PUBLIC HEALTH REPORTS

VOL. 48 MAY 26, 1933 NO. 21

PREPARATION OF A SCARLET FEVER STREPTOCOCCUS TOXOID AND ITS USE IN ACTIVE IMMUNIZATION

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A sufficient number of investigators have demonstrated that the toxin produced by the hemolytic streptococcus of scarlet fever origin can be detoxified, at least in part, by the action of formalin and prolonged storage at 37° C., so that this procedure may be accepted as within the realm of possibility. However, there remain to be solved such problems as (*a*) the most practicable method of manufacture; (*b*) laboratory methods of titrating the antigenic value of this detoxified product; (*c*) the range of doses tolerated by susceptible individuals without undue reactions; and (*d*) the immunity response of susceptible individuals as indicated by the percentage who become Dick-negative subsequent to treatment. The study which is reported here was pursued in an effort to solve some of these problems and thereby to place the manufacture and use of scarlet fever toxoid on a practical basis.

PREPARATION OF THE TOXIN

Culture medium.—Because of the uniformly good growth and toxin production obtained with a modification of Douglas tryptic digest broth, this medium has been used exclusively throughout this study. The basic formula for the preparation of the pancreatic extract used in this broth is given by Cole and Onslow (1) and that for the broth by Watson and Wallace (2). Either beef or veal may be used. Instead of using 90 cc of concentrated hydrochloric acid to 7 kilograms of meat as directed, only 45 cc are added. The reaction is so adjusted before sterilization as to give a pH of 7.6 in the completed broth. Blood is not added.

Full-strength broth prepared in this manner contains between 300 and 400 mg of total nitrogen per 100 cc. This represents a food content probably far in excess of the requirements of the hemolytic streptococcus. Flasks containing 25, 50, 75, and 100 percent broth, respectively, were inoculated and incubated for 3 days. The toxin content of the four batches after incubation was the same as indicated by human skin tests. It is highly desirable to keep the protein content near the minimum consistent with maximum toxin production,

because of the possible connection between such foreign protein and reactions in the individual receiving the injection.

In the beginning of this study 75 percent Douglas broth was used, but toward the latter part this was changed to half-strength broth.

Culture.—In selecting a culture of hemolytic streptococcus suitable for toxin production one should make the selection on the basis of certain definite requirements; namely, (*a*) the toxin produced should be of a high titer, (*b*) the resulting toxin should be neutralizable by a known hemolytic streptococcus antitoxin of scarlet fever origin, and (*c*) the toxin when used as an antigen should stimulate the production of an antitoxin which, in turn, will neutralize the greatest possible range of hemolytic streptococcus toxins. If this wide neutralization range in an antitoxin cannot be obtained by the use of a single-strain antigen, the antigen from one or more additional strains should be added. However, probably nothing is accomplished by using a multiple-strain antigen for antitoxin production, provided the re sulting antitoxins, when the antigens are used separately, neutralize within the same range.

The NY-5 strain has been used exclusively. Because of the hemolytic streptococcus strains available, this one more nearly meets the above criteria. The particular culture used has been carried in broth medium with transfers every second or third day and kept continu ously at 37° C. since October 1929 without animal passage. Wheeler (3) states that of 500 strains studied the NY-5 strain proved of exceptionally broad valence and good toxin production. She selected 8 representative strains out of these 500 and observed their antigenic activities. No strain exceeded NY-5, and only one equaled it. Coburn and Pauli (4) report on 10 toxin-producing strains of hemolytic streptococci which had been isolated from patients suffering from rheumatic fever. The toxins derived from 6 of these 10 strains were neutralized by NY-5 antitoxin. Veldee (5) studied commercial antitoxins and found that those which had been prepared from an NY-5 containing antigen possessed greater neutralizing properties. Veldee and Dunnahoo (unpublished data) have observed that NY-5 antitoxin neutralizes toxins derived from hemolytic streptococci from erysipelas sources as readily as do erysipelas antitoxins.

In spite of this apparent superiority of the NY-5 strain over other known strains, the search for a more suitable strain or strains which will fill in where the NY-5 strain fails, should continue. However, when multiple strains are used for toxoid production, the toxins should be separately prepared and detoxified and later combined on the basis of individual antigenic value.

The inoculated broth is held at 37° C. for 72 hours for toxin production. Longer periods are objectionable because of the probability of unnecessarily increasing the amount of dissolved bacterial protein.

Practically all of the streptococcus growth takes place within the first 24 hours of incubation. Flasks A, B, and C of broth were each inoculated with the D-II strain of hemolytic streptococcus and placed at 37° C. After 24, 48, and 72 hours, respectively, the contents of each flask were filtered through a Berkefeld filter and then reinoculated with the same strain of streptococcus. A scarcely visible growth appeared in the 24-hour flask and none in the other two. Similar results were obtained with the NY-5 strain.

Correspondingly, all toxin production takes place within the first 24 hours. Eight hundred cubic centimeters of broth were inoculated with an NY-5 culture and incubated at 37° C. At the end of each successive 24-hour period thereafter 100 cc were removed from the flask and filtered. Subsequent skin tests on susceptible individuals showed no significant differences between the toxin content of the eight 100-cc batches thus obtained.

Concentration of the toxin.—The quantity of antigen in the form of toxoid which is tolerated by a susceptible individual is sufficiently large to make concentration highly desirable, if not essential. In a previous paper (*loc. cit.*) a method of concentrating the toxin was described which employed precipitation with acetone and acetic acid. The method represented a modification of a method described by Wadsworth and Quigley (6). It gave a highly purified toxin as measured by the small amount of total nitrogen in the finished product, but subsequent experience has shown that such a concentrate seems to lack stability and results in a very considerable loss of toxin. Further, such a highly purified product is not essential in the preparation of a toxoid.

Because of these objections, the concentration method used has been simplified to the following: Two volumes of acetone and one volume of toxin are cooled to 0° C. (If facilities are available, it is well to cool the acetone even further.) The toxin is added to the acetone and thoroughly mixed by rotating the flask vigorously for 3 to 5 minutes (violent shaking is not desirable), after which it is allowed to remain in the cold room until the flocculent precipitate has settled to the bottom (approximately one half to 1 hour). The precipitate is collected in a Büchner funnel by means of suction filtration. By placing a thin layer of paper pulp over the filter paper in the funnel the small holes do not become plugged and filtration proceeds rapidly. Suction is continued until all the acetone has been removed from the precipitate, after which the precipitate, paper pulp, and filter paper are placed in a volume of normal saline equivalent to one tenth the volume of the raw toxin used. Gentle stirring, so as to avoid foam, or allowing to stand in the cold room over night will cause the precipitate to redissolve. A second filtration through a Büchner funnel removes the paper pulp and filter paper. To this filtrate is added sufficient

full-strength broth so as to make the final volume one fifth the volume of the raw toxin used in the beginning. The reaction is adjusted to pH 7.4, and as a last step the concentrated toxin is filtered through a Berkefeld candle.

The end results obtained by this method of concentration are shown in table 1, where there is also a comparison with five lots of unconcentrated commercial toxins which were offered for purposes of active immunization by the Dick method. Those concentrates designated by the letters WA were prepared by precipitating both with acetone and acetic acid, whereas the two marked W were prepared by the method described above. The WA toxins have been concentrated 10 times by volume, as against 5 times concentration of the W toxins, yet each batch contains approximately the same total nitrogen and potency. The use of acetic acid removes more of the nitrogen-containing ingredients, but its use also causes a very great loss of toxin. With the use of a half-strength broth for toxin production, and by concentrating five times by volume with the acetone method, as was done with toxins HL-32W and HL-34W, a final product is obtained whose nitrogen content is no greater than unconcentrated toxin made from full-strength broth and whose potency is three and one half to four times that of a good unconcentrated toxin.

Little was known of the chemical nature of the toxin and of its behavior under various conditions, particularly if removed from its original broth environment. It was known that this toxin could be changed to toxoid by the action of formalin without the loss of much of its antigenic value when retained in the original toxin broth, and therefore, it seemed advisable to retain the concentrated toxin in a menstruum which would be very similar to the original broth. This reasoning has been fortified by the subsequent publication by Bunney (7) of his study on the action of formalin on diphtheria toxin in various stages of purification.

Experiments with detoxification of the toxin before concentration are under way. Should this procedure prove practicable, it would eliminate the need for re-solution in broth and thus reduce the total nitrogen content of the concentrated toxoid by one half as compared with the method just described.

PREPARATION OF THE TOXOID

Method of detoxification.—The practice has been to add 0.4 percent formalin to the concentrated toxin and store at 37° C. On the following day the reaction is adjusted to pH 7.2 by the addition of a solution of sodium carbonate. Skin tests for toxicity are made on the ears of susceptible white rabbits at the end of about 60 days. If considerable toxicity still remains, an additional 0.05 percent of formalin

is added and the pH is adjusted as stated above. The toxoid is allowed to remain in the warm room until tests indicate that the residual skin-reacting factor is not greater than 500 skin-test doses per cubic centimeter, which represents a reduction of more than 99.5 percent in the skin-reacting factor of a toxoid considered suitable for immunization purposes. (See tables 1, 2, and 3.) Table 2 indicates that this was accomplished in 56 to 88 days with toxoids Td-11, Td-12, Td-16, Td-20, and Td-21. The skin-reacting factor in Td-21 was reduced from approximately 175,000 STD per cubic centimeter to 500 in 66 days. Leaving it in storage for another 39 days only reduced the skin-reacting factor to 400 STD per cubic centimeter. Toxoid Td-14 still contained a residual of 1,500 STD after 82 days' storage. This lot contained a total of 526.5 mg of nitrogen per 100 cc (table 1), as against 190.4, 270.0, 323.7, and 323.7 and 317.4 mg, respectively, for the above toxoids. The rate of detoxification is influenced by the concentration of formalin and the total nitrogen content of the toxin. There appears to be an irreducible minimum of skin-reacting factor which cannot be detoxified. It is not entirely clear whether this is true toxin or some other substance.

TABLE 1.—*Total nitrogen and the estimated potency of certain concentrated scarlet fever toxins used for the manufacture of toxoid, as compared with the total nitrogen and potency of certain market samples of commercial toxins*

A. NATIONAL INSTITUTE OF HEALTH CONCENTRATED TOXINS

Designation of toxin	Concentration by volume	Total nitrogen expressed as milligrams per 100 cc	Estimated potency expressed as skin-test doses per cc
1930	Unconcentrated	326.0	50,000
HL23WA	2 times	190.4	75,000
HL25WA	10 times	270.0	200,000
HL26WA	10 times	374.3	200,000
HL27WA	10 times	526.5	200,000
HL32W	5 times	322.3	175,000
HL34W	5 times	317.4	175,000

B. COMMERCIAL UNCONCENTRATED TOXINS

Laboratory:			
A	Unconcentrated	347.6	45,000 STD
A	do	370.1	35,000 STD
D	do	394.6	60,000 STD
E	do	249.3	40,000 STD
F	do	446.6	50,000 STD

Heat stability of toxin and toxoid.—The original unconcentrated toxin which has been used in this study contained 45,000 STD per cubic centimeter. Subjecting this toxin to streaming steam in the Arnold

sterilizer (approximately 99° C.) for varying lengths of time caused the following reductions in the titer of the skin-reacting factor:

Period of exposure to streaming steam	Titer of the heated toxin in terms of skin-test doses as compared with the reaction produced by 1 STD of standard control toxin	
	Less than—	At least as much as—
	STD per cc	*STD per cc*
Before heating		45,000
30 minutes	25,000	10,000
60 minutes	10,000	5,000
120 minutes	5,000	2,000
180 minutes	1,000	100
240 minutes	100	10

From these data it would appear that the skin-reacting factor is heat labile within the limits described for this test and that the rate of destruction proceeds in an orderly manner.

A concentrated toxin (toxin HL-32W, which became toxoid Td-16 after detoxification) was similarly heated for 60 minutes. This reduced the skin-reacting factor from 175,000 STD to approximately 25,000 STD per cubic centimeter, which is an 85.7 percent reduction as compared with an approximate 88.9 percent reduction obtained with the unconcentrated toxin in the same length of time. Similar heating of the toxoid Td-16 reduced the residual skin-reacting factor from the equivalent of 500 STD in the unheated toxoid down to 125 STD, a reduction of 75 percent. The residual skin-reacting factor in the toxoid appears somewhat more resistant to prolonged heating than the raw toxin. The much greater concentration of heated toxoid which must be injected for the skin test may be a factor, and the presence of bacterial proteins must also be considered.

The question now naturally arises as to whether the skin-reacting factor at these various stages of heating is neutralizable with antitoxin, and, if so, how much antitoxin is required as compared with the neutralization of standard control toxin. The standard toxin and antitoxin provided by the National Institute of Health are so standardized that, on the average, one STD of toxin will be neutralized by 0.02 unit (one neutralizing skin-test dose) of antitoxin. The ratio is somewhat different when tested by the rabbit ear method. Neutralization tests with standard toxin and antitoxin on 128 suitable rabbits showed that 25 STD of toxin required on an average 0.081 unit (4.05 neutralizing skin-test doses), which means that antitoxin is 6.17 times more effective in neutralizing toxin by the rabbit ear method than in the human skin. Neutralization according to the same ratio takes place with the toxin concentrated by the acetone method.

Tests on rabbits indicate that the skin-reacting factor still present in unconcentrated toxin after heating in streaming steam for 60 minutes may be neutralized by antitoxin, the ratio of toxin to antitoxin being the same as with the unheated product.

