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EMPLOYMENT OF SOLUBLE ANTIGEN IN SCREENING TESTS FOR TYPHUS COMPLEMENT FIXATION

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Purification of rickettsial suspensions from infected yolk sacs by the ethyl-ether extraction technic was first described by Craigie in a confidential report submitted in 1942 and later published in 1945 (*1*). The development of this method paved the way for greatly simplified technics for the preparation of highly specific rickettsial antigens and of nonspecific soluble antigens which have been increasingly employed in studies concerning serological relationships between various rickettsial strains and groups.

Topping and Shear (*2*) soon noted that treatment of typhus infected yolk sacs by the ether method caused a release of soluble antigen into the aqueous fraction remaining in the supernatant fluid after high speed centrifugation to remove rickettsial bodies. This antigen proved capable of causing positive complement-fixation reactions and immunity in guinea pigs and strongly positive Weil-Felix response in rabbits. Plotz (*3*) found that while the soluble antigen liberated from typhus rickettsiae by ether extraction of infected yolk sacs gave strong cross-fixation with both epidemic and murine convalescent sera, the sedimented rickettsial bodies, after several washings in neutral buffered saline, showed a high degree of specificity. Topping and Shepard (*4*) reported that large quantities of antigen released by ether extraction and contained in the supernate after centrifugation were found with yolk sac preparations of both *Rickettsia prowazeki* and *R. mooseri*, whether the yolk sac suspensions were treated directly or first centrifuged to sediment the rickettsiae before treatment with ether. With *R. rickettsi* a lesser amount of soluble antigen was also released by ethyl ether extraction, while with *R. burneti* and *R. orientalis* there was no release at all and an actual loss in antigen titer resulted.

When rickettsial suspensions were first washed by centrifugation and most of the remaining yolk sac material removed by absorption

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with celite, Shepard and Topping reported (*5*) that no liberation of soluble antigen occurred following ether treatment of the prepared suspensions. However, soluble antigen was liberated by ether when normal yolk sac material was added to the purified suspensions.

Fulton and Begg (*6*) also reported the presence of soluble antigen in purified rat lung murine rickettsial suspensions after storage for 1 month at 4°C. although purified mouse lung suspensions were deficient or lacking in soluble antigen when freshly purified. Significant release of soluble antigen occurred following ether treatment both in purified mouse lung suspensions of murine rickettsiae and in yolk sac emulsions of epidemic typhus rickettsiae. It was considered probable that the soluble antigen was derived from the surface antigen of the rickettsiae.

This view was confirmed by the work of Shepard and Wyckoff (*7*) in which they demonstrated with the aid of the electron microscope that the filter-passing soluble antigen released from suspensions of typhus rickettsiae by ether treatment consisted of sub-microscopic particles of a capsular substance adhering to and partially enveloping the rickettsiae. Liberation of particles from the capsular substance was found to be much more active and complete with warm ether treatment than with cold ether extraction.

Soluble antigen prepared from epidemic strains (Breinl, Cairo, Madrid No. 4) and murine strains (Castaneda, Wilmington) of typhus rickettsiae have been found to show positive complement-fixation reactions with the heterologous as well as homologous immune sera of guinea pigs (*6, 8, 9*). Wishart and Malcomson (*9*) noted that with both epidemic and murine serum, the titer with homologous soluble antigen was higher than with heterologous or heated antigens. When either epidemic or murine serum was absorbed with epidemic rickettsiae previously heated at 65° C., the antibody responsible for the cross-reaction and for reactions with heated antigen was removed from both types of serum. An antibody which reacted only with homologous unheated antigen remained. Absorption of immune serum with homologous unheated rickettsiae removed all antibodies from the serum. Absorption of murine serum with epidemic rickettsiae had no effect upon the titer for murine antibody after an initial reduction due, presumably, to removal of common antibody from the serum. Similarly, absorption of epidemic serum with murine rickettsiae had only slight effect upon epidemic antibody titer. The specific antigen appeared to be identical for both the Breinl and Madrid strains of epidemic rickettsiae. Specific antibody was removed only by absorption with the homologous type of antigen, while "common antibody" was absorbed either by heterologous rickettsiae or by heated homologous rickettsiae. Antigens stable to 65° C. heat (common antigen) were identical for Castaneda murine and Breinl or Madrid epidemic strains.

Commercially prepared typhus vaccines of the Cox-Craigie type have been found to be useful as diagnostic antigens for complement-fixation tests (*10*, *11*). Such vaccines are known to owe a large part of their antigenic activity to the presence of soluble antigen. However, soluble antigen as such, does not appear to have been widely employed in routine typhus complement-fixation procedures. This may be due in part to the fact that such antigen lacks specificity and thus cannot be used to differentiate between epidemic and murine antibodies, and in part because such antigen may show false positive reactions with Wassermann-positive sera when primary incubation is carried out for 18 hours in the cold (*12*, *13*).

Antibody titers against soluble antigen have been determined in this laboratory in almost a thousand complement-fixation tests concurrently with specific rickettsial epidemic (Breinl) and murine (Wilmington) antibody titers, employing antigens prepared from a variety of typhus strains. Results of these tests have made it evident that whenever epidemic or murine positive titers are obtained using specific rickettsial antigens, positive reactions are also obtained employing soluble antigens from either epidemic or murine typhus yolk sac strains. Furthermore, in several instances (unpublished data 1947) where positive diagnoses of murine typhus have been made on the basis of epidemiological and clinical observations, Weil-Felix reactions and rickettsial agglutination tests, soluble antibody complement-fixation titers have been found to be as high as 1:2560 while specific murine titers remained negative or reached a maximum of 1:40. Serological tests were carried out in three different laboratories. Kahn and Kolmer tests in these instances were negative.

The preparation of specific complement-fixing rickettsial antigens involves considerable expense and a high degree of technical skill. As a byproduct in the preparation of such antigens by the ether extraction method using rickettsial yolk sac cultures, a relatively large quantity of soluble antigen may be obtained. Employment of the comparatively easily prepared soluble antigen in the preliminary testing of sera suggests the possibility of conserving highly specific antigens in large-scale typhus serologic studies such as typhus incidence surveys. To be of value in serum "screening" tests, use of soluble antigen should permit elimination of anticomplementary sera and of all sera lacking in specific complement-fixing antibodies, and at the same time permit detection of all sera in which such antibodies are present. If, as has been indicated by previous work, antibody titers with soluble antigen were as high or higher than antibody titers with specific antigens, quantitative or semiquantitative screening tests with soluble antigen should serve to estimate closely the maximum titers which might be expected in subsequent quantitative tests with specific antigens.

MATERIALS AND METHODS

Soluble antigens were prepared from Breinl epidemic and Wilmington murine typhus rickettsiae obtained from the Army Medical Department Research and Graduate School, and from the Ishii and Uchída epidemic typhus strains isolated in the Tokyo field laboratory of the United States of America Typhus Commission during the 1946–1947 typhus season. Infected yolk sacs were ground in a Waring blendor and brought to a 10 or 20 percent emulsion in M/75 phosphate-buffered saline (ph 7.2) containing 0.3 percent formalin. After standing for 24 to 48 hours at 4° C. to 8° C. for inactivation of the rickettsiae, the suspensions were shaken in a separatory funnel with 1½ volumes of ethyl ether, left at room temperature for 4 to 6 hours, and the aqueous portion drawn off. A second extraction was then made with ½ volume of ether and the aqueous layer again drawn off when separation appeared to be complete. The supernate remaining after centrifugation for 30 minutes at 12,000 r.p.m. was employed as the soluble antigen after removal of excess ether by partial vacuum. Specific rickettsial antigens were obtained through the Army Medical Center.

An epidemic immune serum pool was obtained from convalescent guinea pigs inoculated with a single dose of Breinl guinea pig brain passage material. Murine immune serum was similarly obtained from guinea pigs recovered from a single injection of tunica washings from guinea pig Wilmington strain passage material. The complement-fixation technic used throughout was essentially that recommended by the Division of Virus and Rickettsial Diseases, Army Medical Department Research and Graduate School, employing two-fold serial dilutions of serum in 0.25 cc., 2 units of antigen in 0.25 cc., 2 full units of complement in 0.5 cc., fixation overnight in the refrigerator followed by 15 minutes at room temperature, addition of 0.5 cc. of 3 percent washed sheep cells sensitized with an equal volume of amboceptor diluted to contain 3 hemolytic units in 0.25 cc., and secondary incubation for 30 minutes at 37° C. in the water bath. Serum, antigen and hemolytic system controls were always included. Secondary complement titration in the cold was invariably performed.

