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The Relationship Between Tuberculin Reaction and Tuberculous Infection

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The findings from mass investigations on tuberculin sensitivity are often reported in terms of the frequency of positive reactors. On the basis of the degree of reaction to tuberculin, the population is divided into two groups intended to represent those infected with tuberculosis and those not infected.

Division of the population in this way, however, will always be to some extent arbitrary. First, results will depend upon choice of test, technique, and dosage of tuberculin. With increasing dosage there will be an increase in the number of reactions that can justifiably be classified as positive. It is not possible by means of the character of the reaction to decide which is the most appropriate dose for separating infected from noninfected individuals.

Second, there is no sharp dividing line between two kinds of reactions even to a given dose which could appropriately separate positive and negative. The reactions range along a continuous scale which it is difficult to dichotomize.

One method of interpreting the different degrees of reactions is to compare them with quite different criteria of tuberculous infection, such as radiologically detected pulmonary changes.

Another approach is to obtain distributions according to detailed categories of degree of reaction for different groups of the population. From an examination of these distributions, it may be possible to gain further insight into the relationship between level of sensitivity and the existence of tuberculous infection.

In some parts of the scale of reactions, the majority of individuals

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will presumably belong to the infected or to the noninfected group. It has been found that many distribution curves have two definite peaks, and in such cases the reactions in the modal classes can reasonably be designated as definitely positive and definitely negative. The group to which individuals belong is not so easily determined when the reaction is between these two extremes. These in-between reactions can suitably be called doubtful. It is likely that these reactions could be found among tuberculosis infected as well as noninfected individuals. In the latter case the reaction is often referred to as nonspecific, a terminology which will be used throughout the present paper.

The distribution curves will differ from one age-sex group to another and by geographical areas. That the prevalence of infection is not the same in all population groups is demonstrated by differences in the heights of the two peaks of the curves. It is conceivable, however, that not only will the prevalence of infection vary, but the degree of reaction among infected individuals may also vary, and this will be indicated by the different locations of the peak of positive readings along the scale of reactions.

In this study, these aspects are explored by the use of age-sex distributions of reactions to Pirquet's test in a section of Norway.

Material and Methods

The material for this study has been provided through the courtesy of the Aker Tuberculosis Department of the Oslo Public Health Office and of its Chief, Dr. Erling Refsum. The group studied consists of a portion of the population over 14 years of age of the districts of Østre Aker, Nordstrand, and Vestre Aker, near the city of Oslo, who were tuberculin tested in connection with a mass photofluorographic survey in 1947–48.

Pirquet's technique was used in administering the tests. The tuberculin product was standardized Danish old tuberculin from the State Serum Institute in Copenhagen, of a strength 1.7 times the international standard. Immediately after preparation a 0.5 percent solution of phenol was added to the tuberculin; one drop of a 1 percent solution of adrenalin was added just before the test was given. Readings, consisting of measurements of the diameter of the erythema and induration, were made at 72 hours.

The majority of the examinations were performed by the same three nurses, but a part of the examinations were done by substitutes in the absence of the regular nurses. All of the participating nurses, however, were considered well experienced in this work and all had been carefully instructed. The examinations by the substitutes occurred at random throughout the study. Hence, no bias is introduced by a concentration of these examinations in any particular group.

The material is summarized in table 1, where the data are classified by age and sex. Figures on the total surveyed population are also presented. The attendance rate for women was higher than for men, tests having been obtained on 69 and 56 percent of the respective populations. For both sexes, the highest attendance was observed for those 30–59 years of age, and the lowest for those 15–29 years.

Table 1. *Summary of material*

Age	Population	Number examined		
		Total	Previously vaccinated with BCG	Not previously vaccinated with BCG
Male				
15–29	11,749	5,105	711	4,394
30–39	8,736	5,024	177	4,847
40–49	7,986	5,107	40	5,067
50–59	5,790	4,123	5	4,118
60 and over	4,797	2,667	0	2,667
Total	39,058	22,026	933	21,093
Female				
15–29	15,145	7,775	755	7,020
30–39	10,616	8,008	259	7,749
40–49	9,429	7,748	43	7,705
50–59	6,131	5,800	5	5,795
60 and over	6,435	3,637	0	3,637
Total	47,756	32,968	1,062	31,906

In order to limit the investigation to a study of natural infection, information was obtained on previous BCG vaccinations, as shown in table 1. There is a possibility that additional vaccinations had been given among the study group, but the number cannot be very large as most vaccinations are given by the Health Office and are on record there.

The persons examined include some who did not actually receive the test at the time of the examination, but who produced a certificate of a positive reaction to a previous Pirquet test and were exempted from another one. In table 2, which shows the distribution of reactions according to age and sex, the number of such persons is entered in the bottom line. For the purpose of constructing relative frequency distributions, it was assumed that the reactions of persons previously tested and found positive were distributed from 3 mm. induration upwards, in the same proportion as those reactions which were measured. It is probable that individuals with a previously recorded positive reaction and those tested for the first time in the mass survey represent different groups. But in the absence of a better method the assumption that they were similar was applied to construct the distributions shown in table 3.

Table 2. ***Distribution of Pirquet reactions according to size of induration, by sex and age***

Induration in mm.	Age					
	15–29	30–39	40–49	50–59	60 and over	Total
Male						
0	1,588	689	310	149	194	2,930
1	690	430	225	129	220	1,694
2	122	102	60	88	125	497
3	52	34	29	36	62	213
4	217	273	355	419	410	1,674
5	108	166	204	224	149	851
6	235	308	476	425	246	1,690
7	126	298	374	306	196	1,300
8	201	451	573	478	248	1,951
9	82	163	233	153	74	705
10	191	409	540	464	187	1,791
11	24	59	80	53	21	237
12	74	178	241	188	79	760
13	2	11	15	14	4	46
14	8	22	33	30	13	106
15	18	76	111	93	34	332
16	3	27	30	34	11	105
17	1	5	3	3	2	14
18	2	28	35	33	9	107
19	1	2	3	2		8
20	21	48	54	37	15	175
21				1		1
22	1	2	3	4	1	11
23		1	1	1		3
24	2	1	3	3		9
25	2	19	19	16	4	60
26		1	3	3	1	8
27				1		1
28		3	9	2		14
29						
30	2	23	20	12	5	62
31 and over	5	16	23	21	5	70
Not tested [1]	616	1,002	1,002	696	352	3,668
Total	4,394	4,847	5,067	4,118	2,667	21,093
Female						
0	2,984	2,015	1,116	735	634	7,484
1	1,327	1,016	755	622	550	4,270
2	229	224	238	234	217	1,142
3	74	58	85	83	89	389
4	231	431	737	745	538	2,682
5	122	282	410	327	186	1,327
6	312	612	733	595	316	2,568
7	205	472	561	412	172	1,822
8	256	580	678	462	215	2,191
9	88	212	266	153	61	780
10	176	388	472	322	180	1,538
11	28	48	51	41	13	181
12	89	159	206	162	69	685
13	4	7	15	9	3	38
14	8	27	33	20	8	96
15	28	43	74	50	24	219
16	10	22	28	29	9	98
17	1	1	3	4	2	11
18	4	11	19	21	7	62
19			1		1	2
20	11	40	49	35	16	151
21				1		1
22	1	5	4	3		13
23						
24	1	2	4	2	1	10
25	7	12	17	9	4	49
26	1		2			3
27						
28	3	4	6	1	1	15
29						
30	7	17	14	19	1	58
31 and over	5	28	28	36	8	105
Not tested [1]	808	1,033	1,100	663	312	3,916
Total	7,020	7,749	7,705	5,795	3,637	31,906

[1] With previous positive test.

