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THE NATURE OF THE SOLUBLE ANTIGEN FROM TYPHUS RICKETTSIAE [1]

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When a suspension of the rickettsiae responsible for either epidemic or endemic typhus fever is extracted with ether, a "soluble" antigen (*1*) may be liberated which has many of the immunological properties of the organisms themselves. This antigen, whose active principle is small enough to pass the usual bacterial filters, is highly active in the complement-fixation and precipitin reactions (*2*). The epidemic antigen can be used in place of the organisms themselves as an effective preventive vaccine. The electron microscope has been employed to determine the character of the elementary particles in these soluble antigens and to find out how they are derived from the organisms by the ether treatment.

Most of the rickettsial suspensions for these experiments have been prepared from the yolk sacs of chicken embryos diseased with either the Breinl strain of epidemic typhus or the Wilmington strain of endemic typhus. A few observations have been made on endemic typhus rickettsiae from mouse lung and on chick-grown Q fever rickettsiae. Suspensions rich in organisms were prepared by the procedures used for the production of antigen for complement fixation. This was done by freeing diluted, ground yolk sacs from large tissue fragments by a preliminary low-speed centrifugation. The organisms in such a clarified suspension were then sedimented and thus separated from soluble material by a high-speed centrifugation carried out for an hour at 4,000 r. p. m. in an angle centrifuge. Taken up in a limited volume of suspending fluid these rickettsiae have been examined in the electron microscope immediately and after extraction with ether. As usual this extraction was carried out by shaking the suspension with not less than a volume and a half of anesthetic ether. After the mix-

[1] From the Division of Infectious Diseases and the Industrial Hygiene Research Laboratory, National Institute of Health.

ture had stood till there was a separation of phases, the aqueous phase was withdrawn, and the ether removed from it at reduced pressure. The physical characteristics of the extracts prepared in this way depended on whether the ether extraction was made at room temperature or in the cold. If it was done at room temperature, most of the rickettsiae were removed by recentrifugation at high speed without serious loss of antigenically active material. Such an active supernatant is the "soluble" antigen. If, on the other hand, extraction was made in the cold, the antigenic principle remained with the rickettsiae and was thrown down almost quantitatively with them. Electron micrographic study was made: (1) Of suspensions from chicken embryo and mouse lung material after centrifugal purification; (2) of such partially purified suspensions (of chick origin) after cold- and warm-ether extractions; and (3) of soluble antigens prepared, as indicated above, by recentrifugation of warm-ether extracts.

These suspensions were prepared for electron microscopic examination by drying microdrops onto the usual collodion-covered screens which were then washed with distilled water when salts had to be removed and finally were shadowed (*3*) by being covered with suitably thin obliquely deposited films of metal. In most of the present work gold, evaporated in vacuum to a calculated thickness of ca. 8 A, was the shadowing metal. Finished preparations were examined and photographed with an RCA type EMU electron microscope.

A concentrated suspension of typhus, or of Q fever rickettsiae shows the organisms enmeshed in a thin membranous material suggestive of bacterial capsules (figs. 1 and 2). In more dilute suspensions this material is associated with the individual cells (fig. 3). There does not seem to be an observable difference in either cell morphology or in the appearance of this capsular substance between Breinl and Wilmington rickettsiae or between the endemic typhus grown in eggs or in mouse lungs. The cell walls of many bacteria, as seen in the electron microscope, resemble this capsule in being flat, sharply bounded structures surrounding thicker central protoplasm. The present photographs, however, make it clear that while the rickettsial capsule may be attached to individual organisms, it usually does not completely envelop them.

Extraction with ether at room temperature does not alter the appearance of the rickettsiae themselves but it does profoundly affect their capsules. These are more or less completely broken up into shreds and droplets, some of which continue to adhere together and to the cells to which they probably were attached before treatment (fig. 4) while others are also freely distributed as tiny droplets over the surface of the preparation (fig. 5). Centrifugation at 4,000 r. p. m. throws down the rickettsiae from such an extract but leaves the droplets in suspension. A preparation of soluble antigen obtained by such a centrifugation gives electron micrographs (fig. 6) showing nothing but

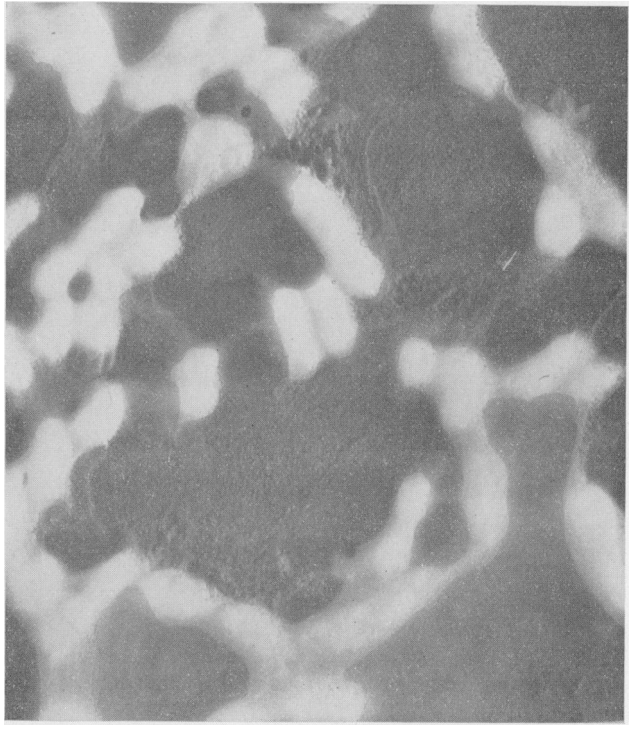

FIGURE 1.—An electron micrograph of a field from a fairly dense suspension of rickettsiae of the Wilmington strain of endemic typhus, grown in yolk sac. This and all the following photographs are negative prints. (Magnification, as determined by calibration with the replica of an optical grating, 18,000 ×.)

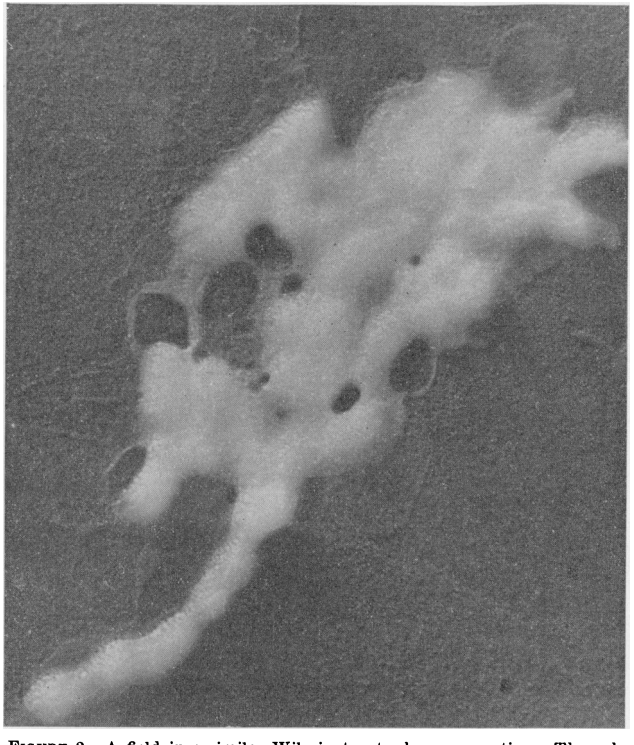

FIGURE 2.—A field in a similar Wilmington typhus preparation. The substrate in this instance was formvar; in all others it was collodion. (Magnification, 18,000 ×.)

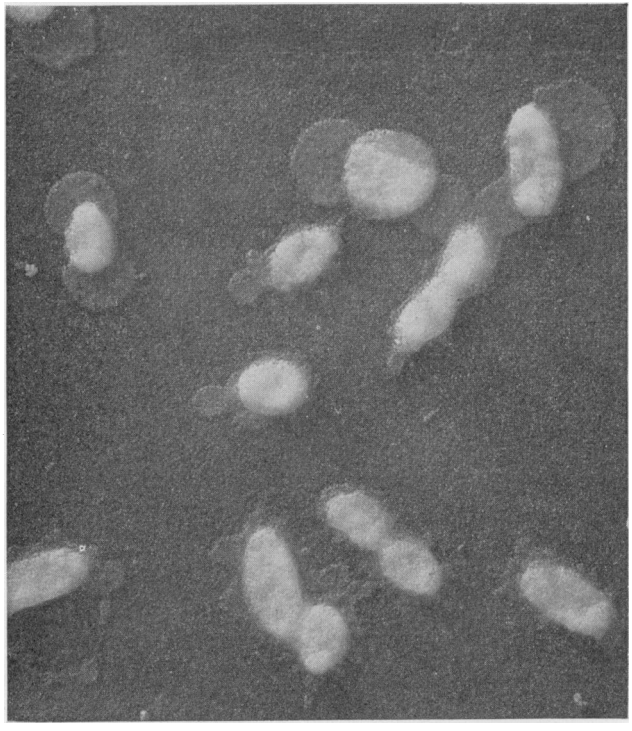

FIGURE 3.—A field in a more dilute Wilmington typhus preparation. This suspension was from infected mouse lung. (Magnification, 18,000 ×.)