Titrations of immune serum were made by testing increasing dilutions of serum against increasing dilutions of homologous soluble antigen and considering the highest dilution of serum showing 3 or 4 plus fixation in the presence of the greatest dilution of antigen as one unit. The highest dilution of each epidemic antigen giving 3 or 4 plus fixation in the presence of 4 units of Breinl antiserum was then taken as one unit of antigen. Murine antigens were titrated in the same way against 4 units of Wilmington antiserum. Dilutions of sera in titrations were made in increments not greater than 1:50, while antigens were diluted in increments of 1:20. None of the anti-

TABLE 1.—*Complement fixation cross titration of guinea pig epidemic and murine antiserum against epidemic and murine soluble and specific rickettsial antigens*

ANTISERUM	Dilution	Units of serum	UNITS OF ANTIGEN																													
			Breinl soluble				Ishii soluble				Uchida soluble				Wilmington soluble				Breinl specific AMS				Epidemic specific Parke-Davis				Wilmington specific AMS				Murine specific Parke-Davis			
			4	2	1	½	4	2	1	½	4	2	1	½	4	2	1	½	4	2	1	½	4	2	1	½	4	2	1	½	4	2	1	½
Epidemic (Breinl) guinea pig pool	20	16	4	4	4	4	4	4	4	3	4	4	4	—	4	4	4	—	4	4	4	0	4	4	4	1	—	0	0	0	0	0	0	0
	40	8	4	4	4	3	4	4	4	1	4	4	4	—	4	4	2	—	4	4	4	±	4	4	4	±	—	0	0	0	0	0	0	0
	80	4	4	4	4	1	4	4	4	±	4	4	3	—	3	1	0	—	4	4	4	0	4	4	4	±	—	0	0	0	0	0	0	0
	160	2	4	4	4	±	4	4	3	0	4	4	1	—	0	0	0	—	4	4	3	0	4	4	4	±	—	0	0	0	0	0	0	0
	320	1	4	4	4	0	4	4	2	0	4	3	1	—	0	0	0	—	1	0	0	0	1	0	0	0	—	0	0	0	0	0	0	0
	640	0.5	±	±	0	0	4	3	1	0	0	0	0	—	0	0	0	—	0	0	0	0	0	0	0	0	—	0	0	0	0	0	0	0
Murine (Wilmington) guinea pig pool	20	16	4	4	4	4	4	4	4	4	4	4	4	—	4	4	4	—	4	3	0	0	4	1	0	0	—	4	4	0	4	4	4	0
	40	8	4	4	4	4	4	4	4	2	4	4	3	—	4	4	4	—	4	1	0	0	4	0	0	0	—	4	4	0	4	4	4	0
	80	4	4	4	4	2	4	4	4	±	4	4	2	—	4	4	4	—	4	±	0	0	3	0	0	0	—	4	3	0	4	4	3	0
	160	2	4	4	4	0	4	4	2	0	4	3	0	—	4	4	3	—	±	0	0	0	±	0	0	0	—	4	1	0	4	3	±	0
	320	1	4	4	±	0	4	2	±	0	±	0	0	—	4	4	1	—	0	0	0	0	0	0	0	0	—	0	0	0	4	±	0	0
	640	0.5	±	0	0	0	4	±	0	0	0	0	0	—	±	0	0	—	0	0	0	0	0	0	0	0	—	0	0	0	±	0	0	0

gens tested was anticomplementary in a dilution of 1:5. After preliminary determination of titers of antisera and antigens, cross-titration of epidemic and murine antisera were carried out with various concentrations of each antigen (table 1). For the sake of clarity, cross-reactions with epidemic and murine antisera in the presence of 2 units of antigen are tabulated separately (table 2).

TABLE 2.—*Abstract: Complement fixation cross-titration of guinea pig epidemic and murine antiserum against 2 units of epidemic and murine soluble and specific antigens*

Antigen 2 units	Guinea pig immune serum [1] (Breinl)						Guinea pig immune serum [1] (Wilmington)					
	20	40	80	160	320	640	20	40	80	160	320	640
Breinl soluble	4	4	4	4	4	±	4	4	4	4	4	0
Ishii soluble	4	4	4	4	4	3	4	4	4	4	2	±
Uchida soluble	4	4	4	4	3	0	4	4	4	3	0	0
Wilmington soluble	4	4	1	0	0	0	4	4	4	4	4	±
Breinl specific, AMS	4	4	4	4	0	0	3	1	±	0	0	0
Epidemic specific, P. D	4	4	4	4	0	0	1	±	0	0	0	0
Wilmington specific, AMS	0	0	0	0	0	0	4	4	4	4	0	0
Wilmington specific, P.D	0	0	0	0	0	0	4	4	4	3	±	0

[1] Titer of both epidemic and murine guinea pig serum pools 1:320 with 2 units of homologous soluble antigen. (Titer of 1:80 represents 4 units of antiserum).

Secondary complement titration at 4°–8° C. Complement containing 2 full units in 0.5 cc.

0.1 cc.	0.15 cc.	0.2 cc.	0.25 cc.	0.3 cc.	0.4 cc.	0.5 cc.
4	2	±	0	0	0	0

With the soluble antigens tested, those prepared from epidemic strains showed a greater degree of cross-reaction than did the murine antigen. With Ishii soluble antigen, positive complement fixation was obtained in higher dilutions of Breinl antiserum than with the homologous antigen. Similarly, when 4 units of Ishii antigen were employed, Wilmington antiserum reacted to a higher titer than when homologous antigen was used.

SCREENING TESTS

In order to determine the suitability of soluble antigens for preliminary screening of sera, complement-fixation tests were set up on a total of 475 sera from presumably normal individuals in Korea, Hokkaido, Kyushu and Okinawa collected in connection with another program. Approximately 39 percent of these sera were tested with Wilmington soluble antigen; 43 percent with Ishii soluble antigen and 18 percent with Uchida soluble antigen. Forty-seven sera were found to be anticomplementary. Of the 428 specimens remaining, 169 gave positive complement-fixation reactions with soluble antigen

in dilutions ranging from 1:10 to 1:80. Seventy-two of the 169 sera positive with soluble antigen were also positive with epidemic or murine specific rickettsial antigen or with both; 97 were negative with specific antigens.

Regardless of which soluble antigen was employed, in no instance was a positive reaction obtained with specific antigen where the reaction with soluble antigen was negative. With the exception of six sera, antibody reacting with soluble antigen was present in at least equal, and usually higher, titer where epidemic or murine specific complement-fixing antibody was present. In each of the six exceptions, specific antigen reactions were positive for epidemic typhus and reaction with Wilmington soluble antigen was positive in one dilution lower than the Breinl rickettsial antigen titer.

Sufficient serum remained in 71 of the 97 specimens which showed positive reactions with soluble antigen but negative fixation with specific antigens to permit of testing by the Kolmer complement-fixation technic. Of these, only 3 specimens were positive, 1 was doubtful, 5 had become anticomplementary, and the remaining 61 were Kolmer negative. Thus, only a small proportion of these reactions could be attributed to false positives due to syphilitic infections.

DISCUSSION

The fact that antibody common to both epidemic and murine typhus rickettsiae has been found to occur invariably in serum from human typhus cases or from guinea pigs recovered from experimental infections with either type of disease, where specific antibodies can be demonstrated, and the fact that such antibody reacts with the soluble antigen liberated by ether treatment of yolk sac preparations of either epidemic or murine strains, makes possible the employment of soluble antigen for preliminary screening of sera in typhus complement-fixation tests. Since soluble antigen is ordinarily obtained as a byproduct in the preparation of specific typhus rickettsial antigens from yolk sac cultures by the ether extraction method, the preparation of this material entails no added cost or effort. Soluble antigen can be derived also from commercial typhus vaccine stocks and, if desired, concentrated by precipitation with sodium sulfate according to the method of van der Scheer, Bohnel and Cox (*13*). These authors found also that treatment of typhus vaccines with benzene followed by sodium sulfate precipitation caused a marked decrease in reaction of the purified and concentrated soluble antigen with human syphilitic sera using complement fixation at icebox temperature.

The considerable expense and technical skill required for manufacture of specific antigens in quantities adequate for large-scale

typhus diagnostic or survey work adds to the desirability of elimination of a majority of negative or anticomplementary specimens by screening with soluble antigen. If an antigen of a type showing strong cross-reactions is employed, results at this laboratory indicate that no typhus positive sera either of epidemic or murine type will be missed, and that an estimation of maximum expected titer with specific rickettsial antigen may be obtained. Consequently, a considerable reduction results in quantities of highly purified rickettsial antigens later required in quantitative complement-fixation tests.

Further work is necessary to determine to what extent positive complement-fixation reactions in human sera with soluble antigens but not with specific antigens is indicative of actual typhus infection. Positive antibody titers with soluble antigen have been found in guinea pigs experimentally infected with murine typhus at stages of the disease before specific murine antibody could be detected by the complement-fixation technic. In human cases diagnosed as murine typhus on the basis of clinical and epidemiological grounds, Weil-Felix and rickettsial agglutination titers, complement-fixing antibody for soluble antigen has been found to occur in significant titer in the absence of specific complement-fixing antibody. It may well be that soluble (common) antibody appears earlier and persists at a measurable titer for a longer period than antibodies of the specific rickettsial type. False positive reactions with soluble antigen may also result in diseases other than syphilis and may account for a further proportion of these apparently anomalous results.

SUMMARY

Soluble antigen prepared by ether treatment of typhus infected yolk sac suspensions may be employed for preliminary screening of sera in typhus complement-fixation studies. Considerable saving in specific rickettsial antigen may be expected by partial elimination of sera lacking in specific complement-fixing antibodies or showing anticomplementary properties, and in the approximate determination of maximum expected titers in quantitative tests.