Table 3. *Percentage of distribution of Pirquet reactions according to size of induration, by sex and age*

Induration in mm.	Age 15-29	30-39	40-49	50-59	60 and over
Male					
0	36.1	14.2	6.1	3.6	7.3
1, 2	18.5	11.0	5.6	5.2	13.0
3, 4	8.9	8.8	9.8	13.6	21.2
5, 6	11.3	13.5	17.3	19.4	17.7
7, 8	10.8	21.4	24.1	23.4	19.9
9, 10	9.0	16.3	19.7	18.4	11.7
11, 12	3.2	6.8	8.2	7.2	4.5
13-17	1.1	4.0	4.9	5.2	2.9
18-22	.8	2.3	2.4	2.3	1.1
23-27	.1	.6	.7	.7	.2
28 and over	.2	1.2	1.3	1.0	.4
Total	100.0	100.1	100.1	100.0	99.9
Female					
0	42.5	26.0	14.5	12.7	17.4
1, 2	22.2	16.0	12.9	14.7	21.1
3, 4	6.4	8.2	13.3	17.0	20.0
5, 6	9.2	15.0	18.5	18.9	16.0
7, 8	9.7	17.6	20.0	17.9	12.4
9, 10	5.6	10.1	11.9	9.7	7.7
11, 12	2.5	3.5	4.2	4.2	2.6
13-17	1.1	1.7	2.5	2.3	1.5
18-22	.3	.9	1.2	1.2	.8
23-27	.2	.2	.4	.2	.2
28 and over	.3	.8	.8	1.1	.3
Total	100.0	100.0	100.2	99.9	100.0

In table 3 the measurement data have been grouped because of irregularities in the observed frequencies. From table 2 it appears that 5, 7, 9, 11, 16–19 mm. of induration are recorded far less frequently than the figures in between, suggesting that the readers have an unconscious tendency to prefer even numbers and round figures. In order to eliminate these irregularities as much as possible, consecutive odd and even numbers (i. e., 1 and 2 mm., 3 and 4 mm. 5 and 6 mm., etc.) were combined and the frequency of reactions for each of these intervals was calculated. For reactions of more than 12 mm. of induration, 5 mm. intervals were used.

It is naturally open to discussion whether or not this is the correct grouping. Perhaps instead, 0 and 1 mm., 2 and 3 mm., 4 and 5 mm., etc., should have been combined. The conclusions in the present study would be the same with either method. The first was chosen because reactions of 0 mm. have been subjected to the most careful scrutiny, and for that reason should perhaps be separated.

Frequency of Reactions

Figure 1 gives a preliminary view of the frequencies of Pirquet reactions according to the definitions currently in use in Norway. The variation with age is shown separately for men and women. The solid curves denote the frequency of definite positive reactions (i. e., reactions with recorded induration of at least 4 mm.); the

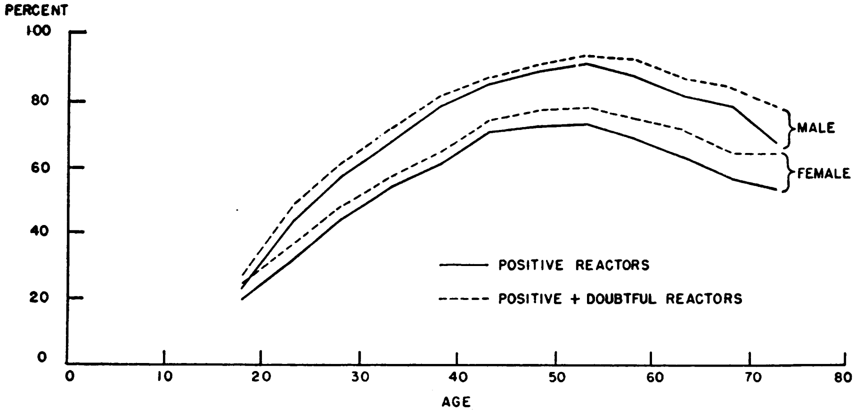

Figure 1. Percentages of positive and doubtful reactors, male and female, by age.

dotted curves, the frequency of definite positive and doubtful reactions (i. e., reactions with a recorded induration of 2–3 mm.).

From these curves it will be seen that the frequency of reactions increases up to 50 or 55 years of age. Above these ages the frequency of positive reactions decreases. Concurrently, there is an increase in the frequency of doubtful reactions.

Most of the previous studies reveal the same fall in the higher age groups. About 20 years ago, however, this decline began at a somewhat higher age—approximately 60–70 years (*1*).

For a more detailed analysis, the distributions according to degree of reaction are presented in figure 2 drawn from the data in table 3.

It is apparent from the graph that the frequency distribution varies with sex and age. First, the frequency of reactions of 0 mm. of induration decreases with increasing age, up to 60 years. Simultaneously the frequency of reactions with an induration of more than 4 mm. rises. Over the age of 60, however, the frequency of 0 mm. of induration increases. This was previously apparent from the age curve for the positive reactors.

In addition it appears, particularly for men, that a shift in the distribution of the definite positive reactions takes place with age, so that, in general, the reactions are strongest in persons between 30 and 59 years old. This can be seen best by noting the frequencies of 5–6, 7–8, and 9–10 mm. of induration. In men between 15 and 29, 5–6 mm. occurs most frequently. In the following age groups (up to 59) 7–8 mm. occurs most often, and the frequency of 9–10 mm. of induration is greater than that of 5–6 mm. At the higher ages, the shift is reversed. Above the age of 60 the majority of the readings are 3–4 mm. The same tendency can be seen from the frequency of induration measuring 11–12 mm. For men in the three lowest age groups (15–49) this frequency increases from 3.2 through 6.8 to 8.2