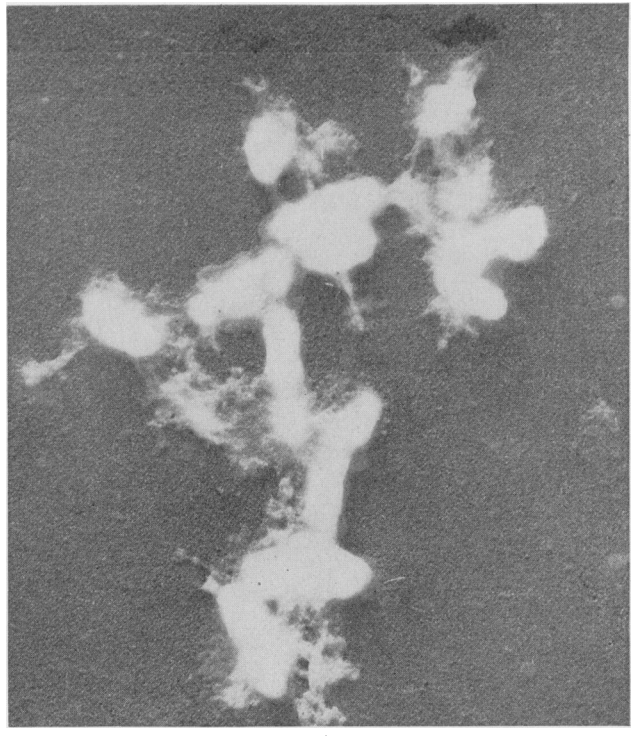

FIGURE 4.—A field from a Breinl typhus preparation, which had been extracted with ether at room temperature. The disintegration of the capsular material is evident. (Magnification, 18,000 ×.)

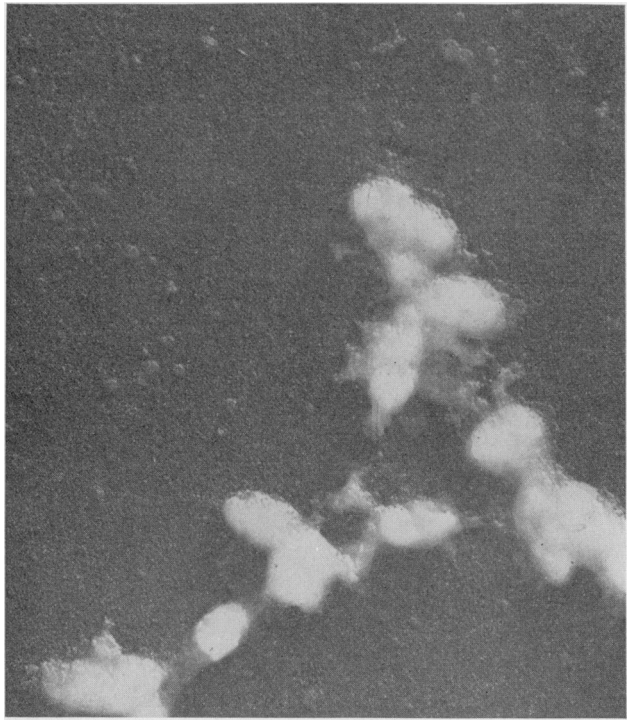

FIGURE 5.—A field in another Breinl typhus preparation extracted with warm ether. Many free droplets of soluble antigen are distributed over the substrate. (Magnification, 18,000 ×.)

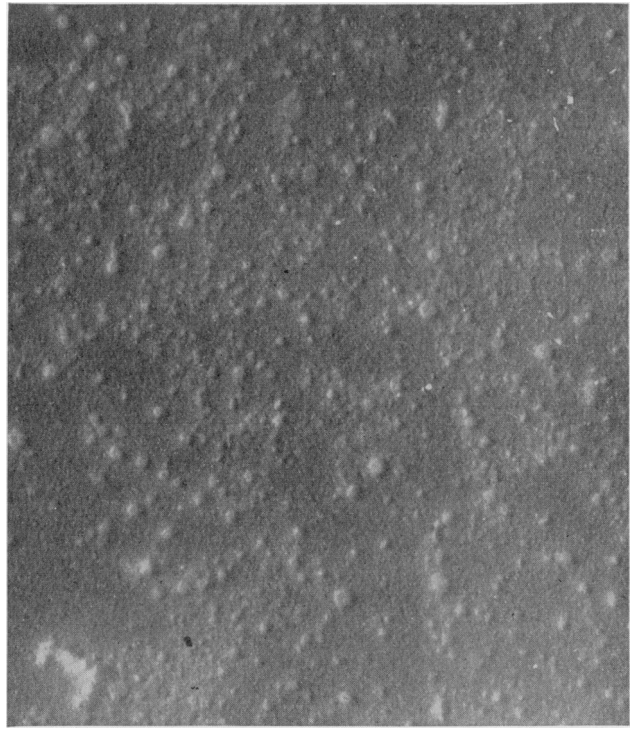

FIGURE 6.—A field in a preparation of Wilmington typhus soluble antigen. (Magnification, 18,000 ×.)

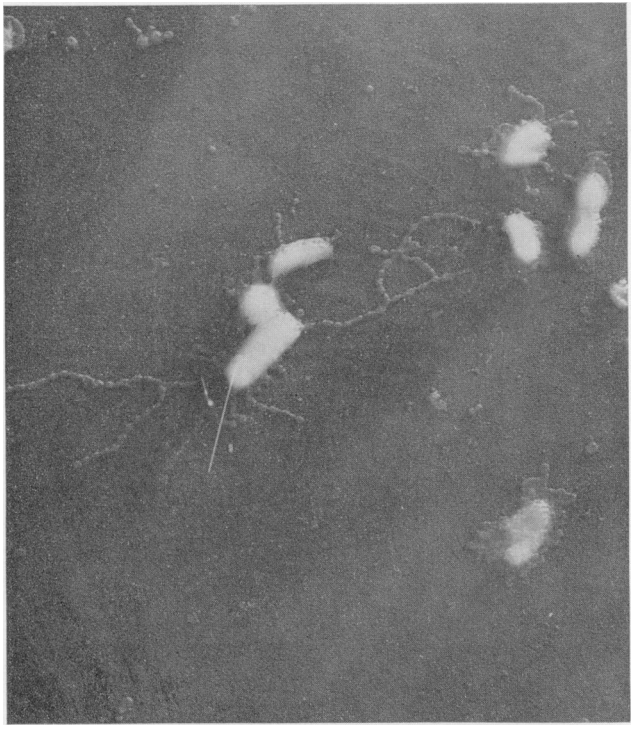

FIGURE 7.—A field in a breinl typhus preparation extracted with ether in the cold. The beaded beginnings in the break-up of the capsular stuff are especially well shown in this micrograph. (Magnification, 11,000 ×.)

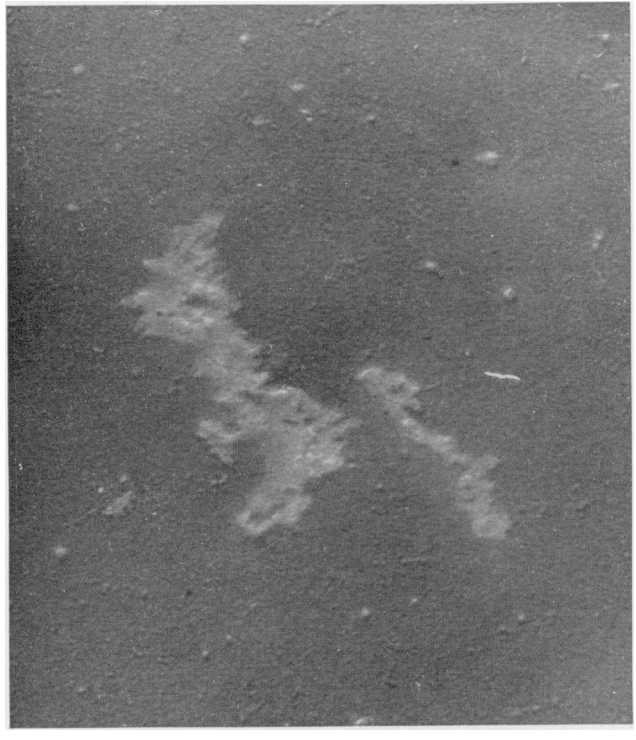

FIGURE 8.—A field in a preparation that is a mixture of Wilmington typhus soluble antigen and anti-Wilmington typhus rabbit serum. Most of the droplets of antigen have been agglutinated by the serum. (Magnification, 18,000 ×.)

these drops, which thus appear as its essential constituent. They are not uniform in size but in the preparations examined their diameters have had such small values that most could pass through bacterial filters.

