Tuberculin Sensitivity of Young Adults in the United States

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THE rapid and continued decline in tuberculosis mortality during the last decades is changing the approach to tuberculosis control. Interest in the mass X-ray survey for detecting persons with active tuberculosis is being supplemented by interest in the tuberculin test for identifying persons who have been infected by the tubercle bacillus. Large-scale use of the tuberculin test may well receive increasing emphasis for tuberculosis control programs during the coming years.

Interest in tuberculin testing programs is not new. One of the purposes of the Tuberculosis Committee of the American Student Health Association, founded in 1931, was to collect information on the prevalence of tuberculin sensitivity among college students throughout the Nation (*1*). And during the 1930's a number of reports were published by Long and associates (*2–4*), as well as by others (*5*, *6*), on the results of tuberculin testing of college students. A standardized tuberculin product (PPD) became available during the later part of the period, and attention was also directed toward the adoption of a uniform testing technique. The reports, in general, indicated a relatively high frequency of tuberculin reactors in the west, lower frequencies in the central part of the country, and high frequencies in the east. Usually, two doses of PPD were used: a first test with 0.00002 mg. and, for nonreactors to that dose, a second test with 0.005 mg. But results were not reported separately for each dose.

By the early 1940's evidence had accumulated from various studies, particularly from the work of Furcolow and associates (*7*), that the so-called intermediate dose test with 0.0001 mg. of standardized PPD was sufficient to detect almost all persons with active tuberculous disease or other signs of tuberculous infection. Results of subsequent studies in this country and abroad (*8–12*) confirmed the earlier findings with the intermediate dose test and, in addition, indicated that most of the sensitivity brought out only by larger doses of tuberculin is not related to tuberculous infection or disease. Such low-grade sensitivity shows pronounced variation with geographic area, being almost

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absent in some localities and highly prevalent in others. It may therefore be assumed that low-grade (nonspecific) sensitivity has inflated the frequency of positive reactors reported from studies in which either 1 mg. of O.T. or 0.005 mg. of PPD has been used as the final dose. The intermediate (0.0001 mg.) dose gradually became more widely accepted, and in 1950 it was recommended by the National Tuberculosis Association for a single-dose testing procedure (*13*). The intermediate dose was adopted also by the World Health Organization for tuberculin testing in its international tuberculosis and BCG programs (*14*).

Testing with the intermediate dose of standardized PPD-S, Palmer and associates (*8*, *9*) found an average frequency of about 12 percent reactors among more than 20,000 young white women entering schools of nursing in various parts of the country between the years 1943 and 1949. The frequencies ranged from less than 10 percent in residents of some of the midwestern States to around 17 percent in girls from the east coast and more than 20 percent in Oklahoma, Texas, and Indiana. Canada and Babione (*15*), using the same dose of tuberculin for testing nearly 80,000 Navy recruits and midshipmen in 1948, reported an average frequency of 9.7 percent positive reactors. Although their results were not given by geographic area of residence, the frequency of reactors was significantly higher in the men at the Naval Training Center at San Diego, Calif., than in those at the Naval Training Center at Great Lakes, Ill.

This paper presents the results and discusses the implications of a tuberculin testing program conducted in 1949–51 among more than 120,000 young white adults—Navy recruits and college students—from almost all parts of the United States.

The study, like most public health research projects, represents the cooperative efforts of many persons and groups. In addition to thousands of young men and women who participated as subjects of study, we had the assistance of the medical corpsmen and officers of the U. S. Naval Training Center, San Diego, and Captains Sidney A. Britten and Charles A. Castle of the Tuberculosis Control Section, Preventive Medicine Division, Bureau of Medicine and Surgery, Department of the Navy. Also cooperating were the directors of student health and their staffs at Berea College, Fort Hays Kansas State College, Iowa State College, Kansas State College, Miami (Ohio) University, Ohio State University, Oklahoma A. and M. College, Purdue University, South Dakota State College, St. Joseph's College and Military Academy, Syracuse University, the universities of Chicago, Colorado, Indiana, Kansas, Kentucky, Minnesota, Missouri, Pennsylvania, and Wisconsin, and various professional schools in New England.

Material and Methods

The major part of the study is based on the results of tuberculin testing of 83,599 white men, 17–21 years of age, as they entered the Naval Training Center at San Diego, Calif., during the years 1949–51. In cooperation with the U. S. Navy, arrangements were made systematically to test each new recruit with tuberculin, histoplasmin (*16*), and coccidioidin and also to obtain a complete residence history. Serious efforts were made to see that no new recruit was missed. The testing was done by a small group of medical corpsmen who were carefully instructed and periodically supervised by Public Health Service research personnel. While some turnover of corpsmen was unavoidable, one principal corpsman was in charge during most of the study period.

In addition, 38,070 white students (22,684 men and 15,386 women) 17–21 years of age were tested during the years 1949–50 in some 35 colleges and universities in 17 States, largely in the middle west. Most of the students were freshmen. The testing was done by a physician or nurse at each college although at the beginning of the program a member of the research staff of the Public Health Service was present to help standardize the testing procedures.

The entire study population, recruits as well as college students, were tested by intradermal injection of 0.1 ml. containing 0.0001 mg. of PPD–S (5 tuberculin units of the international standard PPD). Reactions were read at 48–72 hours by measuring the transverse diameter of induration in millimeters. In this report, a reaction with an induration recorded as measuring 5 mm. or more has been designated as positive.