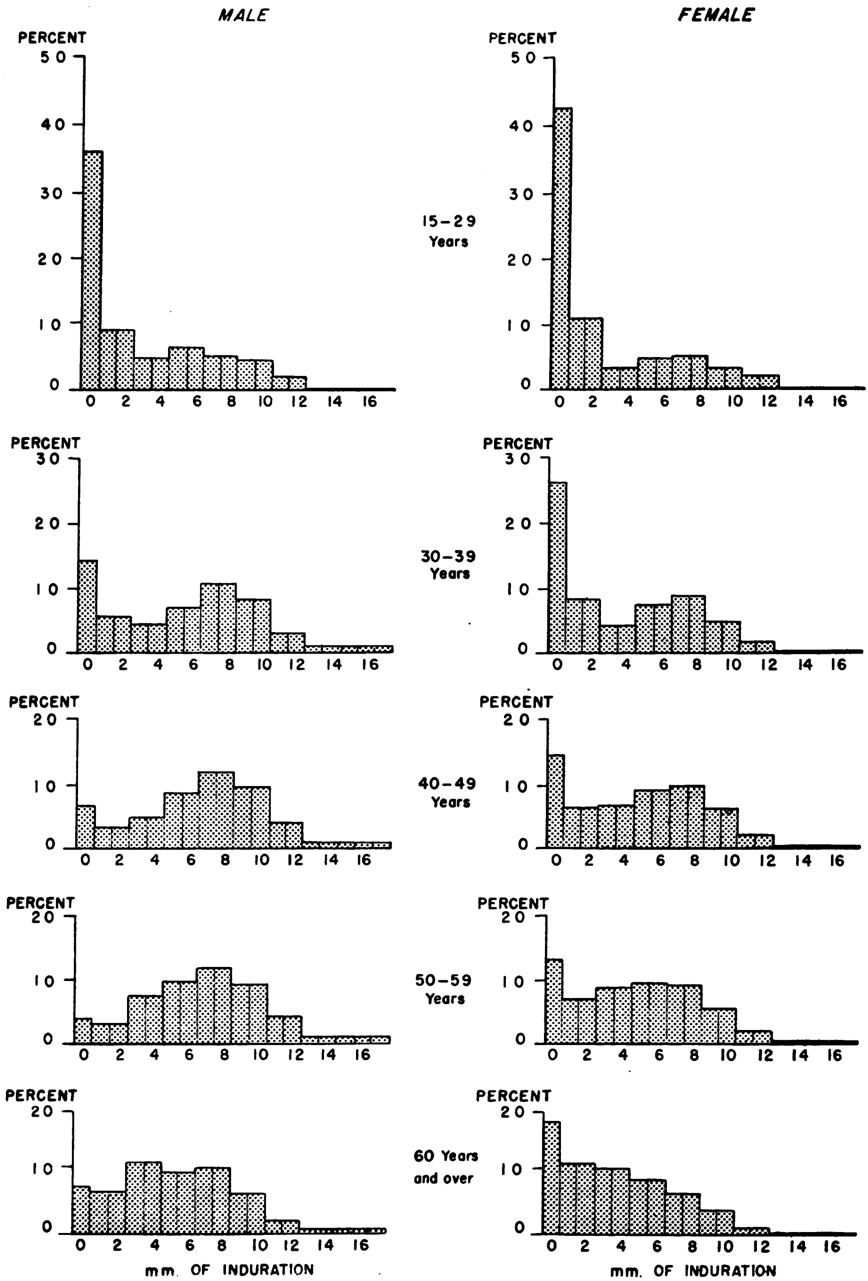

Figure 2. Distributions of Pirquet reactions according to size of induration, by sex and age.

percent. This is relatively more than the increase of all positive reactions. Altogether there are approximately 45, 75, and 90 percent positive individuals in the three age groups, respectively. In older persons there are relatively fewer reactions of 11–12 mm. of induration.

This shift of positive reactions with age is far less marked among women. The reactions seem to be somewhat stronger between the ages of 30 and 39 years than between 15 and 29. But the frequency of indurations measuring 9–10 mm. is uniformly less than the frequency of induration of 5–6 mm. From this it can be deduced that in this middle group, women generally have weaker positive reactions than men. The decrease of allergy in advanced age is even more marked among women than among men.

Table 4 shows more clearly the variation of the definite positive reactions with age and sex. Here the average measurements of all reactions of 4 mm. or more are given (calculated from table 2). For both men and women between the ages of 15 and 29, the intensity of the positive reactions is about the same. In the middle age groups the reactions are stronger in men. In old age the allergy decreases in both sexes.

Table 4. *Average size of induration among reactions of more than 3 mm. by sex and age*

Age	Male	Female
	mm.	*mm.*
15–29	7.82	7.87
30–39	9.00	8.09
40–49	8.99	7.87
50–59	8.58	7.69
60 and over	7.48	6.97

The frequency distributions for the separate age groups by size of reaction differ significantly by chi-square tests. Also the difference between the distributions for men and women in the intermediate age groups is statistically significant.

Several possibilities may be considered to explain the shifts. It is not very likely that reactions of nontuberculous origin can explain the changes in the distribution of definite positive reactions. There is no evidence that Pirquet reactions of much more than 4 mm. of induration can be of nontuberculous etiology, at least not to an extent that can influence the distribution very much. Age in itself may play a role. For example, the condition of the skin may be different at different ages, which perhaps may be considered as an explanation for weak reactions in old persons. It may also be that repeated tuberculous infections play a role by maintaining or possibly increasing the sensitivity. This explanation conforms well with the findings. In the groups in which we have found the strongest reactions, men between 30 and 59, there are presumably a large number of individuals who have been repeatedly exposed to infection. At older ages the possibilities of contact decrease, and for many individuals the last infection has taken place long ago, and allergy may have waned.

In previous studies superinfection has been mentioned as a possible contributory factor to stronger tuberculin sensitivity. Several investigations, including Hertzberg's in Norway (*2*), have shown that the proportion of the reactors to a high dose of tuberculin only (Mantoux, 1 mg. of OT) varies in different population groups. It is smallest in highly exposed groups in which there is a high prevalence of reactors. Further, this proportion of "weak reactors" is greater among women than among men and it decreases with age, at least up to the age of 50–60 years.

This variation with age and sex does to a certain degree correspond to the results previously mentioned. But there is an essential difference. The shift in the level of sensitivity as demonstrated in this material applies to definite positive reactors. On the other hand, Hertzberg and many others reported a shift from a weak to a definite degree of sensitivity. In such a change, the occurrence of nonspecific reactions may also play a part.

Shifts in the distribution curve in the range of doubtful reactions with induration of about 2–3 mm. should be mentioned. It is possible that these may give some information about the nature of the doubtful reactions—the extent to which they are of tuberculous etiology and the extent to which they are nonspecific.

The distribution curve has in the younger age groups a kind of U-shape with two peaks, one at 0 mm. and one at 6 or 7 mm. A natural explanation of this finding is that the population consists of two groups, each of which would give a uni-modal distribution curve. In the composite population, a bi-modal curve will be obtained by combining the two single distributions. In a range around the minimum between the two peaks the distributions will overlap.

Between the ages of 40 and 49 the minimum between the peaks is found at 1–2 mm. In the younger age groups the fewest readings are at 3–4 mm. This may be interpreted to mean that in the younger age groups a majority of the doubtful reactions belong to the noninfected group.

A more detailed analysis in table 5 shows the frequency of reactions per millimeter from 0 to 4 in the two younger age groups for each sex (calculated from the figures in table 2). It can be seen that the frequency of 1, 2, and 3 mm. reactions on the whole decreases with decreasing frequency of 0 mm., but the frequency of 4 mm. reactions changes inversely with this decrease.

According to this, the best distinction between noninfected and infected individuals should be attainable in the younger age groups by using 4 mm. of induration as the boundary between negative and positive reactions. The majority of 1, 2, and 3 mm. reactions should probably be regarded as nonspecific and the majority, if not all, of the 4 mm. reactions, as specific.

Table 5. *Percentage of reactions of 0–4 mm., by sex in the two age groups 15–29 and 30–39*

Sex	Age	0 mm.	1 mm.	2 mm.	3 mm.	4 mm.
Female	15–29	42.5	19.0	3.3	1.1	3.3
Male	15–29	36.0	15.7	2.8	1.2	5.0
Female	30–39	26.0	13.0	2.9	.7	5.6
Male	30–39	14.2	8.9	2.1	.7	5.7

The probable existence of the nonspecific reaction can also be illustrated in another way. The age group of men from 50 to 59 years might be considered an almost pure group of infected individuals, as only 3.6 percent have a reaction of 0 mm. of induration. Here it is seen that the reactions are fairly evenly distributed by size and that the maximum number is 7–8 mm. Close to 14 percent of those infected have a reaction of 3–4 mm. of induration, and about 5 percent have a reaction of 1–2 mm.

If this distribution is applied to the group of men 15–29 years old, of whom approximately 45 percent were definite positive reactors, then by reason of infection, 2.3 percent (i. e., 5 percent of 45 percent) of all individuals in this group should have reactions of about 1 or 2 mm. of induration, and 6.4 percent (i. e., 14 percent of 45 percent) reactions of about 3 or 4 mm. of induration. In reality, however, we find frequencies of 18.5 percent and 8.9 percent. In other words, most of the 1–2 mm. indurations and a fraction of the 3–4 mm. indurations in this age group must be regarded as being nonspecific.

Applying again the ratio of weak to definite reactors found among men 50–59 years of age to reactions among women between 15 and 19 years of age where 35 percent have a definite positive reaction, we find correspondingly that by reason of infection approximately 1.8 and 4.9 percent should have reactions of 1–2 mm. and 3–4 mm. of induration, respectively. In reality, however, we find 22.2 percent and 6.4 percent, and deduce that the number of nonspecific reactions corresponds with that found among men.