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STATISTICAL STUDIES OF HEART DISEASES

I. Heart Diseases and Allied Causes of Death in Relation to Age Changes in the Population[1]

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The annual number of deaths from diseases of the heart, 424,328 in 1945, is not only a staggering figure but is considerably more than twice the mortality from the second most frequent cause of death, cancer, with 177,464 deaths in 1945. Mortality statistics alone do not tell the complete story of the enormous cost to society of diseases of the heart, but they do provide the most reliable index of the course of heart disease in the past, and from them an estimate can be obtained of the size of the problem that confronts doctors and health authorities of the future as well as the present.

Heart disease has not always occupied its present preeminent position as a cause of death. In 1900 it was fourth in the rank order of the leading causes of death in the United States death registration States. About the year 1910 it became for the first time the most frequent cause of death, and since that time heart disease has been, except for the period of the 1918 influenza pandemic, the unchallenged leader of the list.

[1] This is the first of a series of papers dealing with the statistics of heart disease morbidity and mortality The papers are the result of a U. S. Public Health Service study carried on jointly by the National Office of Vital Statistics and the Division of Public Health Methods with the cooperation of the Division of States Relations.

TABLE 1.—*Mortality from selected causes of death in successive decades: Death registration States, 1900–1945* [1]

Cause of death	Death rates (per 100,000 population)						Proportionate mortality (percentage of deaths, all causes)					
	1900	1910	1920	1930	1940	1945	1900	1910	1920	1930	1940	1945
All causes	1,719.1	1,468.0	1,298.9	1,132.1	1,074.1	1,062.1	100.0	100.0	100.0	100.0	100.0	100.0
Communicable diseases:												
Tuberculosis (all forms)	194.4	153.8	113.1	71.1	45.8	40.1	11.3	10.5	8.7	6.3	4.3	3.8
Pneumonia (all forms) and influenza	202.2	155.9	207.3	102.5	70.1	51.8	11.8	10.6	16.0	9.1	6.5	4.9
Diarrhea and enteritis	142.7	115.4	53.7	26.0	10.3	8.7	8.3	7.9	4.1	2.3	1.0	.8
Diphtheria	40.3	21.1	15.3	4.9	1.1	1.2	2.3	1.4	1.2	.4	.1	.1
Typhoid fever	31.3	22.5	7.6	4.8	1.1	.4	1.8	1.5	.6	.4	.1	.04
Chronic diseases of older ages:												
Diseases of the heart (all forms)	137.4	158.9	159.6	214.2	291.9	321.5	8.0	10.8	12.3	18.9	27.2	30.3
Intracranial lesions of vascular origin	106.9	95.8	93.0	89.0	90.8	97.9	6.2	6.5	7.2	7.9	8.5	9.2
Nephritis (all forms)	88.6	94.8	88.8	91.0	81.4	66.7	5.2	6.5	6.8	8.0	7.6	6.3
Cancer	64.0	76.2	83.4	97.4	120.0	134.5	3.7	5.2	6.4	8.6	11.2	12.7
Diabetes mellitus	11.0	15.3	16.1	19.1	26.5	26.6	.6	1.0	1.2	1.7	2.5	2.5

[1] Data from "Vital Statistics Rates in the United States, 1900–1940" (*2*).

Some impression of the increasing significance of heart disease as a cause of death during the period 1900 to 1945 may be gained from the crude death rates for 10 principal causes of death in the United States death registration States. Table 1 shows the mortality from heart disease in relation to other leading causes at the beginning of each decade and also the proportion of all deaths attributed to each specified cause.

In the first 10 years of the United States death registration system, the public health movement was at a stage in which the health officer was still chiefly preoccupied with the problems of sanitation and quarantine of infectious disease cases. As time went on, the success of the efforts of the health officer in preventing the communicable diseases and of the physician in saving the lives of those taken ill began to become apparent in the reduction of mortality from the communicable diseases. During the past 45 years, diseases which were once serious national health problems have been virtually eliminated as causes of death. This is largely the result of sanitary control of environment, isolation of contagious disease cases, artifical immunization, and the development and application of new therapeutic medical and surgical techniques. Among these diseases are typhoid fever, whooping cough, diphtheria, scarlet fever, and diarrhea and enteritis. Great strides have also been taken in the field of infant welfare. Improved sanitation and nutrition have done much to reduce the infant mortality rate from 100 per 1,000 live births in 1915 to 38 per 1,000 live births in 1945. Even tuberculosis and pneumonia, the two most important causes of death at the turn of

the century, are yielding to medical and public health advances. Although there is still a long way to go in the conquest of these diseases, the death rate for tuberculosis in 1945 was only 21 percent of the rate in 1900, and the pneumonia death rate, particularly in recent years, indicates substantial gains in pneumonia control as a result of sera, antibiotics, and chemotherapy. The average pneumonia death rate of 49 per 100,000 population in the 5-year period 1941–45 is in marked contrast to the average rate of 161 per 100,000 population in the years 1900–1904.

Beginning in the second decade of the century a new emphasis was placed upon the broader aspects of health. The programs of nonofficial health agencies began to get under way. There was also a rapid development in the field of public health nursing. Closer integration of medicine into the public health program was sought, and this resulted in the establishment of prenatal clinics and special clinics for tuberculosis, syphilis, cancer, heart disease, and mental hygiene. Such activities tell a story of changing objectives in public health. The death rates for 10 leading causes in table 1 illustrate only one small phase of this story of medical and public-health achievements and shifting objectives, but the figures do show how the most important infectious diseases have given way to the chronic and degenerative diseases as the chief causes of mortality.

During this period of extraordinary advances in public health, the death rate for heart disease climbed steadily. It was one of the few causes that exhibited such a trend; cancer and diabetes were like heart disease in this respect. In the 45 years since 1900, the death rate for heart disease increased from 137 to 322 per 100,000 population while the death rate for all causes dropped from 1,719 to 1,062 per 100,000 population in the United States death registration States.

These trends of mortality from heart disease and other causes of death have been described here in terms of crude annual death rates. Such rates show the proportion of the population lost each year as a result of deaths attributed to the particular cause or causes. As such they are a valid measure of the total impact of these diseases. However, it is well known that a changing age distribution within the population can alter the crude death rates without any accompanying alteration of the rates of dying at specific ages. In fact, the part played by the aging of the population of the United States in the upward trend of the heart disease death rate has already been described many times. Nevertheless, before proceeding to a more detailed analysis of the trend, it is worthwhile to review briefly the reasons for the aging and the evidence that shows it is actually taking place.

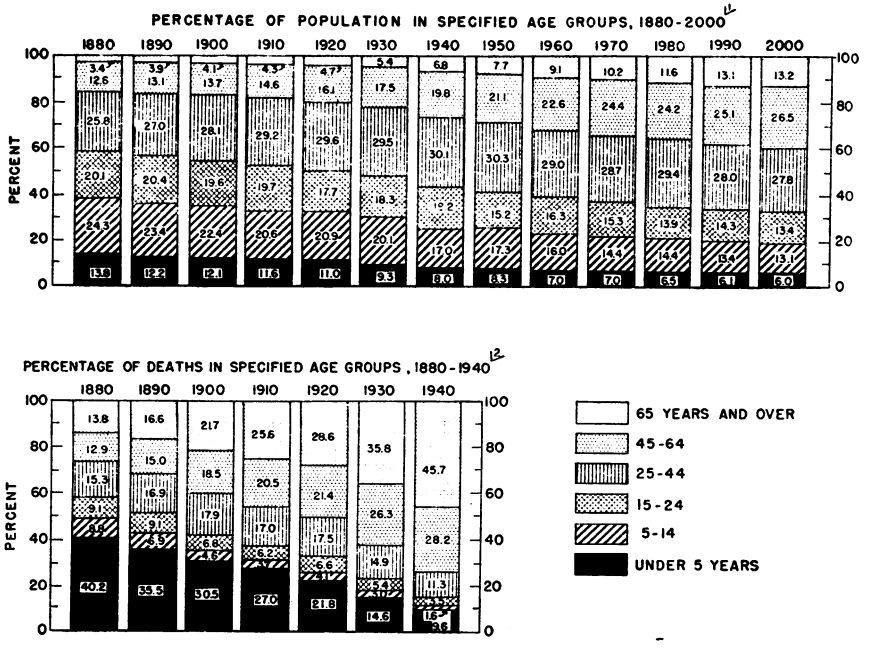

FIGURE 1.

[1] Percentage of the population in specified age groups according to decennial enumerations, 1880–1940; and estimated percentage age distribution of the population, 1950–2000 (*8*).

[2] Percentage of deaths from all causes in specified age groups for the expanding death registration area, 1900–1940. Deaths for 1880 and 1890 were recorded when the population was enumerated.

