of both erythema and induration was measured in millimeters, and the density of the reactions was graded in four qualitative categories. Both the team doctor and the nurse gave injections but all reactions were read by the team doctor. The entire testing and vaccination program in the Darjeeling area was carried out in the period from December 27, 1949, to February 8, 1950.

Findings

Detailed data on the results of tuberculin testing are given in appendix table 1. Text tables 3 and 4 and figures 2, 3, and 4 are presented to summarize the data and to bring out the striking differences in the patterns of tuberculin sensitivity that are associated with altitude of residence and age of the tested populations.

The section to the left in figure 2 shows, separately for each altitude of residence, the change with age in the percentages of the population designated as positive reactors to the 1 TU dose of tuberculin, according to the usual criteria of more than 5 mm. of induration. Among

Table 3. *Percentage of reactors [1] among nonreactors to previous tuberculin test, by age and altitude of residence, Darjeeling, 1949–50*

Age in years	1 TU			10 TU			100 TU		
	Altitude								
	Low	Medium	High	Low	Medium	High	Low	Medium	High
0–4	8.1	5.3	4.6	2.2	1.2	0.0	16.8	5.1	3.3
5–9	19.8	15.5	13.3	9.1	2.7	4.4	44.7	22.1	10.7
10–14	26.7	26.7	28.1	33.6	15.2	9.7	72.5	40.8	19.7
15–19	32.9	40.4	45.4	50.9	30.6	9.2	89.8	64.5	31.6
20–24	57.1	50.9	51.0	64.6	49.4	22.2	94.1	75.0	46.4

[1] A reactor is defined as a person with a reaction of more than 5 mm. induration.

children under 5 years of age, in all altitudes, about 5 percent had reactions of more than 5 mm. of induration to this first low dose of PPD. For the age group 20 to 25 years, the frequency of such reactions increases to about 50 percent. While there are some systematic fluctuations in the age curves it is obvious that altitude of residence does not markedly influence the frequency of reactions ordinarily designated as positive to the 1 TU test.

Table 4. *Combined distributions of reactions to 1, 10, and 100 TU, by age and altitude of residence (percentages [1])*

Mm. of induration	Dose (TU)	Low altitude			Middle altitude			High altitude		
		Age in years								
		0–9	10–14	15–24	0–9	10–14	15–24	0–9	10–14	15–24
0–5	100	51.6	13.4	2.6	72.7	36.9	12.0	81.3	52.1	30.1
6 and over	100	26.9	35.3	24.7	13.4	25.3	24.1	6.6	12.8	16.1
6 and over	10	5.6	24.6	32.1	1.9	11.1	20.1	2.3	6.9	6.6
6–11	1	6.1	12.5	27.1	3.4	11.3	22.2	4.0	5.4	11.0
12 and over	1	9.8	14.2	13.5	8.6	15.4	21.6	5.8	22.8	36.2
Total		100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

[1] The percentages are calculated under the assumption that the reactions not read were distributed in the same way as those read.

The middle section of figure 2 shows the age curves of percentage of reactors (more than 5 mm. of induration) to 10 TU among those not designated as positive reactors to 1 TU. Similar age curves for the 100 TU dose of tuberculin, among nonreactors to 10 TU, are shown in the right hand section of the figure. The enormous influence of altitude of residence on the frequency of reactors to the two larger doses of tuberculin is clearly apparent. As illustrations it may be noted that for the age group 20–25, less than 25 percent of the population living at altitudes above 5,500 feet react to 10 TU, while more than 60 percent of those of similar age react if they live at elevations less than 3,300 feet; among nonreactors to 10 TU, 20-25 years of

