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Studies of Pulmonary Findings and Antigen Sensitivity Among Student Nurses

VI. Geographic Differences in Sensitivity to Tuberculin as Evidence of Nonspecific Allergy

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Evidence accumulated in recent years seems to indicate that the maximum critical dose of tuberculin for identifying persons who are or have been infected with tuberculosis lies in the neighborhood of .0001 mg. of standardized PPD or its equivalent. A few exceptions to this can be considered well established. For example, tuberculin sensitivity apparently wanes in old age, in the terminal stages of tuberculosis, and with some other active infections. Apart from such deviations, however, infected persons usually respond to a low dose of tuberculin.

As a corollary, considerable uncertainty has developed as to the interpretation of reactions elicited only with the higher doses of tuberculin, and during the last few years there has been a growing doubt as to the specificity of at least some of such responses. Actually, the literature on tuberculin testing contains a tremendous volume of material on the wide usage and general acceptance of the higher doses. In contrast, it contains little evidence to justify the use of such doses in testing human beings. Furthermore, much inconsistency in the application of tuberculin test results may be traced to the failure to distinguish and interpret properly high and low dose reactions. With the growing interest in BCG vaccination programs, and the dependence of such programs on the tuberculin test, the

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development of reliable criteria for separating specific from nonspecific responses to tuberculin has become a crucial problem in tuberculosis work.

Previous reports in this series have examined several aspects of this problem, and, though most of the evidence is indirect, the findings definitely support the view that different meanings must be attached to low in contrast to high dose tuberculin reactions. The present study represents further investigation of this question by a detailed analysis of geographic differences in tuberculin reactions among student nurses.

Material

The observations are derived from the comprehensive program for the study of tuberculosis in student nurses, initiated in 1943 by the National Tuberculosis Association, the Public Health Service, and a number of schools of nursing in 10 widely separated metropolitan areas in the United States. A full description of the basic material, techniques, and classifications, will be found in the earlier reports (*1–5*). The immediately preceding report in the series (*5*) contains a fairly detailed consideration of theoretical aspects of interpreting distributions of tuberculin sensitivity.

The nurses were tuberculin tested at regular 6-month intervals by one team of carefully trained personnel of the Public Health Service who took all possible measures to secure and maintain uniform techniques. The group under study constitutes a homogeneous population: young, white girls of approximately the same age, all taking nurses' training. Differences in tuberculin sensitivity which might appear in such a population from different parts of the United States would thus be expected to indicate geographic variations. In reports IV and V, (*4, 5*) in which the nurses were subdivided according to place of training, differences between metropolitan areas were interpreted as geographic. Since, however, a more precise method would be to compare tuberculin sensitivity of longtime residents in different areas, the present analysis is based on a subdivision by residence rather than place of training.

The tuberculin used (PPD–S) was prepared at the Henry Phipps Institute in Philadelphia. All nurses were given a first dose of 0.0001 mg. Those who failed to give a reaction of at least 10 mm. of firm induration were administered a second dose of .005 mg. Reactions were read at 48 hours and the widest transverse diameters of induration and erythema were measured and recorded in millimeters. In addition, all indurations of 5 mm. or more were graded into four qualitative categories: I represented typical, well-circumscribed firm reactions; IV soft, questionable indurations; and II and III, intermediate types.

In this report, the classification of reactors into four groups differs in some respects from that used in earlier reports. Those who reacted to the first dose with at least 5 mm. of induration, description I, II, or III, are classified as "1st dose reactors." Those who did not, but who reacted to the 2d dose with at least 5 mm. of induration, any description, are classified as 2d dose reactors: these are specified as "strong 2d dose reactors" when the induration was 10 mm. or more, description I or II; otherwise they are specified as "slight 2d dose reactors." The fourth class, "nonreactors," are those who showed only erythema or less than 5 mm. of induration to the 2d dose. The two groups designated here as 1st dose reactors and strong 2d dose reactors were defined precisely as "definite" and "questionable" reactors, respectively, in the previous studies.

Subdivision of the entire range of tuberculin sensitivity into four simple classes was considered sufficient for the broad epidemiological purposes of the present study, since it appears appropriate to assume that 1st dose reactors and nonreactors correspond with "positive" and "negative" tuberculin reactors. This assumption is in accordance with the traditional view that "positive" reactors are persons who have been infected with the tubercle bacillus, and "negative" reactors are persons who have not been infected. Lying between the two extremes in the scale of tuberculin sensitivity, 2d dose reactions constitute a critical group because of the uncertainty as to their relation to tuberculous infection and disease. Further, in accordance with evidence presented in earlier reports the very substantial cutaneous responses classified as strong 2d dose reactions merit separate consideration.

The present analysis is limited to the records of the nurses with a "lifetime" residence in one place, the requirement being that they had spent at least five-sixths of their lives in the same place. They were allocated by States, and within each State according to three types of community (1930 census), viz: cities of more than 10,000 inhabitants, cities of 10,000 inhabitants or less, and "farms." Great precautions were taken to include in the last group only nurses who had lived on farms practically all of their lives. The study is also limited to nurses who were tested within 12 months after admission to training. Most of these, however, were tested within the first 2 months and a very high proportion within 6 months of the time they entered training. Tests made this early in training will not be affected very much either by the nurses' exposure to tuberculosis in the hospital or in the wider environment of the city in which the hospital of training is located. These criteria have reduced the group about 16,000 nurses, included in the previous two reports, to a total of 10,058. Classified according to State of lifetime residence (appendix table), nurses from all the States and the District of Columbia are represented. The geographic distribution is very uneven—80 percent of all the nurses originated from 8 States which contributed at least several hundred nurses each, while another 8 States each contributed between 100 and 200 observations. From a total of 29 States more than 30 observations were available.[1]

Results

Differences Among States

The 29 States having at least 30 observations have been arranged according to the percentages of each of thee definitions of reactors (table 1). Variation in the percentage of the 1st dose reactors is apparent—from 4.6 to 27.8 percent. Six States show rates between 5 and 10 percent, 10 between 10 and 15, and 9 between 15 and 20 percent, and, in a general way, the distribution of percentages follow a monomodal frequency curve, without obvious breaks.

Table 1. *Arrays of 29 States by frequencies of 1st dose reactors, strong 2d dose reactors, and all 2d dose reactors among lifetime residents*

(1) 1st dose reactors		(2) Strong 2d dose reactors		(3) All 2d dose reactors	
State	Percentage	State	Percentage	State	Percentage
Alabama	4.6	Indiana	0.0	Indiana	5.6
North Dakota	5.9	Iowa	.8	New Jersey	17.6
Minnesota	7.1	Wisconsin	1.4	Iowa	17.8
Wyoming	8.6	New Jersey	1.4	Wisconsin	18.8
Nebraska	9.0	North Dakota	2.0	New York	19.1
Wisconsin	9.0	Minnesota	2.4	Wyoming	20.0
Mississippi	9.3	New York	2.5	South Dakota	20.7
Ohio	10.0	Ohio	2.6	Michigan	21.5
Kansas-Missouri	10.2	Wyoming	2.9	North Dakota	21.8
Michigan	10.7	South Dakota	3.4	Ohio	24.9
Iowa	11.0	Pennsylvania	3.4	Pennsylvania	25.0
West Virginia	11.3	California	3.6	California	25.0
Virginia	12.1	West Virginia	3.8	Minnesota	25.2
Colorado	12.5	D. C	3.8	Colorado	28.0
Louisiana	12.6	Michigan	4.8	Illinois	29.7
South Dakota	12.6	Maryland	5.4	Nebraska	30.3
North Carolina	13.3	Colorado	5.4	Virginia	31.8
Maryland	15.4	Illinois	5.4	D. C	32.7
California	15.7	Kansas-Missouri	6.0	Maryland	33.0
New Jersey	16.2	Virginia	6.1	West Virginia	34.0
Illinois	16.2	Nebraska	7.9	Kansas-Missouri	35.9
D. C	17.3	Texas	9.7	North Carolina	51.1
Florida	17.5	North Carolina	11.1	Texas	51.4
Pennsylvania	17.7	Florida	11.7	Florida	51.4
New York	17.8	Oklahoma	11.8	Oklahoma	52.9
Arkansas	19.4	Mississippi	13.1	Arkansas	54.8
Oklahoma	20.6	Alabama	14.0	Louisiana	58.2
Texas	25.0	Louisiana	15.5	Alabama	65.1
Indiana	27.8	Arkansas	16.1	Mississippi	66.4

Study of the location of the 29 States according to increasing percentage of 1st dose reactors fails to reveal any very systematic grouping of large geographically contiguous areas. Low rates tend to predominate for States in the north and west and high rates tend to be

[1] The District of Columbia is counted as a State, and Kansas and Missouri as one State, since for technical reasons they were combined when the material was tabulated.

found in the industrial centers of the east and some of the southern States, but there is considerable irregularity in the location of high and low prevalence areas of 1st dose reactors. In some respects, however, the frequency of 1st dose reactors appears to conform with other indices of the prevalence of tuberculosis. Actually, although the details are not given here, there is a substantial though not very high correlation between tuberculosis mortality rates for the white population in the 29 States and the percentage of 1st dose reactors.

Striking differences between reactors to the 1st and 2d doses of tuberculin may be observed by referring again to table 1 where the 29 States are listed according to increasing percentages of strong 2d dose (column 2) and all 2d dose reactors (column 3). First, there is obviously a close association in the frequency of the two classes of 2d dose reactors and almost none apparent between either of them and 1st dose reactors. Actually, the correlation coefficient between strong and slight 2d dose reactors equals 0.9; that between 1st dose and strong 2d dose, 0.04; that between 1st dose and slight 2d dose, −0.06.

Second, a very significant epidemiological observation may be noted from the arrangement of the 29 States in increasing order of frequency of either strong or all 2d dose reactors. All 8 southern States in the group furnish the highest percentages and there is an obvious break or discontinuity in the distributions. The frequencies of all 2d dose reactors vary from 5 to 65 percent, but no States have percentages between approximately 35 and 50. The 8 southern States all show rates above 50, and the other States rates below 35 percent. For strong 2d dose reactors there are only 2 States, Texas and Nebraska, which fall within a range of from about 6 to 11 percent. Excluding the exceptions mentioned, the southern States have rates from 11 to 16 and the other States rates below about 6 percent.

In addition to the sharp contrast between the 8 southern and the 21 other States, detailed study of columns 2 and 3 of table 1 shows that the highest rates outside of the South, i. e., percentages of around 4 to 6 for strong 2d dose and from 25 to 35 percent for all 2d dose reactors, tend to include two groups of States, one in about the center of the country, and another along the middle of the Atlantic seaboard. There may be some question of the appropriateness of attempting to select a geographically distinct group which showed intermediate rates of 2d dose reactions, but it has seemed worth while to do so even though the selection must be arbitrary.