This is illustrated in figure 3, where the heavily shadowed areas indicate the estimated frequency distribution of infected individuals for each size of reaction and the lightly shaded areas indicate the distribution of noninfected individuals.

Some factors which could influence this calculation ought to be considered. The distribution curve for the infected part of the population is not quite the same for different age groups. A certain shift with age in the distribution of the size of the definite positive reactions has already been demonstrated, but, as a rough approximation, the calculation is perhaps permissible.

In the oldest age groups the distribution curve has a different shape. The minimum between definite negative reactions and definite positive reactions becomes less marked and the U-shape disappears.

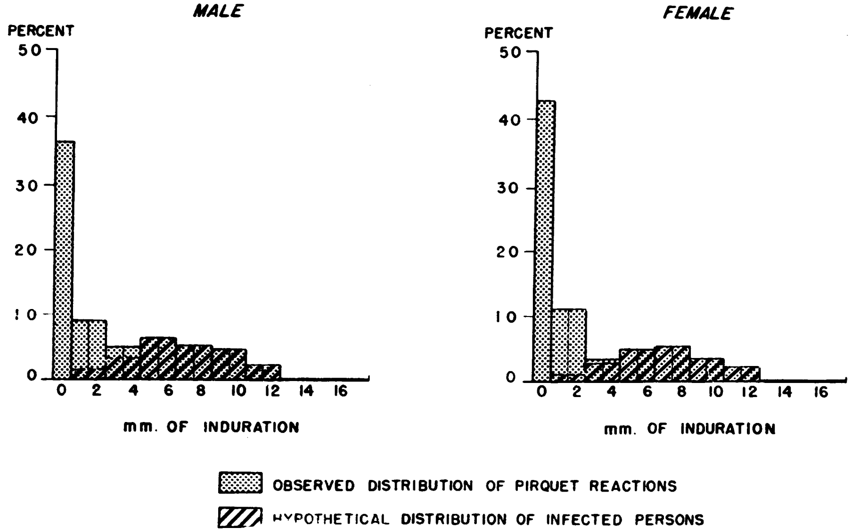

Figure 3. Distributions of Pirquet reaction, according to size of induration, in the age group 15–29 (male and female), showing the hypothetical distribution of infected persons.

The most convenient explanation is that this population essentially consists of one group, namely the infected. The majority of the doubtful and also of the definite negative reactions must be supposed to belong to the infected group. (Among the women there are perhaps some noninfected individuals over 60 years of age because the top at 0 mm. is very high.) This coincides with the fall in the age curve for reactors (fig. 1). The decrease in sensitivity among infected individuals is, therefore, even greater than indicated by the average measurements shown in table 4, because many infected persons over the age of 60 react with indurations of less than 4 mm. and are not included in the calculation of averages.

Pulmonary Findings Related to Tuberculin Sensitivity

The other method of analysis is to assess the relation between tuberculin reactions and another index of tuberculous infection. An investigation can be made of the frequency of roentgenological pulmonary findings of possible tuberculous etiology among individuals with tuberculin reactions of varying intensity. Scheel (*3*) carried out investigations of this kind in 1937 on 1,697 university students in Oslo. In the United States similar studies have been made, but Mantoux tests were used and the reactions were grouped according to the tuberculin dose necessary to produce a positive reaction of a given size.

Among individuals with a definite positive Pirquet reaction (at least 4 mm. of induration), Scheel found that approximately 15 percent had calcified foci. Among those who had a negative Mantoux test

(1 mg. of OT), he found 0.7 percent with calcified foci. Among individuals with a doubtful Pirquet reaction, or with a negative Pirquet reaction but a positive Mantoux, he found calcified foci in approximately 1 percent. Thus this latter group, with a slight tuberculin sensitivity, had about the same frequency of calcification as the definitely negative individuals.

Goddard, Edwards, and Palmer (*4*) reported calcified foci in approximately 10 percent of a population of student nurses with a positive Mantoux reaction of 5 mm. or more of induration to 0.0001 mg. of PPD, and in 0.7 percent of nurses who reacted negatively to 0.005 mg. of PPD. Among questionable reactors, i. e., persons reacting negatively to 0.0001 mg. of PPD but positively to 0.005 mg. (more than 10 mm. of firm induration), the frequency was also low, between 1 and 2 percent. The three groups included only individuals with negative histoplasmin reactions.

If it is assumed that calcification is always detected in a constant percentage of those infected with tuberculosis, it could be concluded that tuberculous infection is about as infrequent among individuals with a weak allergy to tuberculin as among those who are definitely tuberculin negative. And among the definitely tuberculin positive, calcification is at least 10–20 times more frequent.

Objections can of course be raised to such a conclusion. For example, it is possible that a tuberculous infection resulting in calcified foci may also cause a stronger allergy than an infection which is not accompanied by detectable changes. One should bear this reservation in mind. But even so, this method is of value because it attempts to utilize criteria for tuberculous infection different from those offered by the various tuberculin tests.

The investigations mentioned and most others of the same kind have been carried out on fairly young persons. In view of the age variations which appeared in the Pirquet reactions, an investigation of the relationship in different age groups between pulmonary X-ray findings and Pirquet reactions is indicated. Both photofluorograms and tuberculin test results are available for 47,209 individuals. Table 6 shows the frequencies of pulmonary calcification in the different age groups (both sexes) according to whether they had (1) a negative, (2) a doubtful, or (3) a positive Pirquet test.

In all groups the frequency of calcification is considerably less than reported in the investigations previously mentioned. Among other things, this can be attributed to the fact that diagnoses have been made from photofluorographic film. A certain number of calcifications were undoubtedly missed by those interpreting the films and only definite positive findings were recorded. However, the photofluorographic readings were made without knowledge of the tuberculin reactions, so that no bias has been introduced into any group.

Table 6. *Frequencies of pulmonary calcifications among negative, doubtful, and positive reactors, by age (both sexes)*

Age	Negative reactors			Doubtful reactors			Positive reactors		
	Number examined	Calcifications		Number examined	Calcifications		Number examined	Calcifications	
		Number	Percent		Number	Percent		Number	Percent
15-29	6,423	18	0.28	463	2	0.43	4,224	101	2.40
30-44	4,513	17	.38	579	8	1.38	11,810	466	3.92
45-59	2,346	43	1.83	586	14	2.39	11,235	547	4.85
60 and over	1,311	62	4.72	406	23	5.65	3,313	217	6.82

It can be seen that in the two younger age groups calcified foci are far more common among those with a definite positive Pirquet reaction than among those with a negative reaction, the ratio being approximately 10:1. The frequency of calcification in individuals with a doubtful reaction is only slightly higher than in those with a negative reaction. This conforms to the investgiations of Scheel and of Goddard, Edwards, and Palmer, and it is also in accordance with the previous conclusions that the majority of doubtful tuberculin reactions in the younger age groups are nonspecific.

In the older age groups, on the other hand, the difference among the three groups decreases, and in the oldest group, the Pirquet reaction has practically no relation to the frequency of calcification. This agrees with the previous conclusion that most of the old persons with definite negative or with doubtful reactions really belong to the infected group. In other words, the older the person with a negative Pirquet reaction, the greater the chance of his having been infected. The same applies to an even greater extent to persons with a doubtful Pirquet reaction.

Summary

The purpose of the investigation is to study the relation of tuberculous infection and the degree of reaction to the tuberculin test. The distribution of the population according to sensitivity was obtained and the differences by age and sex were studied.

Pirquet tests were performed on about 53,000 individuals over the age of 14 years. The diameter of the induration was used as a measure of the degree of sensitivity.