Residence histories were obtained by a questionnaire in which each Navy recruit and college student specified, in chronological order, each locality where he had lived since birth. Those who had spent their whole life in one State, without residing elsewhere for periods longer than 6 months, were later classified as "one-state residents." Of the Navy recruits, 56,481 could be classified as one-state residents. Of the college students, 15,148 of the men and 11,250 of the women could be so classified.

One-state residents who had never spent more than 6 months away from one section of their home State were further classified as "one-section residents." A section consisted of a number of counties with rough adjustment in size for differences in population density. Sections were small in densely populated areas, larger in areas of low population density. A total of 49,404 recruits were one-section residents.

The questionnaire also requested information on the basis of which the type of residence was classified into four groups. Metropolitan residents were defined as those living in cities of more than 100,000 population (according to the 1940 census) or in the suburbs of these cities. Farm residents were those who lived on farms. All other types of residence were classified under the broad heading of "other." And persons with more than one type of residence were classified as "mixed."

Table 1. Numbers tested and percentage of positive reactors in each group, by age

Age in years at last birthday	Navy recruits		College students				All groups	
			Male		Female			
	Number tested	Percent positive	Number tested	Percent positive	Number tested	Percent positive	Number tested	Percent positive
17	15, 389	8. 9	4, 209	5. 6	3, 532	6. 0	23, 130	7. 9
18	21, 588	8. 4	8, 980	7. 2	6, 583	6. 3	37, 151	7. 7
19	26, 073	8. 7	3, 937	8. 8	2, 668	7. 4	32, 678	8. 6
20	14, 639	10. 4	3, 059	12. 4	1, 712	8. 0	19, 410	10. 5
21	5, 910	11. 4	2, 499	14. 1	891	10. 3	9, 300	12. 0
Total	83, 599	9. 1	22, 684	8. 6	15, 386	6. 8	121, 669	8. 8
Mean age in years	19. 2		19. 1		18. 8		19. 1	

Table 2. Numbers tested and percentage of positive reactors in one-state residents and in residents of more than one State

Residence	Navy recruits		College students			
			Male		Female	
	Number tested	Percent positive	Number tested	Percent positive	Number tested	Percent positive
One-state residents:						
In States with 200 or more tested	55, 706	8. 7	14, 445	7. 5	9, 980	6. 6
In States with less than 200 tested	775	7. 2	703	7. 4	1, 270	6. 8
Residents of more than one State	27, 118	10. 2	7, 536	11. 0	4, 136	7. 7
Total	83, 599	9. 1	22, 684	8. 6	15, 386	6. 8

Study of geographic differences in the prevalence of tuberculin sensitivity is based primarily on the data from the Navy recruits. The Naval Training Center at San Diego draws recruits from all over the country except the north Atlantic States and the Great Lakes region. And, as all of the men were tested in San Diego with the same tuberculin product and by the same personnel, variations (and errors) in technique would be expected to be distributed at random without regard to previous place of residence. Moreover, though the recruits cannot be regarded as representative of the general population of young men of the same age, one could expect those from one locality to be much the same kind of men as those from other localities.

Results

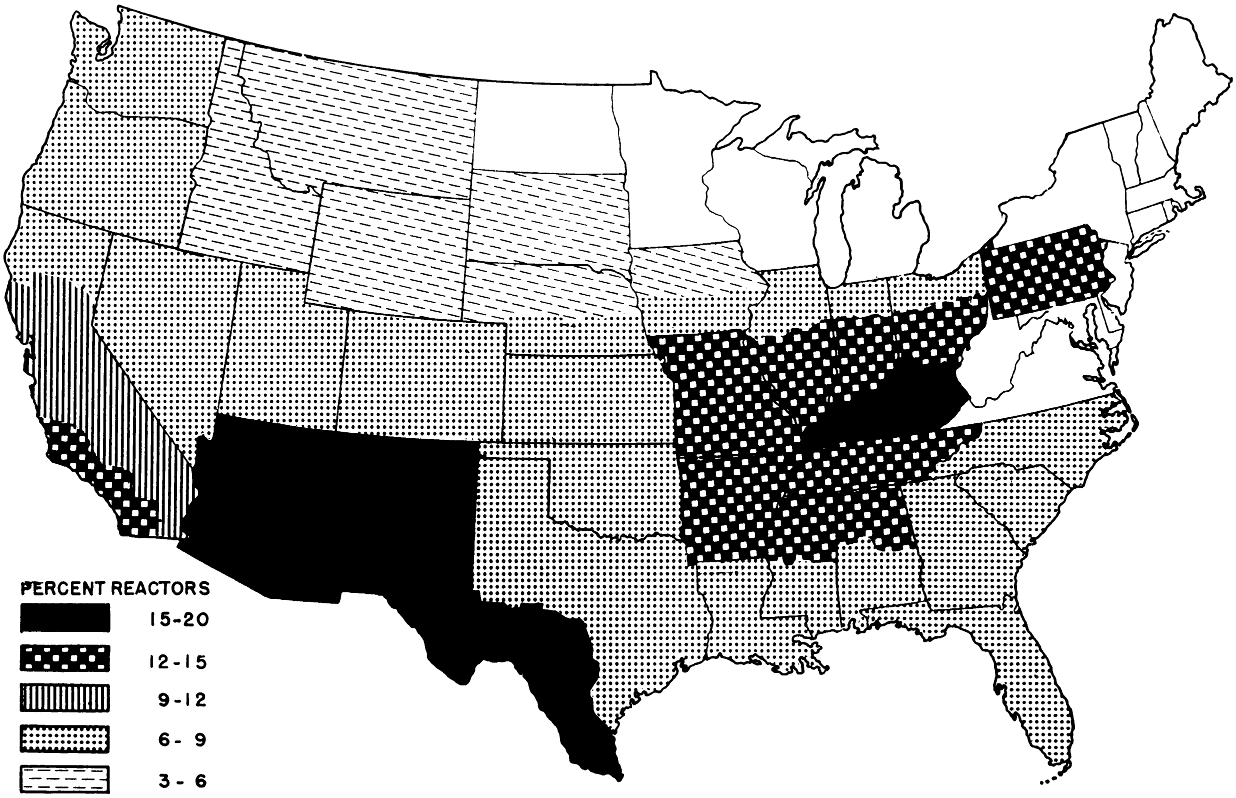
The numbers tested and the percentage with reactions of 5 mm. or more for all of the recruits and college students are given by age in table 1. The overall frequency of positive reactors is 8.8 percent, ranging from 9.1 in the recruits to