When the extraction is carried out in the cold, the capsules about many but not all cells are damaged, but this damage rarely has progressed to the point where the droplets have been broken up and liberated into the preparation (fig. 7). This agrees with the fact that very little antigenic activity is associated with the soluble antigen fraction prepared in the cold.

Confirmation of the rickettsial origin of the droplets in preparations of soluble antigen has been obtained by photographing mixtures of the antigen with antirickettsial serum. When typhus rickettsiae are mixed with antityphus rabbit serum, the organisms are specifically agglutinated; the same serum also agglutinates the particles of the corresponding soluble antigen (fig. 8).

SUMMARY

From these observations it would appear that the so-called soluble antigen of typhus, and presumably of other rickettsiae consists of submicroscopic particles of a capsular substance. This substance adheres to and partly envelops the organisms seen in a centrifugally purified rickettsial suspension. It is broken up, and in a sense emulsified, by treatment with warm ether. Micrographs of cold-extracted suspensions show that in them the capsular breakup has begun but has not progressed to the stage of freeing many droplets of the soluble antigen. These droplets are agglutinated by antityphus serum.

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ANTIBACTERIAL ACTION OF PENICILLIN, PENICILLIN X, AND STREPTOMYCIN ON *HEMOPHILUS INFLUENZAE* [1]

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The use of crude penicillin by Fleming (*1*) to aid in the isolation of *Hemophilus influenzae* illustrates the relative resistance of this organism to penicillin. Recent reports, however, suggest that *H. influenzae* may at times be somewhat sensitive to the penicillin which is now available. Forgacs, Hutchinson, and Rewell (*2*) reported two type b strains isolated from cases of meningitis which were as sensitive to penicillin as the standard Oxford strain of staphylococcus and concluded that one of their two cases showed some evidence of beneficial response to penicillin. Straker (*3*) reported two strains which appeared to be sensitive to penicillin although their precise sensitivity is not given, it being stated that the circle of inhibition obtained with filter-paper discs was less than half that obtained when a sensitive *Staphylococcus aureus* was employed as a test organism. Several cases of *H. influenzae* meningitis have also been treated with sulfonamides and penicillin by Bonaba et al. (*4*), (*5*), all of which recovered, but it is difficult to conclude what action, if any, the penicillin had in attaining clinical cure; the *in vitro* sensitivity of the cultures isolated from these cases was not reported.

In the present investigation we have studied the penicillin sensitivity of a relatively large number of *H. influenzae* cultures. Streptomycin also was studied because of its greater activity against certain gram-negative bacilli. The activity of these agents was tested both *in vitro* and *in vivo*, also in combination with antiserum and with sulfadiazine. The latter seemed indicated in view of the effectiveness of the combination of antiserum and sulfadiazine in the treatment of experimental *H. influenzae* infections in mice, Pittman (*6*) and Alexander and Leidy (*7*), and of meningeal *H. influenzae* infections in humans, Alexander (*8*) and Sako et al. (*9*).

MATERIALS AND METHODS

Cultures.—Thirty-eight cultures of *H. influenzae* and 2 cultures of *H. parainfluenzae* were used. Of the former, there were 3 type a, 23 type b, 1 type c, 1 type d, 1 type e, 2 type f, and 7 non-type-specific strains. All were isolated from human infections, the majority

[1] From the Division of Infectious Diseases and the Biologics Control Laboratory, National Institute of Health.

being isolated from spinal fluid and a smaller number from the respiratory tract and from the blood. All cultures with the exception of 5 had been maintained since isolation under optimum conditions, that is, in defibrinated blood or in the dried state. The other 5, which will be noted later, had been maintained many years on blood agar slants. The type b cultures used in the *in vivo* tests were all of maximum virulence.

Antibiotics.—The sodium penicillin used was a commercial preparation of about 500 units per milligram, the exact potency of which was assayed against a sample of standard calcium penicillin (370 units per milligram), using *S. aureus* 209 as the test organism. A commercial preparation of penicillin X was used which was designated by the manufacturer as "90 percent or over penicillin X." The potency of this preparation was determined as above. A commercial preparation of streptomycin hydrochloride for parenteral use was standardized against a sample of pure streptomycin hydrochloride of potency of 800 units per milligram, using *Bacillus circulans* as the test organism. Standardized solutions of these antibiotic agents were used in performing the *in vitro* and *in vivo* tests.

Method of testing for antibacterial action in vitro.—The simple fluid medium devised by Stebbins and Robinson (*10*) for the assay of streptomycin supported growth of *H. influenzae* satisfactorily if Fildes' peptic digest of blood (*11*) was added to 1 percent concentration. Peptic digest of blood did not interfere with the assay for potency of penicillin, using *Bacillus subtilis*, or of streptomycin, using *B. circulans*.[2] A simple twofold serial dilution technique similar to that described by Randall et al. (*12*) was employed for determining the sensitivity of the different strains of *H. influenzae*. Serial dilutions of the antibiotic agents were made in 13-mm. test tubes; then each tube was inoculated with a 16–18 hour broth culture; the final dilution of the culture was 1: 100 in a volume of 2 ml. The test tubes were incubated 16 to 18 hours at 37° C., then examined for inhibition of growth, which was clearly defined in all cases.

Method of testing for antibacterial action in mice.—The method of preparing the cultures in a solution of mucin for inoculation into 15–19 gm. white mice was as previously described (*6*). The mice were inoculated in groups of 10 or 20. The antibiotic agents dissolved in physiological saline were administered subcutaneoulsy in 0.5-ml. doses, the initial dose being given approximately 30 minutes before intraperitoneal inoculation of the organisms and subsequent doses at 4-hour intervals. The method of preparation and administration of antiserum and sulfadiazine was similar to that used previously by Pittman (*6*); each was given 1 hour preceding the inoculation of the

[2] The cultures of *B. subtilis* and *B. circulans* and samples of standard calcium penicillin and streptomycin hydrochloride were kindly furnished by Drs. Wm. A. Randall and C. W. Price of the Food and Drug Administration.

culture. The serum was administered intraperitoneally and the sulfadiazine orally. The infective dose consisted of approximately 100,000 MLD in mucin administered intraperitoneally. The mice were kept under observation for 96 hours. Peritoneal smears and heart's blood cultures were made from mice that died to determine specificity of death and only specific deaths are recorded in the following tables.

EXPERIMENTAL

The sensitivity of 38 cultures of *H. influenzae* and 2 cultures of *H. parainfluenzae* to commercial penicillin (predominantly penicillin G), penicillin X, and streptomycin is presented in table 1. The range of sensitivity to these substances was as follows:

Penicillin.....0.18–1.5 units per milliliter.
Penicillin X.....0.05–0.75 units per milliliter.
Streptomycin.....1.25–10.0 units per milliliter.

TABLE 1.—In vitro *sensitivity of various cultures of* H. influenzae *and* H. parainfluenzae *to penicillin, penicillin X and streptomycin*