Except for the higher age groups, the distribution curve has a kind of U-shape, with two peaks, one at 0 mm., the second between 5 and 8 mm. The natural explanation for this is that the population consists of two different groups, each of which would give a unimodal distribution.

The shape of the distribution curve varies in different ways according to sex and age. For both sexes the peak at 0 mm. decreases with increasing age up to 50–60 years; above this age it increases again.

As the 0-peak decreases, the second peak at 5–8 mm. increases. But, in addition, the distribution for men between 30 and 59 is distinguished by a displacement of the second peak to the right, as compared with the distribution for males between 15 and 29 and those for females in all age groups. This indicates that stronger reactions occur more frequently in males aged 30–59 than in other groups. It is open to discussion whether this is a result of repeated exposure to infection in this age group or is due to other factors related to age.

In the older age groups, there is a shift in the opposite direction. The peak corresponding to definite positive reactions is displaced so much to the left in the scale that the minimum between the two peaks disappears and the curve loses its U-shape.

The minimum between the two peaks is found at 3–4 mm. in the age group of 15–29 years, at 1–2 mm. in the age group of 40–49 years. Moreover, with this shift of the minimum between the peaks, the frequency of 1–3 mm. reactions decreases along with decreasing frequency of 0 mm. reactions, while the frequency of 4 mm. reactions increases. This may be interpreted to mean that the majority of 1–3 mm. reactors at the younger ages belongs to the noninfected group. On the other hand, in old age most reactors of 0–3 mm. probably belong to the infected group, corresponding to this shift of the second peak toward smaller reactions.

These conclusions concerning the interpretation of the weak reactions are substantiated by study of the frequency of pulmonary calcifications among individuals with reactions of (1) 0–1 mm. of induration, (2) 2–3 mm. of induration, and (3) more than 3 mm. of induration. At the younger ages the frequency is much higher in the third group than in the first two, which are only slightly different. In old age the frequency of calcification is nearly the same in all three groups; this suggests that most individuals with 0–3 mm. reactions belong to the infected group.

Supplement

The results of this study were given in a lecture in Oslo in December 1949. In January 1950 a paper was published by Carroll E. Palmer and O. Strange Petersen (*5*), which dealt with the same problem. They have examined the distributions of sensitivity to histoplasmin and tuberculin among student nurses, and have compared these results by geographic areas. A quantitative method of analyzing the nature of doubtful reactions is given in their paper.

I have had the opportunity to discuss my results with these authors and they have given very valuable help to the final preparation of this paper, which was prepared during my appointment as Consultant in the Tuberculosis Research Office of the World Health Organization. I hope the authors will accept my most sincere thanks.

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Failure of Streptomycin to Enhance the Infectivity of *Histoplasma capsulatum* in Mice

By Charlotte C. Campbell and Samuel Saslaw, Capt., M.C., AUS*

Earlier reports (*1*, *2*) have described the growth enhancement of certain pathogenic fungi in synthetic media containing varying concentrations of streptomycin. Fungi studied at this laboratory (*1*) have included three strains of *Histoplasma capsulatum*, two of which exhibit increased growth in the presence of the antibiotic. The stimulatory effect was observed with the mycelial phase of the organism; the yeast phase was not subjected to *in vitro* tests since the organism invariably reverted to the mycelial type in the culture medium used for testing growth, even at an incubation temperature of 37° C.

Considering this and the fact that histoplasmosis and pulmonary tuberculosis (for which streptomycin is frequently used as a therapeutic agent), are quite similar in clinical appearance, the authors undertook to investigate the *in vivo* effects of the drug. The experiments reported here were therefore conducted to see if streptomycin could accelerate or otherwise alter the mortality rate of mice experimentally infected with *H. capsulatum.*

In all the experiments, young white Swiss mice (Bagg strain) weighing 14 to 17 grams were used. These were separated into groups of five at random, and each group was placed in an individual jar. For the purpose of the initial experiment, 20 of these groups, or a total of 100 mice, were infected with yeast-phase histoplasma organisms and given daily injections of streptomycin in five different dosages, with four groups of mice observed at each dosage level. Daily streptomycin dosages began immediately after infection and amounted to 0.05, 0.125, 0.25, 0.5, and 1.0 mg., respectively.

Eight additional groups, or a total of 40 mice, served as infected controls, and were given no streptomycin at all. Instead, these mice received daily injections of 0.5 ml. of physiologic saline solution. Finally, to provide for drug controls, four more groups, or 20 animals, were given only streptomycin in daily doses of 1.0 mg. (the highest dosage used in the groups receiving both *H. capsulatum* and streptomycin).

All infections were induced by the method described in a previous report from this laboratory (*3*), in which yeast-phase organisms (strain

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G–8)[1] were suspended in 5 percent hog gastric mucin, and challenge doses consisted of approximately 3.5 million organisms suspended in 0.5 ml. of mucin. The unusually large inoculum was used in order to obtain mortality in excess of 50 percent among infected, untreated animals. The strain employed is one in which the *in vitro* stimulatory effect of streptomycin has appeared to be most marked.

The streptomycin used in these studies, commercial streptomycin sulfate (Pfizer), was dissolved in sterile, distilled water at concentrations varying from 0.1 to 10.0 mg. per ml. and stored in sterile, rubber-capped vials at 4° to 6° C. New solutions were prepared every 6th day. Daily dosages consisted of the absolute amounts of streptomycin contained in 0.5 ml. of the various concentrations. It should be noted that the concentrations of streptomycin contained in the daily 0.5 ml. injections paralleled those at which growth enhancement of *H. capsulatum* had been observed *in vitro*, 0.05 to 5.0 mg. (*1*).

All injections were administered intraperitoneally, with streptomycin given daily for a period of 30 days. During this period, all fatalities were necropsied and spleens cultured for *H. capsulatum*. At the close of the 30-day observation period, survivors were sacrificed and examined in similar manner.

The greatest number of fatalities occurred between the 9th and 21st days after injection of the infective agent. Relatively few animals died before or after this time interval in either the untreated or streptomycin therapy groups, and there were no deaths at all among the drug controls.

As indicated in table 1, the death rate among the infected controls was 85 percent, as compared with a range of 65 to 85 percent for the groups receiving daily injections of streptomycin. Since there was no significant difference in either the interval of time between injection and death or the total percentage of fatalities in any of the groups, it would appear that the daily administration of streptomycin under the specified conditions does not accelerate the death rate of mice experimentally infected with histoplasma.

In an effort to see whether the use of larger antibiotic dosages would alter these findings, we next increased the daily concentrations to 0.1, 1.0, 2.5 and the exceedingly high dose of 5.0 mg. The results of three separate experiments based on these higher dosages are shown in table 2. In all three experiments, the total death rate for infected controls (66.7 percent), was similar to the total rate for infected mice receiving 0.1 to 2.5 mg. of streptomycin (73.3 percent, 63.3 percent, 61.7 percent, respectively). Similarly, a single injection of 2.5 mg. of streptomycin given immediately after infection did not materially increase the percentage of fatalities in that group. Even

[1] A human isolate identified at this institution.