The residual skin-reacting factor remaining in the toxoid after detoxification, as well as that residual remaining after heating the toxoid for 60 minutes in streaming steam, can also be neutralized with antitoxin. However, the quantity of antitoxin required was in each instance much greater than that needed for the neutralization of the skin-reacting factor present in the original untreated toxin. The greater concentration of reagents required for the neutralization tests with the residual in the toxoid may be a factor.

Attempts were made to demonstrate the combining power of the toxoid with antitoxin, but all tests ended in failure.

Antigenic tests on white rabbits.—A laboratory method for measuring the antigenic value of the toxoid has been developed which promises to be helpful. In an earlier paper (*loc. cit.*) the writer reported that most adult, white rabbits, as purchased in the open market by the National Institute of Health, when injected with one human skin-test dose of toxin intradermally on the under surface of the pinna of the ear develop an area of inflammation (visible only by transmitted light) very similar in size to the erythematous area produced by a similar intradermal dose in susceptible persons. That this reaction is a toxic one is evident, since it can be prevented by adding antitoxin to the toxin before injecting. Likewise it should be possible to prevent this reaction by stimulating immune body production in the rabbit through the injection of sufficient antigen. Eighteen rabbits, susceptible to one skin-test dose of raw toxin, received from 15,000 to 25,000 skin-test doses of raw toxin subcutaneously, a weighted mean of 20,000 STD per animal. At the end of 2 weeks 13 of these animals gave no reaction to 5 skin-test doses of test toxin when injected intradermally in the ear. As a control, 10 susceptible rabbits each received subcutaneous injections of 0.2 cc of plain broth. When retested 2 weeks later all 10 rabbits gave strong reactions to 5 skin-test doses of test toxin. Twenty-one susceptible rabbits were given subcutaneous injections of 0.2 to 0.3 cc of toxoid, Td-16, a weighted mean of 0.25 cc per animal, and when retested 2 weeks later 16 gave no ear reaction to 5 skin-test doses of test toxin. In each one of these tests the rabbits were also tested with a heated control (1 hour in streaming steam) of the same quantity as the test dose. A few animals reacted to the heated control, and these were considered negative when the reaction approximated in character that produced by the test toxin, an indication of pseudo-reaction. On the basis of these results, toxoid Td-16 would have the antigenic equivalent of at least 80,000 STD of raw toxin per cubic centimeter.

The raw concentrated toxin, table 1, toxin HL-32W, contains 175,000 STD of toxin per cubic centimeter, which would indicate that the process of detoxification destroys some of the antigenic value.

The point has been raised by Okell (8) and others that any antigenic stimulation obtained from scarlet fever toxoid is probably provided by the residual skin-reacting factor in the toxoid. Should this reasoning be correct, then the degree of immunity obtained by the injection of a given volume of the toxoid should be no greater than that produced by the injection of a sufficient number of skin-test doses of raw toxin to correspond to the skin-test doses of residual skin-reacting factor in the toxoid. A total of 1.6 cc of toxoid Td-16 has been used for human immunization. With a residual of 500 STD per cubic centimeter in this toxoid, the 1.6 cc would then represent the equivalent of 800 STD of raw toxin. Nine susceptible rabbits were each injected subcutaneously with 1.6 cc of toxoid Td-16, and a similar number each received 800 STD of raw toxin. Two weeks later all were retested with 1, 2½, and 5 skin-test doses, respectively, of test toxin and a heated control. Of the 9 toxin-treated rabbits, 4 showed immunity to 1 STD of control toxin and none to 2.5 STD, whereas the 9 toxoid-treated rabbits all showed immunity to 2.5 STD and 5 were negative to 5 STD.

ACTIVE IMMUNIZATION WITH SCARLET FEVER TOXOID

Approximately 1,700 persons having positive skin reactions to one human skin-test dose of toxin have been treated with the detoxified toxin, prepared in the manner already described.

Throughout this study a skin reaction was considered positive if one skin-test dose of standard toxin, when injected intradermally on the upper ventral surface of the forearm, produced within 24 hours a reaction measuring 10 mm in its greatest diameter irrespective of the intensity of the reaction.

In order to meet the requirements of practicability, and to meet the approval of physicians and parents, it was felt that the number of injections required should not exceed three, and that the children treated should experience no incapacitating sequelae. (It scarcely need be added that disease-preventive measures of this character are designed for the period of childhood and not for the adult.) At the same time, the object was to give each child no less antigen than is contained in the five immunizing doses of raw toxin as recommended by the Scarlet Fever Committee.

In the beginning of this study antigenic value of the toxoid was calculated volume for volume the equivalent of raw toxin, though it was considered highly probable that some of the antigen would be destroyed by the detoxification process. However, with the development of a rabbit method of measuring antigenic value, it becomes possible to

estimate the antigenic value of each batch of toxoid with at least a fair degree of accuracy.

A wide range of individual doses representing varying quantities of toxoid were tried during the course of this study in order to ascertain the maximum total volume of antigen tolerated as well as the minimum number of injections required. Sufficient toxoid to produce immunity in a high percentage of susceptible individuals could be given in two doses with an interval of 1 month between doses, as is demonstrated by groups A_3, C_1, C_{1A}, C_2, C_{2A}, C_3, E_2, E_3, and E_4. (See table 4.) However, doses of the volume required did produce constitutional symptoms in a certain number of individuals. By distributing the necessary volume of toxoid into three doses it was possible to eliminate constitutional symptoms entirely in children and reduce them to only a rare occurrence in adults. The 3-dose method with 3-week intervals was used with the other groups reported in table 4. The graduation of doses was not correct in each group, and so a few individuals in some of the groups did develop constitutional symptoms, namely, fever, headache, and, in a rare instance, nausea without vomiting. From this experience it was possible to determine the tolerance range; and subsequent clinical experience has shown that three doses of 0.1, 0.5, and 1.0 cc of toxoid, respectively, diluted if necessary to suitable volumes for injection, are tolerated without significant reaction, provided the toxoid meets certain requirements. These minimum requirements are those of toxoid Td-16 (table 2), which had been prepared from concentrated toxin HL-32W (table 1).

TABLE 2.—*Reduction in toxicity of scarlet fever toxin through the action of formalin and storage at 37° C., as measured by the skin-reacting factor*

Designation of toxin	Estimated potency of the raw toxin per cc	Designation of the resulting toxoid	Period of storage at 37° C.	Quantity of formalin used	Estimated residual skin-reacting factor per cc after detoxification
	STD		*Days*	*Percent*	*STD*
1930	50,000	Td- 1	56	0.4	1,000
HL23WA	75,000	Td-11	56	.3	500
HL25WA	200,000	Td-12	69	.4	500
HL26WA	200,000	Td-13	48	.4	1,000
HL27WA	200,000	Td-14	82	.45	1,500
HL32W	175,000	Td-16	64	.45	500
HL32W	175,000	Td-20	88	.45	500
HL34W	175,000	Td-21	66	.45	500

A detailed analysis of the individual doses of an average commercial toxin, offered for active immunization purposes, as compared with the three doses of toxoid, Td-16, is shown in table 3.

Reactions following injections.—The majority of children and all adults developed an area of erythema at the site of injection. This area varied from a few millimeters in diameter up to an area extending

over half the skin area from shoulder to elbow on the injected side of the arm. The intensity usually reached its maximum in 36 to 48 hours. The color was a dull, deep red, as contrasted with the bright scarlet erythema occurring with scarlet fever itself. Induration occurred in a limited number of cases and when present was restricted to a smaller area than the erythema. All cases showing induration showed tenderness on palpation and those with more extensive induration had some localized pain.

Constitutional symptoms were essentially absent in all younger children and occurred rarely in older children. Of 23 children, age 4 to 17 years, held under careful observation, a temperature of 37.5° C. was exceeded 11 times for the 3 injections, the maximum observed temperature being 38.3° C. In a group of 70 children, including the above 23, slight headaches were reported by 5 older children. No other systemic symptoms appeared. A third group of 219 children, 14 years of age or under, showed some local reaction in nearly each instance, with mild systemic symptoms reported in 4 of the older children. A fifth child, a boy of 10 years, became ill with dizziness, leg weakness, and nausea within 2 hours of each of the first 2 injections. He felt entirely well again in a few hours and nothing further developed. The cause of this reaction is not clear, though it does not suggest a toxin reaction.

TABLE 3.—*Comparison of the 5 immunizing doses of raw scarlet fever streptococcus toxin as recommended by the Scarlet Fever Committee and the 3 doses of scarlet fever streptococcus toxoid suggested by the present study*

Raw scarlet fever toxin			Scarlet fever toxoid Td-16				
Dose	Skin-test doses of toxin given per dose	Total mg of nitrogen given in each dose [1]	Dose	Skin-test doses of toxin in each dose before detoxification	Estimated antigenic value of each dose after detoxification	Residual skin reacting factor present in each dose in terms of skin-test doses	Total mg of nitrogen given in each dose
			cc				
1	500	3.9	0.1	17,500	8,000	50	32.2
2	2,000	15.7					
3	8,000	62.8	.5	87,500	40,000	250	161.1
4	25,000	196.2					
5	80,000	628.0	1.0	175,000	80,000	500	322.3
Total	115,500	906.6	1.6	280,000	128,000	800	515.6

[1] These figures represent the mean of the 5 commercial toxins reported in table 1, weighted by the potency of each. Total nitrogen in all instances is reported as milligrams per 100 cc of toxin or toxoid.

Twenty-four pupil nurses all developed local reactions of the character already described, though somewhat more pronounced than with the children. No nurse showed a temperature above 37.7° C., and five nurses developed mild headaches. A group of 36 adults, 44 years or under, showed more pronounced local reactions, and 10

developed systemic symptoms with 2 confined to bed with chills. There was no vomiting, and none developed a rash.

With systemic symptoms essentially absent in the young and occurring only occasionally in the adult, and with the symptoms, when present, limited to fever, headache, and chills, it was believed probable that they constituted reactions to something other than the toxin itself.

Pseudo-reactions.—At the time of the original skin test, 74 persons of various ages received on the opposite arm an injection of one STD of control toxin which had previously been heated for 1 hour in streaming steam (approximately 99° C.). Likewise, 653 persons who were originally skin positive were tested with a heated control at the time of the retest after immunization. The results in the two groups were as follows:

	Group I		Group II	
	Number	Percent	Number	Percent
Total persons tested	74		653	
Negative to toxin and the heated control	55	74.3	467	71.5
Positive to toxin and negative to heated control	18	24.3	145	22.2
Positive to toxin and positive to heated control	1	1.4	41	6.3

In an earlier portion of this paper it was shown that a temperature of 99° C. for 1 hour destroyed only 88.9 percent of the skin-reacting factor, whereas the same degree of heat for 4 hours destroyed at least 99.78 percent. Therefore, the frequency of pseudo-reactions in the above tabulation may be too high, owing to a small amount of active skin-reacting factor remaining in the heated control. It is evident that with this particular control toxin, the test of pseudo-reactions should be made with the same toxin after exposing it to streaming steam for 4 hours. However, if a test toxin of high titer is used (the National Institute of Health standard toxin contains 45,000 STD per cubic centimeter) pseudo-reactions become of such infrequent occurrence that for routine purposes the test may be omitted. Even in the presence of a pseudo-reaction the symptoms developing in the treated individual are sufficiently mild and transitory not to be significant.

First retest after immunization.—An attempt was made to retest each treated person 1 month after the injection of the last immunizing dose. Of 1,700 persons so treated, 1,168 were available for this retest, and of these 972 (or 83.2 percent) were Dick negative. Table 4 is presented to show the age range of the various groups treated, the lot number of the toxoid used, and the results of the retest in the various groups.

TABLE 4.—*Number of Dick positive persons given injections of scarlet fever toxoid and the character of the skin reaction upon retest with 1 human skin-test dose of toxin, 1 month after the last immunizing dose*

Designation of group	Age range in years (both inclusive)	Lot number of toxoid used	Retest 1 month after last immunizing dose		
			Number retested	Number negative	Percent negative
A_1	6–13	Td- 1	21	20	95.2
A_2	3–14	Td-11	22	19	86.3
A_3	4–14	Td-12	22	21	95.5
B_1	18–22	Td- 1	17	12	70.6
B_2	18–22	Td- 1	10	9	90.0
B_3	18–22	Td-13	13	10	77.0
B_4	18–22	Td-13	10	9	90.0
B_5	15–18	Td-11	9	8	89.0
C_1	5–16	Td-12	47	36	76.6
C_{1A}	17–53	Td-12	52	41	80.8
C_2	2–16	Td-12	145	109	75.1
C_{2A}	17–46	Td-12	133	106	79.6
C_3	6–17	Td-12	24	16	66.5
D_1	2–16	Td-12	147	124	84.4
D_2	1–16	Td-16	85	71	83.5
E_1	2–19	Td-12	116	94	81.0
E_2	5–16	Td-13	10	10	100.0
E_3	17–55	Td-13	91	87	95.6
E_4	18–52	Td-13	70	63	90.0
F_1	2–21	Td-11	31	27	87.1
G	5–15	Td- 1	93	80	86.0
Total	2–55		1,168	972	83.2

The Dick positive inmates of three institutions, not included in table 4, which care for tuberculous children, were treated with three doses of toxoid Td-16. On retest the skin reactions were as follows:

Institution	Elapsed time since last injection	Number present for retest	Percent negative on retest
	Weeks		
C_4	4	73	80.9
C_5	4	89	82.0
C_6	10	97	51.5

Institutions C_4 and C_5 were again retested approximately 10 weeks after the last injection so as to give information comparable to institution C_6 when the percent negative was 70.1 and 59.6, respectively. The results are considerably lower than the retests reported for well children in table 5. The children in these institutions were in various stages of tuberculous infection, and, in addition, institution C_6 went through epidemics of mumps and "grippe" during the immunization period. It is not known what influence such intercurrent diseases may have had on the production of scarlet-fever immunity. It may also be that the secondary infections invariably present in pulmonary tuberculosis have caused an excessively high percentage of pseudo-reactions. Unfortunately, no heated control test was made.