Table 2 shows the results of separating the 29 States into three major groups, each representing fairly distinct geographic areas. This division fails to show any difference in the distribution of percentages for 1st dose reactors, while the percentages of both strong and slight 2d dose reactors in the "South" and in the "other States" are distinctly separated, with the other areas in an intermediate

Table 2. *Distribution of 8 Southern,[1] 7 Central and mid-Atlantic,[2] and 14 other[3] States according to the frequencies of 1st dose reactors, strong 2d dose reactors, and all 2d dose reactors among lifetime residents*

1st dose reactors					Strong 2d dose reactors					All 2d dose reactors				
Percentage	All States	Southern	Central and mid-Atlantic	Others	Percentage	All States	Southern	Central and mid-Atlantic	Others	Percentage	All States	Southern	Central and mid-Atlantic	Others
Total	29	8	7	14	----------	29	8	7	14	----------	29	8	7	14
0.0–4.9	1	1	----	----	0.0–1.9	4	----	----	4	0.0–9.9	1	----	----	1
5.0–9.9	6	1	1	4	2.0–3.9	10	----	2	8	10.0–19.9	4	----	----	4
10.0–14.9	10	2	4	4	4.0–5.9	4	----	2	2	20.0–29.9	10	----	1	9
15.0–19.9	9	2	2	5	6.0–7.9	3	----	3	----	30.0–39.9	6	----	6	----
20.0–24.9	1	1	----	----	8.0–9.9	1	1	----	----	40.0–49.9	----	----	----	----
25.0–29.9	2	1	----	1	10.0–11.9	3	3	----	----	50.0–59.9	6	6	----	----
	----	----	----	----	12.0–13.9	1	1	----	----	60.0–69.9	2	2	----	----
	----	----	----	----	14.0–15.9	2	2	----	----	----------	----	----	----	----
	----	----	----	----	16.0–17.9	1	1	----	----	----------	----	----	----	----

[1] Includes: Alabama, Arkansas, Florida, Louisiana, Mississippi, North Carolina, Oklahoma, Texas.
[2] Includes: Colorado, District of Columbia, Kansas-Missouri, Maryland, Nebraska, Virginia, West Virginia.
[3] Includes: California, Illinois, Indiana, Iowa, Michigan, Minnesota, New Jersey, New York, North Dakota, Ohio, Pennsylvania, South Dakota, Wisconsin, Wyoming.

position. In spite of the fact that many of the percentages were computed from quite small numbers, and must be subject to substantial random errors, a fairly well circumscribed area supplies all the high frequencies of 2d dose reactors. Thus it appears that the States covering, roughly, the southeastern quarter of the country constitute an area in which tuberculin sensitivity is distinctly different from that found elsewhere.

Differences Among Zones

In the preliminary survey of the data, States contributing only very small numbers of observations were omitted, but for a further examination it was considered expedient to use a geographic division in which all of the States were grouped into the 10 zones as shown in figure 1. This grouping, which is largely arbitrary, was determined mainly by three considerations: a natural division into areas of a fairly regular shape, a reasonably large number of observations of roughly the same order of magnitude in each area, and contrast between areas with respect to 2d dose sensitivity. These principles were followed as far as possible, but it became desirable to include two numerically small zones both with between 100 and 200 observations. Each of the 10 zones is believed to be fairly homogeneous with respect to high-dose tuberculin sensitivity, although individual States within the same zone differ somewhat. A systematic analysis of these differences is not promising, however, because of the very small number contributed by many States. In fact, each of the 10 zones is dominated by one State.

Figure 1. Division of the United States into 10 zones, showing the numbers of lifetime residents tested and the percentage classified as strong 2d dose reactors in each zone.

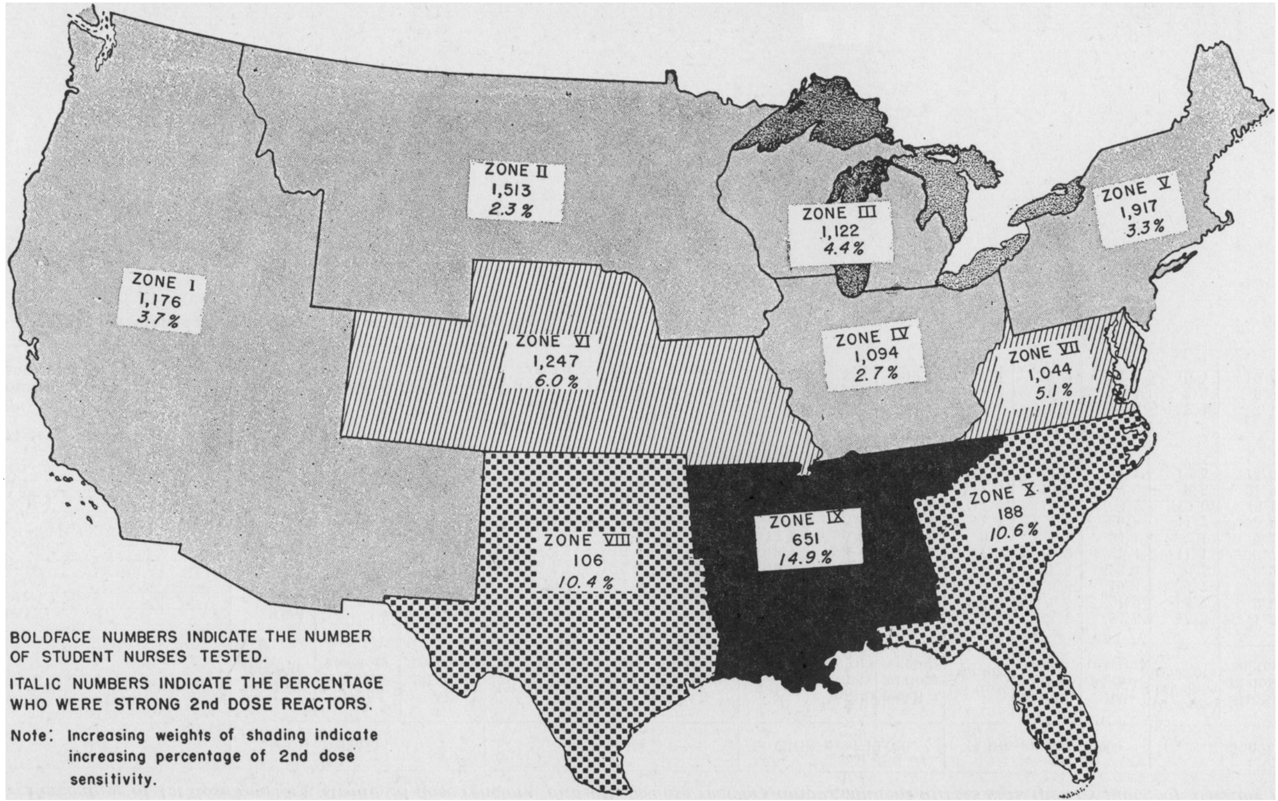

Table 3. *Percentage of 1st dose reactors, strong 2d dose reactors, and all 2d dose reactors among student nurses classified by place of lifetime residence*

Zones and States	Total			All cities			Cities over 10,000			Cities under 10,000			Farm		
	1st dose reactors	Strong 2d dose reactors	All 2d dose reactors	1st dose reactors	Strong 2d dose reactors	All 2d dose reactors	1st dose reactors	Strong 2d dose reactors	All 2d dose reactors	1st dose reactors	Strong 2d dose reactors	All 2d dose reactors	1st dose reactors	Strong 2d dose reactors	All 2d dose reactors
I (Calif., etc.)	16.4	3.7	24.8	16.5	3.9	24.0	16.1	4.0	23.8	18.5	3.6	24.6	15.3	1.6	31.5
II (Minn., etc.)	7.7	2.3	24.0	8.6	2.1	22.3	10.4	2.7	22.7	6.9	1.5	21.9	5.7	2.9	27.6
III (Mich., etc.)	10.5	4.4	21.2	11.3	4.5	20.6	11.4	4.8	21.0	10.8	3.6	19.4	4.7	3.1	24.8
IV (Ohio, etc.)	11.5	2.7	24.9	12.7	2.3	23.9	13.7	2.8	24.2	11.1	1.5	23.4	6.5	4.2	29.0
V (Pa., etc.)	17.8	3.3	24.2	18.2	3.3	24.0	18.7	3.4	25.2	17.0	3.2	21.4	11.1	3.7	26.9
VI (Kans.-Mo., etc.)	10.4	6.0	34.4	11.9	5.5	31.4	13.9	4.0	29.1	9.5	7.3	34.1	7.1	7.1	41.1
VII (Md., etc.)	14.9	5.1	32.8	15.4	5.0	32.5	16.8	5.1	33.4	11.4	4.5	29.8	11.7	5.8	35.0
VIII (Tex., etc.)	23.6	10.4	51.9	24.7	10.6	50.6	27.4	9.7	45.2	(17.4)	(13.0)	(65.2)	(19.0)	(9.5)	(57.1)
IX (La., etc.)	11.7	14.9	59.0	12.6	12.6	55.2	14.4	9.7	52.1	11.0	15.3	58.0	8.8	21.9	70.6
X (Fla., etc.)	13.8	10.6	51.6	14.2	9.5	46.6	15.4	5.1	46.2	12.9	14.3	47.1	12.5	15.0	70.0
Summary of major areas															
I-V ("other")	13.1	3.2	23.8	14.2	3.2	23.1	15.0	3.6	23.6	12.5	2.5	22.0	7.4	3.1	27.9
VI-VII ("central and mid-Atlantic")	12.5	5.6	33.7	13.7	5.2	31.9	15.6	4.7	31.7	10.2	6.2	32.4	8.2	6.8	39.6
VIII-X ("southern")	13.4	13.5	56.7	14.4	11.7	52.9	16.8	8.8	49.7	11.8	14.9	56.3	10.4	19.5	69.2

NOTE: Figures in parentheses are computed from less than 30 observations.

Table 3 shows for each of the 10 zones the percentage distributions of reactors calculated from the figures in the appendix. Zones I–V, covering the West and a broad belt in the north stretching from coast to coast, constitute a very large portion of the country the population of which is characterized by low frequencies of strong 2d dose reactors varying around the average of 3.2 percent. At the same time, this region includes zones with relatively low and high prevalence of 1st dose reactors, varying from 7.7 in zone II (Minnesota, etc.) to 17.8 in zone V (Pennsylvania, etc.).

In zones VI and VII (central States and mid-Atlantic States) there are relatively more strong 2d dose reactors (6.0 and 5.1 percent), but the frequencies of 1st dose reactors are neither very high nor very low. In the remaining major area, the South, the prevalence of 1st dose reactors appears high in zone VIII (Texas and Oklahoma), but not in zones IX and X, and the average for all southern States is not very different from that found for all nurses included in the study. At the same time, 13.5 percent of all nurses with a lifetime residence in the South reacted strongly to the 2d dose as against 3.2 percent of those from zones I–V, and the percentages for zones VIII (Texas and Oklahoma) and zone X (Florida, etc.) were about 10, as against nearly 15 in zone IX (Louisiana, etc.).