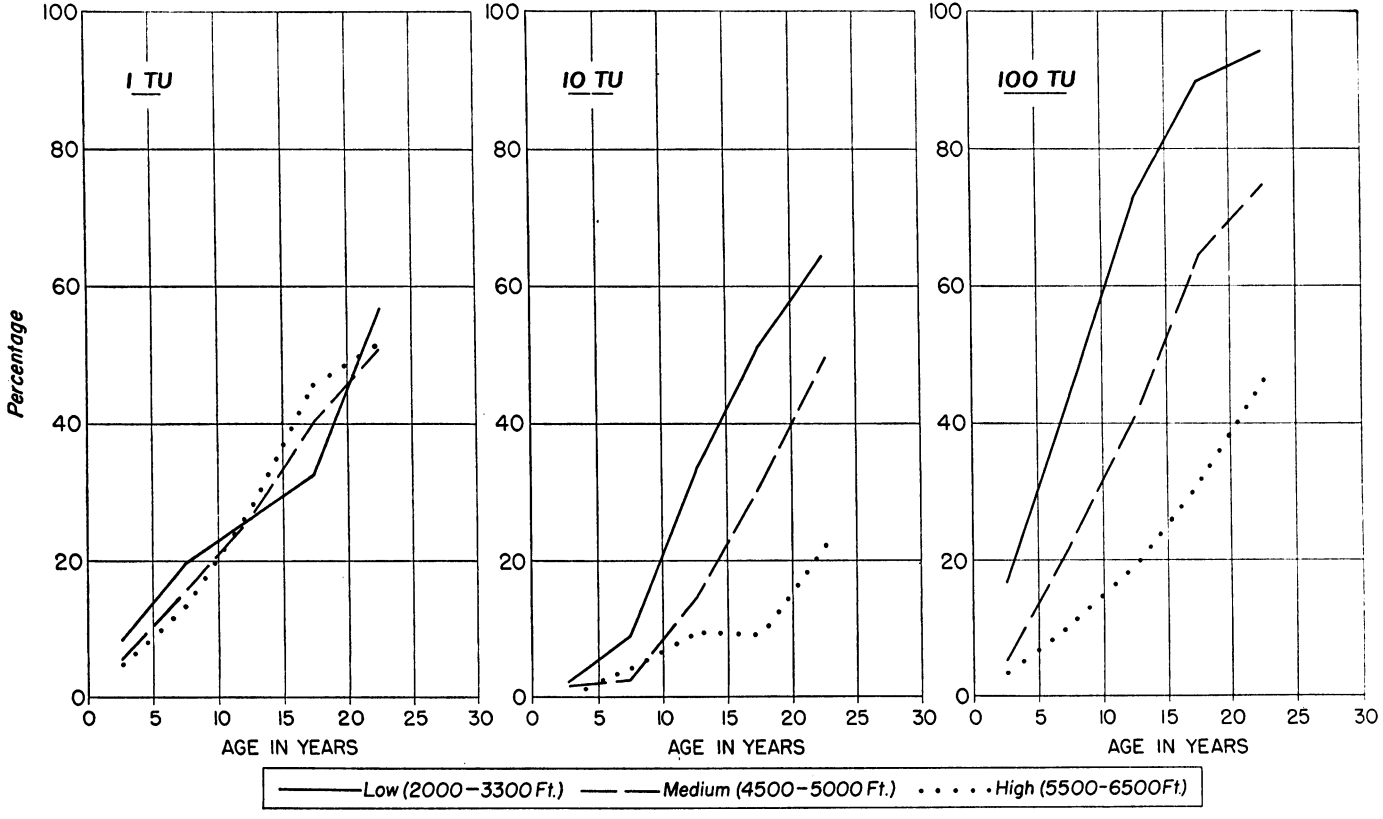

Figure 2. Percentage of reactors among nonreactors to previous tuberculin test, by age and altitude of residence, Darjeeling, 1949–50.

age, 46 percent react to 100 TU if they live above 5,500 feet while nearly 95 percent react if they live below 3,300 feet.

In general, it is evident that there is a marked association between altitude of residence and the frequency of reactors to the 10 and 100 TU doses of tuberculin: the higher the place of residence above sea level the lower the prevalence of reactors to these doses. Further, with increase in the age of the persons tested there are very sharp increases in the frequencies of these reactors, especially of those to the 100 TU test.

Only part of the important differences in the pattern of tuberculin sensitivity according to altitude are brought out by a consideration simply of the prevalence of "positive" reactors to the three graded doses of tuberculin. In figure 3, histograms illustrating the frequency distributions of the measured sizes of reactions are shown for five age groups, for each dose of tuberculin, and for the three altitude groups. Inspection of these 45 histograms reveals several significant facts. First, although the percentages of reactors designated as positive to the 1 TU test are not very different for residents at different altitudes, the distributions of sizes of reactions show sharp contrasts. The characteristic tendency may be noted by comparing, for example, the distribution of reactions to 1 TU for 15–19-year-old children living at high and low altitudes. The distribution for the low altitude group is J-shaped; the most frequent class is that having reactions of 0–2 mm. in diameter, with a gradual decrease in frequency of the larger reactions. Very few children have reactions of 15 mm. or more. The distribution for the high altitude group shows an entirely different pattern. While the 0–2 mm. class contains the greatest number of cases, the remainder of the distribution appears to have the form of a "normal" frequency curve with its mode for the class having reactions 12–14 mm. in diameter. A substantial proportion of the children have reactions measuring 15 mm. or more in diameter. Although it is less apparent for the younger children, there is a general tendency for the size of the 1 TU reactions to be somewhat smaller the nearer the residence of the child is to sea level.

Comparison of the distributions of 100 TU reactions for children 15–19 years of age living at the high and low altitudes reveals a complete reversal in the pattern of sizes of reactions. For this dose of tuberculin the J-shaped form of distribution is found for the high altitude residents while a distribution somewhat similar to a normal curve is found for those living at the low altitude. Thus, it appears that with increasing age there is a tendency for J-shaped distributions to appear for 1 TU tests at the low altitude and for 100 TU tests at the high altitude. Frequency distributions resembling the form of normal curves tend to appear for 1 TU tests at the high altitude and for 100 TU tests at the low altitude.