TABLE 5.—*Durability of the skin-negative phase following the injection of scarlet fever toxoid, insofar as this study has progressed. This table contains data on all persons included in table 4 who were present for the second retests except groups C_1, C_{1A}, C_2, and C_{2A}, which are separately reported*

Designation of group	Number immunized and Dick tested on 2 occasions	First retest			Second retest		
		Elapsed time before first retest	Persons negative		Elapsed time before second retest	Persons negative	
			Number	Percent		Number	Percent
					Months		
A_1	14	1 month	13	92.8	29	14	100.0
A_2	19	do	16	84.2	13	17	89.5
A_3	16	do	15	93.7	12	15	93.7
B_1	11	do	9	81.8	22	9	81.8
B_2	5	do	5	100.0	18	5	100.0
B_3	13	do	11	84.6	10	10	76.9
B_4	9	do	8	89.0	7	8	89.0
C_3	15	do	8	53.4	9	12	80.0
D_1	111	do	96	86.5	10	85	76.6
E_1	114	do	96	84.1	7	102	89.5
E_2	9	do	9	100.0	4	8	89.0
E_3	82	do	79	96.4	4	75	91.5
E_4	53	do	46	86.8	4	47	88.7
F_1	23	do	19	82.6	9	22	95.6
Total	494		430	87.3	8	429	87.0

Influence of age on immunity production.—Of the 1,168 persons reported in table 4, it was possible to study the relations between the age of the individual treated and immunity production in 848. As the following tabulation indicates, age does not appear to be a factor:

Age	Number retested	Percent negative	Age	Number retested	Percent negative
1	2	-------	10	61	86.9
2	14	78.6	11	57	82.5
3	29	72.4	12	55	83.7
4	37	78.4	13	38	79.0
5	38	79.0	14	45	80.0
6	36	86.1	15	25	76.0
7	47	74.4	16	28	92.9
8	86	84.9	16 and over	198	78.2
9	52	88.5	Total	848	81.3

Second retest after immunization.—A second retest on as many of those persons reported in table 4 as were available was made shortly before preparing this manuscript, at which time 773 persons were present who had also received the first retest. Of this number, 494 (table 5) had received no subsequent treatment, and of these, 429 (or 87.0 percent) were negative on the second retest, as compared with 430 (or 87.3 percent) negative on the first retest. The mean weighted elapsed time in this group was 8 months. The remaining 321 persons who were present on the second retest, groups C_1, C_{1A}, C_2, and C_{2A}, respectively, were treated somewhat differently in that those

who were positive on the first retest were given additional injections of toxoid. Their second retests gave the following results:

Of 118 persons 16 years of age or less who had received two immunizing doses, all were negative on the first retest and 105, or 89 percent, were negative on a second retest 9½ months later.

Of 128 persons over 16 years of age who had received two immunizing doses, all were negative on the first retest, and 111, or 85.9 percent, were negative on a second retest 9½ months later.

Of 75 persons of various ages who had received two immunizing doses, all were positive on the first retest. An additional dose was given to 55 of these, and after a lapse of 8½ months 35, or 63.6 percent, had become negative. Three additional doses were given to the remaining 20, and after a lapse of 6 months, 17, or 85 percent, had become negative.

An analysis of the record on each person reported in table 5 shows that there were few changes in the individual skin reactions from one test to the other. Thus, of the 494 persons tested on the two occasions,

385, or 78.0 percent were negative on both tests;
45, or 9.1 percent, were negative on the first test and positive on the second;
20, or 4.0 percent, were positive on the first test and positive on the second;
44, or 8.9 percent, were positive on the first test and negative on the second.

If the size and intensity of the skin reaction can be taken as a criterion, those persons whose skin reactions were still positive at the time of the second retest seem to have built up some immunity. The mean original reaction of 93 such individuals measured 21.3 by 27.7 mm, as compared with a mean measurement of 12.3 by 15.9 mm for the same persons on the second retest when tested with some of the same lot of control toxin. The reactions had been reduced in size in all instances save three, and with these the mean had increased from 8 by 12 mm to 14 by 17 mm. The intensity of the retest reactions was either diminished or the same in each of the 93 persons.

How does the percentage of susceptibles who are rendered Dick negative following the injection of toxoid compare with the results obtained with the injection of raw toxin? Since the attempt was made to approximate in the toxoid dose the same amount of antigen as is contained in the dose of raw toxin recommended by the Scarlet Fever Committee, it is to be expected that the percentage of immunes resulting from the two treatments would be about the same. The results following treatment with toxoid have been presented in tables 4 and 5. There is presented in table 6 results reported by different workers with raw toxin immunization. Of the groups reported in table 6, only the first three received five injections containing the

quantities of toxin which are now recommended by the Scarlet Fever Committee, namely, 500, 2,000, 8,000, 25,000, and 80,000 skin-test doses, respectively, with weekly intervals. Literature contains very few reports of this character which are in sufficient detail for comparative purposes.

TABLE 6.—*Influence of injections of raw scarlet fever streptococcus toxin on the skin reactions of persons known to be susceptible. Both the original skin tests and the retests were made with one skin-test dose of toxin*

Reported by—	Number of persons retested	Total dose of raw toxin given	Interval between last dose and retest	Percent negative to 1 STD of toxin
Anderson [1] [6]	60	115, 500	1 year	83
Rhoads [2] [6]	298	115, 500	2 weeks	81
Smythe and Nesbit [3] [6]	197	115, 500	do	85
Smythe and Nesbit [3]	3, 255	85, 500	do	66
Dyer [1]	34	62, 000	3½ years	91
Dyer [1] [6]	122	42, 000	13 days	96
Do	107	42, 000	10 months	64
Kiefer [4]	114	35, 500	1–2 years	61
Do	41	34, 000	2 years	66
Kiefer [4] [7]	577	5, 000+	3 years	77
Kiefer [4]	799	5, 000	21 days	30

[1] Unpublished data.
[2] J.A.M.A., v. 97:153–156 (July 18, 1931).
[3] J.Prevent.Med., v. 2:243–250 (May 1928).
[4] J.A.M.A., v. 91:1885–88 (Dec. 15, 1928).
[6] The total dose injected in these groups represents the amount of toxin now recommended by the Scarlet Fever Committee.
[6] The same group tested on 2 different occasions.
[7] All these persons received 5,000 STD plus such additional quantities, in 5,000 STD doses, as were needed to render the skin reaction negative within a few weeks (the exact amount is not stated).

Prevention of scarlet fever.—The purpose of the clinical phase of this study has been to observe the tolerance of the toxoid injections and the subsequent effect on the skin reaction. However, in a very limited way there has been an opportunity to observe its protective value in human subjects. Scarlet fever had appeared each season in two of the institutions used. Following the treatment of those Dick positive, one institution has remained free from scarlet fever while the other has had no cases among those immunized, only in more recent admissions of unknown susceptibility. Two other institutions have had cases appear among untreated persons who were known to be skin positive but not in those immunized. A fifth institution experienced an outbreak of scarlet fever among recent admissions who had been neither tested nor treated. To date no cases have developed in the treated population or in persons known to be Dick negative. These experiences are too limited and indefinite to provide evidence for conclusive deductions but are suggestive. There is need for an immunization test on a community-wide basis with the retention of a satisfactory control group of known positive children living under identical conditions and of the same age range.

SUMMARY

A method has been presented for the concentration of the toxin which is elaborated by the hemolytic streptococcus of scarlet fever origin by which the toxin content is increased approximately fourfold without causing an increase in the total nitrogen content of the preparation above that now present in commercial unconcentrated toxins. This concentrated toxin may be detoxified by the action of formalin and storage at 37° C. in approximately 60 days so that there remains less than one half of 1 percent of the skin-reacting factor. This residual appears to be irreducible through continued storage. Its character is not fully understood, though it appears to be neutralizable by antitoxin.

Single injections into susceptible white rabbits indicate that this detoxified product possesses antigenic properties, though the detoxification process apparently does destroy a portion of the antigen.

Tests on susceptible persons indicate that toxoid, possessing the characteristics of toxoid Td-16 which is described in the text, may be given in a 3-dose method to children under 15 years of age without subsequent reactions except local erythema in a majority of children, accompanied by induration in a few and tenderness in a still smaller number and mild systemic symptoms (slight fever, headache) in only an occasional individual. Of the 1,168 persons retested with one STD of control toxin 1 month after the last injection, 972, or 83.2 percent, were Dick negative. Of 494 persons retested again, an average of 8 months after the last dose, 87.0 percent were negative as compared with 87.3 percent on the first retest.

In conclusion it should be emphasized that the results reported in this study were obtained through the use of a single strain of hemolytic streptococcus which had been cultured in the manner described. It is not known whether similar results could have been obtained through the use of other strains and other methods.

ACKNOWLEDGMENTS

The clinical observations reported in this study have been made possible through the kind cooperation of the following:

Dr. Gilbert Daniel, clinician, Beards Fork, W.Va.

Dr. R. F. Feemster, assistant director, division of communicable disease, Massachusetts State Department of Health.

Dr. A. E. Keller, assistant professor of preventive medicine, Vanderbilt University.

Dr. R. A. Lyon, instructor in pediatrics, University of Cincinnati, College of Medicine.

Dr. A. L. McKay, provincial epidemiologist, Department of Health of Ontario.

Dr. Martin D. Ott, pediatrician, Davenport, Iowa.

Dr. John Overton, city health officer, Nashville, Tenn.

Dr. E. L. Stebbins, Virginia State Department of Health.

The nitrogen determinations were made by Senior Chemist Elvove and Assistant Chemist Remsberg, of the National Institute of Health.

The writer takes pleasure in expressing his indebtedness to these associates as well as to others whose names are not here recorded.

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(6) Wadsworth, A., and Quigley, J. J.: (1931) Studies on bacterial toxins. Concentration and purification of the toxin of streptococcus hemolyticus with acetone. J. Immunol., vol. 20, pp. 459–462 (June).

(7) Bunney, W. E.: (1931) The action of formaldehyde on diphtheria toxin. J. Immunol., vol. 20, pp. 47–59 (January).

(8) Okell, C. C.: (1932) Properties of erythrogenic (rash producing) toxin of the streptococci. The Lancet, vol. 222, pp. 815–820 (April).

OBSERVATIONS ON HEART DISEASE IN MARINE HOSPITAL PRACTICE

A Study of Organic Heart Disease in the United States Marine Hospital, Stapleton, N.Y., During the Fiscal Year 1931

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Ninety-one of the 3,517 admissions to the United States Marine Hospital at Stapleton, N.Y., from July 1, 1930, to June 30, 1931, were diagnosed as having evidence of organic heart involvement or angina pectoris. This represented about 2.6 per cent of the admissions for this period. These 91 admissions included a total of 79 individual cases. Among these there were 20 deaths, 15 of which were due to cardiac causes.

These patients, with few exceptions, were examined by the writer, either in his capacity as ward surgeon or in conjunction with electrocardiographic examinations. As far as practicable, statistical data are computed on the basis of individual cases, rather than admissions,

although in considering the clinical conditions at the time of admission, the latter is necessarily adopted.

The official nomenclature of the Public Health Service classifies heart disease from the viewpoint of the clinical interpretation of pathological findings and of certain changes of function, notably the arrhythmias. This omits two important factors in the evaluation of heart disease; namely, etiology and the determination of functional capacity. An endeavor has been made to supply these. The findings here are modeled on the bases of the etiological classifications offered by White,[1] Cabot,[2] the American Heart Association,[3] and others, but none of these systems of etiologic classification has been adopted entirely.

Table 1 takes into consideration the reasons for the admissions of these patients.

TABLE 1.—*Clinical distribution of 91 admissions to the United States Marine Hospital, Stapleton, N.Y., in which heart disease was diagnosed, during the fiscal year 1931*

Basis for admission	Etiologic classification					
	Syphilitic	Rheumatic	Degenerative	Other	Undetermined	Total
Cardiac	12	17	23	5	6	63
Medical	2	8	8	0	2	20
Surgical	2	0	1	1	1	5
Genito-urinary	0	1	0	0	1	2
Syphilis	1	0	0	0	0	1
Total	17	26	32	6	10	91

From Table 1 it will be seen that in approximately two-thirds of the instances in which heart disease was diagnosed it was the basis for the admission. In many other instances cardiac pathology played an important rôle. For example, a patient admitted for cerebral hemorrhage may at the same time show marked evidence of congestive heart failure.

A consideration is next given to the etiology of the various diagnoses made during the year. The diagnoses were all made on ante-mortem findings, and on the bases of the official nomenclature. Some were made by the writer, others, by various members of the staff. In a few instances where obvious omissions were made diagnoses were supplied, but in general the diagnoses in Table 2 represent those made during the course of the year.

[1] Heart Disease. By Paul D. White. Macmillan Co. 1931.

[2] Facts on the Heart. By Richard C. Cabot. W. B. Saunders Co. 1926.

[3] Criteria for the Classification and Diagnosis of Heart Disease. New York Health and Tuberculosis Association. 1929.