It is significant that the major decreases in mortality since 1900 have occurred in the childhood and early adult ages of life. The natural consequence of improving the chances of survival through the younger ages has been an increase in the proportion of the population alive at the older ages. This tendency has been reinforced by the decline in the birth rate (up until about 10 years ago) and the curtailment of immigration. During the period 1900–1940, the median age of the population of the United States increased from 22.9 to 29.0 years. Even more striking was the increase in the proportion of persons in the population 45 years of age and over, which rose from 18 percent in 1900 to 27 percent in 1940. At the same time the proportion under 15 years of age decreased from 35 to 25 percent while the population at ages 15–44 years remained practically stationary at approximately 48 percent. Figure 1 shows the percentage of the population in specific age groups as enumerated in the various censuses from 1880 to 1940 and as estimated to the year 2000. The estimates of the future population, published by the Bureau of the Census (*8*), are a revision of estimates prepared by the Scripps Foundation for Research

in Population Problems and published by the National Resources Planning Board in 1943 (*6*, *7*). The prediction for the year 2000, under certain reasonable assumptions, is that 40 percent of the population will be 45 years of age or over and only 19 percent will be under 15 years.

The age distribution of total deaths has changed in a pronounced manner, reflecting, in part, the change that has been taking place in the age distribution of the living population (fig. 1). In 1880, 40 percent of the recorded deaths occurred under 5 years of age while 14 percent were 65 years of age and over (*9*); in 1940 only 10 percent of deaths were under 5 years of age while 46 percent were 65 years of age or older. In other words, practically half the deaths occurring at the present time are among persons in the definitely older age brackets.

The effect of these changes in the age composition of the population upon the death rates can be eliminated by computing age-adjusted death rates. The so-called "direct method" has been used here. In this method the rates of mortality at specific ages are applied to the numbers of persons alive at corresponding ages in a selected population usually spoken of as the "standard population." In this case the populations by age of the United States in 1940 were used. The same standard population is used for all sets of age-specific rates that are to be compared. Thus, there is found the number of deaths that would be expected in the standard population if any given set of age-specific mortality rates were prevailing. These expected deaths divided by the total standard population give the age-adjusted death rate. The same proportionate distribution of population having been used for each set of age-specific rates, the age-adjusted rates are free from the effect of any changes in the age distribution of the population; the method may be used for comparing rates for one area with another as well as for comparisons over a period of time.

The age changes affect the crude rates for specific causes of death to varying extents. Hence, when age-adjusted rates are computed for each cause, the increasing importance of heart disease in relation to other leading causes can be more meaningfully assessed. Figure 2 shows in rank order the age-adjusted rates for 25 major causes of death in the death registration States of 1900 in the years 1900, 1920, and 1940. Although the changes in relative importance of the various causes, as shown in figure 2, are independent of the increasing proportions of older persons in the population, they are not free from the presumably increasing ability of physicians to make better diagnoses. The causes shown in the chart were selected because they were important causes of death at some time during the period (1900–1940) and are the same for each of the three census years. In general,

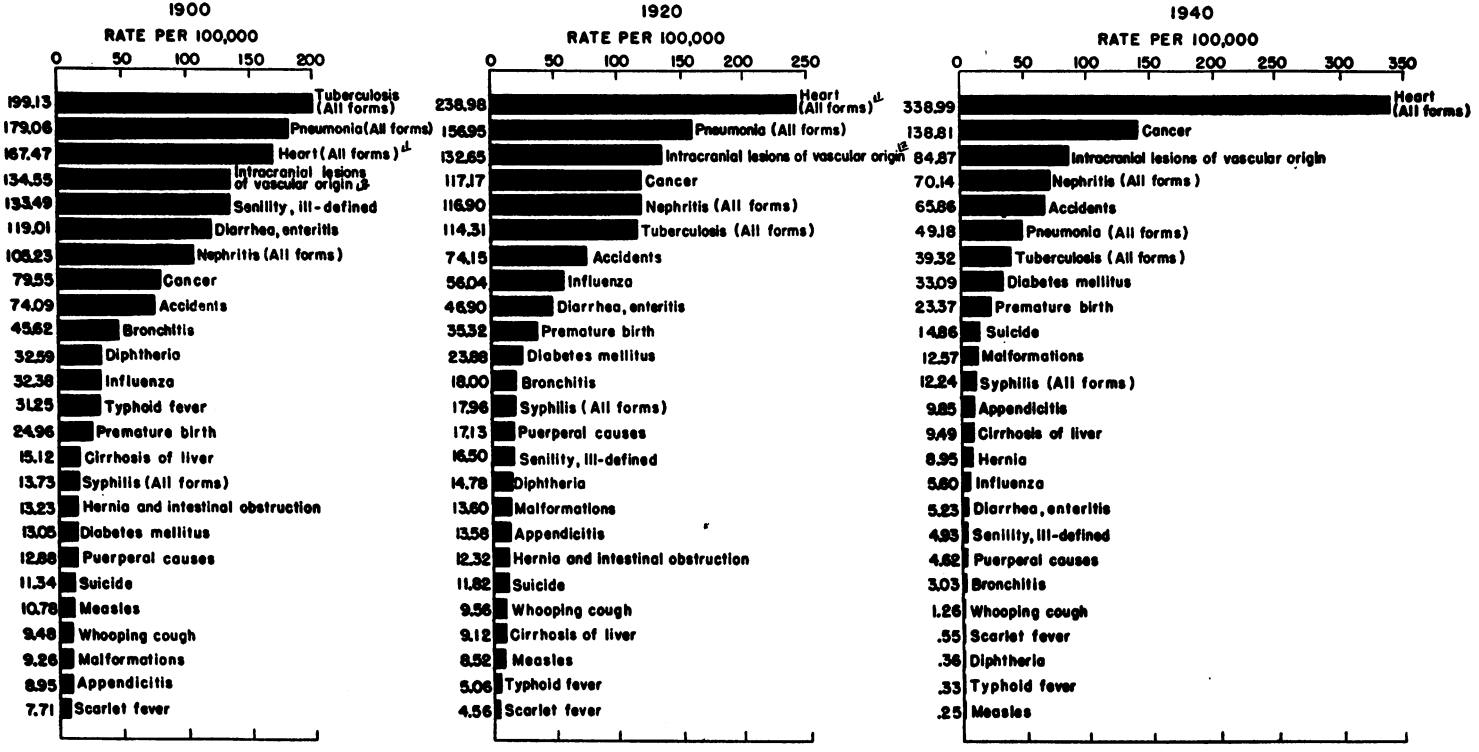

FIGURE 2.—Comparative rank of age-adjusted rates for major causes of death, in the death registration States of 1900, for 1900, 1920, and 1940. Rates are adjusted to the age distribution of the total population, enumerated, 1940.

[1] Excludes diseases of coronary arteries.

[2] Includes all embolism and thrombosis, except puerperal.

it can be seen that the tendency, already described, for the chronic and degenerative diseases of middle and old age to replace the infectious diseases as leading causes of death is not essentially altered when the changing age distribution of the population is taken into account. In particular, the chart shows that "diseases of the heart" has progressed in the 40-year interval from third to first place, nephritis from seventh to fourth, cancer from eighth to second, and diabetes from eighteenth to eighth place, while tuberculosis, pneumonia, diarrhea and enteritis, diphtheria and other communicable diseases have declined from higher to lower ranks.

The course of mortality from 15 of the important causes of death for the period 1900–1945 is shown in greater detail in figure 3. The death rates shown for measles, whooping cough, scarlet fever, and diphtheria are for the age group under 20 years; mortality under 1 year of age from diarrhea and enteritis is expressed in terms of deaths per 1,000 live births; the remainder of the rates are age-adjusted in the manner described above (*3*). The marked drop in mortality from the chief infectious diseases is obvious. Lesser declines in the rates for intracranial lesions of vascular origin and nephritis, and increases for heart disease, cancer, and diabetes are also apparent.

Since the upward trend is evident even in age-adjusted rates for some of the diseases characteristic of middle and old age, the aging of the population could not be wholly responsible. This aging, however, does make it logical to suppose that a further upward movement of the crude death rate for heart disease, at least, is almost inevitable. For it is apparent that the effect of the survival of greater numbers of persons to advanced ages is simply to increase the relative numbers exposed to the chance of death at these ages, and this, in turn, will result in a steady tendency toward higher crude death rates for such diseases as are especially inclined to cause death among the older groups. Thus far, however, the decline in the mortality rates for infectious diseases (including tuberculosis and pneumonia) has been so rapid that, despite the increase in mortality for the "old age" diseases taken as a group (including heart disease, intracranial lesions of vascular origin, nephritis, cancer, and diabetes), there has been a downward trend in the crude death rate for all causes combined. With further public health advances, particularly in the south and southwest, the general mortality rate may continue to decrease somewhat, but it is not expected that the crude or general death rate for the United States will ever fall much below the present level of about 10 per 1,000 population. Indeed, if the age structure of the population continues to change in the manner illustrated in figure 1, a moderate upward trend in the crude death rate is indicated for the future. It