When all reactors to the 2d dose are considered, the differences among the three major areas become still more evident. The third column in table 3 shows distinctly three different levels of frequencies of all 2d dose reactors. In the first five zones, the percentages of all come close to an average of 24; in the South they are more than twice as high, 52, 59, and 52, respectively, in zones VIII to X, while they are 34 and 33 in the central and mid-Atlantic States (VI and VII).

The frequencies of 2d dose reactors in separate States or zones evidently vary much more than is compatible with the notion of a constant probability when the whole country is considered. Within the five first zones, however, the variation is not significantly larger than would be attributable to random fluctuations as measured by χ^2 tests for homogeneity.

Although the important feature is the striking difference between the two major areas in the occurrence of 2d dose reactors, the present material is not sufficient to establish geographic differences within the very large area covered by zones I–V. However, the occurrence of 2d dose reactors varied in fair agreement with the hypothesis of a constant probability of 3.2 percent for strong and 23.8 for all 2d dose reactors.

The percentage of strong 2d dose reactors can be compared to that found in the previous report for separate cities in which the nurses were located as shown in table 4. It appears that the allocation used in this study tends to widen the difference between North and South, suggesting that the geographic difference in the occurrence of 2d dose reactors is associated with previous long-time residency rather than with the place of training.

Table 4. *Number of student nurses tested and percentage classified as strong 2d dose reactors, by place of lifetime residence, and by city of training*

State of lifetime residence	Nurses tested	Strong 2d dose reactors percentage	City of training	Nurses tested	Strong 2d dose reactors percentage
Minnesota	1, 143	2.4	Minneapolis	2, 419	3.1
Ohio	959	2.6	Columbus	1, 330	3.3
Pennsylvania	1, 624	3.4	Philadelphia	2, 179	4.5
California	1, 080	3.6	Los Angeles	1, 778	5.0
			San Francisco	1, 111	4.0
Michigan	978	4.8	Detroit	1, 250	4.2
Total	5, 784	3.4	Total	10, 067	4.0
Maryland	803	5.4	Baltimore	1, 971	5.7
Colorado	168	5.4	Denver	1, 329	5.1
Kansas and Missouri	990	6.0	Kansas City, Kans	532	7.7
			Kansas City, Mo	1, 131	5.4
Louisiana	452	15.5	New Orleans	1, 290	14.3

Urban and Rural Differences

Another striking feature is demonstrated by comparisons between students with urban and rural residence prior to entering nursing school. As shown in table 3, in all 10 zones the proportions of 1st dose reactors is always higher in the cities than in the country, and with one exception highest in the largest cities. The frequencies of 2d dose reactors, on the other hand, tend to vary in the opposite direction. In the south there are many more strong 2d dose reactors in the country than in the cities, and in the central and mid-Atlantic regions there is a small difference in the same direction, but in the other States, strong 2d dose reactors are found among both urban and rural residents with nearly the same frequency. If all 2d dose reactors are considered, the percentages are always higher in the country than in the cities in all parts of the United States, but especially in the South.

All Levels of Tuberculin Sensitivity

To compare the whole range of tuberculin sensitivity in different places, figure 2 was drawn to show the distributions according to four degrees of sensitivity, with separate histograms for residents of larger cities, small cities, and farms for each of the 10 zones. In the left-hand section of the graph representing zones I–V, the general visual impression suggests the existence of a definite configuration, or form of histogram. The configuration can be described roughly as U-shaped, with the two limbs of the U representing 1st dose reactors and nonreactors, respectively, and the middle part representing strong and slight 2d dose reactors. The histograms illustrating the range of tuberculin sensitivity of nurses in zones I–V vary considerably with respect to the relative height of the two "limbs" of the U, that is, with respect to the relative proportions of low dose reactors and of

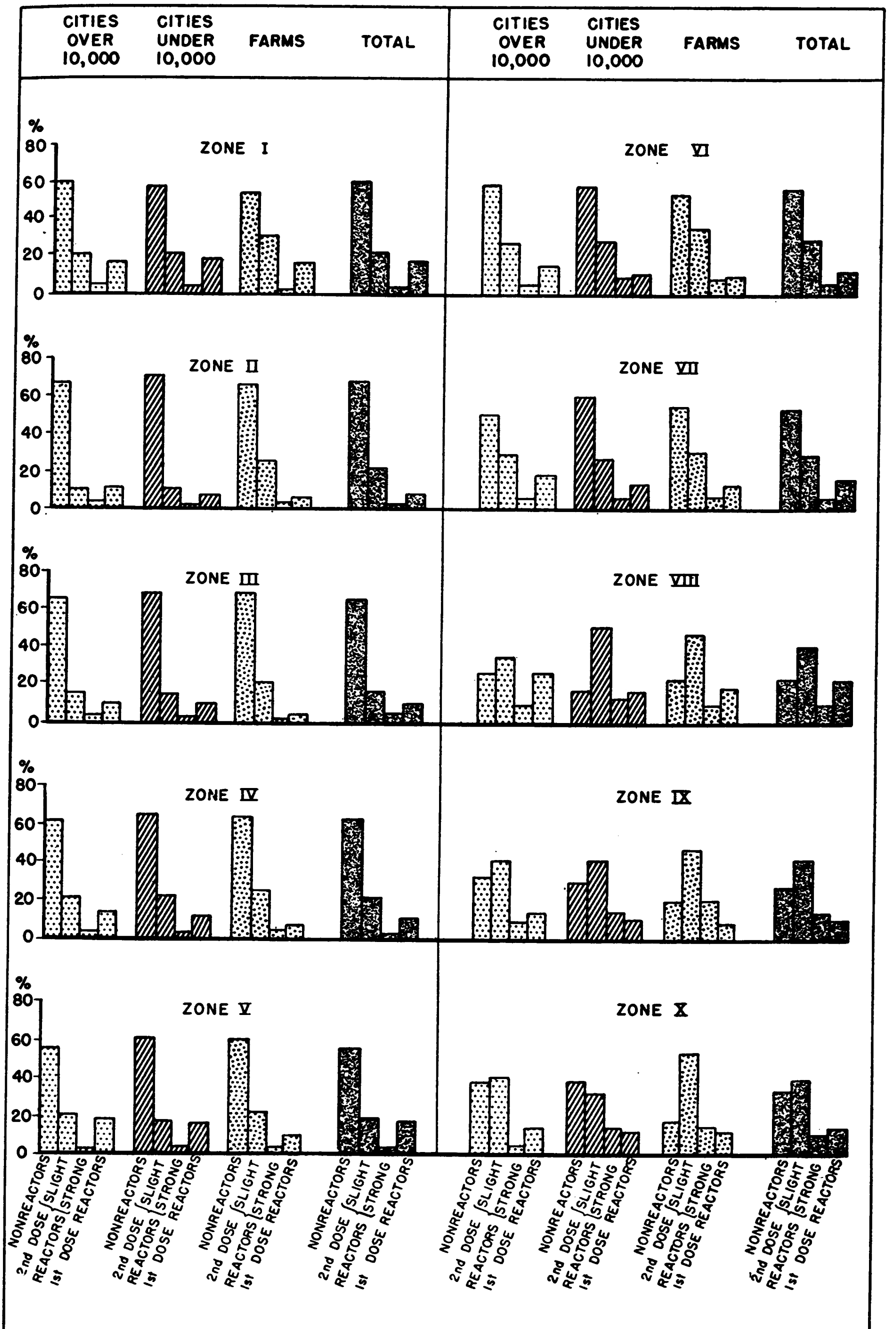

Figure 2. Distributions, according to tuberculin reaction, of lifetime residents from different types of communities in 10 zones of the United States.

nonreactors, but, in spite of these substantial differences, the U-shaped form of the distribution is not disturbed. There is an obvious similarity even between the two extremes, the distribution for nurses from farms in zone III (Michigan and Wisconsin) and those from the large cities in zone V (Pennsylvania, etc.), where the proportion of 1st dose reactors is 4.7 as against 18.7 percent. Actually the percentages of 2d dose reactors in these two groups are almost the same: 3.1 as against 3.4 for strong 2d dose reactors, and 21.7 as against 21.8 for slight 2d dose reactors.

While differences among the distributions in the left-hand side of the chart consist mainly of a transition of cases from one extreme to the other in the scale of tuberculin sensitivity, the histograms for zones VIII–X are distinctly of a different type. In all instances the middle part of the distribution is much more dominant. With one exception only, the modal class is found to be that for slight reactors to the 2d dose, and in several instances similarity to the U-shape has completely disappeared to be replaced by an almost symmetrical monomodal histogram, as in the distribution for nurses from rural districts in zone IX (Louisiana, etc.).

Also, the forms of the distributions for zones VIII–X are much less uniform than those for I–V. For instance, the distribution for the larger cities in zone VIII with the high prevalence of 1st dose reactors has not much resemblance to that for the farms of zone IX, but both deviate radically, because of the high percentage of strong and slight 2d dose reactors, from the typical form of histogram which described nurses in zones I–V. It should be noted especially that within the three southern zones there is not the same similarity between distributions from cities and from country as is found in the North.

If no evidence of a distinctly different type of distribution in the South had been available, the histogram for the Central States of zone VI and the mid-Atlantic States of zone VII would probably have been accepted without hesitation as belonging to the same type as found in zones I–V, in spite of the relatively high frequencies of both strong and slight 2d dose reactors. They do represent, however, the largest deviations found outside the South, possibly representing a transition between the two patterns.

A definite localization of a peculiar distribution of tuberculin sensitivity, manifested by an unusually frequent occurrence of reactions to a large dose of tuberculin, seems to be quite clear. A distortion of the distribution seems to take place within a certain limited geographic area, most violently in the center of this area, and more so for the rural than the urban subdivisions. The center of the "endemic" area appears to cover Louisiana, Mississippi, and presumably the adjoining States. East and west of this center, the frequencies of 2d dose reactors are a little smaller, and to the northeast and northwest, much lower.

It is obvious, of course, that the contours of the endemic area can be determined in only a very crude way with the material in the present study. The zones specifically outlined in figure 1 and the rates given for them must be viewed as first approximations. The initial sorting of the records was made by States only. Many of the States are represented by small numbers of nurses, and the frequencies are subject to large sampling errors. The possibility cannot be excluded that areas having high proportions of 2d dose reactors may be found in certain places outside of the South. The finding that within the large area comprising zones I–V the frequencies of 2d dose reactors did not show variations significantly different from random fluctuations, however, may be taken as some evidence against this possibility.