Culture No.	Type	Penicillin		Penicillin X		Streptomycin	Pathological source
		Unit	Microgram [1]	Unit	Microgram [1]	Microgram [1]	
H. influenzae:							
571	b	0.18	0.11	0.18	0.18	2.5	Meningitis.
572	b	.37	.24	.05	.05	2.5	Do.
573	b	.18	.11	.18	.18	2.5	Do.
574	b	.37	.24	.18	.18	2.5	Do.
575	b	.75	.45	.18	.18	2.5	Do.
576	b	1.5	.91	.18	.18	5.0	Do.
577	b	.37	.24	.18	.18	2.5	Do.
581	b	.18	.11	.18	.18	2.5	Do.
583	b	.37	.24	.18	.18	2.5	Do.
584	b	.37	.24	.18	.18	2.5	De.
591	b	.18	.11	.18	.18	1.25	Do.
599	b	.37	.24	.18	.18	2.5	Do.
623	b	.18	.11	.18	.18	2.5	Do.
635	b	.18	.11	.18	.18	1.25	Do.
641	b	.37	.24	.09	.09	2.5	Do.
645	b	.75	.45	.09	.09	5.0	Do.
647	b	.37	.24	.75	.75	1.25	Bacteremia.
649	b	.37	.24	.18	.18	10.0	Meningitis.
650	b	1.5	.91	.37	.37	2.5	Do.
656	b	.75	.45			5.0	Do.
659	b	.37	.24	.18	.18	5.0	Respiratory infection.
665	b	.37	.24	.18	.18	2.5	Meningitis.
667	b	.37	.24	.18	.18	5.0	Do.
358+	a	1.5	.91	.75	.75	2.5	Respiratory infection.
610	a	.75	.45	.37	.37	5.0	Do.
620	a	1.5	.91	.37	.37	5.0	Meningitis.
624	c	.75	.45	.37	.37	2.5	Respiratory infection.
611	d	.37	.24	.37	.37	5.0	Do.
595	e	1.5	.91	.37	.37	5.0	Not known.
375+	f	.18	.11	.18	.18	2.5	Meningitis.
644	f	1.5	.91	.37	.37	5.0	Do.
51R+	NTS	.18	.11	.09	.09	2.5	Type b meningitis.
525	NTS	.37	.24	.18	.18	5.0	Meningitis.
544+	NTS	.37	.24	.75	.75	2.5	Respiratory infection.
579	NTS	.75	.45	.75	.75	2.5	Eye infection.
596	NTS	.37	.24	.18	.18	2.5	Not known.
640	NTS	.37	.24	.18	.18	2.5	Meningitis.
668	NTS	.37	.24	.18	.18	5.0	Respiratory infection.
H. parainfluenzae:							
535+		.37	.24	.18	.18	2.5	Meningitis.
655		1.5	.91	.09	.09	2.5	Endocarditis.

[1] Calculated on the basis of 1,650 units/mg. for pure penicillin G and 1,000 units/mg. for pure penicillin X. 1 microgram of streptomycin hydrochloride = 1 unit.

+ = Culture had been on blood agar slants 6 to 17 years.
NTS = Non-type-specific.

It was noted that the cultures carried on artificial laboratory media for long periods manifested in general the same degree of sensitivity as those strains recently isolated from pathological sources. A graphic presentation of the sensitivity of the various cultures is shown in figure 1. On the unit basis, the cultures as a whole were sensitive to one-half as much penicillin X as penicillin. The majority of both the non-type-specific and the type b cultures had the same sensitivity to the respective antibiotic. There were only seven in the former group;

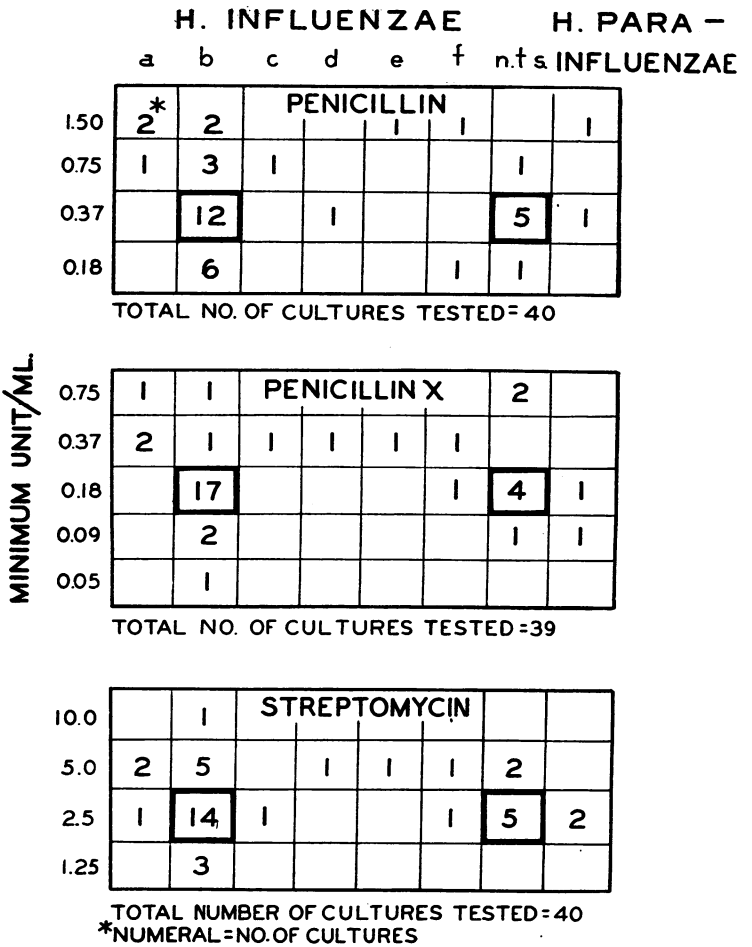

FIGURE 1.—Relative sensitivity of *H. influenzae* to penicillin, penicillin X, and streptomycin.

six had been obtained from pathological sources, the source of the seventh is not known. Straker (*3*) reported that the ordinary throat strains of *H. influenzae* are less sensitive to penicillin than the type specific. We did not have any of these throat cultures available for study.

Although no extensive morphological studies were undertaken, Gram's stains of smears made from the first tube showing growth in

the serial dilution tests showed quite definite departure from the normal control. This was most marked in the case of organisms exposed to streptomycin. The majority of the bacteria stained faintly, manifesting almost a shadowy form; a few showed darker staining granules and only an occasional organism appeared normal. In performing the capsular-swelling test with specific antiserum the organisms took the methylene blue stain poorly, a granular appearance was evident, and some of the organisms had a bulbar, club-shaped end. Very few of the organisms showed a distinct capsular swelling. Organisms exposed to penicillin also took the stain faintly, and showed a tendency to form long, thread-like rods, although some normal-appearing cells were present, and a pronounced irregularity in capsular swelling when tested with specific antiserum, yet the latter was not as marked as in the case of organisms exposed to streptomycin.

Results of treatment of mice with penicillin and streptomycin.—In tables 2 and 3 the results of treatment of experimental infections are presented. Culture 572 was relatively susceptible *in vitro* to all three antibiotic agents tested while culture 576 was relatively resistant. The

TABLE 2.—*Results of treatment of mice infected with a strain of* H. influenzae *sensitive* in vitro *to the antibiotic employed*

Therapeutic agent	Dosage				Survival
	25 units 3×	50 units 3×	100 units 3×	200 units 3×	
Penicillin	10D	9D 1S	3D 7S	2D 8S	50-percent end point—257 units.
Penicillin X	8D 2S	2D 8S	5S	9S	50-percent end point—106 units.
Streptomycin	9D	5D 4S	10S	10S	50-percent end point—160 units.
Culture control	10D				None.

Test organism: *H. influenzae* type b No. 572.

D=Mice died.
S=Mice survived.

TABLE 3.—*Results of treatment of mice infected with a strain of* H. influenzae *relatively resistant* in vitro *to the antibiotics employed*

Therapeutic agent	Dosage				Survival
	25 units 3×	50 units 3×	100 units 3×	200 units 3×	
Penicillin	10D	10D	10D	10D	None. No end point obtained.
Penicillin X	10D	10D	1D 9S	10S	50-percent end point—220 units.
Streptomycin	10D	8D 2S	2D 8S	10S	50-percent end point—212 units.
Culture control	10D				None.

Test organism: *H. influenzae* type b No. 571.

amount of therapeutic agent required to protect mice against infections with the resistant strain was considerably greater than when the infection was caused by a sensitive strain. Both strains were shown by virulence controls to be of similar virulence for mice although these data are not presented in the protocols.

The *in vivo* effect of these agents was tested using non-type-specific culture 640 with results which showed streptomycin to afford the greatest protection followed by penicillin X and penicillin in that order. Although this culture was not as virulent for mice as the type b cultures used, the degree of protection obtained followed closely the *in vitro* sensitivity to the antibiotic agents employed in essentially the same manner as the type b cultures.

Influence of streptomycin on invasion of the blood by H. influenzae.—Table 4 presents the effect of streptomycin on the blood cultures of

TABLE 4.—*The fate of bacteria in the blood of mice experimentally infected with* H. influenzae *and treated with varying doses of streptomycin*

Dose of streptomycin	Time of blood culture after treatment	Mouse No.										Results 4 days
		1	2	3	4	5	6	7	8	9	10	
	Hours											
50 units 1×	2	+	±	±	0	±	±	±	±	+	±	
	5	0	++	±	±	+	++	±	+	++	++	
	7	+	+++	+	±	+++	+++	++	++	+++	+++	
	24	D	D	D	D	D	D	D	D	D	D	10D.
100 units 1×	2	±	+	±	+	++	++	+	+	+	0	
	5	±	+	++	±	±	+	+	+	+	0	
	7	+	++	+++	++	++	++	+++	++	++	±	
	24	D	D	D	S	D	D	D	D	D	S	9D; 1S.
200 units 1×	2	0	0	0	0	0	±	+	0	+	0	
	5	0	±	±	±	±	+	±	±	±	+	
	7	±	+	0	+	+	++	++	±	++	++	
	24	S	D	D	D	D	D	D	D	D	D	9D; 1S.
300 units 1×	2	±	0	0	0	±	0	+	0	±	0	
	5	±	±	±	±	0	0	0	±	0	±	
	7	0	0	±	0	0	0	0	0	±	0	
	24	S	S	S	S	S	S	S	S	D	S	3D; 7S.
Control	2	----	±	±	+	±	±	±	±	+	+	
	5	----	++	++	++	++	++	++	±	++	++	
	7	----	+++	+++	+++	+++	+++	+++	+++	+++	+++	
	24	----	D	D	D	D	D	D	D	D	D	9D.