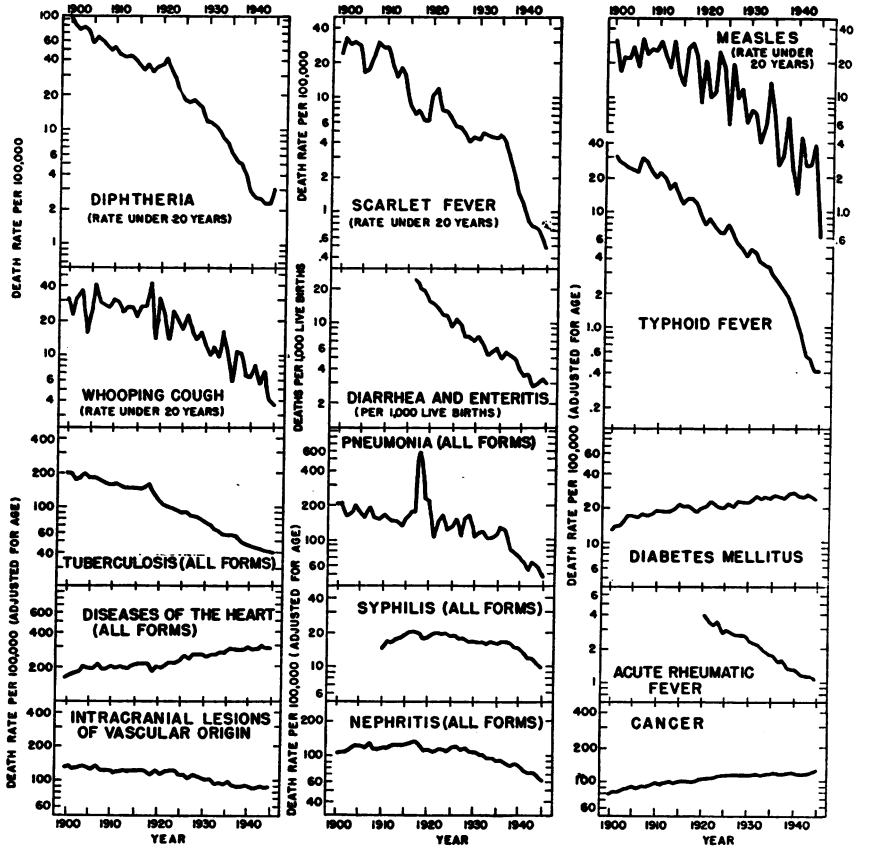

FIGURE 3.—Course of mortality for selected causes of death in the expanding death registration States (logarithmic scale), 1900–1945.

has been variously estimated by Dublin and Lotka (*1*), by Thompson and Whelpton (*5*), and by Perrott and Holland (*4*), that the crude death rate in 1980 will be 13.0, 14.5, and 17.0 per 1,000 population, respectively. The last of these estimates, unlike the other two, takes no account of expected further reductions in the age-specific mortality rates for all causes combined, and the authors state that they think it is unlikely that the actual death rate will reach their estimated figure. Their computation was made solely to show how the expected aging of the population between 1935 and 1980 could alone be responsible for an increase in the death rate from 11 per 1,000 in 1935 to about 17 per 1,000 in 1980, the age-specific rates remaining fixed during that interval.

Although there is some variation in the predicted crude death rate because of differences in the assumptions made, there is no question that heart disease will continue to play the principal role in the upward trend of mortality unless some revolutionary advance is made in medical knowledge bearing upon the prevention or treatment of

cardiac diseases. If the age-specific mortality rates for heart disease in 1945 are applied to the estimated populations at specific ages in 1980, it is found that they would cause 74 percent more deaths in 1980 than they did in 1945. On a rate basis this increase would amount to 40 percent, or a rate of about 452 per 100,000 population in 1980, in contrast to the 1945 rate of 321. It may also be estimated on the basis of a crude general death rate of about 14 per 1,000 population in 1980 that deaths from heart disease will constitute roughly 32 percent of all deaths occurring in that year. If the age-specific death rates for heart disease at ages over 45 continue to increase, even at a reduced rate, the proportion will be considerably higher.[2]

These computations may give some idea of what the magnitude of the health problems relating to heart disease promises to become in the future. Even today they offer a major challenge to society. The cardiovascular-renal diseases are not as amenable to control as are most of the infectious diseases. However, trends of mortality from syphilis and acute rheumatic fever, and other infections which may lead to specific heart conditions, are definitely downward, and, with respect to the larger group of degenerative heart diseases, much can be done at present to postpone the onset of cases and to slow their progress.

A thorough investigation of various statistical aspects of heart disease, based upon morbidity data from surveys and mortality data from the death registration system, is now in progress. This investigation will take the form of a series of studies each of which will present and analyze material on a particular phase of the cardiac disease problem in the United States.

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[2] It is worth noting that a significant decline in mortality from any important cause of death other than heart disease, such as cancer, for example, could also result in the attributing of more deaths to diseases of the heart and, hence, a higher crude death rate for that cause.

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 APRIL 3, 1948

Summary

The incidence of influenza declined from a total of 4,642 cases last week to 3,658 for the current week. For the corresponding week last year the total was 48,968, and the 5-year (1943–47) median is 2,770. Of the 7 States reporting currently more than 67 cases, 4 showed decreases, while 3 (Virginia, South Carolina, and Oklahoma) showed a combined increase of 201 cases. The total for the year to date is 121,308. The peak of reported incidence, 14,253 cases, was reached in the week ended January 31. Last year a rise beginning unusually late (the latter part of February) and increasing sharply brought the total for the corresponding period to 206,662 cases. The highest weekly incidence of that year, 52,115 cases, was reported for the week ended March 22.

Of the current total of 18 cases of poliomyelitis (last week 33, 5-year median 24), the lowest weekly incidence since May 1944, only Texas (5 cases), and New York and Indiana (2 cases each) reported more than 1 case. The total for the year to date is 399, as compared with 667 for the same period last year and a 5-year median of 453.

The total reported incidence to date of the dysenteries (amebic, bacillary, and undefined) is 6,700 cases, or 53 percent above the combined 5-year median (4,371). Of the other diseases listed in the following tables, cumulative figures to date for only infectious encephalitis, Rocky Mountain spotted fever, and undulant fever are above the corresponding median expectancies.

A total of 9,685 deaths was recorded during the week in 92 large cities of the United States, as compared with 9,634 last week, 10,169 and 9,021, respectively, for the corresponding weeks of 1947 and 1946, and a 3-year (1945–47) median of 9,097. The total for the year to date (14 weeks) is 142,350, as compared with 141,212 for the same period last year. Infant mortality for the week in the same cities totaled 696, as compared with 679 last week and a 3-year median of 605. The cumulative figure is 9,708, as compared with 11,307 for the corresponding period last year.

Telegraphic morbidity reports from State health officers for the week ended Apr. 3, 1948, and comparison with corresponding week of 1947 and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none was reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median 1943–47	Week ended—		Median 1943–47	Week ended—		Median 1943–47	Week ended—		Median 1943–47
	Apr. 3, 1948	Mar. 29, 1947		Apr. 3, 1948	Mar. 29, 1947		Apr. 3, 1948	Mar. 29, 1947		Apr. 3, 1948	Mar. 29, 1947	
NEW ENGLAND												
Maine	0	1	0	3	------	------	27	195	27	0	0	0
New Hampshire	0	0	0	------	1	1	3	5	5	1	0	0
Vermont	0	0	0	------	107	------	2	275	171	1	0	0
Massachusetts	4	10	4	------	------	------	1,094	404	1,149	0	0	9
Rhode Island	0	0	1	------	------	1	4	165	11	0	0	3
Connecticut	0	2	2	8	------	3	71	573	455	2	0	5
MIDDLE ATLANTIC												
New York	9	20	17	[1] 7	[1] 9	[1] 6	2,359	383	2,799	8	4	24
New Jersey	4	1	3	9	23	9	1,150	390	1,653	1	1	5
Pennsylvania	8	22	14	[2]	[2]	[2] 2	1,488	291	1,424	5	9	11
EAST NORTH CENTRAL												
Ohio	8	13	13	------	141	9	1,127	647	647	2	7	12
Indiana	7	10	6	------	259	15	634	90	294	0	1	2
Illinois	4	6	15	2	189	14	2,247	77	1,271	4	10	17
Michigan [3]	3	7	7	2	78	4	1,332	41	1,295	3	4	7
Wisconsin	2	8	1	12	1,853	46	1,754	289	1,563	2	1	2
WEST NORTH CENTRAL												
Minnesota	5	2	3	------	13	------	426	73	73	1	1	4
Iowa	0	0	2	1	6,036	------	513	107	118	2	1	2
Missouri	3	1	4	2	230	3	476	4	369	2	3	6
North Dakota	0	0	0	4	20	8	18	16	16	0	0	0
South Dakota	0	0	3	------	------	------	43	13	19	0	0	0
Nebraska	0	2	2	30	9	9	292	4	125	0	0	0
Kansas	1	5	3	4	926	3	59	11	629	1	3	3
SOUTH ATLANTIC												
Delaware	0	0	0	------	------	------	71	2	22	0	0	1
Maryland [3]	10	6	11	3	20	8	107	23	140	2	1	5
District of Columbia	0	0	0	------	4	1	122	31	75	0	0	1
Virginia	5	9	4	398	3,986	259	202	437	621	3	2	5
West Virginia	4	3	2	41	2,474	7	346	95	95	6	1	4
North Carolina	5	7	7	------	------	------	7	265	265	2	3	3
South Carolina	5	7	5	482	2,305	473	126	127	175	0	1	2
Georgia	3	3	4	7	805	35	51	87	264	2	1	2
Florida	5	5	3	2	135	5	296	21	69	1	0	2
EAST SOUTH CENTRAL												
Kentucky	3	10	5	------	------	7	142	4	105	3	4	5
Tennessee	3	4	4	35	1,125	57	301	80	297	5	3	7
Alabama	1	12	7	112	1,085	93	63	145	164	2	4	6
Mississippi [3]	2	6	5	18	255	------	59	19	------	3	1	3
WEST SOUTH CENTRAL												
Arkansas	1	5	4	183	4,576	87	133	117	157	1	0	2
Louisiana	0	1	3	2	315	55	28	119	121	1	1	5
Oklahoma	6	3	3	133	6,891	131	38	8	95	3	2	2
Texas	33	28	29	1,750	12,332	1,143	2,053	289	1,297	1	2	16
MOUNTAIN												
Montana	0	1	1	66	851	21	39	137	137	4	1	1
Idaho	0	1	1	35	242	1	49	4	27	0	0	0
Wyoming	0	0	1	------	53	12	176	15	27	0	0	0
Colorado	8	4	7	67	393	35	792	40	354	1	0	2
New Mexico	4	3	0	4	22	4	22	88	21	0	0	1
Arizona	1	3	2	111	119	98	184	------	31	0	1	0
Utah [3]	0	0	0	3	309	15	44	15	156	0	0	0
Nevada	0	0	0	------	------	------	10	------	------	0	0	0
PACIFIC												
Washington	3	10	7	8	428	2	460	52	261	1	0	2
Oregon	3	1	5	61	220	22	------	31	135	0	2	2
California	16	8	21	53	129	70	2,744	261	1,142	3	3	23
Total	179	250	250	3,658	48,968	2,770	23,784	6,565	26,183	79	78	216
13 weeks	2,725	3,760	3,760	121,308	206,662	175,984	199,206	69,066	210,408	1,119	1,117	3,232
Seasonal low week [4]	(27th) July 5–11			(30th) July 26–Aug. 1			(35th) Aug. 30–Sept. 5			(37th) Sept. 13–19		
Total since low	9,083	11,326	12,430	164,866	239,637	239,637	234,152	91,953	248,341	1,901	2,089	5,684