Table 3. Numbers tested and percentage of positive reactors in one-state residents, by State of residence [1]

State	Navy recruits		College students			
			Male		Female	
	Number tested	Percent positive	Number tested	Percent positive	Number tested	Percent positive
Alabama	1, 981	8. 0				
Arizona	472	22. 7				
Arkansas	1, 785	8. 9				
California	8, 496	11. 6				
Colorado	1, 444	8. 2	308	9. 7		
Florida	1, 469	5. 3				
Georgia	1, 961	7. 2				
Idaho	708	3. 4				
Illinois	879	9. 7	1, 689	8. 5	1, 156	9. 7
Indiana	1, 125	10. 0	1, 478	7. 9	831	6. 0
Iowa	2, 567	4. 9	640	3. 8	318	5. 7
Kansas	1, 900	6. 2	2, 577	4. 5	1, 651	3. 6
Kentucky	1, 010	16. 7	534	15. 5	374	12. 0
Louisiana	1, 533	7. 4				
Massachusetts					433	10. 8
Minnesota					1, 255	5. 1
Mississippi	1, 337	7. 3				
Missouri	2, 336	11. 6	879	9. 6	535	8. 2
Montana	839	5. 6				
Nebraska	1, 580	3. 9				
New Jersey			246	7. 3		
New Mexico	601	18. 0				
New York			1, 333	8. 3	779	7. 3
North Carolina	2, 645	6. 0				
Ohio	1, 341	11. 1	2, 079	7. 8	1, 172	5. 4
Oklahoma	2, 170	8. 9	1, 035	7. 9	837	6. 1
Oregon	1, 182	6. 9				
Pennsylvania	531	10. 9	362	12. 2		
South Carolina	1, 308	5. 0				
South Dakota	401	4. 5	275	5. 5		
Tennessee	1, 788	11. 3				
Texas	6, 834	8. 7				
Utah	976	4. 4				
Washington	2, 180	6. 8				
Wisconsin			1, 010	5. 0	639	6. 9
Wyoming	327	5. 5				
Total	55, 706	8. 7	14, 445	7. 5	9, 980	6. 6

[1] Excludes States represented by less than 200 persons.

Figure 1. Distribution of States or sections of States by prevalence of positive tuberculin reactors in Navy recruits.



States represented by insufficient data are unshaded.

6.8 in the women students. The frequency increases with age, especially in the college men.

The frequency of reactors in the one-state residents was found to be lower than in those who had lived in more than one State (table 2). The latter group also includes all persons born outside of the United States. Further, in the Navy recruits, the frequency of reactors in the States from which 200 or more were tested was higher than in States represented by smaller numbers, mainly States in the north central section of the country and in New England.

The findings among the one-state residents are given in table 3 for States from which 200 or more persons were tested. Except for Kentucky, New Mexico, and Arizona, the percentage of reactors among the recruits does not exceed 12, and for 9 of the 31 States it is less than 6. The same broad pattern of geographic variation is found for the college students although the prevalence of tuberculin sensitivity is generally lower than in the recruits.

Based only on one-section residents among the Navy recruits, the area covered by the 31 States has been divided into five different levels of prevalence of tuberculin sensitivity (fig. 1). States and sections of States have been grouped in order to show the broad geographic pattern of variation in prevalence of sensitivity. Sectional subdivisions of States have been maintained only where groups of sections appeared to have distinctly different rates from those of the neighboring sections. (For continuity, Nevada has been included although only 96 recruits were tested from that State.)

The map shows that the frequency of tuberculin reactors is less than 10 percent over most of the country, from the northwestern to the southeastern coasts. Areas of significantly higher frequencies appear in some east central States and in the southwest, but only among residents of Kentucky, Arizona, New Mexico, and the southern part of Texas do the rates exceed 15 percent.

The frequency of tuberculin reactors varies with type of residence. Table 4 shows it is generally highest in the metropolitan and lowest in the farm residents. It is, therefore, pertinent to consider to what extent the geographic variations shown in table 3 and figure 1 may be influenced by differences in the relative proportions of different types of residence.