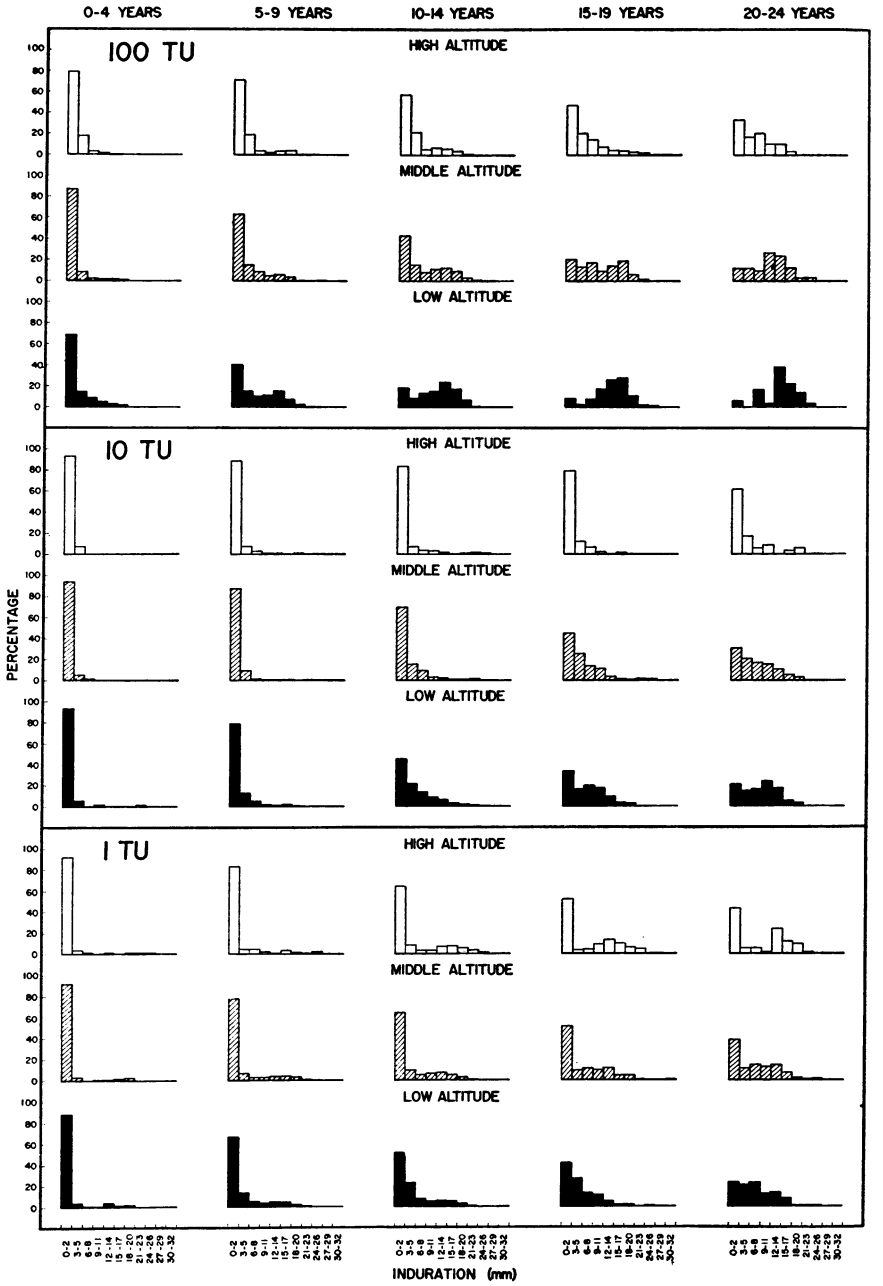

Figure 3. Percentage distribution of reactions in millimeters of induration to each dose of tuberculin by age and altitude of residence, Darjeeling, 1949–50 (derived from appendix table 1).

The detail presented in figure 3 suggests another significant fact: the form of the distribution of 1 TU reactions may be useful in predicting the pattern of sensitivity to the higher doses of tuberculin. Thus it appears that the presence of many 3–5-mm. reactions to the 1 TU test, as revealed in the J-shaped distributions for low-altitude residents, is associated with the finding of many reactors to the higher doses of tuberculin. Relatively few small reactions to 1 TU, as observed among high-altitude residents, indicate the absence of many reactors to the higher doses of tuberculin. This finding probably means that fairly strong reactors to the higher doses, even 100 TU reactors, tend to reveal their presence by showing small reactions below the size usually regarded as positive to the less concentrated doses of tuberculin.

In order to show altitude differences for the whole range of tuberculin sensitivity, table 4 and figure 4 present distributions of the frequency of reactions according to five broad classes for three age groups for each altitude of residence. For these distributions reactions to the 1 TU are subdivided arbitrarily into those measuring more than 11 mm. of induration and those 6–11 mm. in diameter; all reactions larger than 5 mm. to the 10 TU are placed in a single class; 100 TU reactions are subdivided into two classes, those above 5 mm. in diameter and those showing 5 mm. or less of induration.

Differences between the distributions are apparent to some extent in the youngest age group but these differences are in general limited to the frequencies of 100 TU reactions. With increasing age, however, a gradual shift from smaller to larger reactions occurs and at the same time the various altitudes develop singularly diverse patterns. Maximum differences in the pattern of tuberculin allergy may be noted by comparing the upper and lower histograms shown at the right side of figure 4. In the upper histogram, for the group 15–24 years of age living at an altitude above 5,500 feet, the distribution is clearly U-shaped. There are many large reactions to 1 TU, many small reactions less than 6 mm. to 100 TU, and few of those representing intermediate degrees of allergy, particularly reactions to 10 TU. The lower histogram, for 15-24-year olds living less than 3,300 feet above sea level, is strikingly different. It is unimodal, with most of the population showing the intermediate degrees of tuberculin sensitivity, the most frequent reactions being those to the 10 TU test.