Table 1. ***Comparative mortality among mice receiving streptomycin and those receiving no streptomycin following infection with* H. capsulatum *(streptomycin dosages of 1.0 mg. and less)***

Experimental subjects	Daily streptomycin dosage (mg.)	Number dead/number observed		Total death rate (percent)
		Individual groups	All groups	
Infected animals (dosage approximately 3.5 million yeast-phase *H. capsulatum* organisms suspended in 0.5 ml. of 5 percent hog gastric mucin).	[1] None	5/5, 4/5, 4/5, 3/5 5/5, 5/5, 4/5, 4/5	34/40	85.0
	0.05	5/5, 5/5, 3/5, 4/5	17/20	85.0
	.125	4/5, 2/5, 5/5, 4/5	15/20	75.0
	.25	4/5, 2/5, 3/5, 4/5	13/20	65.0
	.5	3/5, 5/5, 5/5, 4/5	17/20	85.0
	1.0	4/5, 3/5, 3/5, 5/5	15/20	75.0
Drug controls [2]	1.0	0/5, 0/5, 0/5, 0/5	0/20	0

[1] Infected controls. Received daily injections of 0.5 ml. of physiologic saline sol ution instead of streptomycin.
[2] Uninfected animals. Received streptomycin only.

in the group receiving daily streptomycin dosages of 5.0 mg. in experiment 3, the death rate was not substantially different from that sustained by the infected controls (55.0 percent and 50.0 percent, respectively). It therefore appears that relatively large doses of the antibiotic also fail to accelerate the death rate of infected mice.

Table 2. ***Comparative mortality among mice receiving streptomycin and those receiving no streptomycin following infection with* H. capsulatum *(streptomycin dosages of 0.1–5.0 mg.)***

Experimental subjects	Daily streptomycin (dosage (mg.))	Number dead/number observed				Death rates (percent)			
		Experiment 1	Experiment 2	Experiment 3	All experiments	Experiment 1	Experiment 2	Experiment 3	All experiments
Infected animals (dosage approximately 3.5 million yeast-phase *H. capsulatum* organisms suspended in 0.5 ml. of 5-percent hog gastric mucin).	[1] None	28/37	26/39	10/20	64/96	75.7	66.7	50.0	66.7
	0.1	15/20	15/20	14/20	44/60	75.0	75.0	70.0	73.3
	1.0	15/20	15/20	8/20	38/60	75.0	75.0	40.0	63.3
	2.5	13/20	16/20	8/20	37/60	65.0	80.0	40.0	61.7
	5.0	------	------	11/20	11/20	------	------	55.0	55.0
	[3] 2.5	16/20	14/20	------	30/40	80.0	70.0	------	75.0
Drug controls [2]	[4] 2.5 and 5.0	0/20	0/20	0/20	0/60	0	0	0	0

[1] Infected controls. Received daily injections of 0.5 ml. sterile, physiologic saline instead of streptomycin.
[2] Uninfected animals. Received streptomycin only.
[3] Single injection only, immediately following infection.
[4] Lower dose used in experiments 1 and 2, and higher dose in experiment 3.

Finally, one additional experiment was undertaken to determine whether the large inoculum of *H. capsulatum* (3.5 million organisms) used in the earlier trials had, perhaps, exaggerated mortality to a point where any acceleration of the death rates caused by the antibiotic might be concealed. In these final experiments, then, a smaller inoculum was used, and the high streptomycin dosage trial repeated.

Five lots of mice, each containing 20 animals, were injected with one-tenth the original inoculum, or approximately 350,000 organisms (this inoculum had not in the past produced mortality in excess of 50 percent). Once again, no significant difference was noted in mortality.

Seven of the infected controls died, as compared with 5, 4, 4, and 4 among those receiving 30 daily injections of 0.1, 1.0, 2.5, and 5.0 mg. of streptomycin, respectively.

In all the experiments, survivors in both the infected controls and the groups receiving streptomycin appeared well and healthy at the end of 30 days. However, the spleens of selected animals in both groups yielded cultures positive for *H. capsulatum*.

Summary and Conclusions

Under the conditions of these studies, streptomycin concentrations varying from 0.05 to 5.0 mg., administered in daily intraperitoneal doses for 30 days, failed to accelerate the fatality rate of mice experimentally infected with the yeast phase of *H. capsulatum*. There was no significant difference in the death rates of mice receiving *H. capsulatum* alone and those receiving streptomycin following infection. Although streptomycin may enhance the growth of the mycelial phase of *H. capsulatum in vitro*, no increased virulence has been observed with *in vivo* studies employing the yeast phase of the fungus.

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Incidence of Disease

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

UNITED STATES

Reports From States for Week Ended December 16, 1950

Measles

For the current week 3,507 new cases of measles were reported, as compared with 3,008 for the previous week, and 1,774 for the same week last year. Nearly one-third of the cases for the current week (1,105) occurred in the East North Central States.

Other diseases

For the current week 27 cases of infectious encephalitis were reported, 15 of which occurred in California. A total of 368 cases of poliomyelitis was reported, which represents a 23 percent decrease since the previous week. The cumulative total for the "disease" year is 31,710 as compared with 41,094 for the same 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
	Dec. 16, 1950	Dec. 17, 1949			1949–50	1948–49		1950	1949	
Anthrax (062)	1	-------	(1)	(1)	(1)	(1)	(1)	44	51	(1)
Diphtheria (055)	128	153	338	27th	[2] 2,700	3,982	5,680	[2] 5,828	7,750	11,977
Acute infectious encephalitis (082)	27	7	8	(1)	(1)	(1)	(1)	980	738	612
Influenza (480–483)	3,157	2,441	2,875	30th	31,614	25,621	29,177	277,873	101,488	217,174
Measles (085)	3,507	1,774	2,592	35th	21,761	14,344	21,111	309,932	602,862	590,719
Meningococcal meningitis (057.0)	81	78	70	37th	822	787	787	3,621	3,303	3,307
Pneumonia (490–493)	1,230	1,523	-------	(1)	(1)	(1)	(1)	77,512	74,572	-------
Acute poliomyelitis (080)	368	243	197	11th	[2] 31,710	41,094	24,493	[2] 32,841	42,007	24,960
Rocky Mountain spotted fever (104)	2	2	2	(1)	(1)	(1)	(1)	454	560	560
Scarlet fever (050)	1,314	1,292	2,070	32d	12,987	14,142	18,949	53,157	71,808	79,935
Smallpox (084)	1	-------	3	35th	[2] 8	7	16	[2] 34	48	163
Tularemia (059)	13	34	34	(1)	(1)	(1)	(1)	854	1,074	1,052
Typhoid and paratyphoid fever (040, 041)[3]	48	36	53	11th	[2] 2,844	3,285	3,317	[2] 3,353	3,773	3,802
Whooping cough (056)	1,823	1,718	2,125	39th	18,787	18,672	20,544	115,982	65,274	96,419

[1] Not computed. [2] Deductions: Diphtheria, North Carolina, week ended Sept. 2, 1 case; poliomyelitis, Georgia, week ended Nov. 25, 1 case; smallpox, Kansas, week ended Nov. 25, 4 cases; typhoid fever, North Carolina, week ended Aug. 19, 1 case and week ended Nov. 25, 1 case of paratyphoid. [3] Including cases reported as salmonellosis.

There was one case of anthrax in West Virginia, one case of psittacosis in Pennsylvania, and one case of smallpox in North Dakota.

Report of Epidemics

Influenza

Dr. J. R. Enright, Department of Health, Hawaii, has reported information on "Influenza Incidence" in the South Pacific Islands which he received from the South Pacific Health Service, Suva, Fiji. The latest figures available are those for October which are as follows in the various island groups: Cook Islands, incl. Niue (1,060 cases); Fiji (94); Gilbert and Ellice Islands (Prevalent); Nauru Islands (366); New Guinea (Netherlands) (28); New Hebrides (69); New Caledonia (4); Oceania (French) (496); Papua (New Guinea) (47); Western Samoa (68); Eastern Samoa (41); British Solomon Islands (4).

This report states that an epidemic of influenza followed a visit by a naval vessel to Oceania Island which lies between the Gilberts and Nauru. The nature of the virus causing the outbreak is being investigated by Dr. Burnet of Melbourne, Australia.

(Note: An outbreak of an upper respiratory infection in Canton Island in June 1950, and an epidemic of influenza in Hawaii, were reported in the Communicable Disease Summary for the week ended November 18, 1950.)