The observations on nurses with a lifetime residence in the South indicate that the high frequency of 2d dose reactors may be widespread over a large contiguous area, though it appears to be most common around the Mississippi delta. It is not possible to determine from the available data whether the somewhat lower proportions of 2d dose reactors toward the east and west is evidence of a gradual decrease in the prevalence or whether the center has sharp contours. If the latter is the case, the center may be supposed to cover all of zone IX, parts of zones VIII and X and stretch some way to the northeast and northwest.

Discussion

The preceding analysis has shown a certain simple pattern in the distribution of degrees of tuberculin sensitivity among student nurses from many different places representing most of the country outside of the southeast. This pattern can be interpreted according to principles presented in the preceding study (*5*) by visualizing the tested populations as composed of two groups: those who have been infected with the tubercle bacillus, and those who have not. If these two groups could be separated quite correctly without the use of the tuberculin test, each of them would provide its own characteristic form of frequency distribution of reactions. The former would include mostly typical reactions to a small dose and the latter mostly negative or slight degrees of sensitivity to the large dose, but both distributions would have a considerable dispersion and would overlap on a certain part of the scale. In the preceding study, the overlapping portion of the scale was shown to correspond approximately to strong 2d dose reactions.

An observed distribution of tuberculin reactions is determined, therefore, by the characteristics of the two components and by their relative magnitude, i. e., by the prevalence of tuberculous infection. While the prevalence varies considerably it may be a plausible working hypothesis to consider both components to be invariant, i. e., to assume: first, that the distribution according to sensitivity among those who have actually been infected is very much the same whether they constitute a large or small proportion of the total population; and, second, that those not infected have the same distribution of low level allergy in all areas.

Under these assumptions, changes in the prevalence of tuberculosis would alter the composite distribution as shown in figure 3, where distribution curves are drawn as rough illustrations without specified degrees of sensitivity. They demonstrate how increasing prevalence of infection changes the composite distribution. Observations are transferred from the nonreactor group to the group of 1st dose reactors without much change of the frequencies in the middle of the scale. The findings from many different places covering the larger part of

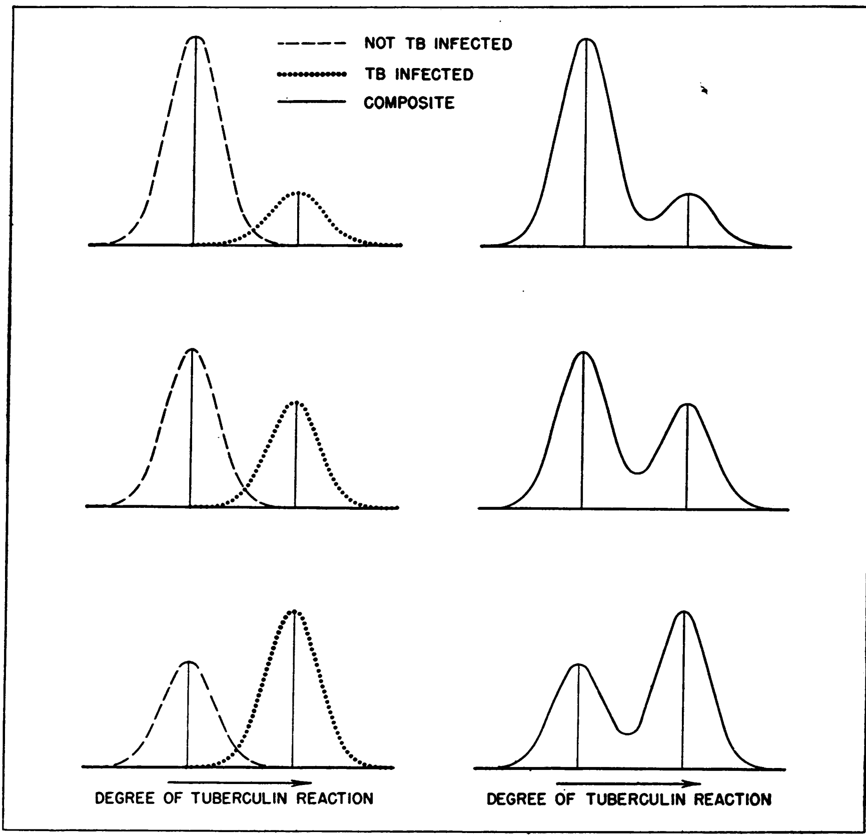

Figure 3. Hypothetical combination of two overlapping components into one composite frequency distribution according to degrees of tuberculin reaction for three populations with different prevalences of tuberculous infection.

the country conform with this model, supporting the view that the strong 2d dose reactors mainly represent cases in which the test has failed to discriminate unequivocally between positive and negative reactions.

The recognition of a certain margin of error does not impair the value of the tuberculin test when only a very small proportion of the population tested falls into the questionable category, which probably includes both persons infected with tuberculosis who failed to react to the first dose, and spurious reactors. It may be that tuberculous infections in a constant low proportion produce a very low degree of sensitivity, and we may speculate that there is a fairly constant "toxic" factor, a physiological reaction to an irritant unassociated with any specific response. In general, it might suffice to interpret the infrequent occurrence of strong 2d dose reactors in terms of experimental errors. The frequent interpretation that high dose reactions essentially represent a low level of specific sensitivity, resulting from a slight but true tuberculosis infection, seems unlikely in view of the almost complete lack of any association between their frequency and that of 1st dose reactors. It is most difficult to visualize how geographic factors could influence the prevalence of severe and slight infections in entirely different ways.

The diagnostic value of the tuberculin test, however, depends on the fact that unequivocal results are found in the very large majority of cases. The problem of erroneous classification becomes serious only when distributions are observed that deviate from the U-shaped model described above. Fortunately, so many populations do conform, that it appears justified to accept them as representative of a "normal" situation. As a consequence, the existence of divergent patterns of distribution calls for careful consideration and explanation. Distributions representative of the southern part of the country could be viewed as "distortions" of the normal form ,which must be explained either by a reduced level of sensitivity among the infected, or by the local existence of nonspecific allergy among those not infected with tuberculosis. The first explanation would necessitate the acceptance of the extremely complex consequences of the assumption that tuberculous infection in certain parts of the country fails to sensitize to the usual degree; the second appears much more acceptable.

The characteristic distribution found in the South may be explained by the superimposition of an additional component, i. e., a population composed of three groups instead of two: One, persons who have been infected with tuberculosis; another, noninfected persons; and a third, those with nonspecific allergy. Each group would represent a different level of sensitivity, and each would vary over a certain range, with considerable overlapping as illustrated in figure 4. In fact, the simplest, and most plausible explanation must be to assume that there

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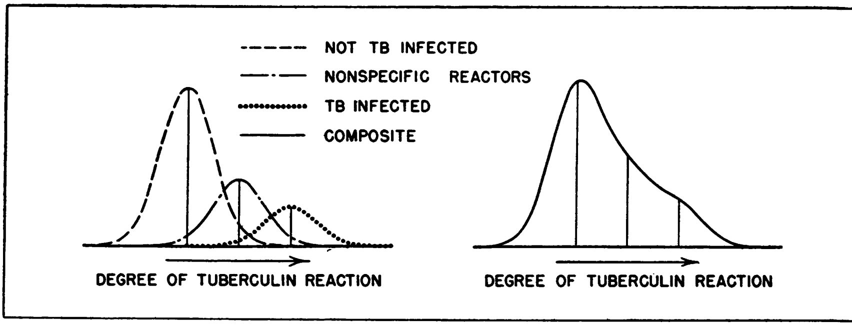

Figure 4. Hypothetical combination of three overlapping components into one composite frequency distribution according to degrees of tuberculin reaction.

exists among those not infected by tuberculosis, a substantial group of nonspecific reactors with a low level of sensitivity.

The most important evidence to support this hypothesis is, basically, the lack of correlation of the frequencies of 2d dose reactions with 1st dose reactions and with other evidence of tuberculosis. First, within major geographical subdivisions, especially in the entire northern and western segment of the country, the level of 2d dose sensitivity is remarkably uniform despite substantial variations in the percentages of 1st dose reactors. Second, from very broad geographic aspects, the existence of a definite endemic center of high prevalence of 2d dose reactors, apparently radiating outward from the Mississippi delta, is not at all closely related to the prevalence of tuberculosis. The third highly significant link in the evidence involves the marked reversal in the South of the urban-rural relationship in the frequency of low and high dose tuberculin reactors.

A nonspecific tuberculin sensitivity, while not related to tuberculous infection, must, when it occurs in sizeable segments of a tested population, indicate the existence of an unknown or not recognized agent.

Although speculations about the nature of this agent must be highly conjectural, the results of this study would appear at least to justify a serious search. That it might be infection with an organism allergenically resembling the tubercle bacillus was suggested in the preceding study (*5*). The most important clue now available is the general geographic localization of frequent 2d dose tuberculin sensitivity which appears to rule out the possibility of infection with the bovine or avian bacilli. In addition, it seems likely that the nonspecific sensitivity in the nurses tested was acquired before admission to training, suggesting that it was not temporary, and further, that the "infection" is highly benign and subclinical.

This localization and the urban-rural relationship would suggest certain geographical conditions like climate and vegetation as important factors rather than person-to-person contact as in tuberculosis The nonspecific reactions are found in an area of low level lands with subtropical vegetation, fairly hot and moist climate, a two-crop growing season, and a predominance of a peculiar soil described by geologists as "red or yellow podzolic soil."

Summary

The study is based on tuberculin tests, using a first dose of 0.0001 mg. and a second of 0.005 mg. of PPD-S, in a selected group of 10,000 white student nurses, who had lived essentially all of their lifetimes in single places in the United States. The distributions according to tuberculin sensitivity among residents from different localities were studied and compared as representative of geographic areas.

Reactions to the low dose, assumed to represent the most certain evidence of tuberculous infection, occurred with frequencies varying from about 5 to nearly 30 percent roughly in accordance with expected geographic variations in the prevalence of tuberculosis.

Reactions to the high dose, on the contrary, were strikingly independent of 1st dose reactions, and showed a peculiar geographic pattern. Throughout the greater part of the country, a remarkably constant proportion of about 24 percent of all residents reacted to the 2d dose in areas with high was well as in areas with low frequency of 1st dose reactors. In sharp contrast, however, the frequencies of high dose reactors were more than twice as high in a large contiguous area east of New Mexico and south of Kansas, Missouri, Kentucky, and Virginia, which at the same time includes parts with very high, with moderate, and with low prevalence of 1st dose reactors. The area showing the highest frequency of 2d dose reactors appears to center in Louisiana and Mississippi, with some indication of lower frequencies toward the east and west. Also the proportion of 2d dose reactors was higher in rural than in urban subdivisions in contrast to the proportions of 1st dose reactors. Among residents from Louisiana farms 72 percent responded to the 2d dose and only 9 percent to the 1st dose.