Test organism: *H. influenzae* type b, No. 641.

0, ±, +, ++, +++=None, very few, few, moderate number, and many colonies which grew from 1 mm. loopful of blood from tail.

Streptomycin 50-percent end point=253 units.

experimentally infected mice. Only one dose of streptomycin was administered followed in 30 minutes by inoculation with the infective dose. Blood cultures were taken at the time indicated by inoculating one loopful of blood from the tail on agar plates. Doses of streptomycin sufficient to produce high blood levels are quite effective in tending to cause rapid disappearance of organisms in the blood stream. Smaller doses of streptomycin insufficient to prevent death of the animal increased the time required for appearance of large numbers

of organisms in the blood of many of the mice. This was also evident in other experiments by the longer time of survival of animals receiving treatment as compared to the controls.

Results of treatment of mice with a combination of antiserum and streptomycin.—In table 5 the effect of combining streptomycin and

TABLE 5.—*Results of treatment of mice with a combination of antiserum and streptomycin*

Therapeutic agent	Results	Survival (percent)
Streptomycin 25 units 3×. Antiserum 0.5 ml. of 1:1600	11D; 9S	45
Streptomycin 50 units 3×. Antiserum 0.5 ml. of 1:1600	3D; 17S	85
Streptomycin 25 units 3×. Antiserum 0.5 ml. of 1:800	2D; 18S	90
Streptomycin 50 units 3×. Antiserum 0.5 ml. of 1:800	1D; 18S	95
Antiserum:		
0.5 ml. of 1:1600	9D; 1S	10
1:800	8D; 2S	20
1:400	1D; 9S	90
1:200	1D; 9S	90
Streptomycin:		
25 units 3×	10D	0
50 units 3×	5D; 5S	50
100 units 3×	2D; 8S	80

Test organism: *H. influenzae* type b, No. 641.
Antiserum 50-percent end point= 0.5 ml. of 1:594 dilution.
Streptomycin 50-percent end point= 171 units.

specific antiserum is shown. The protective activity of serum alone was shown to be slight when 0.5 ml. of 1:1,600 dilution was used inasmuch as only 10 percent of the mice survived. The effect of a total dosage of 75 units of streptomycin divided into three doses at four hourly intervals was not sufficient to prevent 100 percent mortality. However, when these two doses were combined, 45 percent of the mice survived. When antiserum diluted 1:800 was employed (which alone protected 20 percent of the mice) in combination with a total dosage of 75 units of streptomycin, 90 percent survival was obtained. Although there is a marked increase in protection obtained by combining these two therapeutic agents it is difficult to determine whether the effect is more than purely additive.

Results of treatment of mice with a combination of sulfadiazine and streptomycin.—Combined therapy of experimental infections with streptomycin and sulfadiazine is demonstrated in table 6. Whereas 0.1 mg. of sulfadiazine protected 30 percent of the mice and a total of 75 units of streptomycin resulted in no protection, the combination of the two therapeutic agents in the same amounts produced 100 percent protection. In the protocol presented, culture 576 was employed. This culture was the most sensitive to sulfonamides of 6 cultures studied previously by Pittman (*6*). She noted a difference of 6 times in sensitivity. In the present study we have observed a culture (641) which is more than 25 times as resistant to sulfadiazine

TABLE 6.—*Results of treatment of mice with a combination of sulfadiazine and streptomycin*

Therapeutic agent	Dosage				Survival
Sulfadiazine ... Streptomycin ...	0.05 mg 50 units 3×	0.1 mg 25 units 3×	0.1 mg 50 units 3×	0.2 mg 25 units 3×	100 percent survival with each combination.
	8S	10S	10S	9S	
Sulfadiazine	0.05 mg.	0.1 mg.	0.2 mg	0.4 mg	50-percent end point—0.125 mg.
	8D; 2S	6D; 3S	2D; 8S	1D; 9S	
Streptomycin	25 units 3×	50 units 3×	100 units 3×		50-percent end point—178 units.
	10D	6D; 4S	1D; 9S		
Culture control	10D				None.

Test organism: *H. influenzae* type b, No. 576.

as culture 576. This was in an experiment similar to the one given in table 6. Following treatment with the largest dose employed, 3.2 mg., only 10 percent of the mice survived, whereas 0.125 mg. afforded protection to 50 percent of the mice against culture 576 (table 6). However, a combination of 0.4 mg. of sulfadiazine and a total dosage of 150 units of streptomycin resulted in 50 percent protection as contrasted to 20 percent survival when the same amount of streptomycin alone was employed.

Results of treatment of mice with a combination of penicillin and streptomycin.—Inasmuch as streptomycin and penicillin X were the most effective of the three antibiotics studied, it was desirable to determine the influence of a combination of the two agents on the experimental infection. The results of an experiment in which culture 576 was used are given in table 7. The culture which was relativelv resistant to the antibiotics was equally sensitive per unit to streptomycin and penicillin X *in vivo*. Approximately 200 units of each agent alone protected 50 percent of the mice; similar findings were

TABLE 7.—*Results of treatment of mice with a combination of penicillin X and streptomycin*

Therapeutic agent	Dosage			Survival
Penicillin X and streptomycin.	25 units each 3 ×	50 units each 3 ×		75 units of each 73.7 percent.
	5D; 14S	1D; 18S		150 units of each 94.7 percent.
Penicillin X	25 units 3 ×	50 units 3 ×	100 units 3 ×	50 percent end point—204 units.
	10D	9D; 1S	7S	
Streptomycin	25 units 3 ×	50 units 3 ×	100 units 3 ×	50 percent end point—200 units.
	9D	6D; 1S	9S	
Control culture	10D			None.

Test organism: *H. influenzae* type b, No. 576.

reported in table 3. A combination of 75 units of each agent or a total of 150 units protected 73.7 percent of the mice, while only 11.7 percent of all the mice that received 150 units each of streptomycin and penicillin X alone survived. When the amounts were doubled the survival rates were comparable, 94.7 and 100 percent, respectively.

It is apparent that streptomycin and penicillin X are not antagonistic to each other. In combination the effect is at least additive and there is some suggestion of synergistic action, but the latter point remains to be proved.

DISCUSSION

A study of the *in vitro* sensitivity of a number of *H. influenzae* cultures to penicillin, penicillin X, and streptomycin has shown that in general streptomycin is the most effective and that penicillin X is more effective than the usual commercial penicillin (predominantly G) in inhibiting growth. The same relative effectiveness was observed in experiments with mice. The cultures did not show uniformity in relative sensitivity to the respective agents, neither did they show uniform susceptibility to a single agent, although the range of variation was not remarkably large. In the case of the penicillins, the cultures were in general about twice as sensitive per unit of penicillin X as per unit of penicillin G, although a few cultures were equally sensitive to each and one was more sensitive to G than X. Thus the sensitivity of a given strain must be determined in order to treat more intelligently the infection caused by that organism. This is emphasized by the greater amount of drug necessary to confer protection in mice experimentally infected by a culture relatively resistant to a specific drug *in vitro*.

In view of the greater effectiveness of streptomycin as shown experimentally and the fact that blood levels can be attained with streptomycin which on a unit basis are approximately 10 times greater than with penicillin, it appears that streptomycin should prove to be superior to penicillin in the treatment of *H. influenzae* infections. That streptomycin may be effective clinically has been substantiated by the report of Harrell and Nichols (*13*) which appeared just after the completion of our experimental work. They treated four cases of *H. influenzae* meningitis with "good" results; one patient, however, died 2 months later with a postmeningitis hydrocephalus. Additional forms of therapy were used with two cases.