TABLE 2.—*The etiology of various diagnoses made at the United States Marine Hospital, Stapleton, N.Y., during the year 1931*

Diagnosis	Etiology					
	Syphilitic	Rheumatic	Degenerative	Other	Undetermined	Total
Angina pectoris	0	0	2	0	0	2
Aneurysm, aortic	4	0	0	0	0	4
Aortitis	5	0	0	0	0	5
Hypertrophy and dilatation	0	0	2	0	0	2
Chronic cardiac dilatation	0	1	0	0	0	1
Myocardial and cardiac insufficiency	0	1	11	1	0	13
Endocarditis, septic	0	0	0	3	0	3
Myocarditis, chronic	0	3	14	1	5	23
Pericarditis, adhesive	0	0	0	0	1	1
Auricular fibrillation	0	7	3	2	1	13
Valvular diseases:						
Aortic insufficiency	10	1	0	0	0	11
Aortic stenosis	0	0	1	0	0	1
Mitral insufficiency	0	8	0	0	2	10
Mitral stenosis	0	14	0	0	0	14
Combined lesions, aortic and mitral	0	5	0	0	1	6
Total	19	40	33	7	10	109

Among the noteworthy features of Table 2 is the infrequency of the occurrence of the anginal syndrome. This condition was diagnosed in two patients during the year. In one instance it was secondary, the main condition being referable to the cerebrovascular system. The other case was characterized by an almost textbook picture of coronary thrombosis. There was prolonged substernal pain radiating down the left upper extremity and to the abdomen, not notably relieved by nitrites. This was followed by fever, leucocytosis, congestive heart failure, and a coronary T-wave on electrocardiographic examination. It would appear, based on experiences at this hospital and at the United States Marine Hospital at New Orleans, that both the anginal syndrome and coronary occlusion are rather infrequent among beneficiaries of the Public Health Service.

Aneurysm of the aortic arch was observed in four patients during life. An additional diagnosis was made on the basis of findings at necropsy. There were no deaths from aneurysm. In no instance was there severe dysphagia, aphonia, or erosion of bony structures.

Aortitis was diagnosed five times. In only two instances was it diagnosed without evidence of other manifestations of luetic heart disease, such as aneurysm or aortic insufficiency. This illustrates the need for definite criteria as guides in making diagnoses. One clinician will make an observation of the presence of aortitis in a given case while another will not. To what extent clinicians are called upon to go into the minutiæ of pathological diagnoses is a debatable point. Certainly from the viewpoint of clinical research it would be advisable to have definite standards to which diagnoses should conform.

Probably a number of simple cases of luetic aortitis are missed. This condition is easily diagnosed if borne in mind. The cardinal

points are a history of increasing dyspnea on exertion, indefinite anginoid pains, nocturnal dyspnea or cardiac asthma, and physical findings of a widened supracardiac area on percussion, a bell-like aortic second sound usually in the presence of a relatively low blood pressure, frequently an aortic systolic murmur, and characteristic X-ray changes. The serology is generally positive, but the condition should not be ruled out on the basis of a negative blood Wassermann reaction.

Diagnose of cardiac hypertrophy, hypertrophy and dilatation, cardiac dilatation, myocarditis, and cardiac or myocardial insufficiency were used interchangeably to express the findings in congestive heart failure and cardiac enlargement. Using the present nomenclature system, insufficiency of the myocardium would seem preferable in describing physiological changes brought about by the failing myocardium. When it is desirable to describe the anatomical changes in the heart muscle incident to either valvular or nonvalvular heart disease, the terms hypertrophy, hypertrophy and dilatation, dilatation, or fibrosis of the myocardium would appear preferable to that of myocarditis. Myocarditis describes pathological conditions which can usually be described only at the necropsy table. Its use should be restricted to the description of inflammatory changes in the heart muscle. With the exceptions of a few conditions such as the active state of rheumatic heart disease [4], acute diptheritic myocarditis [5], or syphilitic myocarditis as described by Warthin [6], it is not easy to see how this diagnosis can be made ante mortem. Even then, there is still considerable doubt in the minds of many regarding the syphilitic myocarditis described by Warthin. Certainly, it is unfortunate that myocarditis has been used to describe the fibrotic insults due to the involution of advancing years or to the outcome of diseases of the coronary arteries. Fibrosis of the myocardium is a more accurate description.

There is a tendency among clinicians to use certain medical terms quite loosely. "Myocarditis" serves as an example of this inexactness in current medical terminology. Myocarditis has been used as synonymous with congestive heart failure, precordial or substernal distress, almost any type of shortness of breath, senility, as descriptive of nonvalvular heart diseases, and general circulatory weaknesses occasioned by systemic conditions, such as pernicious anæmia, cancer, tuberculosis, the terminal events in acute infectious processes, or the effects of surgical operations and trauma. Similarily, in the past more than at present, "mitral insufficiency" has been ascribed to

[4] Aschoff, L.: Zur Myocarditisfrage. Verhandl. d. deutch. path. Gesellschaft, 1904. vol. VIII, p. 46.
[5] Warthin, A. S.: Myocardial lesions of diphtheria. Jour. Inf. Dis., 1924, vol. XXXV, p. 32.
[6] Warthin, A. S.: Sudden death as an exacerbation of latent syphilitic myocarditis. Am. Heart Jour., 1925, vol. I, p. 1.

practically any type of heart, showing evidence of disease or otherwise, which on auscultation gives evidence of a systolic apical murmur.

The heart committee of the New York Tuberculosis and Health Association has made a commendable effort to rectify this state of affairs by adopting a system of diagnosis and describing the criteria for the diagnostic terms in a booklet entitled "Criteria for the Classification and Diagnosis of Heart Disease." Diagnoses made in the clinics affiliated with the association conform to the definitions set forth in the manual. This is of inestimable value for statistical purposes.

The diagnostic classification of the New York Tuberculosis and Health Association, also adopted by the American Heart Association, considers each case as far as possible from the viewpoints of etiology, anatomical changes, physiological alterations, and functional capacity. This scheme may be too complicated to become that of general usage among practitioners of medicine, but from the viewpoint of clinical research it has much to offer. For example, a case of mitral stenosis showing evidence of rheumatic activity, auricular fibrillation, and congestive heart failure sufficient to cause the patient to be bedridden would fall under the classification of (*A*) etiological, rheumatism (active); (*B*) anatomical changes, mitral stenosis; (*C*) physiological alterations, auricular fibrillation, congestive heart failure; (*D*) functional capacity, Class III, unable to carry on any activities. A case of syphilitic heart disease with a widened aorta, aortic insufficiency, cardiac enlargement, certain electrocardiographic findings, such as left ventricular preponderance and ventricular premature beats (extra systoles), and slight dyspnea on exertion would be considered as (*A*) syphilis (active or inactive); (*B*) aortitis, with dilatation of the aorta, aortic insufficiency, cardiac enlargement, left ventricular preponderance; (*C*) ventricular premature contractions; (*D*) Class IIa, activities slightly limited. A case of arteriosclerotic heart disease with hypertension and anginal syndrome resulting in considerable limitation of activities would be diagnosed (*A*) arteriosclerosis; (*B*) enlargement of the heart, fibrosis of the myocardium, sclerosis of the coronary arteries; (*C*) anginal syndrome; (*D*) Class IIb, activities greatly limited. In addition, patients who show abnormal signs or symptoms referable to the heart, such as murmurs of doubtful significance or precordial distress of undetermined etiology, are considered as "Possible heart disease, Class E." Patients without heart disease, who should be followed because of the presence or history of an etiological factor, such as rheumatism, syphilis, or hypertension, are diagnosed as "Potential heart disease, Class E." When it is considered that each factor in the diagnosis is made according to definition, it can be readily seen that it is possible to obtain a quite accurate conception of the clinical picture.

An elaboration of grouping of patients according to functional capacity will be made later in this paper.

Endocarditis was diagnosed three times during the year. In each instance nonhemolytic streptococci (*S. viridans*) were found in the blood stream. All of these patients died, one of embolic phenomenon, one of pneumonia, and the third of sepsis.

Of the valvular heart diseases, mitral stenosis was diagnosed most frequently. It is gratifying to note the infrequency with which the diagnoses of mitral insufficiency are being made. The day of labeling each individual with a systolic apical murmur as having an organic heart lesion is rapidly passing. It is not to be inferred that mitral insufficiency as a clinical entity does not exist. It is as much a part of the picture of rheumatic heart disease as mitral stenosis, and according to Coombs [7] may even precede it. Aortic insufficiency was diagnosed in 11 instances, 10 of which were considered to be of luetic origin. Aortic stenosis was diagnosed once. It was considered as being due to the type of calcareous heart disease described by Margolis et al.,[8] Christian,[9] and others. Combined aortic and mitral lesions were described five times, each instance being considered of rheumatic origin.

Auricular fibrillation was described 13 times as a diagnosis and 3 times as a physical finding. However, this condition should not be given as a principal diagnosis until every effort to find the lesion responsible for this physiological alteration has been exhausted.

From the viewpoint of etiology there were 15 cases of syphilitic heart disease, involving a total of 17 admissions. The average age was 44.3 years. Two cases of aortic aneurysm were under 30 years of age. Four patients having syphilitic heart disease died, three from heart disease. Among these 15 cases, positive blood Wassermann reactions were the bases for the luetic classification in 7 instances, positive spinal fluid reactions in 2 instances, histories of previous treatments in 2, and histories of penile ulcers in 3 instances. In one instance the diagnosis was based entirely on the type of cardiac findings, despite negative history and serology.

Rheumatic heart disease occurred in 21 cases, being found in 26 admissions. The average age of these patients was 34.7 years. There were four deaths, three of which were from cardiac causes. Histories of rheumatism were elicited in 14 of the 21 cases, 2 of which had scarlet fever, in addition to rheumatism and 2 had histories of tonsilitis. Of the 7 other cases, 1 case gave a history of chorea, 2 cases of tonsilitis, 1 case of scarlet fever, and 1 of repeated sore

[7] Rheumatic Heart Disease. By C. F. Coombs. John Wright and Sons (Ltd.). 1924.

[8] Margolis, H. M., Zielliesen, F. O., and Barnes, A. R.: Calcareous Aortic Valvular Disease. Am. Heart Jour., vol. VI, pp. 349-374, February 1931.

[9] Christian, Henry A.: Aortic Stenosis with Calcification of Cusps; Distinct clinical entity. J.A.M.A., vol. 97, pp. 158-161, July 18, 1931.

throats. In 2 cases the diagnoses were made on the bases of the distinctly rheumatic characteristics of the lesions, despite negative histories. In 11 of the 21 cases there was evidence of active carditis, joint manifestations, or tendencies to respiratory infections, the so-called rheumatic state described by Swift,[10] Coburn,[11] and others.

There is apparently no satisfactory term to describe the degenerative-senile heart changes. Many names have been used, including "hypertensive," "arteriosclerotic," "cardiorenal," "cardiovascular renal," "nephritic," "arteriorenal," "involutionary," "degenerative," "senile," and others. None is very satisfactory. Each tends to place undue emphasis on some particular aspect of the etiology of the types of heart diseases desired to be described. In each the personal views of the clinician plays too large a rôle. All seemingly fail to differentiate between lesions due to degeneration and those due to senility. From a public health viewpoint it is highly desirable to ascertain whether the apparent increase in heart disease is due to more frequent degenerative changes in middle age, or whether by reducing the deaths from infection and other diseases in early life, there are more people dying of senile changes. The 1931 edition of the Manual of the International List of Causes of Death [12] groups certain types of heart disease into those occurring before or after 45 years of age, a step which, although arbitrary, should be of considerable value. In the present study, due to the limited number of cases, the term "degenerative" is used without attempting further to subdivide the cases into the primarily degenerative and the senile. This group accounted for 32 admissions and represents 29 individual cases. The average age of these patients was 60.4 years. Among these 29 cases, in 6 the hypertensive element was dominant, in 7 others hypertension was associated with arteriosclerosis, in 8 there was evidence of arteriosclerosis without hypertension, in 2 nephritis, hypertension, and arteriosclerosis occurred, in 1 instance there was nephritis without hypertension or arteriosclerosis, and in 4 instances the diagnosis was based on the type of the clinical picture. In addition to the above, there were 2 instances of "angina pectoris," one of which was apparently due to a sclerosis with sudden occlusion of a coronary artery, and a symptomatic angina pectoris which was considered part of a general degenerative process.

The relative importance of arteriosclerosis and hypertension in the production of degenerative heart disease is a mooted point. Certain authorities (Cabot, White, et al.) stress the hypertensive factors. The New York Tuberculosis and Health Association, in

[10] Swift, Homer F.: Factors favoring the onset and continuation of rheumatic fever. Am. Heart Jour., June, 1931, vol. VI, p. 629.

[11] The Factor of Infection in the Rheumatic State. By Alvin F. Coburn. Williams and Wilkins, 1931.

[12] Manual of the International List of Causes of Death. Based on the Fourth Decennial Revision by the International Commission, Paris. October 16 to 19, 1929. U.S. Department of Commerce, 1931.

its manual on the criteria for diagnosis of heart disease, advises that when practicable a diagnosis of arteriosclerosis as the etiological factor be made, considering hypertension as a physiological rather than etiological factor in most cases. This presupposes a certain degree of arteriosclerosis, although not clinically evident, in most cases.

The ascribing of the dominance of arterioclerosis, hypertension, and in some cases nephritis in the production of this type of heart disease is dependent to a large degree on the views of the individual studying the cases. There is apparently no line of demarcation in determining just where each of these conditions begins or any gauge of their relative significance.

Of the miscellaneous cases, two showed evidence of thyrocardiac disease (hyperthyroidism) and three of subacute bacterial endocarditis. In each instance of subacute bacterial endocarditis, there was evidence that the infection was engrafted upon a pre-existing valvular lesion.