[1] New York City only. [2] Philadelphia only.
[3] Period ended earlier than Saturday.
[4] Dates between which the approximate low week ends. The specific date will vary from year to year.

Telegraphic morbidity reports from State health officers for the week ended Apr. 3, 1948, and comparison with corresponding week of 1947 and 5-year median—Continued

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever		
	Week ended—		Median 1943–47	Week ended		Median 1943–47	Week ended—		Median 1943–47	Week ended—		Median 1943–47
	Apr. 3, 1948	Mar. 29, 1947		Apr. 3, 1948	Mar. 29, 1947		Apr. 3, 1948	Mar. 29, 1947		Apr. 3, 1948 [5]	Mar. 29, 1947	
NEW ENGLAND												
Maine	0	0	0	5	25	32	0	0	0	1	0	0
New Hampshire	0	0	0	1	3	10	0	0	0	0	0	0
Vermont	0	0	0	4	8	10	0	0	0	0	0	0
Massachusetts	0	0	0	130	146	431	0	0	0	1	7	0
Rhode Island	0	0	0	16	10	14	0	0	0	0	0	0
Connecticut	0	0	0	43	63	70	0	0	0	0	0	0
MIDDLE ATLANTIC												
New York	2	3	3	251	406	749	0	0	0	2	1	3
New Jersey	0	0	0	90	150	167	0	0	0	1	0	1
Pennsylvania	0	0	0	294	256	472	0	0	0	1	4	2
EAST NORTH CENTRAL												
Ohio	0	0	0	342	398	409	0	0	0	1	0	2
Indiana	2	0	0	66	85	122	0	0	0	1	1	1
Illinois	0	0	0	112	132	271	0	0	0	1	0	3
Michigan [3]	1	2	0	113	205	205	0	0	0	1	1	2
Wisconsin	0	0	0	58	57	317	0	0	0	0	0	0
WEST NORTH CENTRAL												
Minnesota	0	1	0	42	40	49	0	0	0	0	2	0
Iowa	1	0	0	41	34	60	0	1	1	1	1	0
Missouri	0	0	0	33	42	80	0	0	0	1	3	1
North Dakota	0	1	0	10	24	24	0	0	0	0	2	0
South Dakota	0	0	0	10	8	11	0	0	0	0	0	0
Nebraska	0	2	0	33	16	41	0	0	0	0	0	0
Kansas	0	0	0	20	52	74	0	0	0	0	0	0
SOUTH ATLANTIC												
Delaware	0	0	0	1	14	11	0	0	0	0	0	0
Maryland [3]	0	0	0	18	37	146	0	0	0	1	2	0
District of Columbia	0	0	0	5	14	25	0	0	0	1	0	0
Virginia	1	0	0	21	41	104	0	0	0	0	1	1
West Virginia	0	0	0	16	19	38	0	0	0	3	3	1
North Carolina	0	0	0	15	36	36	0	0	0	0	0	0
South Carolina	0	0	0	4	19	10	0	0	0	0	1	1
Georgia	0	0	0	19	12	15	0	0	0	1	1	2
Florida	1	0	0	5	10	9	0	0	0	3	1	1
EAST SOUTH CENTRAL												
Kentucky	0	0	1	18	70	68	0	0	0	1	2	1
Tennessee	0	0	0	23	51	45	0	2	0	0	0	1
Alabama	0	2	1	7	26	26	0	0	0	3	2	2
Mississippi [3]	0	1	0	0	9	9	0	0	1	3	0	0
WEST SOUTH CENTRAL												
Arkansas	0	0	1	3	9	10	0	0	0	0	1	1
Louisiana	0	1	0	1	6	13	0	0	0	5	1	2
Oklahoma	0	0	0	5	14	14	0	0	0	2	1	1
Texas	5	2	2	31	36	118	0	9	1	5	4	4
MOUNTAIN												
Montana	1	0	0	14	7	14	0	0	0	0	0	0
Idaho	1	0	0	8	4	8	0	0	0	0	0	0
Wyoming	0	0	0	4	6	10	0	0	0	0	0	0
Colorado	0	0	0	17	50	50	0	0	0	0	0	0
New Mexico	0	0	0	9	21	18	0	0	0	0	0	1
Arizona	0	0	0	3	8	19	0	0	0	0	0	0
Utah [3]	0	0	0	12	19	49	0	0	0	0	0	0
Nevada	0	0	0	2	0	1	0	0	0	0	0	0
PACIFIC												
Washington	1	0	0	85	22	41	0	0	1	0	2	2
Oregon	1	0	0	18	20	29	0	0	0	0	1	0
California	1	9	4	70	152	229	0	0	0	4	4	3
Total	18	24	24	2,148	2,892	4,336	0	12	18	44	49	54
13 weeks	399	667	453	30,853	35,869	51,038	33	61	136	566	570	692
Seasonal low week [4]	(11th) Mar. 15–21			(32nd) Aug. 9–15			(35th) Aug. 30–Sept. 5			(11th) Mar. 15–21		
Total since low	51	55	52	53,392	62,555	89,359	54	115	219	93	85	98

[3] Period ended earlier than Saturday.
[4] Dates between which the approximate low week ends. The specific date will vary from year to year.
[5] Including paratyphoid fever reported separately, as follows: Massachusetts 1 (salmonella infection), Georgia 1, California 2.

Telegraphic morbidity reports from State health officers for the week ended Apr. 3, 1948, and comparison with corresponding week of 1947 and 5-year median—Continued

Division and State	Whooping cough			Week ended Apr. 3, 1948							
	Week ended—		Median 1943–47	Dysentery			Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever, endemic	Undulant fever
	Apr. 3, 1948	Mar. 29, 1947		Amebic	Bacillary	Unspecified					
NEW ENGLAND											
Maine	35	10	12								
New Hampshire		5	5								
Vermont	16	11	37								2
Massachusetts	51	130	150		1						
Rhode Island	2	4	15								
Connecticut	19	42	42	1			1				1
MIDDLE ATLANTIC											
New York	118	160	200	11	3						1
New Jersey	51	110	110								1
Pennsylvania	68	197	122								
EAST NORTH CENTRAL											
Ohio	79	121	121	1						1	2
Indiana	24	15	15			3	2		1		
Illinois	45	56	57	1			3		1		13
Michigan[3]	82	212	121	7							6
Wisconsin	56	107	81								14
WEST NORTH CENTRAL											
Minnesota	17	8	16								1
Iowa	7	9	9			1					2
Missouri	14	15	8			2					
North Dakota	4			8							
South Dakota	1										
Nebraska	14	15	8								5
Kansas	70	16	37								2
SOUTH ATLANTIC											
Delaware	3	3	3								
Maryland[3]	12	46	46			1					2
District of Columbia	1	6	5								
Virginia	51	81	54			74			1		4
West Virginia	12		15								
North Carolina	49	75	98								
South Carolina	111	45	67	1	3		1			2	1
Georgia	14	2	22	1					3	2	8
Florida	19	25	22	4		2				3	
EAST SOUTH CENTRAL											
Kentucky	9	51	28								1
Tennessee	28	72	18	2		1					2
Alabama	31	66	31	2						1	
Mississippi[3]		8			1				1	2	1
WEST SOUTH CENTRAL											
Arkansas	21	33	17	4					3		1
Louisiana	10	3	3	3	1						
Oklahoma	43	30	13								
Texas	401	568	302	18	229	34			1	4	12
MOUNTAIN											
Montana	4	8	9								
Idaho	16		5								2
Wyoming	5		2								
Colorado	65	13	22				1				6
New Mexico	12	23	10								
Arizona	35	16	19			8					
Utah[3]	10	3	32								3
Nevada											
PACIFIC											
Washington	33	38	31	2							2
Oregon	26	17	27	7							1
California	87	164	164	5	13						2
Total	1,881	2,639	2,551	78	251	126	8	0	11	15	98
Same week, 1947	2,639			81	213	170	11	0	5	18	167
Median, 1943–47	2,551			40	213	74	9	1	16	33	[4] 95
13 weeks: 1948	28,738			828	3,273	2,599	119	6	235	187	1,185
1947	33,138			627	4,267	2,849	92	12	473	561	1,372
Median, 1943–47	31,641			383	2,602	1,386	106	4	246	609	[4] 1,099

[3] Period ended earlier than Saturday.