The findings by type of residence for recruits

Table 4. Numbers tested, percentage distribution, and percentage of positive reactors, by type of residence [1]

Type of residence	Navy recruits			College students						All groups
				Male			Female			
	Tested		Percent positive	Tested		Percent positive	Tested		Percent positive	Percent positive
	Number	Percent		Number	Percent		Number	Percent		
Metropolitan	10, 853	24	10. 1	4, 836	36	8. 5	4, 254	42	7. 2	9. 1
Farm	11, 858	26	6. 0	2, 721	20	5. 3	1, 486	15	4. 3	5. 7
Other	22, 467	50	9. 3	5, 983	44	8. 0	4, 412	43	6. 9	8. 7
All types	45, 178	100	8. 6	13, 540	100	7. 6	10, 152	100	6. 6	8. 1
Adjusted to distribution by type of residence of Navy recruits						7. 4			6. 3	

[1] Excludes persons of mixed residence.

Table 5. Numbers tested and percentage of positive reactors, by State and by type of residence,[1] for Navy recruits from 20 States

States arranged by decreasing frequency of positive reactors	Metropolitan		Farm		Other residence		All types		Adjusted [2] percent positive	States arranged by adjusted frequency of positive reactors
	Number tested	Percent positive	Number tested	Percent positive	Number tested	Percent positive	Number tested	Percent positive		
1 Kentucky	217	13. 8	304	14. 8	320	16. 6	841	15. 2	15. 4	1
2 Missouri	746	12. 5	490	6. 1	665	14. 7	1, 901	11. 6	12. 0	2
3 California	3, 666	10. 9	712	10. 0	2, 648	11. 8	7, 026	11. 1	11. 1	4
4 Tennessee	417	10. 8	562	9. 6	477	12. 6	1, 456	10. 9	11. 4	3
5 Indiana	229	9. 6	170	8. 8	531	11. 5	930	10. 5	10. 3	5
6 Ohio	524	10. 5	147	8. 8	469	10. 9	1, 140	10. 4	10. 3	6
7 Illinois	224	7. 1	162	7. 4	355	13. 5	741	10. 3	10. 2	7
8 Texas	1, 006	11. 1	1, 100	4. 6	2, 900	10. 3	5, 006	9. 2	9. 2	8
9 Oklahoma	287	7. 3	566	8. 0	850	9. 9	1, 703	8. 8	8. 7	9
10 Colorado	342	7. 6	250	4. 8	549	10. 7	1, 141	8. 5	8. 4	11
11 Alabama	202	7. 9	556	5. 9	801	9. 7	1, 559	8. 1	8. 3	12
12 Louisiana	225	14. 2	337	6. 2	665	6. 3	1, 227	7. 7	8. 6	10
13 Oregon	219	5. 5	245	3. 7	426	10. 6	890	7. 4	7. 5	13
14 Georgia	201	9. 5	493	4. 5	800	7. 8	1, 494	6. 9	7. 5	14
15 Washington	641	8. 4	389	6. 4	669	5. 4	1, 699	6. 8	6. 5	16
16 Kansas	160	11. 2	485	3. 3	852	6. 9	1, 497	6. 2	7. 3	15
17 Florida	302	7. 9	186	3. 8	739	4. 2	1, 227	5. 1	5. 2	18
18 Iowa	205	7. 3	701	2. 6	1, 163	5. 9	2, 069	4. 9	5. 5	17
19 Utah	261	7. 7	205	. 5	308	4. 2	774	4. 4	4. 3	20
20 Nebraska	214	7. 9	454	2. 6	623	3. 4	1, 291	3. 9	4. 5	19
Total	10, 288	10. 2	8, 514	6. 0	16, 810	9. 4	35, 612	8. 8	8. 9	----------

[1] Excludes persons of mixed residence.
[2] Adjusted to distribution by type of residence of the total.

from the 20 States in which metropolitan, farm, and other residents were each represented by reasonably large numbers are given in table 5. Relative frequencies of reactors for the three types of residence vary considerably from one State to another. However, as shown by the last column in the table, adjustment for the differences in distribution by type of residence has only a limited effect on the order of the 20 States as arranged by frequency of tuberculin reactors. It must be assumed, nevertheless, that type of residence is of greater importance for total frequency of reactors in other States where metropolitan areas, as defined, do not exist, or where the distribution by type of residence is for other reasons less uniform.

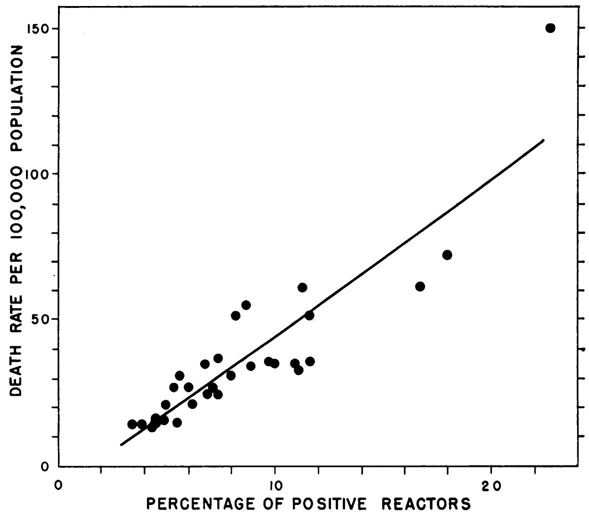
The frequency of tuberculin reactors in the total study population, as well as in the population used for studying geographic variations, is highest in the recruits, lower in the college men, and lowest in the college women. The differences are statistically significant. They cannot be accounted for by differences in age distribution since that was essentially the same in each group. Nor can they be ascribed to the unequal geographic distribution of the groups.