Gastro-enteritis

Dr. V. A. Getting, Commissioner of Public Health, Massachusetts, has reported that gastro-enteritis is epidemic in many parts of the State. Cases are mild with nausea, vomiting, and diarrhea. Average durations of symptoms is 24 hours.

Deaths During Week Ended December 16, 1950

	Week ended Dec. 16, 1950	*Corresponding week, 1949*
Data for 94 large cities of the United States:		
Total deaths	9, 588	9, 426
Median for 3 prior years	9, 497	----------
Total deaths, first 50 weeks of year	458, 578	458, 805
Deaths under 1 year of age	674	599
Median for 3 prior years	660	----------
Deaths under 1 year of age, first 50 weeks of year	31, 329	32, 665
Data from industrial insurance companies:		
Policies in force	69, 600, 812	69, 962, 439
Number of death claims	12, 856	12, 845
Death claims per 1,000 policies in force, annual rate	9. 6	9. 6
Death claims per 1,000 policies, first 50 weeks of year, annual rate	9. 2	9. 1

Reported Cases of Selected Communicable Diseases: United States, Week Ended December 16, 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	**128**	**27**	**3,157**	**3,507**	**81**	**1,230**	**368**
New England	**4**	**1**	**2**	**142**	**3**	**39**	**12**
Maine	-	-	-	2	1	1	1
New Hampshire	-	-	1	-	-	-	-
Vermont	-	-	-	88	-	-	-
Massachusetts	2	1	-	38	2	-	6
Rhode Island	1	-	-	5	-	1	1
Connecticut	1	-	1	9	-	37	4
Middle Atlantic	**8**	**1**	**3**	**650**	**25**	**280**	**80**
New York	4	1	[1] 3	163	8	195	54
New Jersey	2	-	-	172	1	40	11
Pennsylvania	2	-	-	315	16	45	15
East North Central	**6**	**4**	**46**	**1,105**	**13**	**91**	**80**
Ohio	2	-	1	348	4	-	23
Indiana	1	-	-	5	-	5	8
Illinois	2	1	1	344	7	61	10
Michigan	1	2	4	121	1	14	29
Wisconsin	-	1	40	287	1	11	10
West North Central	**10**	-	**13**	**387**	**6**	**78**	**32**
Minnesota	6	-	-	50	2	5	2
Iowa	-	-	-	4	-	5	8
Missouri	4	-	4	142	1	12	7
North Dakota	-	-	8	7	-	55	-
South Dakota	-	-	-	5	1	-	10
Nebraska	-	-	-	-	1	-	-
Kansas	-	-	1	179	1	1	5
South Atlantic	**40**	**4**	**433**	**102**	**10**	**146**	**39**
Delaware	-	-	-	-	-	-	-
Maryland	2	-	4	2	-	26	7
District of Columbia	-	-	1	5	-	8	-
Virginia	1	-	231	27	1	43	10
West Virginia	9	-	130	5	-	17	4
North Carolina	12	1	-	30	1	-	6
South Carolina	7	-	44	6	3	17	-
Georgia	7	-	18	24	2	7	5
Florida	2	3	5	3	3	28	7
East South Central	**19**	**2**	**57**	**142**	**3**	**60**	**13**
Kentucky	7	-	-	101	-	-	2
Tennessee	7	1	23	22	2	-	5
Alabama	1	1	29	3	1	41	2
Mississippi	4	-	5	16	-	19	4
West South Central	**29**	-	**2,350**	**324**	**13**	**422**	**18**
Arkansas	5	-	137	65	2	65	1
Louisiana	2	-	-	4	-	34	2
Oklahoma	5	-	111	54	2	21	2
Texas	17	-	2,102	201	9	302	13
Mountain	**4**	-	**243**	**238**	**1**	**71**	**16**
Montana	-	-	8	5	-	1	1
Idaho	-	-	7	41	-	12	3
Wyoming	-	-	-	7	-	-	-
Colorado	2	-	10	157	1	16	3
New Mexico	2	-	-	12	-	11	4
Arizona	-	-	214	9	-	30	3
Utah	-	-	4	7	-	-	2
Nevada	-	-	-	-	-	1	-
Pacific	**8**	**15**	**10**	**417**	**7**	**43**	**78**
Washington	2	-	-	126	3	2	12
Oregon	-	-	8	16	-	14	8
California	6	15	2	275	4	27	58
Alaska	-	-	-	-	2	-	9
Hawaii	-	-	-	-	-	-	-

[1] New York City only.

Anthrax: West Virginia, 1 case; *Psittacosis:* Pennsylvania, 1 case.

Reported Cases of Selected Communicable Diseases: United States, Week Ended December 16, 1950—Continued

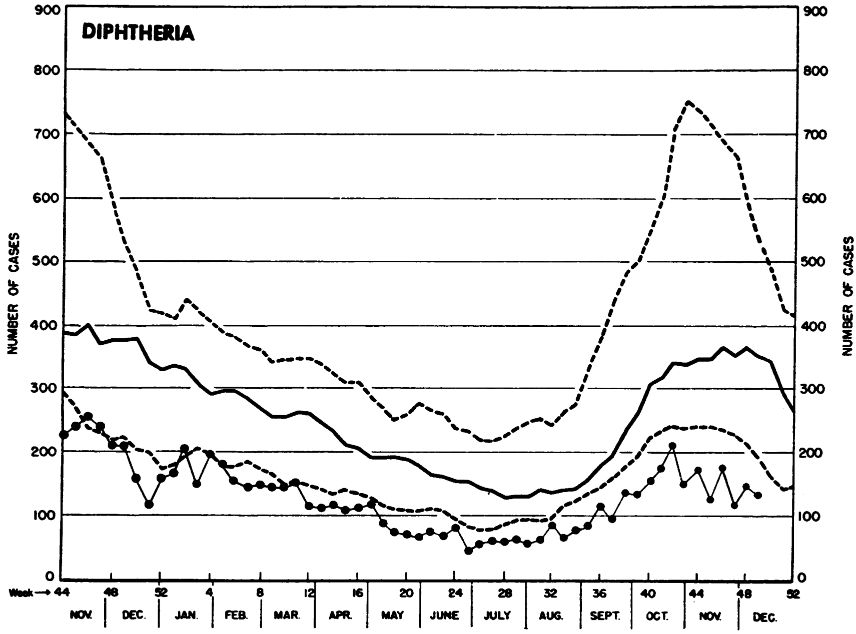
[Numbers under diseases are International List numbers, 1948 revision]