Among the 9 instances in which the etiologic diagnoses were undetermined, 2 were probably of rheumatic origin and 1 was of syphilitic etiology. Another case had pericardial adhesions of unknown origin. Another was considered as being a case of valvular heart disease due to trauma. This was not proved. The etiology of the remainder was entirely undetermined.

From the viewpoint of physiological changes this discussion is limited to whether or not the patient had heart disease severe enough to produce symptoms or evidence of congestive heart failure. Arrhythmias will not be considered.

Evidences of symptomatic disturbances due to heart disease include dyspnea, effort syndrome, palpitation, indefinite precordial or even anginal pains, pressure symptoms due to aneurysms, cardiac enlargement or distension of the pericardial sac, and peripheral manifestations, such as digestive disturbances, headaches, dizziness, faintness, etc., when of cardiac origin. Manifestations of congestion include, in addition to certain of the symptomatic disturbances just mentioned, congestion of the lungs, enlargement of the liver, cardiac asthma, orthopnea, œdema of the lower extremities, ascites, etc. As this study is made on the basis of the conditions of the patients at the time of admission, it is necessary to consider admissions rather than individual cases. As will be seen below, certain patients were admitted showing no symptoms of heart disease. These represent individuals showing stigmata of heart disease on physical examination, frequently unaware of its existence. The "symptomatic" group include those who had various subjective manifestations previously mentioned, but who gave no histories of congestive attacks. The group entitled "symptomatic—previously congested"

include those having only subjective complaints, but who gave histories of previous attacks of congestive failure. Those grouped under the heading of "congestive—first attack" include those admitted to the hospital in a state of heart failure of the congestive type, who had never experienced such a state before. Those considered as "congestive—previously congested" include those entering the hospital with manifestations of congestive heart failure who admitted histories of earlier attacks.

TABLE 3.—*Condition of 91 admissions to the United States Marine Hospital at Stapleton, N.Y., during the fiscal year 1931, regarding the presence or histories of symptoms of heart disease or manifestations of congestive heart failure. (Studied from the viewpoint of the etiological diagnoses)*

Presence or history of heart symptoms	Etiologic					
	Syphilitic	Rheumatic	Degenerative	Other	Undetermined	Total
Asymptomatic	2	4	1	0	3	10
Symptomatic	7	7	5	3	3	25
Symptomatic—previously congested	2	5	2	2	1	12
Congestive—first attack	3	2	10	0	0	15
Congestive—previously congested	3	8	14	1	3	29
Total	17	26	32	6	10	91

While it is not possible to reach any conclusions from so small a series, it is noted that the syphilitic group shows relatively little evidence of repeated bouts of heart failure. This is in keeping with the clinical observation that while rheumatic and, to lesser extent, degenerative cases show many attacks of heart failure, the patient suffering from syphilitic heart disease infrequently survives more than two or three such states. The observation that only two admissions among those having rheumatic heart disease involved the first attack of congestive heart failure is probably accounted for by the fact that the patients of the Public Health Service represent an age group older than that in which the first attacks of heart failure due to this disease ordinarily occur. The frequency with which both the first and subsequent attacks of congestion occur in cases of degenerative heart disease is accounted for, to a large extent, by the economic status of the beneficiaries. These patients enter the hospitals in states of congestive heart failure and undergo rest and enough treatment for them to be discharged from the hospitals. They are unable, however, to carry on the rigorous duties demanded of merchant seamen and other beneficiaries of the service, and soon find themselves back in the marine hospitals.

A further study was made from the viewpoint of the patients' functional capacity. This study, while similar in many respects to that presented here, embodies the system of classification of func-

tional capacity developed by the American Heart Association and the New York Tuberculosis and Health Association and used in their clinics. It is based on the ability of the patients to carry on the ordinary activities of life, and the restriction of these activities due to heart disease. Allowance must be made for age and factors other than cardiac which may affect the patient's activities. The classification is as follows:

Class I: Patients with organic heart disease able to carry on ordinary activities without discomfort.

Class II–a: Patients with organic heart disease whose activities are slightly limited. Ordinary physical activities produce undue fatigue, palpitation, dyspnea, and chest pain. Patients in this class rarely show any evidence of active cardiac infection, congestive heart failure, or anginal syndrome.

Class II–b: Patients with organic heart disease whose activities are greatly limited. Patients in this class suffer from dyspnea, palpitation, fatigue, or chest pain on less than ordinary activity. They also present some evidence of active cardiac infection, congestive heart failure, or anginal syndrome.

Class III: Patients with organic heart disease showing symptoms and signs of heart failure when at rest. These patients are unable to carry on any exertion without discomfort. They invariably show marked evidence of active cardiac infection, congestive heart failure, or anginal syndrome.

TABLE 4.—*Functional capacities, with reference to various etiologic factors, of 91 admissions involving cardiac diagnoses to the United States Marine Hospital at Stapleton, N.Y., during the fiscal year 1931, based on the condition of patients on entering the hospital. (The system of functional classification is that used by the American Heart Association)*

Classification of functional capacity	Etiologic classification					
	Syphilitic	Rheumatic	Degenerative	Other	Undetermined	Total
Class:						
I	2	3	1	0	3	9
II–a	5	7	6	2	1	21
II–b	3	6	10	0	2	21
III	7	10	15	4	4	40
Total	17	26	32	6	10	91

The basic figures in Table 4 are too small to justify any definite conclusions. That so many of the degenerative group are in Classes II–b and III offers an explanation why so many beds are filled with chronic cardiac cases.

It is suggested that ward surgeons and others keep this classification in mind in determining whether patients should be admitted for cardiac conditions and when they are fit for discharge. Class I obviously requires no treatment. Class II–a should not be admitted as in-patients, but can frequently be quite satisfactorily treated as out-patients. Class II–b represents borderline cases which would not usually be admitted to civilian institutions, but which frequently should be admitted to marine hospitals, preferably for short periods.

until their functional capacity has improved. Included in Class III are those cases which require rest in bed.

The adoption of such a system of functional diagnosis would have the added value that, upon transfer from one institution to another or upon subsequent admission, those handling the patients could obtain better ideas as to their conditions when last treated.

SUMMARY

Heart disease was found in 91 admissions among 79 patients during the fiscal year 1931 at the United States Marine Hospital at Stapleton, N.Y., and was responsible for 15 deaths. Degenerative types of heart disease were found in 29 cases and resulted in 7 cardiac deaths. Rheumatic heart disease was found in 21 cases and was the cause of 3 deaths. Syphilitic heart disease occurred in 15 individuals and was responsible for 3 deaths. The low incidence of syphilitic heart disease is noteworthy. The approximate age of the patients with rheumatic heart disease was 35 years; of luetic heart disease, 45 years; and of the degenerative group, 60 years. The average age of all cases of heart disease was approximately 48 years.

CONCLUSIONS

1. The etiology of heart disease should be given greater consideration in making cardiac diagnoses.
2. A study of patients' functional capacity is of value in determining their ability to carry on.
3. Angina pectoris and coronary thrombosis are apparently infrequent among the beneficiaries of the Public Health Service.
4. Syphilitic heart disease is not clinically as frequent as might be expected.

COURT DECISIONS RELATING TO PUBLIC HEALTH

Sexual sterilization law held constitutional.—(Oklahoma Supreme Court; In re Main, 19 P. (2d) 153; decided Feb. 14, 1933.) Acting under the 1931 law providing for the sexual sterilization of mental defectives (Session Laws 1931, pp. 80–82), the State board of public affairs ordered the sterilization of the appellant. This order was affirmed by the district court, and an appeal was taken to the supreme court. The appellant was afflicted with a hereditary form of insanity that was recurrent and was about to be discharged from the Central Oklahoma State Hospital.

One contention made on appeal was that the lower court had erred in finding that an operation of vasectomy and the resultant sterilization of the appellant would be without detriment to his general health, but the court held that the record sustained such finding. Another

contention was that the power conferred by the act upon the State board of public affairs, an administrative body, was judicial in character and, therefore, inhibited by the State constitution. The supreme court said that the board's duties were to some extent judicial or quasi-judicial in character, but, by reason of the act's provisions for a review and a trial *de novo* and a stay pending such review and trial before a judicial tribunal, held that the patient was not injuriously affected by the bestowal of quasi-judicial powers upon an administrative board, and, such being the case, he had no concern relative to the grant of those powers to such a board.

Concerning the appellant's view that the sterilization act was violative of the State constitutional provision inhibiting the infliction of cruel or unusual punishments, the court said that it was apparent that the constitutional inhibition had no application to surgical treatment of feeble-minded persons, but had reference to punishment after conviction of crime.

Another contention was that the act violated the provision of the State constitution that no person should be deprived of life, liberty, or property without due process of law, in that it deprived "a man of a part of his life, to-wit, the ability to produce life" or procreate. With respect to this, the court stated as follows:

> The phrase "without due process of law" is not without import in this connection. Therefore, assuming that the right to beget children is a natural and constitutional right, yet this right cannot be extended beyond the common welfare. Under the police power of the State and acting for the public good, the State may impose reasonable restrictions upon the natural and constitutional rights of its citizens. This statutory provision for sterilization of feeble-minded inmates of public institutions constitutes a reasonable restriction upon such natural and constitutional rights of such persons. [Case cited.]

A like contention as to unconstitutionality of the act, based upon the provision that "All persons have the inherent right to life, liberty, the pursuit of happiness, and the enjoyment of the gains of their own industry," was held to be without merit.

In concluding its opinion, the supreme court said:

> The attack is upon the procedure and the substantive law. The first is adequate and liberal—the latter is an enactment of public policy within the scope of the power of the legislature.

The judgment of the lower court was affirmed.

Sexual sterilization statute held unconstitutional as denying due process.—(North Carolina Supreme Court; *Brewer* v. *Valk* et al, 167 S.E. 638; decided Feb. 8, 1933.) Under the sexual sterilization law of North Carolina, it was the duty of the board of county commissioners, upon the petition and request of the legal guardian of a mentally defective person who was a resident of the county and not an inmate of any public institution, to have a sterilization operation

performed upon such defective. It was required, also, that such operation should have the approval of the State commissioner of charities and public welfare, the secretary of the State board of health, and the chief medical officers of any two of the institutions for the feeble-minded or insane of the State.

The plaintiff was adjudged incompetent to manage her affairs and a legal guardian was appointed. Such guardian thereupon requested the board of commissioners of the county to have a sterilization operation performed. In compliance with this request the commissioners authorized and ordered a certain physician to perform such operation upon the plaintiff. The latter, by her next friend, then brought an action to enjoin the performance of the operation, contending that the statute involved was unconstitutional because violative of the due process provisions of the Federal and State constitutions. The supreme court stated that the question was whether, under the due process requirement, the sterilization could be done without giving the plaintiff notice and an opportunity to be heard. Because of the absence in the act of any provision for such notice and hearing, the court declared the statute to be unconstitutional as violative of the due process requirement.

DEATHS DURING WEEK ENDED MAY 6, 1933

[From the Weekly Health Index issued by the Bureau of the Census, Department of Commerce]

	Week ended May 6, 1933	Corresponding week, 1932
Data from 85 large cities of the United States:		
Total deaths	7,957	8,276
Deaths per 1,000 population, annual basis	11.1	11.8
Deaths under 1 year of age	611	701
Deaths under 1 year of age per 1,000 estimated live births [1]	52	57
Deaths per 1,000 population, annual basis, first 18 weeks of year	12.0	12.5
Data from industrial insurance companies:		
Policies in force	68,357,913	73,403,421
Number of death claims	12,654	14,370
Death claims per 1,000 policies in force, annual rate	9.7	10.2
Death claims per 1,000 policies, first 18 weeks of year, annual rate	10.9	10.5

[1] 1933, 81 cities; 1932, 80 cities.