Table 6. Percentage of positive reactors in Navy recruits (one-state residents [1]) and average annual tuberculosis death rates per 100,000 white population, by State, 1939–41

State	Percent positive	Tuberculosis death rate [2]
Alabama	8. 0	32
Arizona	22. 7	150
Arkansas	8. 9	34
California	11. 6	51
Colorado	8. 2	51
Florida	5. 3	27
Georgia	7. 2	26
Idaho	3. 4	14
Illinois	9. 7	36
Indiana	10. 0	35
Iowa	4. 9	16
Kansas	6. 2	21
Kentucky	16. 7	62
Louisiana	7. 4	37
Mississippi	7. 3	25
Missouri	11. 6	36
Montana	5. 6	32
Nebraska	3. 9	14
New Mexico	18. 0	72
North Carolina	6. 0	27
Ohio	11. 1	33
Oklahoma	8. 9	34
Oregon	6. 9	25
Pennsylvania	10. 9	35
South Carolina	5. 0	21
South Dakota	4. 5	15
Tennessee	11. 3	61
Texas	8. 7	55
Utah	4. 4	14
Washington	6. 8	35
Wyoming	5. 5	15

[1] Excludes States represented by less than 200 persons.
[2] Computed from mortality and population figures given in Vital Statistics of the United States, 1939–41.

Figure 2. Correlation for 31 States between percentage of positive tuberculin reactors in Navy recruits and average annual death rates from tuberculosis (all forms) for 1939–41 in the white population.



As shown in table 3, for the 8 States from which more than 200 persons (all one-state residents) were tested within each of the three groups, the prevalence of reactors ranges from relatively high (Kentucky) to low (Iowa). Correction for the inequality in geographic distribution of the recruits and the college students does not reduce the differences in the total prevalence of reactors in those 8 States. The proportion of metropolitan residents is lowest in the recruits, higher in the college men, and highest in the college women (table 4). Consequently, an adjustment of the college student rates to the distribution, by type of residence, of the recruits tends to increase rather than decrease the differences between the groups.

Differences between recruits and college men with respect to tuberculin sensitivity are not found in those who had been residents of more than one State, nor in the one-state residents from States represented by small numbers

Table 7. Frequency distributions of sizes of reactions among

Transverse diameter of induration (in millimeters)

State of residence [1]	Number tested [2]	00	01	02	03	04	05	06	07	08	09	10	11	12
Alabama	1,981	1,795	----	17	7	4	21	12	4	13	6	19	6	7
Arizona	472	355	----	4	3	3	6	5	3	7	7	14	1	14
Arkansas	1,785	1,599	----	14	8	5	8	5	8	14	5	22	9	10
California	8,496	7,438	----	46	15	14	30	21	30	42	34	101	36	73
Colorado	1,444	1,320	----	5	1	-----	3	2	4	5	-----	12	10	3
Florida	1,469	1,364	----	10	14	3	9	4	4	10	3	17	3	6
Georgia	1,961	1,788	1	14	13	4	17	4	6	10	10	27	5	10
Idaho	708	679	----	4	-----	1	1	-----	1	-----	-----	1	3	3
Illinois	879	788	----	3	1	2	4	2	3	4	2	5	5	6
Indiana	1,125	1,005	----	5	1	1	4	1	5	2	2	15	2	13
Iowa	2,567	2,421	----	8	7	5	7	-----	6	8	6	12	8	5
Kansas	1,900	1,771	----	8	2	2	8	6	5	4	4	18	4	7
Kentucky	1,010	832	----	2	2	5	4	6	4	19	6	23	5	17
Louisiana	1,533	1,390	----	12	9	8	11	9	14	15	10	7	6	10
Mississippi	1,337	1,213	----	14	9	3	7	10	8	8	5	21	4	8
Missouri	2,336	2,027	----	16	12	9	20	10	11	20	6	41	9	20
Montana	839	788	----	-----	3	1	-----	3	1	1	-----	3	3	1
Nebraska	1,580	1,499	----	9	5	5	2	5	3	3	2	4	1	5
New Mexico	601	487	----	2	1	3	4	1	2	5	3	17	5	6
North Carolina	2,645	2,453	1	15	8	10	11	8	7	13	8	21	5	7
Ohio	1,341	1,186	----	-----	4	2	12	4	6	4	6	22	6	12
Oklahoma	2,170	1,939	----	21	7	9	9	9	10	10	8	28	14	14
Oregon	1,182	1,087	----	10	3	1	-----	-----	1	4	1	7	3	1
Pennsylvania	531	466	----	7	-----	-----	-----	1	3	6	-----	12	3	2
South Carolina	1,308	1,222	----	14	4	3	7	2	4	8	3	9	4	5
South Dakota	401	381	----	2	-----	-----	1	-----	2	-----	-----	2	-----	2
Tennessee	1,788	1,573	----	4	1	8	8	7	10	14	7	21	9	17
Texas	6,834	6,130	----	53	28	29	40	26	44	51	31	78	28	45
Utah	976	925	----	3	3	2	1	2	1	-----	2	6	3	4
Washington	2,180	2,014	----	11	5	1	3	4	2	3	5	13	4	8
Wyoming	327	305	----	3	1	-----	-----	-----	-----	1	-----	6	1	1
Total	55,706	50,240	2	336	177	143	258	169	212	304	182	604	205	342

[1] Excludes States represented by less than 200 persons. [2] Includes only persons classified as one-state residents.