Although it is indicated that streptomycin may be the best of the antibiotics tested for the treatment of *H. influenzae* infections, it is indicated that penicillin, particularly penicillin X, might also have some clinical efficacy. Relatively high antibiotic blood and spinal fluid levels may be obtained in man by large intramuscular and re-

peated intraspinal injections. It must be emphasized that since a high concentration of penicillin is required to inhibit growth of *H. influenzae*, initial treatment by large doses should be used to avoid the possibility of rendering the organism penicillin-resistant under conditions of subcurative levels. The influence of penicillin in interfering with or inhibiting the swelling of the capsule further serves to demonstrate an injurious action on the organism by penicillin. This action may explain the failures to obtain a direct typing of the bacteria in spinal fluids from patients who have been treated with penicillin. Several such cultures have been sent to one of the authors (Pittman) and typing by capsular swelling was successful only after repeated subculture.

In the treatment of experimentally infected mice, combinations of streptomycin and antiserum, streptomycin and sulfadiazine, and streptomycin and penicillin X seemed to be more effective than might have been expected from a summation of the activity of the respective agents. The work has not been sufficiently extensive to prove that the action is synergistic nor to conclude which combination is the most effective. We have shown that there is no correlation in sensitivity to the three antibiotic agents and sulfadiazine. Previously it had been shown that there was no correlation in sensitivity to sulfadiazine and antiserum (*6*). The latter combination has been effective in reducing the mortality of *H. influenzae* meningitis in children (*8*), (*9*), and it might be expected in treatment with an antibiotic agent that under certain conditions the most effective therapy would result from simultaneous treatment with antiserum, sulfadiazine, or another antibiotic agent.

SUMMARY

1. *In vitro* tests of 38 cultures of *H. influenzae* and 2 cultures of *H. parainfluenzae* showed their sensitivity to penicillin to vary from 0.18 to 1.5 units per milliliter, to penicillin X from 0.05 to 0.75 units per milliliter, and to streptomycin from 1.25 to 10.0 micrograms per milliliter.

2. Using a three-dose technique, streptomycin was found to be the most effective single agent in protecting mice against *H. influenzae* infections; penicillin X was the next most effective single agent.

3. Bacterial strains of the same virulence but of different *in vitro* sensitivity to the antibiotic agents tested produced infections in mice which required varying amounts of therapeutic agents for protection depending upon the *in vitro* sensitivity of the particular strain used.

4. The results of combined treatment with streptomycin and specific antiserum and with streptomycin and sulfadiazine showed a very marked complementary effect. Similar results were obtained by combining streptomycin and penicillin X.

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A METHOD FOR THE PREPARATION OF TSUTSUGAMUSHI (SCRUB TYPHUS) ANTIGEN FROM INFECTED YOLK SACS [1]

By NORMAN H. TOPPING,[2] *Surgeon*, and CHARLES C. SHEPARD,[3] *Passed Assistant Surgeon, United States Public Health Service*

Rickettsia orientalis,[4] the causative agent of tsutsugamushi, grows well in the yolk sacs of embryonated hen's eggs. Suspensions of infected yolk sacs in sterile skimmed milk have been found, at times, lethal for white mice when 0.5 cc. is given intraperitoneally in dilutions of 10^{-8} and 10^{-9}. Smears of infected yolk sacs have repeatedly shown large numbers of rickettsiae, yet great difficulty has been experienced in preparing satisfactory antigens from this material. When yolk sacs have been ground, a stable emulsion has formed that

[1] From the Division of Infectious Diseases, National Institute of Health. This paper was approved for publication February 7, 1945, and scheduled for publication in PUBLIC HEALTH REPORTS in the issue of March 2, 1945. Because of the subject matter the paper was withheld from publication at that time.

[2] Member of the United States of America Typhus Commission.

[3] Assigned to the United States of America Typhus Commission.

[4] Strains of *R. orientalis* for this and other studies of tsutsugamushi have been obtained through the courtesy of the United States of America Typhus Commission.

could be deemulsified with difficulty. Alternate slow freezing and thawing has sometimes broken the emulsion with the formation of a cream layer at the top of an aqueous layer. At times, insoluble tissue has separated, either falling to the bottom or rising to the cream. This deemulsification has not occurred with any great degree of regularity.

Diethyl ether has been tried in a manner similar to its use in the preparation of epidemic typhus vaccine. Here, however, the antigen has usually been found in the emulsion interface that separates the aqueous phase from the excess ether. Some modifications of this technique have been tried, such as coupling the method with freezing and thawing, but antigens satisfactory either in potency or appear, ance did not result. Other fat solvents such as carbon tetrachloride-chloroform, toluene, xylene, and petroleum ether have been substituted for ether in this method with no success in breaking the emulsion.

Centrifugation of the emulsions has resulted in a splitting of the antigen into the sediments and supernatants even when slow speeds were used. On the other hand 1 hour at 4,000 r. p. m. in the angle centrifuge did not result in sedimentation of all the antigen. However, a method has been developed which produces an antigen specific in the complement-fixation test and very clear in appearance.

METHODS [5]

Infected yolk sacs which had been stored at approximately −40° C. were thawed, weighed, and pooled. They were placed in a wide-mouthed bottle together with about 10 volumes of cold diethyl ether (U. S. P.). The mixture was shaken for 2 hours in the cold room (4° C.) in a mechanical shaking machine. (Glass beads may be used to facilitate the disruption of the membranes and thereby aid in the lipoidal extraction.) The ether turned a deep orange color; the membranes partially disintegrated and became a brownish red amorphous mass.

The mixture was removed from the shaker and allowed to stand in the cold for a few moments until the tissue had completely settled to the bottom of the bottle. The colored ether was removed by decantation and the ether in solution was reduced by a partial vacuum from a water pump. The amorphous mass was then suspended in 2 or 3 volumes of saline containing 0.1 percent formalin and thoroughly ground in a Waring blender. Additional formol-saline was added so that the final fluid volume was approximately 10 times the original weight of the infected yolk sacs. The resulting suspension bore but little resemblance to an ordinary crude 10-percent emulsion of yolk sac. Since the yolk sacs were defatted before blenderizing, the result was a suspension rather than an emulsion.

[5] Since this manuscript was submitted for publication several modifications in this technique have been made by the authors and are to appear in a later publication.

Further purification and concentration at this stage can be accomplished by a variety of procedures. Centrifugation at speeds up to 4,000 r.p.m. for 10 or 15 minutes throws down a considerable quantity of sediment which when resuspended to volume in saline is inactive by complement fixation and for this reason probably can be discarded. The supernatant is active and therefore may be fractionated further. Occasionally there may be some fat and bits of tissue in the supernatant that can be removed by filtering through a layer of cotton.

Ammonium sulfate, $(NH_4)_2\ SO_4$, may be used to precipitate and concentrate the antigen. With some modifications, the method described by Stanley (*1*) for the isolation and purification of tobacco mosaic virus has been found useful. The centrifuged supernatant that has passed through cotton is further clarified by filtration through "Hyflo Supercel." [6] The antigen in the filtrate is insoluble in 40-percent ammonium sulfate but soluble in saline, distilled water, or 20-percent ammonium sulfate. These differences in solubility allow for fractionation and concentration. The clarified filtrate is brought to a 20-percent concentration by adding, with constant agitation, the proper amount of ammonium sulfate (A. C. S. specification). A turbidity develops after the filtrate stands a few minutes. This is removed by filtering through another layer of Supercel. Sufficient ammonium sulfate is added to the filtrate to bring the total concentration of the salt to 40 percent. A heavy precipitate forms if the mixture is allowed to stand for a few moments. This precipitate, containing the antigen, is collected upon Supercel. The filtrate has, after dialysis, been found to be inactive by complement fixation and is therefore discarded. The filter paper and Supercel are placed in saline or distilled water and shaken vigorously for a few moments to elute the antigen and aid in its solution. The quantity of saline or water used for elution will determine the amount of concentration of the antigen. We have been concentrating 10 times (10 ×) by this method. The Supercel is removed by a final filtration with the antigen remaining this time in the filtrate. The antigen may contain an undesirable concentration of ammonium sulfate which can be reduced by dialysis in a cellophane tube against running water.

An alternate method using cold ethanol in varying concentrations in the cold also can be used. The main portion of the antigen is soluble in 8-percent ethanol but insoluble in 25-percent. The relatively inactive precipitate which forms in 8-percent ethanol can be separated by centrifugation at 0° to 4° C. The supernatant, containing the antigen, can then be brought to a 25-percent concentration by adding cold ethanol.

[6] A filter aid produced by the Johns Manville Co.

A heavy precipitate forms which can be separated by centrifugation in the cold. The precipitate can then be brought to the desired volume in saline. Traces of ethanol remaining may be removed by dialysis.