PREVALENCE 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

CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers

Reports for Weeks Ended May 13, 1933, and May 14, 1932

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended May 13, 1933, and May 14, 1932

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932
New England States:								
Maine	-------	4	2	5	3	202	0	0
New Hampshire	-------	-------	-------	-------	40	16	0	0
Vermont	1	-------	-------	-------	3	190	0	0
Massachusetts	20	33	1	3	623	1,015	0	2
Rhode Island	2	3	-------	-------	-------	51	1	0
Connecticut	-------	3	4	7	305	296	0	1
Middle Atlantic States:								
New York	80	97	[1] 12	[1] 20	3,205	2,437	5	5
New Jersey	33	33	4	14	1,575	917	1	2
Pennsylvania	56	80	-------	-------	1,635	1,937	6	9
East North Central States:								
Ohio	41	30	122	86	610	3,984	0	1
Indiana	12	17	14	15	292	123	4	9
Illinois	20	61	15	60	791	1,428	15	6
Michigan	19	11	16	6	822	2,715	2	3
Wisconsin	2	6	20	31	458	2,629	1	0
West North Central States:								
Minnesota	4	6	1	-------	676	51	2	1
Iowa	12	11	-------	-------	83	9	2	1
Missouri	24	23	8	4	202	127	3	3
North Dakota	6	18	-------	-------	115	14	0	1
South Dakota	3	1	2	-------	17	8	0	0
Nebraska	6	12	-------	-------	184	4	1	0
Kansas	7	2	-------	1	301	496	2	0
South Atlantic States:								
Delaware	2	-------	1	-------	18	2	0	0
Maryland [2]	7	10	4	17	21	65	0	1
District of Columbia	6	7	-------	-------	30	26	1	2
Virginia	11	-------	-------	-------	340	-------	0	1
West Virginia	6	14	7	39	51	234	0	0
North Carolina	12	20	2	172	635	830	1	2
South Carolina	4	7	165	635	283	180	0	0
Georgia [3]	1	7	37	86	121	73	0	1
Florida [3]	11	5	2	7	32	9	0	0

See footnotes at end of table.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended May 13, 1933, and May 14, 1932—Continued

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932
East South Central States:								
Kentucky	7	10	12	52	17	41	1	2
Tennessee	4	7	30	144	45	22	4	5
Alabama [3]	7	10	11	47	157	16	3	2
Mississippi	7	5	----	----	----	----	0	0
West South Central States:								
Arkansas	2	13	11	13	181	5	0	0
Louisiana	11	27	11	5	24	82	0	1
Oklahoma [4]	6	6	11	50	204	10	1	2
Texas [3]	54	16	108	18	1,569	563	4	0
Mountain States:								
Montana [5]	3	----	2	1	24	149	0	2
Idaho [5]	----	----	3	----	29	2	0	0
Wyoming [5]	----	1	----	----	30	27	0	0
Colorado	5	5	27	----	10	132	0	1
New Mexico	3	10	----	----	8	36	0	0
Arizona	3	9	----	2	74	----	0	0
Utah	1	----	2	----	17	2	0	0
Pacific States:								
Washington	3	3	1	----	65	258	1	1
Oregon [5]	----	5	28	36	97	282	0	1
California	30	66	37	57	1,388	717	2	2
Total	554	714	733	1,651	17,410	22,428	63	70

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932
New England States:								
Maine	0	0	33	23	0	0	3	6
New Hampshire	0	0	8	50	0	0	0	0
Vermont	0	0	8	11	0	10	0	0
Massachusetts	1	0	305	461	0	0	2	5
Rhode Island	0	0	24	47	0	0	1	0
Connecticut	0	0	113	97	0	0	1	2
Middle Atlantic States:								
New York	0	1	770	1,556	0	1	14	13
New Jersey	1	0	252	341	0	0	5	2
Pennsylvania	1	0	873	707	0	0	13	5
East North Central States:								
Ohio	0	1	1,029	440	7	17	6	5
Indiana	1	0	127	67	2	6	2	2
Illinois	3	2	432	407	10	6	28	10
Michigan	1	1	508	506	0	14	5	2
Wisconsin	0	2	114	84	5	1	2	2
West North Central States:								
Minnesota	0	0	93	98	0	2	0	4
Iowa	0	0	22	38	8	26	1	0
Missouri	0	0	58	51	11	5	1	1
North Dakota	0	0	5	8	0	1	0	0
South Dakota	0	0	13	2	0	0	2	0
Nebraska	0	0	10	24	1	11	0	1
Kansas	1	0	51	42	2	6	2	2
South Atlantic States:								
Delaware	0	0	15	11	0	0	0	0
Maryland [2]	0	0	81	77	0	0	6	0
District of Columbia	0	0	17	25	0	0	0	0
Virginia	0	----	34	----	0	----	6	----
West Virginia	0	0	24	18	0	0	5	5
North Carolina	0	0	37	41	2	2	7	4
South Carolina	0	0	4	5	0	0	17	12
Georgia [3]	0	0	10	8	0	2	8	19
Florida [3]	1	0	2	2	0	9	2	10

See footnotes at end of table.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended May 13, 1933, and May 14, 1932—Continued

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 1932	Week ended May 13, 1933	Week ended May 14, 932
East South Central States:								
Kentucky	0	0	32	32	0	6	4	10
Tennessee	0	0	33	43	4	15	13	9
Alabama [3]	0	1	8	10	23	10	7	13
Mississippi	0	0	5	4	0	11	2	5
West South Central States:								
Arkansas	0	0	4	0	3	6	4	0
Louisiana	0	0	8	13	1	9	16	12
Oklahoma [4]	1	0	7	8	37	7	4	5
Texas [3]	2	1	52	13	31	49	13	3
Mountain States:								
Montana [5]	0	0	6	15	0	4	6	1
Idaho [5]	0	0	3	3	3	2	1	1
Wyoming [5]	0	0	11	12	0	0	0	0
Colorado	0	0	28	20	4	5	0	0
New Mexico	0	0	5	11	0	1	1	1
Arizona	0	0	5	1	0	0	0	0
Utah	0	0	4	3	0	0	0	0
Pacific States:								
Washington	2	2	50	27	7	25	3	0
Oregon [5]	0	0	37	7	11	9	1	2
California	1	4	150	174	42	9	7	5
Total	16	15	5,520	5,649	214	288	221	179

[1] New York City only.
[2] Week ended Friday.
[3] Typhus fever, week ended May 13, 1933, 26 cases: 5 cases in Georgia, 1 case in Florida, 14 cases in Alabama, and 6 cases in Texas.
[4] Figures for 1933 are exclusive of Oklahoma City and Tulsa and for 1932 are exclusive of Tulsa only.
[5] Rocky Mountain spotted fever, week ended May 13, 1933, 15 cases: 2 cases in Montana, 4 cases in Idaho, 5 cases in Wyoming, and 4 cases in Oregon.

SUMMARY OF MONTHLY REPORTS FROM STATES

The following summary of cases reported monthly by States is published weekly and covers only those States from which reports are received during the current week.

State	Meningococcus meningitis	Diphtheria	Influenza	Malaria	Measles	Pellagra	Poliomyelitis	Scarlet fever	Smallpox	Typhoid fever
February 1933										
Puerto Rico	----	59	229	3,122	282	18	0	----	0	17
March 1933										
Puerto Rico	----	60	142	2,402	203	6	0	1	0	22
April 1933										
Florida	2	36	13	7	----	3	1	20	0	9
Iowa	10	43	1	----	115	----	0	140	70	1
Michigan	8	55	39	4	5,006	----	4	2,516	4	14
New Jersey	8	82	56	2	7,670	----	2	1,120	0	11
New York	16	274	----	6	14,905	----	3	3,797	0	35
North Dakota	2	8	15	----	317	----	----	34	----	1
Tennessee	12	56	405	93	303	32	2	192	4	18
Wyoming	3	2	----	----	45	----	0	55	0	6

February 1933

	Cases
Puerto Rico:	
Chicken pox	72
Dysentery	971
Filariasis	7
Leprosy	3
Mumps	27
Ophthalmia neonatorum	2
Puerperal septicemia	9
Tetanus	18
Tetanus, infantile	32
Trachoma	15
Whooping cough	118

March 1933

	Cases
Puerto Rico:	
Chicken pox	191
Dysentery	660
Filariasis	3
Mumps	32
Ophthalmia neonatorum	11
Puerperal septicemia	12
Tetanus	11
Tetanus, infantile	25
Trachoma	9
Whooping cough	100
Yaws	1

April 1933

	Cases
Actinomycosis:	
Wyoming	1
Anthrax:	
New Jersey	1
New York	1
Chicken pox:	
Florida	162
Iowa	179
Michigan	1,724
New Jersey	1,711
New York	3,688
North Dakota	56
Tennessee	326
Wyoming	61
Dysentery:	
New York	4
Tennessee	3
German measles:	
Iowa	12
Michigan	7,018
New Jersey	97
New York	216
Tennessee	136
Impetigo contagiosa:	
Tennessee	11
Lead poisoning:	
New Jersey	3
Lethargic encephalitis:	
Michigan	3
New Jersey	5
New York	14
North Dakota	7
Tennessee	1
Mumps:	
Florida	291
Iowa	397
Michigan	1,427
New Jersey	1,321
North Dakota	7
Tennessee	164
Wyoming	3
Ophthalmia neonatorum:	
New Jersey	4
New York	8
Tennessee	7
Paratyphoid fever:	
New York	6
Tennessee	1
Puerperal septicemia:	
Tennessee	2
Rabies in animals:	
New Jersey	27
New York	[1] 3
Rabies in man:	
Florida	1
Rocky Mountain spotted fever:	
Wyoming	13
Scabies:	
Tennessee	22
Septic sore throat:	
Michigan	33
New York	21
Tennessee	26
Wyoming	12
Tetanus:	
New York	5
Tennessee	2
Trachoma:	
New Jersey	1
North Dakota	1
Tennessee	32
Trichinosis:	
New Jersey	1
New York	12
Tularaemia:	
Tennessee	3
Typhus fever:	
Florida	1
Undulant fever:	
Iowa	23
Michigan	4
New Jersey	1
New York	25
Vincent's angina:	
Iowa	4
New York	[1] 83
Tennessee	14
Wyoming	1
Vincent's infection:	
North Dakota	14
Whooping cough:	
Florida	59
Iowa	53
Michigan	1,058
New Jersey	482
New York	1,841
North Dakota	8
Tennessee	200
Wyoming	14

[1] Exclusive of New York City.

WEEKLY REPORTS FROM CITIES

City reports for week ended May 6, 1933

State and city	Diphtheria cases	Influenza cases	Influenza deaths	Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
Maine:											
Portland	0	-------	0	1	1	2	0	0	0	19	22
New Hampshire:											
Concord	0	-------	0	0	0	1	0	0	0	0	5
Manchester	0	-------	0	0	1	2	0	1	0	0	29
Nashua	0	-------	0	0	0	0	0	0	0	0	-------
Vermont:											
Barre	0	-------	0	0	1	0	0	0	0	9	4
Burlington	0	-------	0	0	0	5	0	0	0	0	7
Massachusetts:											
Boston	7	1	0	192	22	70	0	9	0	39	217
Fall River	1	-------	0	1	1	9	0	1	0	7	40
Springfield	1	-------	0	1	0	14	0	1	0	9	34
Worcester	3	-------	0	7	2	18	0	2	0	11	35
Rhode Island:											
Pawtucket	0	-------	0	0	0	2	0	0	0	0	18
Providence	0	-------	0	2	1	21	0	3	0	20	68
Connecticut:											
Bridgport	0	-------	0	31	0	12	0	3	0	0	27
New York:											
Buffalo	3	-------	1	73	22	46	0	10	0	46	140
New York	45	26	5	1,592	160	259	0	84	7	127	1,542
Rochester	0	-------	0	2	6	26	0	2	0	11	69
Syracuse	0	-------	0	2	2	22	0	2	0	5	54

City reports for week ended May 6, 1933—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
New Jersey:											
Camden	4			6		19	0		0	0	
Newark	0	2	0	260	3	23	0	7	0	33	94
Trenton	0		0	21	4	14	0	2	0	0	41
Pennsylvania:											
Philadelphia	1		1	398	35	133	0	24	0	5	473
Pittsburgh	2	5	4	8	11	62	0	6	0	29	134
Reading	1		0	35	2	9	0	1	0	7	32
Scranton	0			4		15	0		0	0	
Ohio:											
Cincinnati	4		1	6	8	34	0	10	0	14	133
Cleveland	6	44	0	5	14	201	0	15	1	38	206
Columbus	3		0	13	3	31	0	3	0	0	65
Toledo	3	2	2	252	6	137	0	6	0	13	88
Indiana:											
Fort Wayne	4		0	0	3	10	0	1	0	0	31
Indianapolis	0		0	181	5	20	1	6	0	3	
South Bend	0		0	5	3	3	0	3	0	11	26
Terre Haute	0		1	25	1	13	0	1	0	0	18
Illinois:											
Chicago	0	2	4	574	43	224	0	38	1	22	680
Springfield	2		0	2	0	2	0	0	1	0	24
Michigan:											
Detroit	14	9	1	368	15	150	0	17	2	124	223
Flint	0	2	0	31	1	5	0	0	0	3	15
Grand Rapids	0		0	9	3	5	0	1	0	15	36
Wisconsin:											
Kenosha	0		0	0	0	3	0	0	0	12	3
Madison	1			102		3	0		0	0	
Milwaukee	0	2	2	1	2	39	0	5	1	39	94
Racine	1		0	0	0	9	0	0	0	17	12
Superior	0		0	0	1	0	0	0	0	9	8
Minnesota:											
Duluth	0		0	11	3	0	0	3	0	21	19
Minneapolis	1		3	34	10	50	0	5	1	31	119
St. Paul	0		0	532	0	20	0	0	0	99	51
Iowa:											
Des Moines	1			0		10	1		0	0	35
Sioux City	2			1		0	0		0	0	
Waterloo	0			0		0	2		0	0	
Missouri:											
Kansas City	2		0	59	8	42	0	2	0	3	80
St. Joseph	2		0	38	0	2	0	1	0	0	30
St. Louis	10	1		58	4	14	0	1	0	13	179
North Dakota:											
Fargo	0		0	2	1	0	0	0	0	0	14
Grand Forks	0		0	0	0	2	0	0	0	0	
South Dakota:											
Aberdeen	0			0		1	0		0	0	
Sioux Falls	0			0		2	0		0	0	10
Nebraska:											
Omaha	0		0	74	4	3	0	2	0	3	56
Kansas:											
Topeka	0		0	176	0	2	0	0	0	7	5
Wichita	0		1	0	1	0	0	0	0	1	34
Delaware:											
Wilmington	0		1	2	4	2	0	0	0	4	29
Maryland:											
Baltimore	4	3	1	1	15	77	0	14	0	30	199
Cumberland	0		0	7	0	1	0	0	0	0	9
Frederick	0		0	0	0	1	0	0	0	1	
District of Col.:											
Washington	2		0	16	7	14	0	9	0	7	147
Virginia:											
Lynchburg	2		0	4	0	0	0	1	0	15	19
Norfolk	0		0	4	0	5	0	1	0	6	24
Richmond	0		0	5	2	6	0	3	1	0	40
Roanoke	0		0	21	0	2	0	1	0	2	20
West Virginia:											
Charleston	0	2	1	0	0	1	0	1	1	0	19
Huntington	2			2		4	0		0	0	
Wheeling	0		0	4	4	1	0	0	0	8	15
North Carolina:											
Raleigh	0		0	2	2	2	0	0	0	3	10
Wilmington	0		0	91	1	0	0	0	0	2	12
Winston-Salem	0		0	9	1	3	0	4	0	1	11