(table 2). Nor is the relative frequency of reactors in college women consistently the lowest in all States represented in the study (table 3).

Tuberculin Sensitivity and Tuberculosis Deaths

The prevalence of positive reactors in each of the 31 States from which 200 or more recruits were tested was related to the average annual tuberculosis death rates in the white population, by State, for the 3-year period 1939–41, the midpoint in the lives of the 17- to 21-year-old recruits (table 6 and fig. 2). A high positive correlation was found, the coefficient of correlation being 0.88. That finding led to an examination of the relation between the prevalence of positive reactors and other tuberculosis death rates: sex-specific rates for the period 1939–41 and average annual rates for 1929–31 and for 1949–51, as well as the mean annual death rates for all three periods (1929–31, 1939–41, 1949–51). Coefficients of correlation range from 0.84 to 0.93. The difference is not statistically significant.

Variation in Size of Tuberculin Reactions

Results thus far have been presented in terms of the conventional definition of a positive reaction as one measuring 5 mm. or more. The use of that definition, according to recent studies in many countries (*10*), may mean that reactions of quite different significance are being classed as positive in different geographic areas. Distributions of the sizes of the reactions were therefore studied, and the basic data are given in table 7.

While the data are inadequate for detailed analysis by single States, pooled results from several States illustrate the difference that may be found between two geographic areas (fig. 3). The figure shows percentage distributions, by size, for reactions measuring 2 mm. or more, for recruits from four northwestern States,

Navy recruits to the intradermal 0.0001 mg. tuberculin test

Transverse diameter of induration (in millimeters)

13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28+	State of residence [1]
4	5	22	2	6	3	2	16	----	5	----	----	1	1	1	2	Alabama.
3	2	7	1	4	7	3	5	2	6	2	2	3	2	----	1	Arizona.
7	6	16	8	5	6	1	11	3	3	1	2	6	1	----	2	Arkansas.
29	64	109	43	33	58	19	84	11	34	16	18	34	4	6	54	California.
2	3	13	6	5	7	3	13	3	3	2	1	9	----	1	8	Colorado.
3	4	6	----	1	1	1	2	----	----	1	----	3	----	----	----	Florida.
4	5	10	----	1	6	2	8	----	3	4	1	2	----	----	6	Georgia.
1	----	----	1	2	1	----	3	----	3	----	1	1	----	1	1	Idaho.
4	4	9	5	4	4	2	8	1	1	3	----	7	----	1	1	Illinois.
3	7	11	5	4	7	----	10	1	8	2	1	2	2	1	5	Indiana.
4	9	9	6	9	2	2	8	3	3	----	3	5	3	3	5	Iowa.
4	2	11	6	5	3	----	7	3	5	3	1	6	----	1	4	Kansas.
5	8	20	5	5	6	1	14	----	4	3	1	7	----	----	6	Kentucky.
3	7	6	----	----	6	1	6	----	1	----	----	----	----	----	2	Louisiana.
1	3	11	3	1	1	----	5	----	----	----	1	1	----	----	----	Mississippi.
9	14	24	6	6	15	2	26	2	5	3	3	9	----	----	11	Missouri.
2	7	2	2	2	2	1	6	1	3	1	----	3	----	----	3	Montana.
1	3	8	4	1	3	----	11	----	1	----	----	1	1	----	3	Nebraska.
1	5	10	2	5	8	1	13	1	3	1	1	8	1	----	5	New Mexico.
2	8	14	1	4	4	3	17	3	3	3	----	5	2	----	9	North Carolina.
7	8	16	3	7	8	1	10	1	1	1	2	1	2	2	7	Ohio.
2	11	17	5	3	6	5	22	2	3	2	4	3	----	1	6	Oklahoma.
5	8	7	4	3	5	4	11	2	3	1	2	2	----	1	6	Oregon.
----	2	9	1	----	1	----	8	----	4	----	----	4	----	----	2	Pennsylvania.
1	1	5	2	2	3	1	3	----	1	----	----	2	----	----	2	South Carolina.
1	1	2	1	1	2	1	1	----	1	----	----	----	----	----	----	South Dakota.
5	8	22	8	8	10	4	16	1	6	1	1	10	----	----	9	Tennessee.
17	22	58	15	18	23	9	33	6	14	5	9	10	2	----	10	Texas.
----	4	5	2	2	1	1	4	----	1	1	1	----	----	1	1	Utah.
2	10	18	5	5	10	5	20	2	11	2	----	4	2	2	9	Washington.
1	1	3	----	----	1	----	2	----	1	----	----	----	----	----	----	Wyoming.
133	242	480	152	152	220	75	403	48	140	58	55	149	23	22	180	Total.

Idaho, Montana, Oregon, and Washington, and from four southeastern States, Alabama, Georgia, Louisiana, and Mississippi.