Discussion

The population dealt with in this investigation comprised groups of persons comparable with respect to race, age, sex, and major habits of life. Persons in the age groups studied were exceedingly restricted in their travel. As far as could be determined by inquiry the preva-

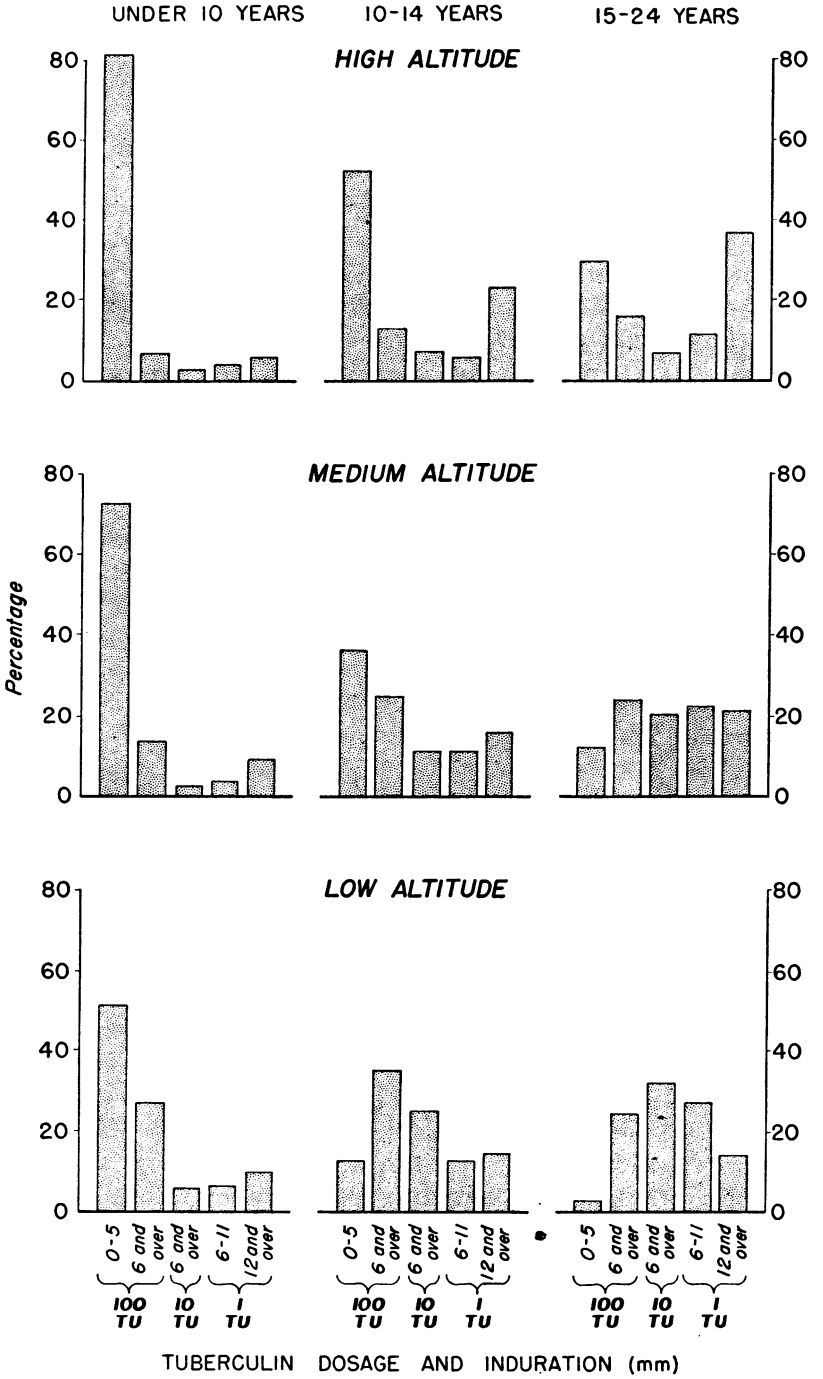

Figure 4. Combined distributions of reactions to 1, 10, and 100 tuberculin units by age and altitude of residence, Darjeeling, 1949–50.

lence of tuberculosis was the same throughout the whole area. Consequently, so far as is known the difference in altitude of residence is the most obvious single variable in the population.

Many factors—constitutional make-up of the people, dosage and mechanism of infection, inherent characteristics of the infecting organism—may be pertinent in attempts to explain the observed variations in tuberculin sensitivity. It is possible that environmental factors, such as climate, affect the quantity or the quality of infecting organisms or that different modes of infection may occur at different altitude levels. It is conceivable also that fundamental differences in allergic response to tuberculous infection may occur in persons living at different altitudes. But considerations of how these factors could produce such large variations predominantly in sensitivity to the higher doses of tuberculin without producing greater change in sensitivity to the low dose or without an obvious influence on tuberculosis morbidity and mortality, become so complex that one is tempted to seek other and perhaps simpler explanations of this phenomenon.

The common occurrence of cross reactions among skin testing antigens, and the similarity between the pattern of sensitivity produced in cases of known cross reactions and the pattern of sensitivity found in the low altitude at Darjeeling (and in certain other regions) suggest that some of the sensitivity to tuberculin observed in these locations may be due to infection with an agent other than the ordinary human strain of tubercle bacillus.