DISCUSSION

The defatting of whole yolk sacs by ether in the cold allows the preparation of a crude tissue suspension that is susceptible to further purification and concentration. It appears that this procedure had best be done with temperature control. Extractions made at room temperature have indicated a loss of antigen. When extracting, the amount of ether is also a factor, as with 5 volumes the fat is not entirely removed, since the resulting suspension is more turbid than when 10 volumes have been used. There seems to be no advantage in using larger volumes. When several changes of ether were used there was a considerable loss in antigen, perhaps as much as 50 percent (as estimated by complement fixation). Fulton and Begg (*2*) have indicated some slight denaturation of epidemic typhus antigen when ether was used in processing the yolk-sac emulsions. Such change, however, does not seem to interfere with the immunogenic properties of epidemic typhus vaccine.

There is some loss of antigen, probably by adsorption, in passing through Supercel. Stanley's studies (*1*) of tobacco mosaic virus indicated that some virus could always be demonstrated on the celite filter. His final highly purified product contained, however, approximately 80 percent of the original infectious material. In our studies, by dissolving the precipitate that occurs in 40-percent ammonium sulfate in less than the original volume of saline, not only the loss can be compensated for but actual concentration can be accomplished.

The ethanol or the ammonium sulfate may further denature the antigen; both final products are, however, active when tested by complement fixation. In limited studies it seems that there is more loss with the ethanol technique than with ammonium sulfate. The potency by complement fixation does not seem to depend upon the presence of rickettsiae stainable with methylene blue. The immunizing properties of the various preparations of antigens are under investigation at the present time.

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A CHARTER FOR SCHOOL HEALTH

A Review

The 1945 revision of "Suggested School Health Policies," [1] carries the significant subtitle "A Charter for School Health." The report is offered as "a clear, comprehensive, printed statement of the consensus of well-informed professional opinion concerning many specific policies which directly or indirectly affect the health of children and adults." The report is not a blueprint of a school health program that can be applied uniformly and inflexibly to every community, but it is a guide which all concerned with school health programs in any capacity can consider and adapt to their local conditions.

Schools have definite responsibilities for protecting the health of pupils and have tremendous opportunities to improve the health of pupils and communities. The title "Suggested School Health Policies" indicates that these responsibilities may be met and these opportunities utilized by action based on the following recommendations.

Schools can:

Organize a school health council;

Make provision for healthier school living by raising their standards of inspection for safety and sanitation, by employing more understanding and emotionally stable teachers, by paying more attention to the health of school personnel, and even by serving better food;

Improve the quality of health and safety instruction by according more time, securing better-qualified teachers, granting more scholastic credit and providing more adequate teaching materials;

Clarify and sharpen their programs for the prevention and control of communicable diseases and avoidable accidents:

Institute wider programs of health counseling, including keener teacher observation, more frequent screening tests, and more useful medical and psychological examinations;

Enforce more intelligent precautions in physical education and athletic programs;

Identify sooner and provide more sensibly for handicapped children;

Provide in-service education to help teachers to understand the health problems of children;

Participate in programs of parent and community health education; and

Seek qualified medical advisers, nurses, health educators, and other necessary specialized health personnel.

School health programs are recognized as cooperative activities in which many individuals take part, including teachers, school administrators, physicians, nurses, psychologists, and dentists. The protection and improvement of the health of children requires coordinated efforts by parents, pupils, the schools, the health department, pro-

[1] Report prepared by the National Committee on School Health Policies of the National Conference for Cooperation in Health Education.

fessional health groups and others. "Cooperation is the keynote essential to the coordination of the efforts of all concerned with child health. Only in this way can schools and communities develop balanced programs of health education and health care. Only thus can a school avoid false emphasis on one phase of its health program with corresponding neglect of other equally vital areas. School health policies must be formulated to achieve the maximum cooperation and coordination both within each school and each school system and between each school and the community."

The report recommends that school health programs include health counseling. This is described as "the planned, cooperative effort on the part of teachers, nurses, physicians, psychologists, dentists and others to discover the health needs and health problems of students and to help them and their families find ways of meeting the needs and solving the problems. Determining health needs and problems involves the use of teacher observations, screening tests, reports from pupils and parents, psychological examinations and medical examinations. Each of these methods is used effectively in a well-planned program. The value of health counseling depends in part on the complete utilization of all community resources for protecting and improving health and, if necessary, augmenting these resources."

In order that health counseling shall actually improve the health of pupils it is essential that resources for medical and dental treatment be adequate. "A school may properly insist that all community resources be made available to meet the health needs of the students in the school. Such resources would naturally include appropriate opportunities for specialized medical consultation of a diagnostic nature. When resources outside the school or school system are utilized (whether private physicians, public clinics or voluntary agencies), efficient liaison arrangements must be made by the school. In particular, full provision should be made for two-way exchange of pertinent information between the school and the cooperating community agencies."

Suggested School Health Policies,[2] a 46-page pamphlet, includes recommendations relating to all aspects of school health programs. Specific sections are devoted to each of the following topics: (1) Provisions for healthful school living, (2) health and safety instruction, (3) services for health protection and improvement, (4) health aspects of physical education, (5) education and care of the handicapped, and (6) qualifications of school health personnel.

The National Committee on School Health Policies included representation from different national professional groups. The

[2] Single free copies may be secured from the American Medical Association, 535 N. Dearborn St., Chicago 10, Ill. Sale copies may be obtained from the Health Education Council, 10 Downing St., New York 14, N. Y.

names of members, together with the name of the organizations which nominated them for membership, are as follows:

W. E. Ayling, M. D., American School Health Association.
W. W. Bauer, M. D., American Medical Association.
Edward S. Evenden, Ph. D., American Association of Teachers Colleges.
Raymond A. Green, M. A., Secondary School Principals Association.
W. H. Lemmel, Ed. D., American Association of School Administrators.
S. S. Lifson, M. A., U. S. Public Health Service.
Ben Miller, Ph. D., American Association for Health, Physical Education and Recreation.
Harold H. Mitchell, M. D., American Academy of Pediatrics.
Dorothy Nyswander, Ph. D., American Public Health Association.
Thurman B. Rice, M. D., Joint Committee on Health Problems in Education of the National Education Association and American Medical Association.
Justus J. Schifferes, (Secretary).
Maycie Southall, Ph. D., Educational Policies Commission.
Frank Stafford, M. A., U. S. Office of Education.
George M. Wheatley, M. D., U. S. Children's Bureau.
Alberta B. Wilson, R. N., National Organization for Public Health Nursing.
Charles C. Wilson, M. D. (Chairman).
J. M. Wisan, D. D. S., American Dental Association.

Every community can advantageously evaluate its present school health program and plan ways for improving it. An important step is the development of specific policies. This needs to be followed by action, by translating the policies into procedures. As this is done the health of our Nation will be improved.

OUTBREAK OF Q FEVER IN THE UNITED STATES[1]

By J. V. Irons, *Acting Director of Laboratories, Texas State Department of Health;* N. H. Topping, *Senior Surgeon, United States Public Health Service;* C. C. Shepard, *Passed Assistant Surgeon, United States Public Health Service;* and H. R. Cox, *Director of Virus Research, Lederle Laboratories, Inc.*

During the second and third weeks of March 1946 an explosive outbreak of an acute febrile illness which has been identified as Q fever occurred at Amarillo, Tex. More than 40 cases, mostly in men, have been found. The illnesses varied from mild influenza-like attacks to severe pneumonitis or atypical pneumonia. It appears that inapparent infections also occurred. There were two deaths. Cases occurred among employees of a stockyards and meat-packing company, and in railroad workers and others working around the stockyards. In the stockyards, cattle, sheep, and hogs are unloaded and loaded, fed and watered, and bought and sold. Animals are transported in and out both by train and truck. Some of the animals are slaughtered and processed at the nearby packing plant. Although

[1] From the Division of Infectious Diseases, National Institute of Health.

the packing plant handles both hogs and cattle, preliminary investigations suggested that cattle were probably involved in the human infections.

Recognition of the outbreak as Q fever has been so far based upon both the clinical and serological findings. Early acute phase serums from the cases were negative in complement-fixation tests, while convalescent serums or serums from recovered cases had high complement-fixation titers with several Q fever antigen preparations. Agglutination tests with Q fever rickettsial suspensions gave positive results in agreement with complement-fixation findings. All tests performed for other acute febrile conditions gave negative results.

Recovery of *Rickettsia burneti* is being attempted from specimens obtained during acute illness and stored in the frozen state. Further details concerning the outbreak and results of laboratory studies in progress will be published at a later date.