City reports for week ended May 6, 1933—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
South Carolina:											
Charleston	0	9	1	0	0	1	0	3	0	9	20
Columbia	0	----	1	0	4	0	0	0	0	0	22
Greenville	0	----	0	6	0	0	0	0	0	0	4
Georgia:											
Atlanta	1	15	2	32	5	2	0	4	0	26	61
Brunswick	0	----	0	1	0	0	0	1	0	0	3
Savannah	0	19	0	0	3	2	0	1	1	0	33
Florida:											
Miami	1	----	0	1	0	0	0	4	0	4	28
Tampa	0	1	1	0	0	0	0	1	0	3	18
Kentucky:											
Ashland	0	----	0	5	0	0	0	0	1	5	----
Tennessee:											
Memphis	0	----	0	26	2	3	0	9	1	40	71
Nashville	0	----	1	4	2	2	0	1	0	0	50
Alabama:											
Birmingham	0	4	2	3	3	1	0	5	0	8	52
Mobile	0	----	2	8	0	0	0	2	0	0	22
Montgomery	2	----	----	19	----	0	0	----	0	5	----
Arkansas:											
Fort Smith	0	----	----	1	----	0	0	----	0	2	----
Little Rock	0	----	0	120	2	0	0	2	0	1	4
Louisiana:											
New Orleans	8	8	0	8	7	6	0	5	4	1	114
Shreveport	0	----	0	0	5	0	0	4	0	0	50
Texas:											
Dallas	13	1	1	----	3	14	0	3	1	6	55
Fort Worth	1	----	----	7	----	2	1	0	0	0	----
Galveston	0	----	0	2	2	2	0	3	1	0	18
Houston	4	----	2	2	4	3	0	3	3	0	73
San Antonio	3	----	0	28	6	0	0	10	0	0	71
Montana:											
Billings	0	----	0	0	0	0	0	0	0	0	9
Great Falls	0	----	0	2	0	2	0	0	0	3	3
Helena	0	----	0	0	0	0	0	0	0	0	5
Missoula	0	1	1	2	0	0	0	0	0	0	7
Idaho:											
Boise	0	----	0	14	0	0	7	0	0	0	7
Colorado:											
Denver	0	27	1	1	5	10	0	5	0	4	71
Pueblo	0	----	0	0	0	0	0	0	0	9	10
Utah:											
Salt Lake City	0	----	0	5	0	6	0	1	0	18	23
Nevada:											
Reno	0	----	0	0	0	1	0	0	0	0	4
Washington:											
Seattle	0	7	----	6	----	16	0	----	0	5	----
Spokane	0	2	----	2	----	1	0	----	0	0	----
Tacoma	0	----	0	0	3	4	0	2	0	1	25
Oregon:											
Salem	0	----	----	12	----	0	0	----	0	0	----
California:											
Los Angeles	19	9	1	553	13	43	19	24	1	55	271
Sacramento	0	2	0	2	2	1	0	2	0	49	23
San Francisco	0	----	0	2	10	9	0	15	0	71	145

City reports for week ended May 6, 1933—Continued

State and city	Meningococcus meningitis		Poliomyelitis cases
	Cases	Deaths	
Massachusetts:			
Boston	1	2	1
New York:			
New York	2	0	1
Pennsylvania:			
Pittsburgh	0	1	0
Ohio:			
Cleveland	1	0	0
Indiana:			
Fort Wayne	1	0	0
Indianapolis	0	0	1
Illinois:			
Chicago	8	4	0
Michigan:			
Detroit	1	2	0
Flint	2	0	0
Iowa:			
Sioux City	1	0	0
Missouri:			
St. Joseph	1	0	0
St. Louis	1	1	0
Nebraska:			
Omaha	2	0	0
Maryland:			
Baltimore	1	1	0
Virginia:			
Roanoke	1	0	0
Tennessee:			
Memphis	0	0	1
Texas:			
Houston	0	0	1
California:			
Los Angeles	0	0	1
Sacramento	0	1	0

Lethargic encephalitis.—Cases: Toledo, 1; Pittsburgh, 1; Tampa, 1.
Pellagra.—Cases: Baltimore, 1; Winston-Salem, 1; Charleston, S.C., 2; Savannah, 1; New Orleans, 4; Dallas, 1.
Rabies (in man): 1 death at Birmingham.
Typhus fever.—Cases: Montgomery, 1.

FOREIGN AND INSULAR

ITALY

Communicable diseases—4 weeks ended January 8, 1933.—During the 4 weeks ended January 8, 1933, cases of certain communicable diseases were reported in Italy as follows:

Disease	Dec. 12–18		Dec. 19–25		Dec. 26–Jan. 1		Jan. 2–8	
	Cases	Communes affected	Cases	Communes affected	Cases	Communes affected	Cases	Communes affected
Anthrax	21	21	14	11	11	10	18	16
Cerebrospinal meningitis	10	7	5	5	5	5	6	6
Chicken pox	332	120	248	91	197	80	365	113
Diphtheria and croup	1,030	444	739	358	812	382	881	398
Dysentery	3	3	2	2	6	4	4	4
Lethargic encephalitis	2	2	2	2			3	3
Measles	1,458	219	962	166	1,039	181	1,414	226
Poliomyelitis	11	10	6	6	9	9	14	14
Scarlet fever	725	215	413	153	441	177	386	148
Typhoid fever	685	357	392	218	430	263	391	229

JAMAICA

Communicable diseases—Four weeks ended March 25, 1933.—During the 4 weeks ended March 25, 1933, cases of certain communicable diseases were reported in Kingston, Jamaica, and in the island of Jamaica, outside of Kingston, as follows:

Disease	Kingston	Other localities	Disease	Kingston	Other localities
Chicken pox	4	8	Tuberculosis	37	94
Dysentery	5	4	Typhoid fever	11	38
Puerperal fever		6			

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

From medical officers of the Public Health Service, American consuls, International Office of Public Hygiene, Pan American Sanitary Bureau, health section of the League of Nations, and other sources.. The reports contained in the following tables must not be considered as complete or final as regards either the list of countries included or the figures for the particular countries for which reports are given.

CHOLERA

[C indicates cases; D, deaths; P, present]

Place		Oct. 16–Nov. 12, 1932	Nov. 13–Dec. 10, 1932	Dec. 11, 1932–Jan. 7, 1933	Jan. 8–Feb. 4, 1933	Week ended—												
						February 1933			March 1933				April 1933					May 1933
						11	18	25	4	11	18	25	1	8	15	22	29	6	13
China:																			
Amoy	C			6															
Canton	C		1																
Macao	C											1							
	D											1							
Swatow	C	3																	
India	C	2,411	3,453	4,524	3,396	573	762	768	1,068	1,052									
	D	1,336	1,907	2,400	1,721	288	364	395	523	530									
Bombay	C	5			1				1						1				
Calcutta	C	69	53	54	110	14	35	41	24	50	53	93	131	136	184				
Chittagong	C						1					1	4	3	8	5			
Karachi	C																1		
Rangoon	C														1				
India, French: Chandenagor	C				1	2													
Indo-China (see also table below):																			
Pnom-Penh	C			1									1						
Saigon and Cholon	C	1			2								1		1	2	1		
Philippine Islands:																			
Cebu Province	C						7	8	2	2									
Iloilo Province—Iloilo	C																	1	
	D																	1	
Leyte Province	C		7	80	110	21	7	26	24	23		1	2		9	3	38	9	
	D		7	44	76	14	6	23	13	21		1	2		7	4	35	8	
Rizal Province	C																	1	
Samar Province	C	53	35	135	121							[1] 186			67				
	D	42	26	101	75							[1] 144			50				
Siam	C	1		1	2											1			

Place		October 1932	November 1932	December 1932			January 1933			February 1933			March 1933	
				1-10	11-20	21-31	1-10	11-20	21-31	1-10	11-20	21-28	1-10	11-20
Indo-China (French) (see also table above):														
Cambodia [2]	C	4	1	1	1	3				9		1		2
	D	3	1	1		1				6				1
Cochin-China [2]	C	10	1	2	3	3	1	4	2	9	2	1	8	4
	D	7	1	2	3	1	1	1		6	2	1	7	3

[1] For month of March 1933.

[2] Reports incomplete.

PLAGUE [1]

Place		Oct. 16–Nov. 12, 1932	Nov. 13–Dec. 10, 1932	Dec. 11, 1932–Jan. 7, 1933	Jan. 8–Feb. 4, 1933	Week ended—											
						February 1933			March 1933				April 1933				
						11	18	25	4	11	18	25	1	8	15	22	29
Angola	C		P				P										
Argentina:																	
Cordoba Province	C			2	1	5						5				1	
Jujuy Province	C				10				6								
La Rioga Province	D	4															
Rosario	C											2					
Salta Province	C	7	12													7	
San Luis Province [2]	C		P														
Santa Fe	C			1													
Belgian Congo	C			1													
British East Africa (see also table below):																	
Tanganyika	D		1		2					1							
Uganda	C	192	194	141	58	11	7	14	8	9	10	9					
	D	189	169	134	58	10	7	14	9	9	10	9					
Ceylon:																	
Central Province	C				9						4	2					
	D				7						4	2					
Colombo	C	9	11	4	5	4	1	3	2	11		1	1		1		
	D	8	7	3	3	2	1	2	2	9		1	1				
Plague-infected rats		5		4			3	1									

[1] Including plague in the United States and its possessions.

[2] Several cases of plague with 1 death were reported at Quines, San Luis Province, Argentina, on Dec. 9, 1932.

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

PLAGUE—Continued

[C indicates cases; D, deaths; P, present]

Place		Oct. 16–Nov. 12, 1932	Nov. 13–Dec. 10, 1932	Dec. 11, 1932–Jan. 7, 1933	Jan. 8–Feb. 4, 1933	Week ended— February 1933			March 1933				April 1933				
						11	18	25	4	11	18	25	1	8	15	22	29
Dutch East Indies:																	
Batavia	C										[3]1						
West Java	C	502	610	1,152	1,329	262	312	299	278								
	D	502	608	745													
Ecuador. (See table below.)																	
Egypt:																	
Alexandria	C			2	1					1						1	
Assiout	C			6	4	1	2	1		4	2		2	4	4	2	2
Minieh	C	1									1	1				1	
France: Marseille	C			1													
Hawaii Territory:																	
Hawaii Island:																	
Hamakua—Kukaiau	C				1												
	D				1												
Plague-infected rats				2	7												
Paauilo—Plague-infected rats			1	11	1												
Maui Island—Makawao:																	
Plague-infected rats					1												
Omaopio—Plague-infected rats					1												
India	C	5,422	6,104	6,900	6,662	1,446	1,935	1,494	1,524	1,587							
	D	3,074	3,060	4,349	4,191	898	1,304	914	859	970							
Bassein	C	1			1			1	1	1	4	3	4	4		6	
Plague-infected rats		1	1	1	1	1	1						1		1		
Bombay	C	3						3		2	1	6	6	2	2	3	
Plague-infected rats		34	15	16	28	11	21	14	22	26	26	25	44	22	23	28	
Madras Presidency	C	266	546	446	508	95	93	107	83	57	60						
	D	92	197	249	170	43	32	47	51	27	30						
Rangoon	C	2	3	1	1		1		1	2							
Plague-infected rats					1		1		1	1							
Indo-China. (See table below.)																	
Iraq: Baghdad	C	3	1			1	1		1		1						
Madagascar. (See table below.)																	
Morocco	C		10	16				3	1	14	8	9	2		12		
Peru. (See table below.)																	
Senegal. (See table below.)																	

Siam	C	7	9	12	7	1	1	13	1	10	1			1	1		
South-West Africa.[4]																	
Straits Settlements: Singapore	C															1	
Syria: Beirut	C	9	12													1	
Union of South Africa: Orange Free State	C	P	P	P	4	1											
United States: California—San Benito County—Plague-infected ground squirrels					1												
On vessels:																	
S.S. Kingsborough at port in Argentina	C											1					
S.S. Patris at Beirut	C	3															

Place		November 1932	December 1932	January 1933	February 1933	March 1933	April 1933
British East Africa (see also table above): Kenya	C	5	8	6	11	6	2
Ecuador	C			1		3	
Indo-China	C	2	3	4	4	4	6
	D	2	3	2	4	4	5
Madagascar:							
Province:							
Ambositra	C	41	149	158			
	D	35	125	146			
Antisirabe	C	25	57	63			
	D	26	56	61			
Maevatanana	C	8	9	2			
Miarinarivo	C	35	37	75			
	D	34	36	14			
Moramanga	C	229	186	163			
	D	228	183	159			
Madagascar—Continued							
Province—Continued							
Tamatave	C	1	1			1	
	D	1	1			1	
Tananarive	C	209	186	198			
	D	199	179	190			
Peru	C	10	12	4	18	7	
Department:							
Ancachs	C	[5] 2					
Libertad	C	[5] 2					
Lima	C	8					
Piura	C	[5] P					
Senegal: Dakar[6]	C	6	19	2	4	1	1
	D	4	17	2	4		

[3] Imported.
[4] 227 cases of plague with 53 deaths were reported in Ovamboland, South-West Africa, up to Dec. 17, 1932. Antiplague measures have been taken.
[5] Suspicious cases.
[6] Incomplete reports.