This evidence of a distinctly different pattern of tuberculin sensitivity predominant within a limited geographic region suggests the existence of a local widespread nonspecific sensitivity to tuberculin, possibly caused by infection by an organism allergenically related to the tubercle bacillus. While other hypotheses are not impossible they appear to involve very complex implications, and the most plausible explanation seems to be the existence of an unrecognized nonspecific factor within an endemic area centered around the Mississippi delta, covering roughly the southeastern quarter of the country.

ACKNOWLEDGMENT

The authors are indebted to the many members of the staff of the Field Studies Branch and of the cooperative schools of nursing, all of whom have contributed to the field, clinical, statistical, and clerical work of making possible these studies of tuberculosis among student nurses. Special thanks are due Miss Jennie Goddard, statistician, for supervising the preparation of the material for the present study. Grateful acknowledgment is also made to the Committee on Research and Therapy, National Tuberculosis Association, for support and sponsorship.

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APPENDIX TABLE

Number of student nurses according to tuberculin reaction and place of lifetime residence

Zones and States	Total					All cities					Cities with more than 10,000 population [1]					Cities with less than 10,000 population [1]					Farm				
	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors
Total United States	10,058	1,307	476	2,457	5,818	8,261	1,163	365	1,915	4,818	5,433	827	228	1,245	3,133	2,828	336	137	670	1,685	1,797	144	111	542	1,000
I																									
California	1,080	170	39	231	640	976	155	37	201	583	813	125	32	165	491	163	30	5	36	92	104	15	2	30	57
Washington	18	2	----	3	13	15	2	----	2	11	12	1	----	2	9	3	1	----	----	2	3	----	----	1	2
Utah	6	2	----	----	4	6	2	----	----	4	4	2	----	----	2	2	----	----	----	2	----	----	----	----	----
New Mexico	18	4	1	2	11	17	4	1	2	10	10	4	----	1	5	7	----	1	1	5	1	----	----	----	----
Idaho	13	1	----	3	9	6	----	----	----	6	3	----	----	----	3	3	----	----	----	3	7	1	----	3	3
Arizona	24	9	2	7	6	18	7	2	5	4	9	5	1	2	1	9	2	1	3	3	6	2	----	2	2
Oregon	8	2	1	1	4	6	1	1	----	4	5	1	1	----	3	1	----	----	----	1	2	1	----	1	----
Nevada	9	3	----	1	5	8	3	----	1	4	1	----	----	----	1	7	3	----	1	3	1	----	----	----	1
II																									
Minnesota	1,143	81	27	261	774	797	66	17	167	547	416	41	11	84	280	381	25	6	83	267	346	15	10	94	227
Montana	29	2	1	6	20	18	1	1	3	13	8	1	1	1	5	10	----	----	2	8	11	1	----	3	7
Wyoming	35	3	1	6	25	29	3	1	4	21	9	1	----	1	7	20	2	1	3	14	6	----	----	2	4
North Dakota	101	6	2	20	73	63	3	1	15	44	16	----	----	5	11	47	3	1	10	33	38	3	1	5	29
South Dakota	87	11	3	15	58	38	6	----	6	26	11	2	----	1	8	27	4	----	5	18	49	5	3	9	32
Iowa	118	13	1	20	84	79	9	1	12	57	30	6	1	6	17	49	3	----	6	40	39	4	----	8	27
III																									
Michigan	978	105	47	163	663	893	102	43	146	602	736	83	37	120	496	157	19	6	26	106	85	3	4	17	61
Wisconsin	144	13	2	25	104	100	10	2	14	74	35	5	----	5	25	65	5	2	9	49	44	3	----	11	30
IV																									
Ohio	959	96	25	214	624	760	85	16	166	493	455	56	12	98	289	305	29	4	68	204	199	11	9	48	131
Illinois	74	12	4	18	40	71	12	4	17	38	57	10	3	15	29	14	2	1	2	9	3	----	----	1	2
Kentucky	25	8	----	9	8	14	5	----	5	4	8	2	----	3	3	6	3	----	2	1	11	3	----	4	4
Indiana	36	10	----	2	24	35	10	----	2	23	26	7	----	1	18	9	3	----	1	5	1	----	----	----	1

See footnote at end of table.

Number of student nurses according to tuberculin reaction and place of lifetime residence—Continued

Zones and States	Total					All cities					Cities with more than 10,000 population [1]					Cities with less than 10,000 population [1]					Farm				
	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors	Total	1st dose reactors	Strong 2d dose reactors	Slight 2d dose reactors	Nonreactors
V																									
Pennsylvania	1,624	288	56	350	930	1,539	281	52	328	878	1,031	192	35	231	573	508	89	17	97	305	85	7	4	22	52
Vermont	1	----	----	----	1	1	----	----	----	1	----	----	----	----	----	1	----	----	----	1	----	----	----	----	----
Rhode Island	4	3	----	1	----	4	3	----	1	----	4	3	----	1	----	----	----	----	----	----	----	----	----	----	----
Connecticut	21	4	1	3	13	20	4	1	3	12	17	3	1	3	10	3	1	----	----	2	1	----	----	----	1
Maine	6	----	----	1	5	3	----	----	----	3	----	----	----	----	----	3	----	----	----	3	3	----	----	1	2
New Hampshire	2	1	----	----	1	2	1	----	----	1	1	1	----	----	----	1	----	----	----	1	----	----	----	----	----
Massachusetts	28	5	2	6	15	27	5	2	6	14	22	4	2	6	10	5	1	----	----	4	1	----	----	----	1
New York	157	28	4	26	99	149	26	4	26	93	133	22	4	25	82	16	4	----	1	11	8	2	----	----	6
New Jersey	74	12	1	12	49	64	9	1	10	44	32	7	----	4	21	32	2	1	6	23	10	3	----	2	5
VI																									
Kansas and Missouri	990	101	59	296	534	676	77	35	186	378	392	51	15	107	219	284	26	20	79	159	314	24	24	110	156
Colorado	168	21	9	38	100	125	20	6	24	75	68	13	2	10	43	57	7	4	14	32	43	1	3	14	25
Nebraska	89	8	7	20	54	54	5	6	11	32	14	2	2	2	8	40	3	4	9	24	35	3	1	9	22
VII																									
Maryland	803	124	43	222	414	719	116	39	197	367	557	98	30	160	269	162	18	9	37	98	84	8	4	25	47
Delaware	17	3	----	3	11	16	3	----	2	11	7	2	----	1	4	9	1	----	1	7	1	----	----	1	----
West Virginia	106	12	4	32	58	92	10	4	28	50	42	3	2	12	25	50	7	2	16	25	14	2	----	4	8
District of Columbia	52	9	2	15	26	51	9	2	14	26	51	9	2	14	26	----	----	----	----	----	1	----	----	1	----
Virginia	66	8	4	17	37	46	4	1	13	28	22	2	1	5	14	24	2	----	8	14	20	4	3	4	9
VIII																									
Texas	72	18	7	30	17	62	16	6	25	15	50	15	5	16	14	12	1	1	9	1	10	2	1	5	2
Oklahoma	34	7	4	14	9	23	5	3	9	6	12	2	1	6	3	11	3	2	3	3	11	2	1	5	3
IX																									
Louisiana	452	57	70	193	132	343	47	44	140	112	166	23	18	67	58	177	24	26	73	54	109	10	26	53	20
Mississippi	107	10	14	57	26	77	8	6	44	19	33	7	----	20	6	44	1	6	24	13	30	2	8	13	7
Arkansas	31	6	5	12	8	23	5	4	7	7	7	2	1	2	2	16	3	3	5	5	8	1	1	5	1
Tennessee	18	1	2	3	12	12	1	2	2	7	7	1	----	2	4	5	----	2	----	3	6	----	----	1	5
Alabama	43	2	6	22	13	36	1	6	16	13	23	1	4	9	9	13	----	2	7	4	7	1	----	6	----

X																									
Florida	103	18	12	41	32	87	15	9	32	31	42	10	3	16	13	45	5	6	16	18	16	3	3	9	1
South Carolina	23	2	1	13	7	17	2	1	9	5	11	1	-----	7	3	6	1	1	2	2	6	-----	-----	4	2
North Carolina	45	6	5	18	16	28	4	2	10	12	15	1	-----	7	7	13	3	2	3	5	17	2	3	8	4
Georgia	17	-----	2	5	10	16	-----	2	4	10	10	-----	1	2	7	6	-----	1	2	3	1	-----	-----	1	-----
SUMMARY BY ZONES																									
I	1,176	193	43	248	692	1,052	174	41	211	626	857	138	34	170	515	195	36	7	41	111	124	19	2	37	66
II	1,513	116	35	328	1,034	1,024	88	21	207	708	490	51	13	98	328	534	37	8	109	380	489	28	14	121	326
III	1,122	118	49	188	767	993	112	45	160	676	771	88	37	125	521	222	24	8	35	155	129	6	4	28	91
IV	1,094	126	29	243	696	880	112	20	190	558	546	75	15	117	339	334	37	5	73	219	214	14	9	53	138
V	1,917	341	64	399	1,113	1,809	329	60	374	1,046	1,240	232	42	270	696	569	97	18	104	350	108	12	4	25	67
VI	1,247	130	75	354	688	855	102	47	221	485	474	66	19	119	270	381	36	28	102	215	392	28	28	133	203
VII	1,044	156	53	289	546	924	142	46	254	482	679	114	35	192	338	245	28	11	62	144	120	14	7	35	64
VIII	106	25	11	44	26	85	21	9	34	21	62	17	6	22	17	23	4	3	12	4	21	4	2	10	5
IX	651	76	97	287	191	491	62	62	209	158	236	34	23	100	79	255	28	39	109	79	160	14	35	78	33
X	188	26	20	77	65	148	21	14	55	58	78	12	4	32	30	70	9	10	23	28	40	5	6	22	7
SUMMARY BY MAJOR AREAS																									
I-V	6,822	894	220	1,406	4,302	5,758	815	187	1,142	3,614	3,904	584	141	780	2,399	1,854	231	46	362	1,215	1,064	79	33	264	688
VI-VII	2,291	286	128	643	1,234	1,779	244	93	475	967	1,153	180	54	311	608	626	64	39	164	359	512	42	35	168	267
VIII	945	127	128	408	282	724	104	85	298	237	376	63	33	154	126	348	41	52	144	111	221	23	43	110	45

[1] According to the 1930 census.

Geographic Distribution of Pulmonary Calcification Among University Students in Ohio

By John A. Prior, M. D., John W. Wilce, M. D., and William Palchanis, M. D.*

In 1943, Long and Stearns (*1*) demonstrated a higher prevalence of pulmonary calcification among selective service inductees who were residents of the Middle West than among those from any other section of the country. Two years later, Palmer (*2*) and Christie and Peterson (*3*) reported on the first widespread use of the histoplasmin skin test. Their results indicate that most of the tuberculin negative persons who had pulmonary calcifications, especially in the Midwestern States, were reactors to histoplasmin. The following year, Palmer (*4*) demonstrated that there was a definite geographic pattern to the prevalence of histoplasmin reactors throughout the country. In the Midwest, 68.3 percent of those tested reacted to histoplasmin and the prevalence of reactors in contiguous areas was much lower. It will be noted that this area of high prevalence of calcified pulmonary lesions corresponds rather closely to the area of high prevalence of histoplasmin reactors, as well as to the endemic center of the reported cases of histoplasmosis.