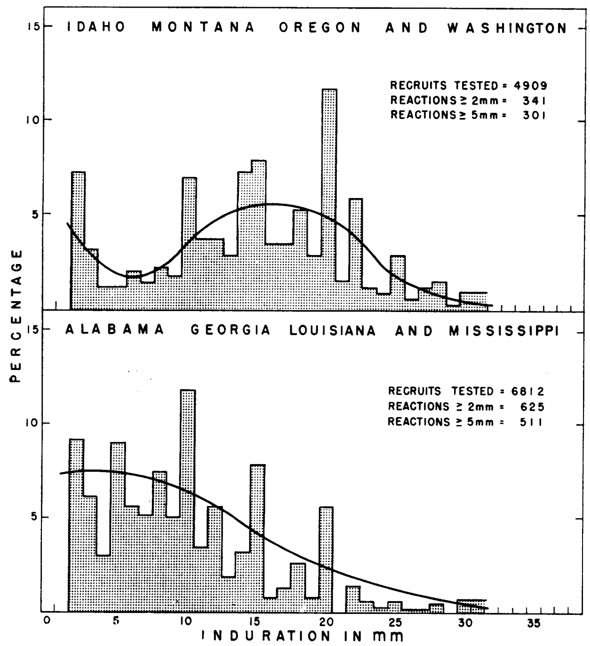
The concentration of reactions on "round" numbers (5, 10, 15, and 20 mm.) is obvious and indicates inaccuracy of reading even though serious efforts had been made to obtain precise measurements. (It may be recalled in this connection that each observer tested recruits from all over the country, and thus his inaccuracy would not be expected to bias the measurement of reactions of men from different geographic areas.) A smoothed curve is superimposed on each distribution to bring out the striking contrast between their shapes. While the distribution of reactions for the northwestern States is bimodal with a minimum at about 5 mm., that representing the southeastern group of States is unimodal with a relative concentration of readings in the 2 to 10 mm. range.

Among reactions commonly classed as positive, those measuring 5 mm. or more, the results obtained in the two geographic areas may be compared numerically by expressing the frequency of reactions measuring 5–9 mm. as a percentage of all reactions measuring 5 mm. or more. In the four northwestern States, only 10 percent of the positive reactions are less than 10 mm. in diameter; in the four southeastern States, 40 percent are less than 10 mm. Although the two groups of States represented in figure 3 were selected to show the greatest difference in the relative frequencies of small reactions, the data in table 7 indicate that the proportion of small reactions varies considerably from one geographic area to another.

Discussion

The findings of the present study confirm a number of recent reports that the frequency of tuberculin reactors among young white adults from over a large part of the United States is, today, very low—less than 10 percent at about

Figure 3. Percentage distributions of reactions measuring 2 mm. or more to the intradermal 0.0001 mg. tuberculin test in Navy recruits from four northwestern and four southeastern States.



20 years of age. In a few areas the frequency may be twice as high; but in many, and particularly in the rural parts of the country, it is below 5 percent.

In interpreting these findings it is important to appreciate that the frequency of reactors at 20 years of age represents the result of tuberculous infections that have occurred during the previous two decades. On the assumption that reversion of tuberculin sensitivity is rare, an average prevalence of less than 10 percent corresponds to an average infection rate of about 5 per 1,000 per year. A prevalence of around 5 percent found in many parts of the country implies a still lower infection rate, an average of around 2 per 1,000 per year. There is every reason to believe, however, that the risk of infection has not been constant but has declined during recent years. (Deaths from tuberculosis for the 0- to 19-year-old white population have dropped from 8.2 per 100,000 in 1939–41 to 0.7 in 1954.) At present, the annual rate of tuberculous infection in white children and adolescents over a large part of the country may well be less than 1 per 1,000 per year. Under such circumstances, most of our children can now be expected to reach adulthood without having acquired a tuberculous infection (*19*).

Type of residence has been shown by many workers to have considerable influence on the prevalence of tuberculin sensitivity, and our findings are in accord. The frequency of reactors is generally higher in urban than in rural residents. Had metropolitan residents in this study been defined as persons living strictly within city limits, the difference in rates between metropolitan and other residents might have been even greater.

Significant differences are shown in the percentage of reactors among the Navy recruits and the college students, differences that cannot be accounted for by age or by type of residence. They undoubtedly reflect the various factors, including socioeconomic status, that govern whether young men join the Navy or go to college. Among the college students, a higher frequency of reactors among men than women agrees with results of earlier investigations (*4*, *5*). It is not inconceivable that women students on the whole generally come from a higher social stratum than men. The fact that the frequency of reactors is usually about the same among boys and girls up to high school age (*17*, *18*) points again to some form of selection as accounting for the differences between sex-specific rates in college students.

Age, sex, race, and, to some extent, type of residence and probably socioeconomic factors do not, however, account for the broad geographic variations in the frequency of tuberculin reactors among Navy recruits (fig. 1). The variations must be ascribed to other factors, some of which are known to be of influence and some whose influence is entirely unknown. To the former belong ethnic differences and the well-known tendency of tuberculosis patients to move to certain areas, particularly the southwestern part of the country. Factors like those may, to a large extent, account for the high prevalence of reactors in California, Arizona, New Mexico, and part of Texas. Of particular interest is the relatively high percentage of reactors in some of the east central States, where such factors are presumably of less importance.

The high correlation between tuberculosis death rates and percentage of tuberculin reactors, by States, represents one of the critical results of the present study and must mean that both the frequency of low-dose reactors and the tuberculosis death rates reflect the same general features of tuberculosis in a community.