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

SMALLPOX

[C indicates cases; D, deaths; P, present]

Place		Oct. 16–Nov. 12, 1932	Nov. 13–Dec. 10, 1932	Dec. 11, 1932–Jan. 7, 1933	Jan. 8–Feb. 4, 1933	Week ended— February 1933 11	18	25	March 1933 4	11	18	25	April 1933 1	8	15	22	29
Arabia—																	
Algeria:																	
Algiers	C	2	1	1													
Constantine Department	C										1						
Aden	C	1	3	1	2			1									
Argentina:																	
Chaco Territory	C							P									
Jujuy Province	C	1															
Belgian Congo	C		122	88													
Belgium	C	1															
Bolivia	C			5				39									
Brazil:																	
Parahyba—Joao Pessoa	C		P														
Pernambuco—Recife	C	7	4														
Porto Alegre (alastrim)	C	26	8	16	1												
British East Africa:																	
Kenya	C						1		13	1	18	4					
Tanganyika	C	74	66	49	95	18	15		23	25	18						
British South Africa:																	
Northern Rhodesia	C	40		6		1					13	8					
Southern Rhodesia	C	27	1	1	25	22											
Canada:																	
Alberta	C		1														
British Columbia	C													[1] 6			
Manitoba	C	2		13													
Ontario	C		3	5						3		2					
Toronto	C		3	3										[1] 3			
Saskatchewan	C		3	1	5	22		9		4		10		[1] 2			
Ceylon:																	
Colombo	C		28	72	75	18	7	5	4	1	1	1	1	1	1		
Galle	C															39	

China:																	
Amoy	C				1	1	1	2	1	1		1	1	1			
Canton	C	28	180	762	504	85	86	41	22	26	17	10	14	13	10	11	6
	D	2	14	23	13		1									1	1
Chemulpo	C					17											
Dairen	C		2	1	4				5		2						
Foochow	C	P	P	P	P		P		P		P						
Hong Kong	C		2	18	78	32	28	63	46	53	43	37	36	36	14	20	14
Macao	C			P	3	2	2	2	2	2	2	2	5	3	1		
Nanking	C		6	11	38		23	17	49	10	1		5				
Shanghai	C	5	13	23	41		17	9	2	16	7	8	7	9	8	15	7
Swatow	C	4	8	7	22	9	8	2	2	3	8	9	6	6	7	3	
Chosen. (See table below.)																	
Colombia: Cali	D		1											•			
Dahomey	C	6		5	22	21	4	7									
Dutch East Indies	C	2			1												
Egypt:																	
Alexandria	C	23	77	583	987	301	300	195	147	104	82	59	32	12	11	11	8
	D	13	18	116	227	52	56	40	35	25	23	11	11	3	22	8	2
Cairo	C		1	8	37	6	9	9	1	7		2		1	2	2	5
Gharbieh	C			37													
Port Said	C				2					1	2	3		3			
Suez	C				2				4	1	2						
Gold Coast. (See table below.)																	
Great Britain:																	
England and Wales	C	116	72	79	66	25	20	22	9	15	23	15	18	31	14	18	
London	C	76	68	73	59	22	16	20	8	13	21	11	17	24	9	13	
London and Great Towns	C	110	71	76	66	24	20	22	9	13	22	14	17	30	9	14	
Greece. (See table below.)																	
Honduras:																	
Puerto Castilla	C		1							2							
Tegucigalpa	D																
Tela	C										8	6				1	
India	C	2	1	2	4	3	1	2		1	2					1	
	C	4,179	7,919	11,284	20,423	6,699	7,516	8,807	8,802	8,021							
	D	1,013	2,239	3,523	5,907	1,906	1,889	2,188	2,320	1,932							
Bassein	C					2	1	2	2	5	2	3	3	14	12	10	
	D						1		1	1	1	1	2	3	3	3	
Bombay	C	33	87	230	805	332	408	377	405	358	341	259	217	159	141	115	
	D	15	35	98	391	164	210	206	215	286	178	142	111	94	72	65	
Calcutta	C	53	103	301	961	322	399	533	383	299	392	460	369	295	245		
	D	24	47	213	672	263	213	355	316	188	281	314	270	244	188		
Cochin	C	1								2	2			2	1	1	
Karachi	C		14	25	45	8	15	13	11	29	22	23	41	34	31	31	
Madras	C	140	119	156	351	117	104	130	213	153	143	195	175	138	125	115	
Moulmein	C					1											
Negapatam	C	3	4	2	3	1		1			2		2	1		2	
Rangoon	C	3	2	2	5	1	6	3	10	3	2	2	4	7	1	2	
Tuticorin	C	12	13											1			
Vizagapatam	C			1									5	1			
India (French): Pondichery Territory	C		3	2													
Indo-China (see also table below): Saigon and Cholon	C	1		2			2		1		4	2	1			2	

[1] For 2 weeks.

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

SMALLPOX—Continued

[C indicates cases; D, deaths; P, present]

Place		Oct. 16–Nov. 12, 1932	Nov. 13–Dec. 10, 1932	Dec. 11, 1932–Jan. 7, 1933	Jan. 8–Feb. 4, 1933	Week ended— February 1933 11	18	25	March 1933 4	11	18	25	April 1933 1	8	15	22	29
Iraq:																	
Baghdad	C	10	31	13	8	2	1	1		1			1			1	1
Basra	C	85	81	25	6	2		1				1	1				
Ireland: Belfast	C							1									
	D							1									
Japan:																	
Kobe	C									1	1	1	2				
Nagoya	C							1									
Osaka	C					1	1	1		1	1		1	3	4		
Tokyo	C										1	1					
Yokohama	C															1	
Mexico:																	
Coahuila	C								1								
Juarez	C					3											5
Mexico, D. F	C	4	2		10	3	1	1				6					
Monterrey	C	1															
Saltillo	D	3	11	8	4	1	3			1		2			1		
San Luis Potosi	D	3		2												1	
Torreon	C	1															
Morocco. (See table below).																	
Nigeria	C	56	1,581	583	401		291	2	1,585		444	3					
Persia	C	404	341	216	108		14	6	9	4	12	5	5	3	5		
	D	166	150	82	41		3		1	1	1	1	1	1	2		
Peru. (See table below.)																	
Poland	C			1													
Portugal:																	
Lisbon	C	5	9	12	4	3			1		1	1		1		1	
Oporto	C	1	14	9	5	2	1	2		1		1					
Siam: Bangkok	D				2		1	1			2	2					
Sierra Leone	C		13	10	217		29		7				63				
Sudan (Anglo-Egyptian)	C	8			57	13	12	4	5	19	6	3	4		12	1	5
Syria. (See table below.)																	
Turkey. (See table below.)																	
Union of Socialist Soviet Republics. (See table below.)																	

Union of South Africa:																		
Cape Province	C	P	P	P			P	P	P	P	P	P						
Orange Free State	C	P	P	P					P	P	P	P	P					
Transvaal	C		P	P														
Zanzibar	C						2											
On vessels:																		
S.S. Amassis at Alexandria	C				1													
S.S. British Engineer at Marseille	C		1															
S.S. Somersetshire at Suez	C		1		1													
S.S. British Splendour en route to Gibraltar	C		1															
S.S. Jervis Bay en route to Southampton	C		1															
	D		1															
S.S. Star of Alexandria at Alexandria	C			1														
S.S. Kohistan at Aden from Basra	C		1															
S.S. Volturno at Alexandria	C									1								
S.S. Arimondi at Massaoua	C									2								
S.S. Hatasu at Malta	C										1							
S.S. Talma at Hong Kong	C								1									
S.S. Karapara at Rangoon	C								1									
S.S. Nawab at Rangoon	C				1													
S.S. California at Liverpool	C												1					
S.S. Kalgan at Bangkok from Swatow	C											1						

Place		October 1932	November 1932	December 1932	January 1933			February 1933			March 1933			April 1933	
					1-10	11-20	21-31	1-10	11-20	21-28	1-10	11-20	21-31	1-10	11-20
Indo-China (see also table above)	C	157	180	213	168	65	20	29	98	60	167	83			
	D	46	51	45	38	17	3	16	33	28	55	30			
Syria: Beirut	C		41	49	5	10	19	11	8		2	11	7	3	35

Place		October 1932	November 1932	December 1932	January 1933	February 1933	March 1933
Chosen	C				7	17	30
Gold Coast	C	3					
Greece	C					3	55
Morocco	C	33	53	81	14	14	
Peru	C	75	67		38		

Place		October 1932	November 1932	December 1932	January 1933	February 1933	March 1933
Turkey	C	13			5		
	D	1					
Union of Socialist Soviet Republics	C	641					

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

TYPHUS FEVER

[C indicates cases: D, deaths; P, present]

Place		Sept. 18–Oct. 15, 1932	Oct. 16–Nov. 12, 1932	Nov. 13–Dec. 10, 1932	Dec. 11, 1932–Jan. 7, 1933	Week ended— January 1933			February 1933				March 1933				April 1933				
						14	21	28	4	11	18	25	4	11	18	25	1	8	15	22	29
Algeria:																					
Algiers	C	11	7	2			1	2	1	1			30	24	35	39	18	4	41	101	
Bone	C	2		1			1			1			1								
Constantine Department	C			3		1		2		1	3	34	26	21	32	16	4	3	36	96	
Argentina: Buenos Aires	C							6													
Bolivia. (See table below.)																					
British East Africa: Uganda	C	16	19	16	17	3	8	2	4	4	4	7	4	3	9						
Bulgaria	C			12	5	2						4	5	24	18	6					
Chile (see also table below)	C	61	41	166	223	81	65	84	68	47	34	51	52	23	30						
Antofagasta	C		1						1		1								1		
China: Hankow	C					3						5									
Colombia: Cali	D	1		1																	
Egypt:																					
Alexandria	C				1	1														6	6
Beheira	C	21		2					40							43					
Cairo	C															2	4	1	10	19	12
Gharbieh	C	1												70							
Port Said	C	1	1	1																	
Provinces	C	3			59	28			143				134		178						
Greece. (See table below.)																					
Guatemala. (See table below.)																					
Ireland: Belfast	C											1									
Irish Free State:																					
Cork County—Bandon	C	1																			
Dublin	C	2																			
Kerry County—Killarney district	C		1	16	5																
Lithuania. (See table below.)																					
Mexico:																					
Mexico, D.F.	C	3	11	10	3			2		3	6	2		5	1	4					
San Luis Potosi	D															1					
Torreon	C			2																	
Morocco	C	2		22	43	10	9	14	30	4	4	66	64	11	26	9		3	6	6	
Palestine	C	5	2	2	1	1						1	1	1		2		1		1	
Persia	C	16	2	11	16	3	3	6	4	7	13	1	19	9	4	2	13		18		
Peru. (See table below.)																					

Poland	C	120	63	65	152	40	68	74	95	86	77	94	93	91	93	64	87	92	87	------	------
	D	9	13	6	8	6	9	4	7	6	4	5	5	8	6	2	4	8	6	------	------
Portugal: Oporto	C	1	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------
Rumania	C	9	7	121	254	59	89	71	------	71	62	80	63	61	63	66	------	------	------	------	------
Tunisia: Tunis	C	------	------	1	9	4	6	25	------	1	20	8	5	2	10	24	9	4	17	26	------
Turkey. (See also table below): Istanbul	C	1	1	------	3	------	------	5	------	------	------	1	------	3	------	1	------	------	------	------	------
Union of Socialist Soviet Republics. (See table below.)																					
Union of South Africa:																					
Cape Province	C	P	P	P	P	P	P	P	------	P	P	P	P	------	------	P	P	------	------	------	------
Natal	C	P	P	P	P	P	------	------	------	P	P	P	P	P	------	P	------	------	------	------	------
Orange Free State	C	P	P	P	P	P	P	P	------	P	P	P	P	P	------	P	P	------	------	------	------
Transvaal	C	------	------	P	P	P	P	P	------	------	------	------	------	P	------	------	------	------	------	------	------
Yugoslavia. (See table below.)																					
On vessel: S.S. Munplace at New Orleans from Progresso	C	------	------	------	------	------	------	1	------	------	------	------	------	------	------	------	------	------	------	------	------

Place		October 1932	November 1932	December 1932	January 1933	February 1933	March 1933
Bolivia	C	------	------	4	29	33	------
Chile: Coquimbo Province	C	------	60	------	------	------	------
Greece	C	4	------	15	10	2	------
Guatemala	C	------	------	3	6	9	11
Lithuania	C	------	1	10	36	13	12

Place		October 1932	November 1932	December 1932	January 1933	February 1933	March 1933
Peru	C	81	75	111	81	------	------
Turkey	C	11	15	14	23	11	8
Union of Socialist Soviet Republics	C	1,727	------	------	------	------	------
Yugoslavia	C	------	3	11	35	125	12

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

YELLOW FEVER

[C indicates cases; D, deaths; P, present]

Place		Oct. 16–Nov. 12, 1932	Nov. 13–Dec. 10, 1932	Dec. 11, 1932–Jan. 7, 1933	Jan. 8–Feb. 4, 1933	Week ended— February 1933			March 1933				April 1933					May 6, 1933
						11	18	25	4	11	18	25	1	8	15	22	29	
Brazil:																		
Ceara State	C	1	1															
Piauhy State	D			1														
French West Africa: Guinea	C	2	4															
	D	2	4															
Gold Coast	C						1		1									1
	D						1		1									
Guinea (Portuguese): Bissagos Islands	C				44													
	D				14													
Senegal	C	8																
	D	5																
Bakel	C												1					
Dagana	C										1							
	D										1							
Podor	C											1						
Sudan (French): Keyes	C	4	2															
	D	4	2															