Within States that lie on the border of this region of high prevalence of histoplasmin reactors, e. g., Ohio on the east and Kansas on the west, a definite geographic pattern of prevalence of histoplasmin reactors is noted (*4*). As one moves across these States away from the center of high prevalence, a rapid decline in prevalence of histoplasmin reactors is seen. In a histoplasmin and tuberculin survey of 5,087 Ohio State University freshmen and student nurses, representing every county in Ohio, conducted in 1946, the geographic pattern of histoplasmin reactors throughout the State was confirmed (*5*). That survey showed the prevalence of histoplasmin reactors in residents of southwestern Ohio to be very high, 75.8 percent, and that it steadily decreased to the north and east across the State, reaching the lowest prevalence, 16.8 percent, in the extreme northeastern section. No similar geographic distribution for tuberculin reactors was noted. Correlation of the skin test results with pulmonary calcifications was not possible at that time.

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It is the purpose of the present paper to report on the relationship of the presence of pulmonary calcification to the results of histoplasmin and tuberculin skin tests, as revealed by surveys conducted in the autumn of 1946 and 1948 among students entering Ohio State University.

Material and Method

The present study is based on the records of 4,829 students who entered Ohio State University in the fall quarters of 1946 and 1948 and met certain criteria. Preliminary histoplasmin and tuberculin skin tests were required, and a satisfactory chest film taken at the time of admission had to be available. The group was further limited to lifetime residents of a given county. As in the preceding study (*5*), a student was considered to be a lifetime resident of a county if he had not lived more than 4 years outside that county.

The 4,829 acceptable records were chosen from among more than 10,000 admissions in the specified periods. There were 3,844 males and 985 females. Only 640 were farm residents; the remaining 4,189 lived in nonfarm areas.

Skin tests consisted of the intradermal injection of 0.1 cc. histoplasmin (H-15) in 1:1000 dilution, and 0.1 cc. of tuberculin (PPD) containing 0.0001 mg. as advocated by Furcolow (*6*). Five mm. or more of induration at 48 hours was considered to be a positive reaction.

Routine 70 mm. chest X-rays were taken of each student when the skin tests were applied. To insure uniform interpretation, all of the X-rays were read by one of the authors (Prior) without the knowledge of the skin test reaction.

The authors recognize that 70 mm. films may not be entirely adequate for detecting the presence of pulmonary calcification. Further, the character of the calcification produced by histoplasmosis is believed by some workers to be larger, more discrete and well defined, hence more easily discernible, than some forms of tuberculous calcification. The figures cited, therefore, probably underestimate the absolute frequencies, perhaps more so for tuberculosis than for histoplasmosis. Nevertheless, they are useful in indicating relative levels among different geographic areas.

Results

Since the rates for histoplasmin reactors and calcified pulmonary lesions differed according to a definite geographic pattern throughout Ohio and because the numbers from some counties were too small to provide a reliable rate for the county, contiguous counties with similar rates were combined into 11 areas. For each of these areas the results of the skin tests and film reading are shown in table 1. The data

Table 1. *Number and percentage of "lifetime" students with pulmonary calcification in each reaction group by geographic areas, Ohio State University, fall 1946 and fall 1948*

Area number	Areas and large cities	H+ T+			H+ T−			H− T+			H− T−		
		Number of reactors	Number with calcification	Percent calcification	Number of reactors	Number with calcification	Percent calcification	Number of reactors	Number with calcification	Percent calcification	Number of reactors	Number with calcification	Percent calcification
	Total	308	71	23.1	2,049	432	21.1	373	24	6.4	2,099	73	3.5
1	Total	21	6	28.6	133	26	19.5	118	5	4.2	638	11	1.7
	Akron	1	------	0	18	3	16.7	10	------	0	55	2	3.6
	Cleveland	8	2	25.0	40	12	30.0	51	3	5.9	250	3	1.2
	Rest of area	12	4	33.3	75	11	14.7	57	2	3.5	333	6	1.8
2	Total	19	3	15.8	69	16	23.2	79	3	3.8	328	1	0.3
	Canton	3	------	0	11	2	18.2	14	1	7.1	57	1	1.8
	Youngstown	7	1	14.3	16	4	25.0	21	------	0	59	------	0
	Rest of area	9	2	22.2	42	10	23.8	44	2	4.6	212	------	0
3	Total	11	2	18.2	77	16	20.8	11	1	9.1	71	------	0
4	Total	7	2	28.6	80	16	20.0	30	1	3.3	151	4	2.6
5	Total	15	3	20.0	95	18	18.9	9	------	0	77	6	7.8
6	Total	13	3	23.1	88	18	20.5	11	2	18.2	52	3	5.8
7	Total	13	2	15.4	50	8	16.0	13	------	0	123	2	1.6
	Toledo	3	------	0	11	2	18.2	6	------	0	48	------	0
	Rest of area	10	2	20.0	39	6	15.4	7	------	0	75	2	2.7
8	Total	24	3	12.5	163	29	17.8	8	2	25.0	95	4	4.2
9	Total	130	35	26.9	878	182	20.7	71	8	11.3	436	33	7.6
	Columbus	80	27	33.8	528	116	22.0	58	7	12.1	313	19	6.1
	Rest of area	50	8	16.0	350	66	18.9	13	1	7.7	123	14	11.4
10	Total	14	4	28.6	116	30	25.9	7	------	0	47	3	6.4
11	Total	41	8	19.5	300	73	24.3	16	2	12.5	81	6	7.4
	Cincinnati	3	1	33.3	68	19	27.9	5	1	20.0	19	------	0
	Dayton	13	5	38.5	80	23	28.8	5	------	0	17	------	0
	Rest of area	25	2	8.0	152	31	20.4	6	1	16.7	45	6	13.3

derived from table 1 are presented in table 2 and these rates are used in the map of Ohio (fig. 1).

The distribution of histoplasmin reactors in this study of students whose chest X-rays were available is essentially the same as that already reported (*5*). In area 11, the histoplasmin reactor rate is

Table 2. *Percent of "lifetime" students in each geographic area with pulmonary calcification, percent reacting to histoplasmin and percent reacting to tuberculin, Ohio State University, fall 1946 and fall 1948*

Area	Calcification	Histoplasmin sensitivity	Tuberculin sensitivity
2	4.6	17.8	19.8
1	5.3	16.9	15.3
7	6.0	31.7	13.1
4	8.6	32.5	13.8
3	11.2	51.8	12.9
8	13.1	64.5	11.0
5	13.8	56.1	12.2
6	15.9	61.6	14.6
9	17.0	66.5	13.3
10	20.1	70.7	11.4
11	20.3	77.9	13.0

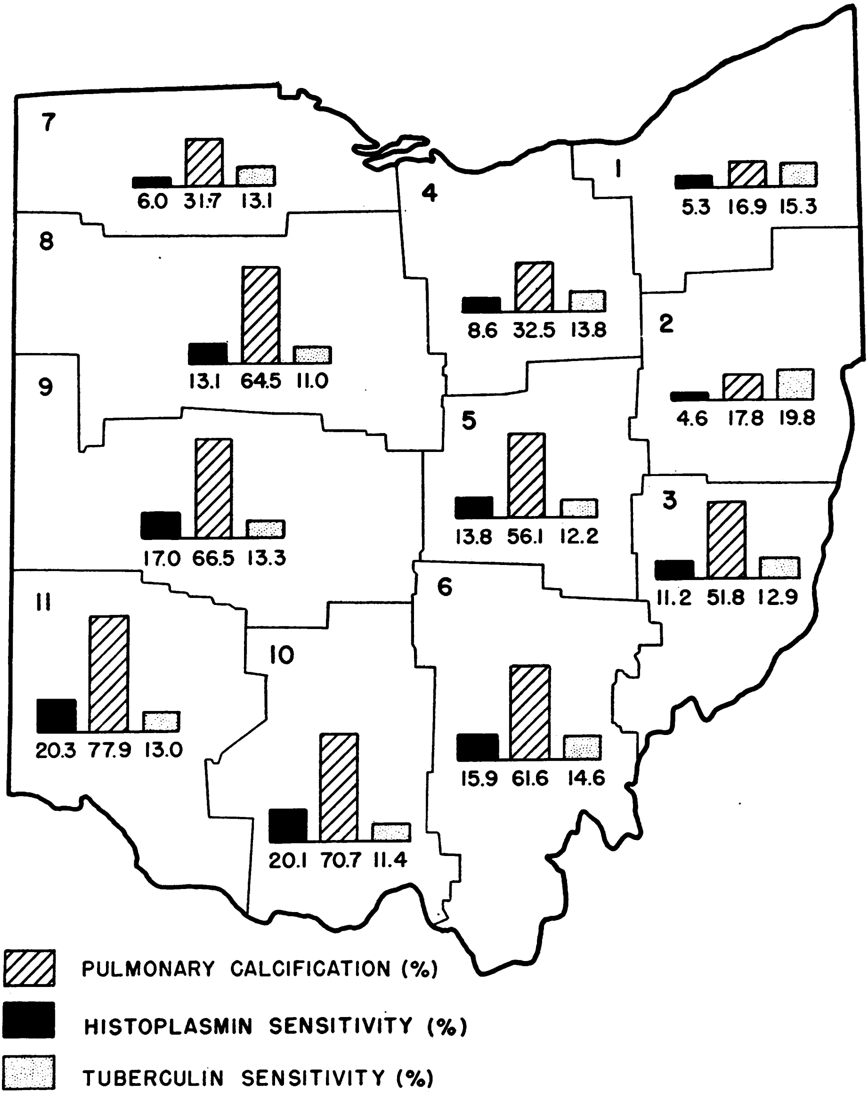

Figure 1. Percent of persons with pulmonary calcification, histoplasmin, and tuberculin sensitivity in 11 selected areas of Ohio.

highest, 77.9 percent. The prevalence gradually decreases across the State to the north and east, reaching a minimum of 16.9 percent in the northeastern corner. The average throughout Ohio is 48.8 percent. The prevalence of histoplasmin reactors in area 11 is approximately four and one-half times greater than in area 1. The prevalence of reactors among the male students is 49.6 percent, and among female students, 45.6 percent. The prevalence of reactors among students from farms is greater (60.6 percent) than among nonfarm residents (47 percent).

No similar pattern is noted for the prevalence of tuberculin reactors (fig. 1). It tends to be highest, 15.3 percent and 19.8 percent, in the most highly industrialized areas, 1 and 2, and lowest in the agricultural areas, 8 and 10—11.0 percent and 11.4 percent, respectively. The average for the State is 14.1 percent.