Recent years have seen a growing interest in large-scale tuberculin testing surveys. In communities where tuberculosis mortality rates are not adequate or not available, results of tuberculin testing may well be the best yardstick of the tuberculosis problem. For pinpointing localities and special situations where infection rates are still high and where energetic control measures could with profit be instituted or strengthened, the test is of unchallenged value. Where, on the other hand, the prevalence rates are low, the use of the tuberculin test as an index of time changes in the tuberculosis problem has distinct limitations. To obtain stable and representative rates would require the testing of very large groups; to estimate conversion rates or to identify an appreciable number of converters would require the retesting of literally tens of thousands of persons.

A number of studies in this country and elsewhere have shown that a high proportion of new cases of tuberculosis—in some areas most of the new cases—come from among the positive tuberculin reactors (*20–25*). Moreover, the risk of developing clinical disease is apparently much greater for those who have large reactions than for those who have small reactions to a low-dose tuberculin test (*23*, *25*). Perhaps one of the most tangible benefits to be derived from tuberculin testing programs is therefore the identification of the infected persons in the community and, by careful measurement of the reactions, the selection of those most at risk of developing tuberculosis. Careful followup of that selected group can be expected to facilitate early diagnosis and treatment of active disease. And, looking to the future, research studies now in progress offer reason to hope that the antimicrobial agents already found so effective in the treatment of clinical tuberculosis may also prove effective in preventing the development of disease in persons already infected (*26*).

How efficient are present-day tuberculin testing procedures for excluding from among the persons being called positive those who have not been infected with the tubercle bacillus? Material from this study, as illustrated in figure 3, shows considerable geographic difference in the sizes of tuberculin reactions generally considered positive. In the north, most of the positive reactions are large and undoubtedly represent specific infection with virulent tubercle bacilli. But in the south, and to a lesser extent in other areas, many of the reactions are small, measuring from 5 to around 10 or 12 mm. in diameter. Distributions similar to those found in the south have been reported from many countries (*10*) where high proportions of the population have the low-grade kind of sensitivity referred to as nonspecific and where many of the small reactions obtained with a low-dose of tuberculin are believed to be cross reactions representing infection with some organism (probably nonpathogenic) which produces sensitivity to tuberculin.

Many years ago the veterinarians had to face a similar situation with the problem of the "no-lesion reactor"—cattle that reacted to tuberculin yet showed no evidence of tuberculous infection. While the problem is still far from solved, it has long been known that tuberculin sensitivity in cattle may be caused by infection with a variety of micro-organisms, including the avian tubercle bacillus, *Mycobacterium johnei*, and others. The term "nonspecific" is commonly used by veterinarians to denote the tuberculin sensitivity caused by such organisms. Although that term may not be entirely satisfactory, Paterson has recently written that: "Provided the tuberculin is defined—then the reactions it produces may be classified as 'specific' or 'nonspecific.' The reactions produced by mammalian (human or bovine) tuberculin in the subject infected by mammalian tubercle bacilli are specific, by avian tubercle bacilli, nonspecific. The reaction of an avian type sensitized individual to avian tuberculin is also a specific reaction, to a mammalian sensitized, nonspecific" (*27*).

In the tuberculin testing of cattle, the problem of the no-lesion reactor did not become of practical concern until the prevalence of bovine tuberculosis fell to low levels, until the nonspecific reactors became a significant proportion of all positive tuberculin reactors. We are now entering the same stage in the tuberculin testing of humans. Our problem is no longer simply to separate persons having tuberculin sensitivity from those having no sensitivity; it includes also the discrimination between specific and nonspecific tuberculin sensitivity. While the separation of the two kinds of sensitivity has been improved by using only a small dose of tuberculin, further improvement cannot be expected by further change in dosage (*28, 29*). The crux of the matter is that with the tuberculin products at present available the smaller specific reactions do not differ in size from larger nonspecific reactions. We need to develop new techniques for distinguishing the two kinds of sensitivity; perhaps a more specific testing product, perhaps comparative testing techniques along the lines developed by the veterinarians to deal with the analogous problem in cattle.

Summary

Tuberculin sensitivity was studied during 1949–51 in more than 120,000 white men and women, 17–21 years of age, by testing with the intermediate (0.0001 mg.) dose of the international standard tuberculin PPD–S. The study population comprised Navy recruits from all parts of the country, tested as they entered the Naval Training Center at San Diego, Calif., and students, mostly freshmen, attending colleges and universities in 17 States. Residence histories obtained from each person at the time of the testing provided material for studying geographic differences in the prevalence of tuberculin sensitivity.

The average frequency of reactors was 8.8 percent, corresponding to an average annual infection rate of less than 5 per 1,000 during the last two decades. However, prevalence rates among Navy recruits ranged from about 20 percent in lifetime residents of Arizona and New Mexico to less than 4 percent in Idaho and Nebraska. Rates in the college students, while generally lower, reflected similar geographic differences. Residents of metropolitan areas generally had higher rates than farm residents.

A high positive correlation was found between the frequency of reactors among the Navy recruits and tuberculosis death rates in the white populations of their home States.

The sizes of tuberculin reactions generally classified as positive showed considerable geographic differences in the relative proportions of small and large reactions. In four northwestern States about 10 percent of the reactions measuring 5 mm. or more were from 5 to 9 mm. in diameter in contrast to 40 percent in four southeastern States. The relative preponderance of small reactions is ascribed to a low-grade kind of sensitivity not related to tuberculous infection; whereas most of the larger reactions represent specific sensitivity. Careful measurement of reactions is essential for the efficient identification of persons most at risk of developing clinical tuberculous disease.

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