Furthermore, the patterns of tuberculin sensitivity observed at the high and low altitudes in Darjeeling resemble those found in student nurses in widely separated geographic areas in the United States, for example, in Philadelphia and Louisiana. Since regional differences in the United States could not be adequately explained by differences in the prevalence of tuberculosis morbidity and mortality, the possibility of a nonspecific infection by some agent closely resembling and antigenically related to the tubercle bacillus was offered as an explanation (*1*). It is possible that the same type of nonspecific infection may exist in the Darjeeling area.

In an area where a nonspecific agent is present it is reasonable to expect that some persons will be infected with both the tubercle bacillus and the "nonspecific" agent. If it is supposed that the tuberculin sensitivity of such individuals is increased by the double infection, there should be relatively more large reactions (a higher level of sensitivity) to the low dose of tuberculin in areas where the nonspecific infecting agent is most prevalent, other factors in the two communities being the same. In this study the opposite is true; there are relatively more large low dose reactions at the higher altitudes where the nonspecific theory assumes that there are fewer non-

specific reactions. To conform to the patterns of sensitivity observed in Darjeeling, the nonspecific theory must now postulate that infection with both the nonspecific agent and the tubercle bacillus does not result in higher sensitivity but, in fact, results in diminished sensitivity. The idea that persons first infected and sensitized by the nonspecific agent resist further development of allergy upon subsequent infection with the tubercle bacillus or that persons first infected and sensitized by the tubercle bacillus are partially desensitized by subsequent infection with the nonspecific agent, merits consideration in the light of the experience in Darjeeling.

While the nonspecific theory is offered as the most probable explanation of these findings, the main purpose of this paper is to report that remarkable real differences in the patterns of tuberculin sensitivity do occur in a homogeneous population living in close proximity but at different altitudes. The people studied live within a few air miles of one another in a type of mountainous country where transportation difficulties and economic conditions are such that most of the people spend their lives very close to their homes on the tea plantations. Yet, within such a homogeneous group, great differences are found in tuberculin sensitivity at different altitudes of residence.

These findings are not explained adequately by any of our traditional notions of how tuberculous infection and allergy production operate. A proper explanation would contribute to the value of the tuberculin test and might lead to substantial contributions in the general field of allergy.

Summary

A homogeneous population of about 4,000 persons, 0–25 years of age, from tea plantations of a small mountainous area around Darjeeling in northern India, was tested serially with graduated doses of 1, 10, and 100 units of tuberculin. Very marked differences in the pattern of allergy were shown to exist at different altitudes of residence. While the frequency of reactions designated as positive to the 1 unit test were approximately the same at all altitudes, reactions to this dose tended to be larger at the high altitude. With the 10 and 100 unit tests a remarkably higher proportion of reactors occurred at the lower altitudes.

The hypothesis is offered that these variations in sensitivity at different altitudes, resembling those found in different areas in the United States, are due to the presence in the lower altitudes of a very prevalent, nonpathogenic organism, closely related to the tubercle bacillus, which produces sensitivity to tuberculin. It is further speculated that infection with both the nonspecific organism and the tubercle bacillus results in a lower level of sensitivity than that produced by the tubercle bacillus alone.

The material also suggests that the general form of a 1 unit distribution of reactions may be useful in predicting the pattern of sensitivity to the higher doses of tuberculin.

The investigation illustrates the opportunities that exist for wider geographic research and the value of carefully planned and executed studies which take advantage of these opportunities.

ACKNOWLEDGMENTS

Grateful acknowledgments are made to various members of the staff of the Tuberculosis Research Office, World Health Organization, and of the Field Research Branch, Division of Chronic Disease and Tuberculosis, Public Health Service, who offered suggestions and technical assistance in the preparation of the report. The investigation was especially dependent on Birthe Johansen, Tuberculosis Research Office nurse, for careful and untiring work in the collection of the original field data, and on Dr. Lydia B. Edwards, Chief of Field Operations, Tuberculosis Research Office, for valuable assistance in the planning and conduct of the study. We are indebted to the managers of the tea estates and the Indian authorities for their generous cooperation and in many instances their active assistance.

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(*2*) Tuberculosis studies in Muscogee County, Ga. IV. To be published.

Appendix table 1. *Distributions of tuberculin reactions in millimeters of induration, by age, dose of tuberculin, and altitude of residence, Darjeeling 1949–50*