A definite geographic pattern for the incidence of pulmonary calcification is noted. The prevalence is greatest in the southwestern corner of the State in areas 10 and 11—20.1 percent and 20.3 percent, respectively. As one moves to the north and east across Ohio, the prevalence of such lesions gradually decreases, until it reaches a minimum in areas 1 and 2—5.3 percent and 4.6 percent, respectively. Thus, the prevalence of calcific pulmonary lesions in area 11 is approximately four times greater than in area 1. The average prevalence throughout the State is 12.4 percent.

When we return to the number and percentage of students with calcification in each reaction group by geographic area, as shown in table 1, it is seen that among students who reacted to tuberculin alone, only 6.4 percent showed the presence of calcified pulmonary lesions. Among those who reacted to histoplasmin alone, the prevalence of pulmonary calcification is considerably greater, 21.1 percent. The highest prevalence of pulmonary calcification, 23.1 percent is found among those who reacted to both histoplasmin and tuberculin. Among those who reacted to neither tuberculin nor histoplasmin, 3.5 percent had calcified lesions in their lungs. It would appear from

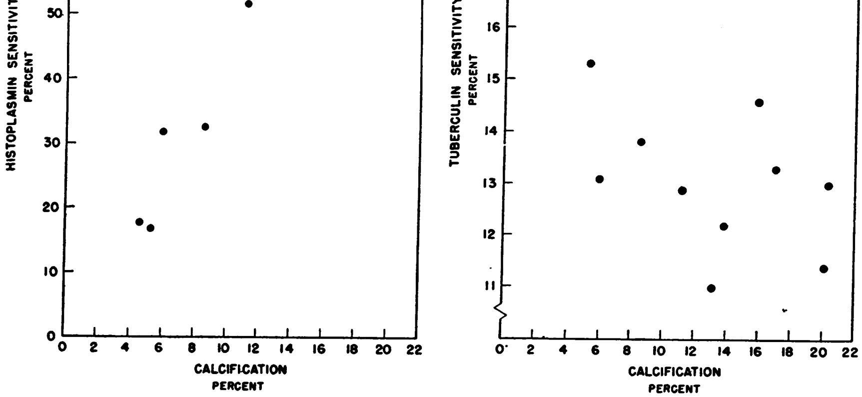

Figure 2. Relationship of frequency of the occurrence of pulmonary calcification to histoplasmin sensitivity and to tuberculin sensitivity in eleven selected areas of Ohio.

the data presented that pulmonary calcifications in Ohio are more commonly associated with histoplasmin sensitivity than with tuberculin sensitivity.

This conclusion is even more evident from an inspection of the scatter diagrams in figure 2. Using the data from table 2, the frequency of calcification has been plotted first against the frequency of histoplasmin reactors and then against the frequency of tuberculin reactors in each of the 11 areas. Although the correlation between the prevalence of calcification and of histoplasmin sensitivity is obvious, no such relationship appears to exist between calcification and tuberculin sensitivity.

A greater prevalence of calcified pulmonary lesions was found among male students, 12.9 percent, than among females, 10.3 percent. Calcifications were also more common among farm residents than among those from urban areas, 15.5 percent and 12.0 percent, respectively. These patterns are similar to those of histoplasmin sensitivity in these groups.

Summary and Conclusions

Studies of 4,829 students by means of chest X-ray, tuberculin, and histoplasmin tests, conducted in the fall of 1946 and 1948, demonstrated that the distribution of the prevalence of pulmonary calcification in Ohio followed a definite geographic pattern. This pattern of prevalence very closely parallels the geographic distribution of histoplasmin reactors, but does not correspond to the distribution of tuberculin reactors. The prevalence of tuberculin reactors tends to be higher in the metropolitan areas and lower in rural sections. In contrast, the prevalence of both pulmonary calcification and histoplasmin reactors tends to be higher in the rural sections than in urban areas, and also shows a definite geographic pattern. Although many calcifications are undoubtedly due to tuberculosis, these facts tend to support the growing belief that most pulmonary calcifications in Ohio and other Middle Western States are probably the result of a benign widespread form of histoplasmosis or an antigenically related agent or agents.

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Notice

The Index of Hospitals and Sanatoria with Tuberculosis Beds in the United States and Territories, as of January 1, 1950, issued this month by the Division of Tuberculosis, is now available for free distribution. Copies may be obtained upon request from the Publications Section, Division of Tuberculosis, Public Health Service, Washington 25, D. C.

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 occuring

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UNITED STATES

Reports from States for Week Ended August 12, 1950

For the current week, new cases of acute poliomyelitis reported in the Nation numbered 1,442, a 22-percent increase over the 1,186 reported last week. However, this rate of increase is roughly comparable to preceding weeks. The total for the current week is less than the 3,153 cases reported for the corresponding week in 1949.

The cumulative total, 7,610 cases of poliomyelitis reported for the current "disease" year, was below the corresponding total of 12,963 for last year, the highest on record. The "disease" year for acute poliomyelitis begins with the twelfth week of the calendar year.

The cumulative total for the calendar year was 8,744 reported cases of poliomyelitis compared with the total of 13,878 for the corresponding period last year.

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 1945–49	Seasonal low week	Cumulative total since seasonal low week		5-year median 1944–45 through 1948–49	Cumulative total for calendar year		5-year median 1945–49
	Aug. 12, 1950	Aug. 13, 1949			1949–50	1948–49		1950	1949	
Anthrax (062)	------	3	[1]	[1]	[1]	[1]	[1]	29	38	[1]
Diphtheria (055)	83	98	144	27th	322	464	663	3,450	4,232	6,960
Acute infectious encephalitis (082)	23	32	21	[1]	[1]	[1]	[1]	495	365	309
Influenza (480–483)	709	538	580	30th	1,568	1,046	1,046	247,827	76,913	140,197
Measles (085)	1,305	1,106	1,129	35th	304,795	638,873	582,899	285,665	586,480	547,953
Meningococcal meningitis (057.0)	41	48	48	37th	3,497	3,143	3,399	2,584	2,298	2,427
Pneumonia (490–493)	639	804	------	[1]	[1]	[1]	--------	59,981	54,943	------
Acute poliomyelitis (080)	1,442	3,153	1,409	11th	[2] 7,610	12,963	6,558	[2] 8,744	13,878	7,025
Rocky Mountain spotted fever (104)	23	36	29	[1]	[1]	[1]	[1]	322	413	382
Scarlet fever (050)	257	245	455	32d	56,609	80,210	88,789	40,170	57,666	62,103
Smallpox (084)	------	1	2	35th	44	50	199	24	40	145
Tularemia (059)	19	23	22	[1]	[1]	[1]	[1]	631	781	641
Typhoid and paratyphoid fever [3] (040, 041)	105	182	140	11th	[4] 1,502	1,813	1,813	[4] 2,012	2,301	2,301
Whooping cough (056)	2,250	1,604	2,183	39th	105,588	46,743	88,432	84,052	36,710	62,414

[1] Not computed.
[2] Deductions—Arkansas, weeks ended July 22, and 29, 1 case each; Georgia, week ended August 5, 1 case.
[3] Including cases reported as salmonellosis.
[4] Deduction—Montana, week ended July 8, 2 cases.

For the current week, total poliomyelitis reported in all geographic divisions except the East South Central and Mountain increased over the preceding week. The increases ranged from 79 (168 to 247) cases reported in the Middle Atlantic States to 3 (199 to 202) cases in the East North Central States. The East South Central States decreased by 5 cases (117 to 112) and the Mountain States decreased by 2 (25 to 23).

For the current week, the States reporting the largest numbers of cases of poliomyelitis were: New York (172), Texas (131), Virginia (94), California (83), Illinois (69), and Michigan (66).

The total number of cases of influenza reported for the current week was 709, compared with 538 for the corresponding period last year. Of this current total, 522 cases were reported by Texas (378) and Virginia (144). The next highest number was reported by Arizona (45).

The total number of cases of infectious encephalitis reported for the week was 23, compared with 32 reported for the corresponding period last year. For the calendar year, a total of 495 cases was reported, the highest total in the past 5 years.

Total reported cases of scarlet fever were lower for the "disease" year ending with the current week than for any corresponding period during the past 5 years. This total was 56,609 which may be compared with 124,866 for 1945–46, the highest disease year in the 5-year period. The median for this period was 88,789.

No smallpox was reported in the United States.

The New Mexico State Health Department reports positive laboratory specimens for bubonic plague from an Arizona patient.

Deaths During Week Ended August 12, 1950

	Week ended August 12, 1950	*Corresponding week, 1949*
Data for 94 large cities of the United States:		
Total deaths	8, 093	8, 813
Median for 3 prior years	8, 813	
Total deaths, first 32 weeks of year	298, 951	299, 285
Deaths under 1 year of age	606	741
Median for 3 prior years	686	
Deaths under 1 year of age, first 32 weeks of year	19, 867	20, 910
Data from industrial insurance companies:		
Policies in force	69, 654, 924	70, 253, 019
Number of death claims	12, 092	11, 175
Death claims per 1,000 policies in force, annual rate	9. 1	8. 3
Death claims per 1,000 policies, first 32 weeks of years, annual rate	9. 5	9. 4

Reported Cases of Selected Communicable Diseases: United States, Week Ended August 12, 1950

[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	**83**	**23**	**709**	**1,305**	**41**	**639**	**1,442**
New England	**3**	**2**		**100**	**3**	**14**	**64**
Maine	1			4			5
New Hampshire						1	
Vermont				3			2
Massachusetts	2	2		80	3		27
Rhode Island							1
Connecticut				13		13	29
Middle Atlantic	**5**	**1**	**1**	**389**	**7**	**176**	**247**
New York	1	1	1 [1]	163	2	115	172
New Jersey	1			124		35	30
Pennsylvania	3			102	5	26	45
East North Central	**6**	**3**	**15**	**352**	**10**	**67**	**202**
Ohio			3	70	3	7	25
Indiana	3			3		2	22
Illinois	3	2		104	2	39	69
Michigan		1		57	1	16	66
Wisconsin			12	118	4	3	20
West North Central	**2**	**2**	**8**	**65**	**4**	**77**	**186**
Minnesota			3	20	2	14	34
Iowa				1	1		72
Missouri	2	1	3	20		9	14
North Dakota		1	2	5		52	8
South Dakota				4	1		12
Nebraska							25
Kansas				15		2	21
South Atlantic	**12**		**163**	**84**	**3**	**72**	**267**
Delaware							2
Maryland			4	7	2	22	29
District of Columbia			2	3		15	15
Virginia	1		144	25	1	25	94
West Virginia	2		5	11			18
North Carolina	3			2			51
South Carolina	3			3		1	24
Georgia	2		8	25		3	17
Florida	1			8		6	17
East South Central	**27**		**14**	**49**	**7**	**31**	**112**
Kentucky	4		1	17		6	33
Tennessee	1		7	23	4		38
Alabama	6		3	5	2	9	18
Mississippi	16		3	4	1	16	23
West South Central	**21**	**1**	**413**	**126**	**5**	**170**	**215**
Arkansas	3		21	4	2	10	15
Louisiana	2			2		12	30
Oklahoma	2		14	5	1	11	39
Texas	14	1	378	115	2	137	131
Mountain	**2**	**2**	**82**	**70**	**1**	**17**	**23**
Montana	1		31	2			
Idaho			2	11			2
Wyoming							2
Colorado	1		3	39		7	7
New Mexico						3	3
Arizona			45	5	1	6	7
Utah		2	1	13		1	2
Nevada							
Pacific	**5**	**12**	**13**	**70**	**1**	**15**	**126**
Washington	1			7			20
Oregon	2	1	1	20		5	23
California	2	11	12	43	1	10	83
Alaska							
Hawaii			24	4			

[1] New York City only.