[4] 3-year median 1945–47.

Anthrax: Pennsylvania 1.

Alaska: Week ended Mar. 27—Influenza 3, rheumatic fever 4, whooping cough 2, scarlet fever 2; week ended Apr. 3—chickenpox 2, influenza 8, measles 1, meningitis 1, mumps 9, pneumonia 3, scarlet fever 1.

Territory of Hawaii: Week ended Apr. 3—Rabies 0, bacillary dysentery 7, measles 6, whooping cough 13.

WEEKLY REPORTS FROM CITIES *

City reports for week ended Mar. 27, 1948

This table lists the reports from 89 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

Division, State, and city	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland	0	0	-----	0	-----	0	0	0	1	0	0	18
New Hampshire:												
Concord	0	0	-----	0	-----	0	2	0	0	0	0	-----
Vermont:												
Barre	0	0	-----	0	-----	0	0	0	0	0	0	-----
Massachusetts:												
Boston	1	0	-----	0	511	1	5	0	44	0	0	7
Fall River	0	0	-----	0	-----	0	0	0	1	0	0	4
Springfield	0	0	-----	0	3	0	0	0	2	0	0	1
Worcester	0	0	-----	0	1	0	5	0	8	0	0	4
Rhode Island:												
Providence	0	1	1	0	-----	0	1	0	10	0	0	7
Connecticut:												
Bridgeport	0	0	-----	0	1	0	0	0	5	0	0	-----
Hartford	0	0	1	0	4	0	1	0	2	0	0	3
New Haven	0	0	2	0	1	1	2	0	0	0	0	5
MIDDLE ATLANTIC												
New York:												
Buffalo	0	0	-----	0	20	0	5	0	4	0	0	13
New York	8	3	13	2	1,581	9	82	1	112	0	0	22
Rochester	0	0	-----	0	2	0	2	0	10	0	0	1
Syracuse	0	0	-----	0	14	0	1	0	5	0	0	5
New Jersey:												
Camden	0	0	-----	0	11	0	0	0	3	0	0	1
Newark	0	0	3	0	124	0	3	0	8	0	0	3
Trenton	0	0	-----	0	2	1	2	0	3	0	0	2
Pennsylvania:												
Philadelphia	1	0	7	1	421	1	21	0	48	0	0	16
Pittsburgh	1	0	1	1	3	0	13	0	23	0	0	1
Reading	0	0	-----	0	10	0	2	0	10	0	0	3
EAST NORTH CENTRAL												
Ohio:												
Cincinnati	0	0	-----	0	42	6	13	0	22	0	0	3
Cleveland	0	0	1	0	17	2	8	0	46	0	1	7
Columbus	0	0	-----	0	117	0	6	0	4	0	0	5
Indiana:												
Fort Wayne	0	0	-----	0	15	0	2	0	8	0	0	-----
Indianapolis	2	0	-----	0	117	1	1	0	4	0	0	12
South Bend	0	0	-----	0	5	0	0	0	2	0	0	-----
Terre Haute	0	0	-----	0	9	0	2	0	2	0	0	-----
Illinois:												
Chicago	0	0	-----	1	1,020	2	32	0	46	0	0	21
Springfield	0	0	-----	1	26	0	1	0	0	0	0	-----
Michigan:												
Detroit	2	0	-----	0	297	0	10	0	75	0	0	15
Flint	0	0	-----	0	-----	0	4	0	3	0	0	-----
Grand Rapids	0	0	-----	0	138	1	0	0	5	0	0	-----
Wisconsin:												
Kenosha	0	0	-----	0	118	0	0	0	0	0	0	-----
Milwaukee	0	0	-----	0	41	0	5	0	13	0	0	4
Racine	0	0	-----	0	196	0	0	0	1	0	0	2
Superior	1	0	-----	0	58	0	0	0	0	0	0	-----
WEST NORTH CENTRAL												
Minnesota:												
Duluth	0	0	-----	0	106	0	1	0	4	0	0	-----
Minneapolis	0	0	-----	0	30	0	4	0	20	0	0	1
St. Paul	1	0	-----	0	34	0	4	0	3	0	0	3
Missouri:												
Kansas City	0	0	2	0	36	0	2	0	2	0	0	12
St. Joseph	0	0	-----	0	-----	0	0	0	0	0	0	-----
St. Louis	6	0	1	0	290	0	9	0	14	0	0	7

* In some instances the figures include nonresident cases.

City reports for week ended March 27, 1948—Continued

Division, State, and city	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL—continued												
South Dakota:												
Fargo	0	0	------	0	1	0	0	0	2	0	0	3
Nebraska:												
Omaha	0	0	------	0	67	0	1	0	1	0	0	1
Kansas:												
Topeka	0	0	------	0	13	0	2	0	0	0	0	------
Wichita	0	0	------	0	2	0	3	0	3	0	0	5
SOUTH ATLANTIC												
Delaware:												
Wilmington	0	0	------	0	33	0	4	0	4	0	0	------
Maryland:												
Baltimore	0	0	3	0	40	1	6	0	7	0	0	14
Cumberland	2	0	------	0	------	0	1	0	0	0	0	2
Frederick	0	0	------	0	------	0	1	0	0	0	0	------
District of Columbia:												
Washington	0	0	------	0	135	0	8	0	11	0	0	15
Virginia:												
Richmond	0	0	------	0	2	0	3	0	4	0	0	1
Roanoke	0	0	------	0	------	0	0	0	0	0	0	------
West Virginia:												
Charleston	0	0	------	0	2	0	11	0	0	0	0	------
Wheeling	0	0	------	0	12	0	5	0	0	0	0	------
North Carolina:												
Raleigh	0	0	------	0	------	0	0	0	1	0	0	------
Wilmington	0	0	------	0	------	0	1	0	0	0	0	7
Winston-Salem	0	0	------	0	------	0	0	0	0	0	0	1
South Carolina:												
Charleston	0	0	21	0	------	0	0	0	0	0	0	2
Georgia:												
Atlanta	0	0	1	1	1	0	2	0	9	0	0	2
Brunswick	0	0	------	0	------	0	0	0	0	0	0	------
Savannah	0	0	1	1	2	0	1	0	0	0	0	1
Florida:												
Tampa	0	0	2	1	12	0	3	0	1	0	1	3
EAST SOUTH CENTRAL												
Tennessee:												
Memphis	0	0	------	5	134	0	7	0	3	0	0	12
Nashville	0	0	------	0	------	0	2	0	1	0	0	2
Alabama:												
Birmingham	0	0	4	1	------	4	5	0	2	0	0	6
Mobile	0	0	18	3	------	0	1	0	0	0	0	------
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock	0	0	3	1	7	0	0	0	1	0	0	------
Louisiana:												
New Orleans	1	0	3	0	------	4	5	0	1	0	2	8
Shreveport	0	0	------	0	------	0	5	0	0	0	0	------
Oklahoma:												
Oklahoma City	0	0	1	0	11	2	4	0	4	0	0	1
Texas:												
Dallas	0	0	------	0	72	0	2	0	6	0	0	3
Houston	0	0	------	1	19	0	4	0	1	0	0	3
San Antonio	2	0	1	0	16	0	6	0	1	0	0	------
MOUNTAIN												
Montana:												
Billings	0	0	------	0	------	0	3	0	0	0	0	1
Great Falls	0	0	------	0	5	0	0	0	0	0	0	2
Helena	0	0	------	0	------	0	0	0	0	0	0	------
Missoula	0	0	------	0	1	0	0	0	0	0	0	------
Idaho:												
Boise	0	0	------	0	------	0	2	0	0	0	0	------
Colorado:												
Denver	1	0	------	0	372	0	5	0	3	0	0	11
Pueblo	1	0	------	0	56	0	2	0	4	0	0	10
Utah:												
Salt Lake City	0	0	------	1	21	0	1	0	6	0	0	------

City reports for week ended March 27, 1948—Continued

Division, State, and city	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle	1	0	-----	0	18	0	4	0	12	0	0	9
Spokane	0	0	-----	0	4	0	2	0	0	0	0	-----
Tacoma	0	0	-----	0	33	0	0	0	1	0	0	2
California:												
Los Angeles	2	0	4	2	168	3	7	2	27	0	0	7
Sacramento	0	0	-----	0	3	0	0	0	4	0	0	-----
San Francisco	0	0	4	0	267	3	5	[illegible]	12	0	0	6
Total	33	4	[illegible]8	23	6,950	42	375	5	705	0	4	348
Corresponding week, 1947[1]	89	-----	1,118	55	1,513	-----	483	-----	867	0	10	615
Average 1943–47	68	-----	248	[2] 33	[3] 6,714	-----	[2] 423	-----	1,611	1	10	629

[1] Exclusive of Oklahoma City.
[2] 3-year average, 1945-47.
[3] 5-year median, 1943–47.