Mm. induration	Low altitude					Middle altitude					High altitude				
	Age in years														
	0–4	5–9	10–14	15–19	20–24	0–4	5–9	10–14	15–19	20–24	0–4	5–9	10–14	15–19	20–24
100 TU dose															
0–2	86	84	44	12	2	137	157	139	30	5	71	86	75	47	10
3–5	18	31	20	3		12	37	50	20	5	16	23	27	20	5
6–8	11	21	31	11	6	3	21	26	25	4	2	4	6	14	6
9–11	6	23	34	25	1	2	11	34	13	10	1	2	8	7	3
12–14	2	31	53	38	13	2	14	37	19	9		3	7	4	3
15–17	2	14	37	39	7	1	8	26	25	5		4	3	3	1
18–20		4	13	15	4			5	7	1			1	2	
21–23			1	3	1			2	2	1				1	
24–26				1			1								
Total	125	208	233	147	34	157	249	319	141	40	90	122	127	98	28
10 TU dose															
0–2	128	200	166	106	20	150	232	266	91	24	91	120	129	86	22
3–5	7	31	79	52	14	8	25	58	52	16	7	10	11	13	6
6–8		12	51	64	16	2	3	35	28	13		3	5	7	2
9–11	2	4	31	56	22		1	9	22	12		1	4	2	3
12–14		2	22	27	16		1	7	6	8		1	2		
15–17		4	9	10	5			1	2	4				1	1
18–20		1	7	7	3		1	2	1	2		1	1		2
21–23	1		2				1	4	2				2		
24–26			2						2				1		
Total	138	254	369	322	96	160	264	382	206	79	98	136	155	109	36
1 TU dose															
0–2	141	218	266	200	51	157	256	349	180	62	100	137	143	106	33
3–5	6	45	115	127	46	5	22	52	32	18	4	7	18	6	4
6–8	1	17	40	62	50		8	28	38	23	1	7	6	8	4
9–11	1	11	25	54	27	1	8	34	34	20		3	6	18	1
12–14	6	15	29	25	31	1	11	40	40	23	1	1	14	26	18
15–17	2	14	27	7	18	3	13	26	15	11		5	16	20	9
18–20	3	6	15	9	1	4	9	14	15	3	1	2	12	12	7
21–23		2	2		1		2	4	1	1	1	1	7	9	1
24–26				3	1					2	1	3	2		
27–29															
30–32			1						1						
Total	160	328	520	487	226	171	329	547	356	163	109	166	224	205	77

Incidence of Disease

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

Reports From States for Week Ended October 6, 1951

In reports of malaria, transmitted through the Kentucky State Health Department from two military establishments located in that State, it was shown that the first cases were recognized late in March in one establishment and late in April in the other. A peak in the number of cases reported was reached late in August in both establishments. Total cases reported from these sources in Kentucky since September 1 suggest a secondary peak late in September. The reports indicate that vivax infections only have been recognized.

For the current week the number of cases of malaria classified as civilian was 55 as compared with 47 for the previous week. Of the 55 cases, 25 were reported by Georgia, 22 by Wisconsin, 5 by Texas and 1 case each by Kentucky, Oregon, and California. The 440 cases of malaria from military establishments for the current week include 283 reported from New Jersey. A large proportion of the 283 cases are delayed reports according to information received from the New Jersey Department of Health.

Poliomyelitis incidence decreased 20 percent in the current week as compared with the previous week. The rate of decline at this period of 1951 is slightly more than it was in 1950. The cumulative total for the calendar year is now 22,791 as compared with 24,937 for the same period last year, and the cumulative total since the seasonal low week is 21,579 as compared with 23,806.

For the current week 33 States reported fewer cases than for the previous week, 5 reported no change, and 10 States reported 1 to 13 more cases. Wisconsin showed the largest numerical decrease from 102 cases for the week ended October 6 to 64 cases for the current week.

Epidemiological Reports

Gastroenteritis

Dr. R. F. Feemster, Massachusetts Department of Health, has reported an outbreak of gastroenteritis in a mental disease hospital in which the custard of a Boston cream pie was the vehicle of infection. This article of food was kept at room temperature about 3 hours

before serving. None was available for bacteriological examination.

Dr. M. Goodman, New York State Department of Health, has reported an outbreak of food intoxication in an institution, involving 56 patients and 31 of the personnel. Symptoms appeared 2 to 4 hours after eating a salad containing several sea foods, eggs, and mayonnaise. Of those eating the salad, 56 percent became ill, while the attack rate among those not eating the salad was 1.6 percent. *Staphylococcus aureus* and an organism having the characteristics of *Bacillus subtilis* were recovered from this article of food.

Dr. F. D. Yoder, Wyoming Health Officer, has reported an outbreak of staphylococcus food poisoning following the eating of chicken salad sandwiches at an auction sale. In the investigation by Dr. O. C. McCandless, it was found that 75 persons were ill, 28 of whom were hospitalized, out of a total of 500 to 600 who attended the sale. The food was prepared 24 hours before being eaten and was not refrigerated. *Staphylococcus aureus* was recovered from a specimen of the food.

Dr. G. W. Cox, Texas Health Officer, has reported a small outbreak of staphylococcus food poisoning in Travis County following the eating of chocolate eclairs. A hemolytic staphylococcus was recovered from eclairs collected from three sources—a home, the bakery, and the mix from which they were prepared.