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Reported Cases of Selected Communicable Diseases: United States, Week Ended August 12, 1950—Continued

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

Area	Rocky Mountain spotted fever (104)	Scarlet fever (050)	Smallpox (084)	Tularemia (059)	Typhoid and paratyphoid fever [1] (040,041)	Whooping cough (056)	Rabies in animals
United States	**23**	**257**		**19**	**105**	**2,250**	**115**
New England		**21**			**4**	**234**	
Maine		4				54	
New Hampshire						1	
Vermont						33	
Massachusetts		10			2	80	
Rhode Island		2			2	36	
Connecticut		5				30	
Middle Atlantic		**45**			**12**	**349**	**32**
New York		[2] 17			3	172	32
New Jersey		4			2	84	
Pennsylvania		24			7	93	
East North Central		**57**		**1**	**17**	**491**	**30**
Ohio		17			4	79	5
Indiana		4		1	8	26	[3] 19
Illinois		9			3	68	2
Michigan		19			1	193	3
Wisconsin		8			1	125	1
West North Central		**16**			**5**	**121**	**7**
Minnesota		4			1	37	
Iowa						32	3
Missouri		8			4	30	
North Dakota		1				1	
South Dakota						4	
Nebraska							
Kansas		3				17	4
South Atlantic	**19**	**40**		**1**	**18**	**394**	**13**
Delaware		1				2	
Maryland	6	6			2	63	
District of Columbia		2				2	
Virginia	10	7			6	58	1
West Virginia	1	2			1	89	1
North Carolina	2	16			3	148	
South Carolina		2			3	7	5
Georgia		3		1	2	24	4
Florida		1			1	1	2
East South Central	**1**	**30**		**2**	**13**	**77**	**14**
Kentucky	1	6			4	21	5
Tennessee		14		2	7	37	2
Alabama		3			1	9	4
Mississippi		7			1	10	3
West South Central		**12**		**12**	**21**	**273**	**15**
Arkansas		1		10	3	45	1
Louisiana		1		1	2		
Oklahoma		3		1	8	8	2
Texas		7			8	220	12
Mountain	**2**	**6**		**3**	**4**	**149**	
Montana						15	
Idaho					1	27	
Wyoming						5	
Colorado	2	2			2	41	
New Mexico				1	1	21	
Arizona		3				30	
Utah		1		2		7	
Nevada						3	
Pacific	**1**	**30**			**11**	**162**	**4**
Washington		3				35	
Oregon	1	2				24	
California		25			11	103	4
Alaska					1		
Hawaii							

[1] Including cases reported as salmonellosis.
[2] Including cases reported as streptococcal sore throat.
[3] Two weeks report.

FOREIGN REPORTS

CANADA

Reported Cases of Certain Diseases—Week Ended July 15, 1950

Disease	New-foundland	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Brucellosis					6	2	1		1		10
Chickenpox	1		14	1	51	139	16	18	61	57	358
Diphtheria					3						3
Dysentery:											
Amebic						1					1
Bacillary					5		1				6
Encephalitis, infectious						1					1
German measles			4		2	177	1	16	8	22	230
Influenza			1			8	1				10
Measles			10		168	304	6	14	24	82	608
Meningitis, meningococcal			1	1				2		1	5
Mumps			21		25	131	5	30	46	52	310
Poliomyelitis					1	3				2	6
Scarlet fever	8		2		11	15	5	4	10	3	58
Tuberculosis (all forms)	15		4	24	67	15	15	12	54		206
Typhoid and paratyphoid fever				2	6	2			1	2	13
Venereal diseases:											
Gonorrhea	4		11	4	78	58	29	8	55	102	349
Syphilis	2		19	2	25	11	5	6	2	11	83
Whooping cough	1		15	2	41	67	3	3	2	30	164

Week Ended July 22, 1950

Disease	New-foundland	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Brucellosis					4	1	1			1	7
Chickenpox			29		32	91	30	13	41	39	275
Diphtheria					3	1			1	1	6
Dysentery, bacillary					5		64			3	72
Encephalitis, infectious									2		2
German measles	3		16	3	2	73		7	11	31	146
Influenza			22				4				26
Measles			1		56	193	12	19	22	37	340
Meningitis, meningococcal						1	3		1		5
Mumps			16	1	11	84	7	28	52	32	231
Poliomyelitis				1	5		2	2	1	5	16
Scarlet fever			2		14	8	3	3	11	4	45
Tuberculosis (all forms)	8		9	20	131	6	30	9		74	287
Typhoid and paratyphoid fever					4	2				1	7
Venereal diseases:											
Gonorrhea	8		16	14	30	52	25	31	47	62	285
Syphilis			2	3	32	17	6	13	3	6	82
Whooping cough	3		32		37	35	3			36	146

Poliomyelitis. The reported incidence of poliomyelitis in England and Wales during the current year has been markedly high. It is in excess of either of the epidemic years of 1947 or 1949. The epidemic of 1949 was second to that of 1947, but exceeded considerably those of pre-war years. A total of 7,791 cases was reported in 1947; 5,969 cases in 1949.

The total number of cases reported for the current year through week ended July 22 is 1,919 (corresponding figures for 1947, 1948, and 1949, respectively, 805, 789, and 847). The numbers of cases reported for the weeks ending in the period July 1 to July 22 are as follows (corresponding figures for 1947, 1948, and 1949, respectively, in parentheses): Weeks ended—July 1, 160 (67, 38, 81); July 8, 212 (88, 25, 77); July 15, 212 (126, 38, 117); July 22, 260 (193, 45, 99).

A similar situation exists in Scotland. Numbers of reported cases in recent weeks are as follows: Weeks ended—June 24, 37; July 1, 47; July 8, 42; July 15, 49; total for the four weeks, 175. Totals for the corresponding periods of 1947, 1948, and 1949 were 18, 10, and 13, respectively.

Numbers of cases reported in Northern Ireland during July 1950, are as follows (figures for 1949 in parentheses): Weeks ended—July 1, 10 (0); July 8, 10 (0); July 15, 12 (2); July 22, 18 (0).

MADAGASCAR

Reported Cases of Certain Diseases and Deaths—June 1950

Disease	Aliens		Natives	
	Cases	Deaths	Cases	Deaths
Beriberi			2	
Bilharziasis	1		104	2
Diphtheria	2		3	2
Dysentery:				
Amebic	14		293	3
Bacillary			2	
Erysipelas			19	
Influenza	80		11,561	71
Leprosy	1		40	
Malaria	278		42,705	89
Measles	8		95	
Mumps	6		254	
Plague			1	1
Pneumonia (all forms)	8	2	1,193	234
Puerperal infection			10	
Relapsing fever			4	
Scarlet fever			1	
Tuberculosis, respiratory	9	1	113	17
Typhoid fever			1	
Whooping cough	6		376	6

NIGERIA

Cerebrospinal meningitis. Incidence of cerebrospinal meningitis has been reported in epidemic proportions in Nigeria during the current year. It is the highest ever recorded in that country. The maximum annual total of cases previously registered was that of 1949. During the period January 1–June 10, 1949, a total of 40,081 cases (7,757 deaths) was reported. The total number of reported cases for the same period of 1950 is 56,185 (7,056 deaths). More than half of the total for the period has been reported in Sokoto Province, where 28,935 cases have registered.

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. A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

Cholera

Burma. During the week ended July 22, 1950, 40 cases of cholera, with 31 deaths, were reported.

India. The latest information on the epidemic of cholera in Bombay, received August 8, 1950, states that as of July 31, 217 cases, with 26 deaths, had been officially reported since the beginning of the outbreak on July 16. Epidemic incidence was also noted in Malad, a suburb of Bombay, and in Hubli, a city of 150,000 population, about three hundred miles southeast of Bombay, but no official reports of the numbers of cases occurring in these areas were available. For the week ended August 5, 58 cases were reported in Bombay. In Calcutta the outbreak reached its peak during the week ended April 22, with a total of 777 reported cases; 141 cases (51 deaths) were reported during the week ended July 29, and 115 cases for the week ended August 5. One fatal case was reported in Tiruchirappalli during the week ended July 29, the first this year.

Indochina. During the week ended July 29, 1950, 1 case of cholera was reported in the Longxuyen area, Viet Nam.

Plague

Belgian Congo. During the week ended July 29, 1950, 1 fatal case of plague was reported in Stanleyville Province at Julo, southwest of Blukwa.

Burma. On June 30, 1950, 1 case of plague was reported in the port of Minhla, and during the week ended July 22, 2 cases were reported in Rangoon.

Indonesia. During the week ended July 15, 1950, 9 fatal cases of plague were reported in Jogjakarta, Java.

Smallpox

Chile. During the outbreak of smallpox reported in Chile in recent months, 3,336 cases were recorded for the period January 1–May 27.

India. During the week ended August 5, 1950, 57 cases of smallpox were reported in Calcutta, and 46 cases in Madras.

Indonesia. In Surabaya, Java, 213 cases of smallpox were reported for the week ended July 15, 1950, and 193 cases for the week ended July 22. In Pontianak, Borneo, 27 cases were reported for the week ended July 8, and 21 cases for the week ended July 15.

Rhodesia (Southern). During the month of June 1950, 74 cases of smallpox (9 deaths) were reported in Southern Rhodesia.

Venezuela. During the period January 1–March 31, 1950, 706 cases of smallpox were reported in Venezuela.

Typhus Fever

Ecuador. During the month of June 1950, 43 cases of typhus fever, including murine type, were reported.

Jamaica. During the week ended July 29, 1950, 3 cases of typhus fever (murine type) were reported in Kingston.

Netherlands New Guinea. One case of typhus fever was reported in the port of Hollandia during the week ended July 15, 1950.

Errata

In the article "Effect of Formaldehyde on the Direct Microscopic Count of Raw Milk" by B. S. Levine, published in the July 28 issue, the entries in table 1, page 934 for "Significance of difference between means" should be changed as follows: "Not significant" should read "High" in both instances and "High" should read "Very high".