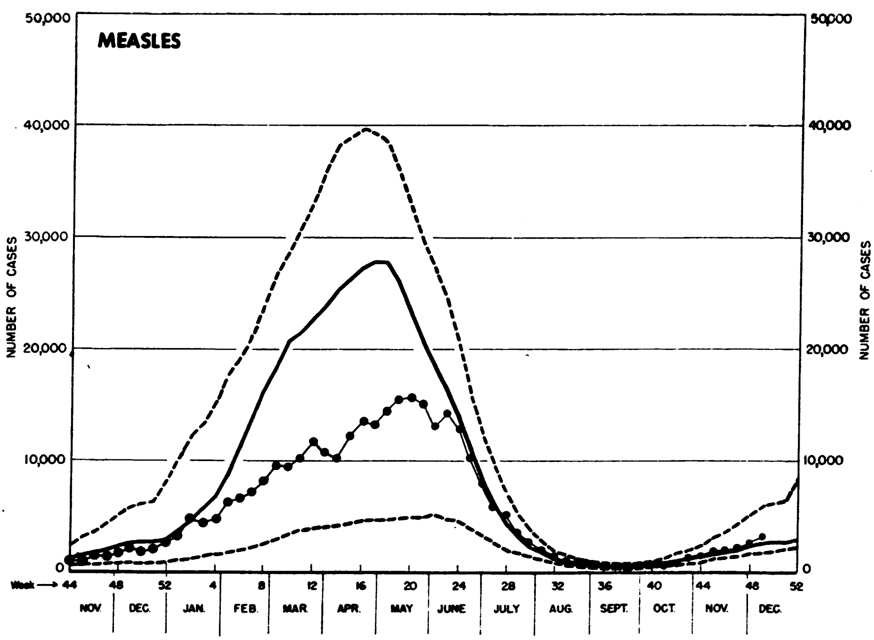
Area	Rocky Mountain spotted fever (104)	Scarlet fever (050)	Smallpox (084)	Tularemia (059)	Typhoid and paratyphoid fever [1] (040, 041)	Whooping cough (056)	Rabies in animals
United States	**2**	**1,314**	**1**	**13**	**48**	**1,823**	**148**
New England		**153**			**3**	**282**	
Maine		12			2	32	
New Hampshire		6				1	
Vermont		7				82	
Massachusetts		112			1	100	
Rhode Island		4				31	
Connecticut		12				36	
Middle Atlantic		**174**		**1**	**7**	**307**	**15**
New York		[2] 96			3	110	15
New Jersey		28				113	
Pennsylvania		50		1	4	84	
East North Central		**277**		**2**	**6**	**299**	**52**
Ohio		77			4	48	5
Indiana		12			1	23	[3] 43
Illinois		51		2	1	24	1
Michigan		112				103	2
Wisconsin		25				101	1
West North Central		**100**	**1**	**1**	**5**	**112**	**11**
Minnesota		17				13	1
Iowa		13			1	9	10
Missouri		18		1	3	28	
North Dakota		11	1				
South Dakota		5				3	
Nebraska		5				2	
Kansas		31			1	57	
South Atlantic	**1**	**175**		**4**	**9**	**312**	**13**
Delaware		1				2	
Maryland		20			1	36	
District of Columbia		11				13	
Virginia		12		2	2	115	1
West Virginia		3				66	3
North Carolina		94			1	39	
South Carolina		8				11	4
Georgia	1	17		2	3	16	5
Florida		9			2	14	
East South Central	**1**	**96**		**2**	**4**	**68**	**19**
Kentucky		24				26	8
Tennessee		42		2	2	24	3
Alabama		19				15	6
Mississippi	1	11			2	3	2
West South Central		**71**		**2**	**8**	**308**	**34**
Arkansas		2		1		40	2
Louisiana		6			6	2	
Oklahoma		4		1	1	5	1
Texas		59			1	261	31
Mountain		**56**		**1**	**1**	**57**	
Montana		4		1	1	1	
Idaho		8				2	
Wyoming						1	
Colorado		13				15	
New Mexico		4				19	
Arizona		4				16	
Utah		23				3	
Nevada							
Pacific		**212**			**5**	**78**	**4**
Washington		64			1	30	
Oregon		23				9	
California		125			4	39	4
Alaska					1	7	
Hawaii							

[1] Including cases reported as salmonellosis. [2] Including cases reported as streptococcal sore throat.
[3] Report for November.

Communicable Disease Charts

All reporting States, November 1949 through December 9, 1950





The upper and lower broken lines represent the highest and lowest figures recorded for the corresponding weeks in the 5 preceding years. The solid line is a median figure for the 5 preceding years. All three lines have been smoothed by a 3-week moving average. The dots represent numbers of cases reported for the weeks of 1950.

FOREIGN REPORTS

CAMEROON (FRENCH)

Influenza. The numbers of cases of influenza reported during August and September were 191 and 197, respectively. For the corresponding months of 1947, 1948, and 1949, influenza was almost nonexistent except for September 1949, when 248 cases were reported. The cases reported for August and September 1950 were chiefly in the Bamoun Region.

CANADA

Reported Cases of Certain Diseases—Week Ended Dec. 2, 1950

Disease	Newfoundland	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Brucellosis					4	1					5
Chickenpox	5		67		253	467	49	106	149	273	1,369
Diphtheria					4			1			5
Dysentery, bacillary					3	10	1			18	32
Encephalitis, infectious								1			1
German measles			7		3	62		8	14	52	146
Influenza			9			5					14
Measles	2		13		255	1,198	40	22	15	52	1,597
Meningitis, meningococcal						1	1			1	3
Mumps	1		26		120	343	51	89	259	187	1,076
Poliomyelitis							3	4		1	8
Scarlet fever	3		2	5	85	38	22	23	82	51	311
Tuberculosis (all forms)	12		5	21	98	34	22	9	7	21	229
Typhoid and paratyphoid fever					8	1		1			10
Venereal diseases:											
Gonorrhea	7		9	8	55	50	25	17		63	234
Syphilis	4		11	4	41	15	9	13		9	106
Primary			2	1	2	2		3		1	11
Secondary					2	2		2			6
Other syphilis	4		9	3	37	11	9	8		8	89
Whooping cough	1		5		70	116	22	2	9	30	255

JAMAICA

Reported Cases of Certain Diseases—4 Weeks Ended Nov. 25, 1950

Disease	Kingston	Other localities	Total
Chickenpox		7	7
Diphtheria		3	3
Dysentery, unspecified		2	2
Erysipelas		2	2
Meningitis, meningococcal		1	1
Ophthalmia neonatorum		1	1
Tuberculosis, pulmonary	24	45	69
Typhoid fever	7	76	83
Typhus fever (murine)		1	1

JAPAN

Influenza. An outbreak of influenza has been reported in Southern Japan where more than 2,000 cases occurred during the 5-week period ended November 18, 1950. The estimated number of cases for the corresponding period in 1947, 1948, and 1949 were 222, 83, and 43, respectively. The number of cases for the whole of Japan during the epidemic last year did not exceed 2,000 for a period twice as long (Nov. 1949–Jan. 1950).

MADAGASCAR

Reported Cases of Certain Diseases and Deaths—October 1950

Disease	Aliens		Natives	
	Cases	Deaths	Cases	Deaths
Beriberi			4	
Bilharziasis	6		89	
Dysentery:				
Amebic	9		165	11
Bacillary			18	
Erysipelas			11	
Influenza	12		6,748	40
Leprosy			118	
Malaria	166	4	27,472	113
Measles	8		206	
Meningitis, meningococcal			2	1
Mumps			71	
Plague			20	19
Pneumonia (all forms)	4	3	1,210	118
Puerperal infection			4	
Tuberculosis, respiratory	5	1	100	14
Typhoid fever	1		8	1
Whooping cough	3		307	3

VENEZUELA

Diphtheria. During the period October 29–December 15, 1950, 91 cases of diphtheria were reported in the urban zone of Maracaibo. For the period October 29–December 2, 34 cases were reported in the rural zone of the city. The authorities reported that all recommended measures have been taken.

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.

Plague

Belgian Congo. One fatal case of bubonic plague was reported in Rukemba, north of Lubero in Costermansville Province.

Smallpox

Burma. During the week ended December 9, 1950, three cases of smallpox were reported in Rangoon and one case in Moulmein.

Dahomey. During the period December 1–10, 1950, 10 cases of smallpox were reported in Dahomey. For the period November 21–30, 8 cases were reported.

India. For the week ended December 2, 1950, 98 cases of smallpox were reported in Nagpur as compared with 21 for the previous week. For the year through November 25, a total of 91 cases were reported.

Tanganyika. During the week ended October 28, 1950, 74 cases (14 deaths) of smallpox were reported in Tanganyika.

Typhus Fever

Egypt. During the week ended December 9, 1950, one case of typhus fever was reported in Alexandria.

Turkey. For the week ended December 9, 1950, six cases of typhus fever were reported in Turkey, one of which was in Istanbul.