Anthrax

Dr. L. L. Parks, Florida Board of Health, has reported a case of

Comparative Data for Cases of Specified Reportable Diseases: United States

[Numbers after diseases are International List numbers, 1948 revision]

Disease	Total for week ended—		5-year median 1946–50	Seasonal low week	Cumulative total since seasonal low week		5-year median 1945–46 through 1949–50	Cumulative total for calendar year—		5-year median 1946–50
	Oct. 13, 1951	Oct. 14, 1950			1950–51	1949–50		1951	1950	
Anthrax (062)	1	3	1	(1)	(1)	(1)	(1)	48	36	41
Diphtheria (055)	117	171	287	27th	[2] 960	1,347	2,421	[2] 2,968	4,475	7,031
Encephalitis, acute infectious (082)	18	27	19	(1)	(1)	(1)	(1)	835	763	515
Influenza (480–483)	245	734	734	30th	3,357	4,796	4,796	119,412	143,560	132,188
Measles (085)	1,212	698	779	35th	5,833	3,606	3,685	474,744	291,777	556,638
Meningitis, meningococcal (057.0)	58	69	58	37th	209	226	189	3,270	3,025	2,823
Pneumonia (490–493)	538	895	[3]	(1)	(1)	(1)	(1)	49,838	66,780	[3]
Poliomyelitis, acute (080)	1,016	1,596	1,122	11th	21,579	23,806	21,160	22,791	24,937	21,510
Rocky Mountain spotted fever (104)	8	10	8	(1)	(1)	(1)	(1)	310	441	526
Scarlet fever (050)[4]	567	659	873	32d	3,277	3,576	4,670	56,663	43,746	61,544
Smallpox (084)				35th		1	3	11	27	51
Tularemia (059)	12	6	15	(1)	(1)	(1)	(1)	536	745	784
Typhoid and paratyphoid fever (040, 041)[5]	78	76	76	11th	2,085	2,332	2,705	2,520	2,842	3,166
Whooping cough (056)	822	1,328	1,328	39th	1,651	2,905	2,905	55,426	100,100	78,899

[1] Not computed. [2] Deduction: District of Columbia, 1 case for week ended September 22. [3] Data not available. [4] Includes cases reported as streptococcal sore throath. [5] Includes cases reported as salmonellosis.

anthrax in a person, living in Broward County, who had skinned a cow. Laboratory test from the patient as well as examination of the organs of the cow revealed the presence of the organism. It is also reported that 100 cattle have died of anthrax in the same area of Florida. The human case was the first in the state of Florida since 1941, and the disease among animals had not been observed in the immediate area for a number of years.

Infectious Hepatitis

Dr. Goodman, New York State Health Department, reports the occurrence of infectious hepatitis in three members of a family consisting of five persons. The onsets were June 26, August 2, and September 7. The source of infection of the first case was not determined.

970389—51——3

Reported Cases of Selected Communicable Diseases: United States, Week Ended Oct. 13, 1951

[Numbers under diseases are International List numbers, 1948 revision]

Area	Diphtheria (055)	Encephalitis, infectious (082)	Influenza (480–483)	Measles (085)	Meningitis, meningococcal (057.0)	Pneumonia (490–493)	Poliomyelitis (080)
United States	**117**	**18**	**245**	**1,212**	**58**	**538**	**1,016**
New England	**1**		**1**	**138**	**2**	**21**	**14**
Maine	1			41		3	1
New Hampshire				3	1	1	
Vermont				12			
Massachusetts				58			3
Rhode Island				11	1		1
Connecticut			1	13		17	9
Middle Atlantic	**6**	**2**	**3**	**366**	**5**	**74**	**104**
New York	3	1	(1)	210	3		54
New Jersey	1	1	3	48	1	53	16
Pennsylvania	2			108	1	21	34
East North Central	**3**	**1**	**10**	**236**	**10**	**39**	**282**
Ohio	2			36	1		66
Indiana	1	1	7	10		1	12
Illinois			3	48	3	24	65
Michigan				69	6	14	75
Wisconsin				73			64
West North Central	**2**	**1**	**2**	**27**	**5**	**19**	**102**
Minnesota	1			1		2	30
Iowa				5	2		8
Missouri	1			3	1	1	16
North Dakota			2	8	1	14	4
South Dakota				1			3
Nebraska				3			17
Kansas		1		6	1	2	24
South Atlantic	**48**		**13**	**112**	**8**	**126**	**57**
Delaware							
Maryland				59		52	5
District of Columbia			1		1	17	1
Virginia	3			24		50	14
West Virginia	2			11	4		12
North Carolina	16			4			7
South Carolina	11		10			1	2
Georgia	13		2	9		6	10
Florida	3			5	3		6
East South Central	**28**	**2**	**2**	**46**	**18**	**41**	**94**
Kentucky	5			17	4	17	10
Tennessee	8	1		7	12		28
Alabama	15			8	2	5	14
Mississippi		1	2	14		19	42
West South Central	**26**		**108**	**26**	**4**	**153**	**115**
Arkansas	1		61	5	3	18	16
Louisiana	3					4	14
Oklahoma	5		47	1		16	29
Texas	17			20	1	115	56
Mountain	**3**		**66**	**142**		**20**	**96**
Montana				80			5
Idaho				5			13
Wyoming				2		2	15
Colorado	2		8	9		3	30
New Mexico				24		7	15
Arizona	1		58	7		8	11
Utah				15			16
Nevada							1
Pacific		**12**	**40**	**119**	**6**	**45**	**152**
Washington			18	25		1	10
Oregon			12	20	1	14	17
California		12	10	74	5	30	125
Alaska							
Hawaii			66	121			

[1] New York City only.
Anthrax: Massachusetts, 1 case.