Rates (annual basis) per 100,000 population, by geographic groups, for the 89 cities in the preceding table (latest available estimated population, 34,520,900)

	Diphtheria case rates	Encephalitis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Poliomyelitis case rates	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
			Case rates	Death rates								
New England	2.6	2.6	10.5	0.0	1,362	5.2	41.8	0.0	191	0.0	0.0	128
Middle Atlantic	4.6	1.4	11.1	1.9	1,013	5.1	60.6	0.5	105	0.0	0.0	31
East North Central	3.0	0.0	0.6	1.2	1,348	7.3	51.1	0.0	140	0.0	0.6	42
West North Central	13.9	0.0	6.0	0.0	1,152	0.0	51.7	0.0	97	0.0	0.0	64
South Atlantic	3.3	0.0	46.3	5.0	396	1.7	76.1	0.0	61	0.0	1.7	79
East South Central	0.0	0.0	129.8	53.1	791	23.6	88.5	0.0	35	0.0	0.0	118
West South Central	7.9	0.0	21.0	5.3	329	15.8	68.4	0.0	37	0.0	5.3	39
Mountain	15.9	0.0	0.0	7.9	3,614	0.0	103.3	0.0	103	0.0	0.0	191
Pacific	4.7	0.0	12.7	3.2	780	9.5	28.5	6.3	89	0.0	0.0	38
Total	5.0	0.6	14.8	3.5	1,053	6.4	56.8	0.8	107	0.0	0.6	53

Dysentery, amebic.—Cases: Boston 1, New York 8, Cleveland 1, Flint 1, Memphis 1, New Orleans 1, Los Angeles 6, San Francisco 1.
Dysentery, bacillary.—Cases: New York 2, New Orleans 1.
Dysentery, unspecified.—Cases: Baltimore 2, San Antonio 2.
Typhus fever, endemic.—Cases: New York 1, New Orelans 1.

TERRITORIES AND POSSESSIONS

Puerto Rico

Notifiable diseases—4 weeks ended February 28, 1948.—During the 4 weeks ended February 28, 1948, cases of certain notifiable diseases were reported in Puerto Rico as follows:

Disease	Cases	Disease	Cases
Chickenpox	42	Poliomyelitis	1
Diphtheria	46	Syphilis	124
Dysentery, unspecified	4	Tetanus	5
Gonorrhea	199	Tuberculosis (all forms)	958
Influenza	18	Typhoid fever	9
Malaria	171	Typhus fever (murine)	2
Measles	1,066	Whooping cough	233

DEATHS DURING WEEK ENDED MAR. 27, 1948

[From the Weekly Mortality Index, issued by the National Office of Vital Statistics]

	Week ended Mar. 27, 1948	Corresponding week 1947
Data for 92 large cities of the United States:		
Total deaths	9,634	10,795
Median for 3 prior years	9,436	
Total deaths, first 13 weeks of year	132,665	131,043
Deaths under 1 year of age	679	827
Median for 3 prior years	695	
Deaths under 1 year of age, first 13 weeks of year	9,012	10,518
Data from industrial insurance companies:		
Policies in force	71,146,501	67,328,480
Number of death claims	13,380	15,305
Death claims per 1,000 policies in force, annual rate	9.8	11.9
Death claims per 1,000 policies, first 13 weeks of year, annual rate	10.3	10.0

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended March 13, 1948.—During the week ended March 13, 1948, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox		49	1	240	301	61	14	29	118	813
Diphtheria				8	1		2	2		13
Dysentery, bacillary				1					19	20
Encephalitis, infectious						1				1
German measles				27	27	1	1	9	10	75
Influenza		51			18	8			417	494
Measles		1		1,223	1,566	5	4	20	142	2,961
Meningitis, meningococcus				1	2	1				4
Mumps		36	3	359	344	56	49	51	24	922
Poliomyelitis						2				2
Scarlet fever		2	8	54	92	1	2	7	4	170
Tuberculosis (all forms)		7	19	84	41	27	4	52	64	298
Typhoid and paratyphoid fever				10	1				1	12
Undulant fever				1	4			10	2	17
Venereal diseases:										
Gonorrhea	1	13	8	63	70	21	14	43	70	303
Syphilis		12	4	105	40	9	7	13	39	229
Other forms									1	1
Whooping cough				48	26	10	4	52	8	148

JAPAN

Notifiable diseases—4 weeks ended February 28, 1948, and accumulated totals for the year to date.—For the 4 weeks ended February 28, 1948, and for the year to date, certain notifiable diseases were reported in Japan as follows:

Disease	4 weeks ended February 28, 1948		Total reported for the year to date	
	Cases	Deaths	Cases	Deaths
Diphtheria	1,594	182	3,659	418
Dysentery, unspecified	138	33	282	74
Gonorrhea	18,249		35,948	
Influenza	400		869	
Malaria	226	1	493	1
Measles	3,636		7,016	
Meningitis, epidemic	174	41	334	79
Paratyphoid fever	114	9	301	17
Pneumonia	16,818		34,269	
Scarlet fever	171	2	457	4
Smallpox	4	0	6	0
Syphilis	16,071		31,403	
Tuberculosis	23,422		44,772	
Typhoid fever	408	59	961	117
Typhus fever	86	7	182	16
Whooping cough	3,402		7,029	

NOTE.—The above figures have been adjusted to include delayed and corrected reports.

NORWAY

Notifiable diseases—December 1947.—During the month of December 1947, cases of certain notifiable diseases were reported in Norway as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis	14	Measles	51
Diphtheria	78	Mumps	2,908
Dysentery	7	Pneumonia (all forms)	1,999
Encephalitis, epidemic	5	Poliomyelitis	17
Erysipelas	435	Rheumatic fever	114
Gastroenteritis	2,996	Scabies	3,604
Gonorrhea	454	Scarlet fever	336
Hepatitis, epidemic	169	Syphilis	124
Impetigo contagiosa	3,526	Tuberculosis (all forms)	410
Influenza	2,654	Typhoid fever	2
Laryngitis, including bronchitis	10,778	Whooping cough	368
Malaria	2		

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

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-named diseases, except yellow fever, during recent months. 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 of each month.

Cholera

Indochina (French)—Cochinchina—Rachgia.—For the period March 1–10, 1948, 32 cases of cholera with 20 deaths were reported in Rachgia, Cochinchina, French Indochina.

Plague

Belgian Congo—Stanleyville Province.—On March 20, 1948, 1 fatal case of plague was reported in Stanleyville Province, Belgian Congo, northeast of Blukwa. The last cases of plague previously reported from Belgian Congo were 1 case each on January 17 and January 24, 1948, both in Stanleyville Province.

Ecuador—Chimborazo Province—Alausi Canton—Allpachaca Farm.—On February 17, 1948, 1 fatal case of plague was reported from Allpachaca Farm, Alausi Canton, Chimborazo Province, Ecuador.

India.—Plague has been reported in India as follows: For the week ended March 13, 1948, 22 cases with 6 deaths were reported in Lucknow, and information received March 30, 1948, reports 9 cases with 4 deaths in Sewri, a suburb of Bombay.

Smallpox

Ceylon—Colombo.—Information dated March 15, 1948, reports 6 cases of smallpox in Colombo, Ceylon, imported from India. (Last reported case in Ceylon, January 4, 1947).

China—Shanghai.—For the week ended March 20, 1948, 182 cases of smallpox with 43 deaths were reported in Shanghai, China.

Colombia.—For the month of February 1948, 534 cases of smallpox with 7 deaths were reported in Colombia.

Ecuador.—For the month of February 1948, 362 cases of smallpox with 13 deaths, were reported in Ecuador, including 25 cases in Guayaquil, 21 cases in Manta, and 19 cases, 2 deaths in Quito.

India—Calcutta.—Smallpox has been reported in Calcutta, India, as follows: Week ended March 13, 1948, 328 cases; week ended March 20, 1948, 344 cases.

Indochina (French)—Annam State.—For the period March 11–20, 1948, 136 cases of smallpox with 41 deaths were reported in Annam State, French Indochina.

Typhus Fever

Colombia.—For the month of February 1948, 300 cases of typhus fever with 11 deaths were reported in Colombia.

Yellow Fever

Colombia.—For the month of February 1948, yellow fever was reported in Colombia as follows: Antioquia Department—Maceo, 2 fatal cases, Yolombo, 1 fatal case; Boyaca Department, Campohermoso, 1 fatal case; Cundinamarca Department, 3 fatal cases.

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