Reported Cases of Selected Communicable Diseases: United States, Week Ended Oct. 13, 1951—Continued

[Numbers under diseases are International List numbers, 1948 revision]

Area	Rocky Mountain spotted fever (104)	Scarlet fever [1] (050)	Smallpox (084)	Tularemia (059)	Typhoid and paratyphoid fever [2] (040, 041)	Whooping cough (056)	Rabies in animals
United States	8	567		12	78	822	112
New England		44			2	59	
Maine						10	
New Hampshire		8				2	
Vermont		2				4	
Massachusetts		31			1	36	
Rhode Island		1			1		
Connecticut		2				7	
Middle Atlantic		67			8	144	21
New York		38				62	13
New Jersey		12				39	
Pennsylvania		17			8	43	8
East North Central		169			8	186	14
Ohio		56			5	56	4
Indiana		11			1	19	8
Illinois		33			2	38	
Michigan		56				36	
Wisconsin		13				37	2
West North Central		36		1	4	20	14
Minnesota		9				4	7
Iowa		5			1	1	1
Missouri		12		1	3	13	2
North Dakota		3					
South Dakota		2					
Nebraska							3
Kansas		5				2	1
South Atlantic	2	86		3	20	70	19
Delaware		2					
Maryland	1	9				16	
District of Columbia		6				1	
Virginia		9		1	5	5	
West Virginia		5				14	1
North Carolina	1	47		2	4	8	
South Carolina		4			6	6	9
Georgia		3			5	16	9
Florida		1				4	
East South Central	1	51		1	15	29	20
Kentucky		18			2	5	7
Tennessee		21		1	5	18	3
Alabama		12				5	4
Mississippi	1				8	1	6
West South Central		22		1	7	198	23
Arkansas		1		1	2	47	8
Louisiana		1			2	4	
Oklahoma		6			2	14	1
Texas		14			1	133	14
Mountain	5	12		6	7	41	
Montana		7				8	
Idaho		1				8	
Wyoming				2			
Colorado		2				2	
New Mexico					6	7	
Arizona		1			1	15	
Utah	5	1		4		1	
Nevada							
Pacific		80			7	75	1
Washington		7				7	
Oregon		10			1	3	
California		63			6	65	1
Alaska							
Hawaii		1					

[1] Includes cases reported as streptococcal sore throat.
[2] Includes cases reported as salmonellosis.

FOREIGN REPORTS

CANADA

Reported Cases of Certain Diseases—Week Ended Sept. 29, 1951

Disease	Total	Newfoundland	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia
Brucellosis	4						3		1		
Chickenpox	333	3		7	1	58	91	14	70	46	43
Diphtheria	6					4	2				
Dysentery, bacillary	70					5	3		57		5
German measles	53			4		18	4		4	14	9
Influenza	6			4				1	1		
Measles	321	26		33	1	54	46	24	7	53	77
Meningitis, meningococcal	11	2			1		3	4		1	
Mumps	185	5		1		28	78	10	8	28	27
Poliomyelitis	112			12	2	12	68	4	6	3	5
Scarlet fever	165			1	1	20	22	13	7	34	67
Tuberculosis (all forms)	212	9		4	31	88	12	21	13	4	30
Typhoid and paratyphoid fever	8					6	1				1
Venereal diseases:											
Gonorrhea	305	8		10	4	76	39	25	21	33	89
Syphilis	76	1		1	7	31	14	4	9	3	6
Primary	6					2		1	2	1	
Secondary	4					1			2	1	
Other	66	1		1	7	28	14	3	5	1	6
Whooping cough	173					56	46	6	36	22	7

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

The following reports include only items of unusual incidence or of special interest and the occurrence of these diseases, except yellow fever, in localities which had not recently reported cases. All reports of yellow fever are published currently.

Cholera

Burma. During the week ended October 6, 1951, eight cases of cholera were reported in the seaport of Tavoy.

Pakistan. Two imported cases of cholera were reported in Chittagong for the week ended October 6, 1951. These are the first cases since the middle of August.

Smallpox

Bechuanaland. During the month of August 1951, 17 cases of smallpox were reported in Districts of Bechuanaland.

Egypt. One case of smallpox was reported for the week ended September 29. The last previous case was for the week ended March 3.

India. Smallpox was reported in ports of India for the week ended October 6, as follows: Trichinopoly, 3 cases; Bombay, 2; and Vizagapatam, 1.

Indonesia. For the week ended September 29, nine cases of smallpox were reported in Surabaya, Java. For the week ended September 22, two cases each were reported in Balik Papan and Bandjarmasin, Borneo.

Iraq. A sharp increase was noted in the incidence of smallpox for the week ended October 6, when 34 cases were reported as compared with only one for the previous week.

Sierra Leone. Three cases of smallpox were reported for the week ended September 1.

Typhus Fever

Libya. For the week ended September 29, 1951, three cases of typhus fever were reported in Tripolitania.

Turkey. One case each of typhus fever was reported in Istanbul and Izmir for the week ended October 6.

Yellow Fever

Costa Rica. During the period September 29–October 6, 1951, three deaths from jungle yellow fever were reported in Alajuela Province. From the beginning of the outbreak to September 26, about 70 cases with 34 deaths, have been reported. The outbreak began in Limon Province and spread to the jungle areas of the Provinces of Alajuela and Heredia.

French West Africa. One suspected case of yellow fever was reported on October 10, in Bembereke about 340 miles north of Catonon, Dahomey. Another case was reported on September 16 in Dahomey at Parakou.

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