NOTICE TO AIR TRAVELERS REGARDING YELLOW FEVER IMMUNIZATION

The International Sanitary Convention for Aerial Navigation of 1933 as amended by the Convention of 1944 provided for isolation of persons who do not hold a valid anti-yellow fever inoculation certificate and who are traveling by air from an endemic yellow fever area to one in which the disease does not exist, but in which conditions may permit of its development. Such persons may be isolated in screened quarters until such a certificate becomes valid or until 6 days shall have elapsed, whichever is the lesser period. The Convention also provided that, in exceptional cases, the countries signatory to the Convention may issue "Certificates of Urgency" to persons not immunized against yellow fever "whose unobstructed passage is absolutely and immediately essential on grounds of high policy, certifying that a passage without hindrance to the bearer of the certificate is urgently necessary."

Official information has been received that the Government of the Union of South Africa and the Government of Southern Rhodesia no longer accept these certificates of urgency issued to persons traveling through endemic yellow fever areas to the respective countries, nor issue such certificates to persons leaving these countries.

In consequence, persons who have not been inoculated against yellow fever will no longer be able, by means of a certificate of urgency, to avoid quarantine delays on arriving in Southern Rhodesia or the Union of South Africa from those parts of Africa in which yellow fever is endemic. Such travelers may be held in quarantine if they have not strictly complied with the yellow fever immunization requirements.

DEATHS DURING WEEK ENDED MAY 4, 1946

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

	Week ended May 4, 1946	Corresponding week, 1945
Data for 93 large cities of the United States:		
Total deaths	8,974	8,920
Average for 3 prior years	9,123	
Total deaths, first 18 weeks of year	178,222	171,652
Deaths under 1 year of age	648	598
Average for 3 prior years	619	
Deaths under 1 year of age, first 18 weeks of year	10,989	11,359
Data from industrial insurance companies:		
Policies in force	67,173,242	67,274,267
Number of death claims	12,517	15,085
Death claims per 1,000 policies in force, annual rate	9.7	11.7
Death claims per 1,000 policies, first 18 weeks of year, annual rate	10.9	11.1

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

REPORTS FROM STATES FOR WEEK ENDED MAY 11, 1946

Summary

Of the total of 4 cases of smallpox, 2 occurred in Texas and 1 each in Ohio and Colorado. The total for the year to date is 193, as compared with 198 for the corresponding period last year and 419 for the 5-year median (see p. 794).

Increased incidence of measles was reported during the week in only 2 of the 9 geographic divisions—the South Atlantic, where moderate increases occurred in 5 States, and in the Mountain area. In the latter, 1,684 cases were reported in Colorado, as compared with 446 last week. The total for the week is 35,208 (more than for a corresponding week since 1941), as compared with 39,902 last week and a 5-year (1941–45) median of 25,813. The cumulative figure is 454,338, as compared with 480,684 for the same period in 1944 and a 5-year median of 368,642.

Of the current total of 245 cases of diphtheria, the same number as reported last week, Texas reported 25, New York and Colorado 18 each, Ohio 17, California 16, and Pennsylvania 13. The total for the year to date is 6,670, as compared with a 5-year median of 5,253. Both the current and cumulative totals are more than reported for the respective corresponding periods of any year since 1939.

Of the total of 56 cases of poliomyelitis (as compared with 23 last week, 47 for the next earlier week, and a 5-year median of 28), Florida reported 17, and Texas 16. The total for the country as a whole since March 16, the week of lowest incidence (except last week) for both this year and last, is 263, as compared with 251 for the corresponding period last year.

Of 115 cases of meningococcus meningitis reported for the week (as compared with 95 last week and a 5-year median of 178), New York reported 13, Pennsylvania 12, and Virginia and California 9 each. The cumulative total is 3,286, as compared with an average of 7,845 for the corresponding periods of the past 3 years, and a 5-year median for the period of 4,345.

Deaths recorded for the week in 93 large cities of the United States aggregated 9,144, as compared with 8,974 last week, 9,147 and 9,098, respectively, for the corresponding weeks of 1945 and 1944, and a 3-year (1943–45) average of 9,229. The cumulative figure is 187,366, as compared with 180,799 for the same period last year.

Telegraphic morbidity reports from State health officers for the week ended May 11, 1946, and comparison with corresponding week of 1945 and 5-year median

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

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median 1941-45	Week ended—		Median 1941-45	Week ended—		Median 1941-45	Week ended—		Median 1941-45
	May 11, 1946	May 12, 1945		May 11, 1946	May 12, 1945		May 11, 1946	May 12, 1945		May 11, 1946	May 12, 1945	
NEW ENGLAND												
Maine	4	0	0	1			143	3	51	1	0	1
New Hampshire	0	0	0				42	2	38	0	0	1
Vermont	1	0	1	2			39	13	66	0	0	0
Massachusetts	8	4	4				2,683	216	971	1	2	6
Rhode Island	1	0	0		21	1	35	6	52	1	1	1
Connecticut	2	0	0	1		1	411	77	422	2	3	3
MIDDLE ATLANTIC												
New York	18	12	15	[1] 5	(1)	[1] 5	4,265	89	1,555	13	24	24
New Jersey	11	2	3	4	2	5	4,170	54	1,192	5	6	6
Pennsylvania	13	6	10	1	1	1	3,414	417	1,329	12	12	12
EAST NORTH CENTRAL												
Ohio	17	2	6	3	1	8	999	52	497	5	12	12
Indiana	6	7	7	1	8	1	493	33	219	3	4	4
Illinois	8	4	14	9	11	11	792	237	695	7	14	14
Michigan [2]	5	3	3			2	1,027	215	902	5	1	2
Wisconsin	0	1	1	14	22	28	2,968	63	1,800	3	1	1
WEST NORTH CENTRAL												
Minnesota	7	3	3				43	9	379	1	2	2
Iowa	2	2	2			1	156	70	223	3	1	1
Missouri	1	10	4	1		2	126	8	251	3	7	7
North Dakota	2	0	1	2	2	2	16	4	21	0	3	1
South Dakota	5	1	1				39	6	19	0	0	0
Nebraska	0	2	1		4	4	344	32	80	0	1	0
Kansas	6	4	4			1	320	47	542	0	1	1
SOUTH ATLANTIC												
Delaware	0	0	0				22	3	13	0	0	0
Maryland [2]	8	9	3	4	2	5	682	22	356	3	1	5
District of Columbia	2	1	0	1	1	1	338	4	123	5	1	2
Virginia	8	3	3	102	77	114	763	27	326	9	5	5
West Virginia	1	2	2		55	10	302	8	159	1	1	1
North Carolina	8	4	6			4	537	45	706	0	2	2
South Carolina	4	6	4	205	163	163	439	18	127	0	1	1
Georgia	1	3	3	2	8	35	141	21	175	0	1	1
Florida	3	1	3			11	201		219	1	7	2
EAST SOUTH CENTRAL												
Kentucky	11	1	3			1	157	30	113	4	3	3
Tennessee	0	1	2	12	26	29	279	63	154	2	9	9
Alabama	2	8	4	11	29	29	228	13	205	1	5	5
Mississippi [2]	7	9	8							3	3	3
WEST SOUTH CENTRAL												
Arkansas	3	1	2	29	23	21	123	34	161	1	2	2
Louisiana	0	5	4	7	5	2	190	26	43	0	2	2
Oklahoma	3	4	4	8	117	44	254	40	153	0	1	1
Texas	25	32	23	385	518	472	1,694	441	991	6	10	10
MOUNTAIN												
Montana	0	2	2	5	11	4	85	19	118	0	0	0
Idaho	1		0	3			141	49	49	1	0	0
Wyoming	0		0			1	38	7	93	0	1	0
Colorado	18	8	7	10	11	23	1,684	30	260	0	1	2
New Mexico	*0	2	0		1	1	67	6	27	0	0	0
Arizona	2	3	2	14	34	34	150	9	78	0	0	0
Utah [2]	0	0	0		15	6	343	283	252	0	1	1
Nevada	0	0	0		36				4	0	0	0
PACIFIC												
Washington	4	5	1		1		527	178	236	2	5	4
Oregon	1	4	0	4	4	8	330	95	185	2	2	0
California	16	20	8	10	12	29	2,968	1,510	1,510	9	19	17
Total	245	197	187	856	1,221	1,150	35,208	4,634	25,813	115	178	178
19 weeks	6,670	5,336	5,253	183,596	60,323	73,372	454,338	59,109	368,642	3,286	4,345	4,345

[1] New York City only.
[2] Period ended earlier than Saturday.

*Correction: New Mexico, week ended Apr. 27, diphtheria 3 cases (instead of 0).

Telegraphic morbidity reports from State health officers for the week ended May 11, 1946, and comparison with corresponding week of 1945 and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever [2]		
	Week ended—		Median 1941-45	Week ended—		Median 1941-45	Week ended—		Median 1941-45	Week ended—		Median 1941-45
	May 11, 1946	May 12, 1945		May 11, 1946	May 12, 1945		May 11, 1946	May 12, 1945		May 11, 1946	May 12, 1945	
NEW ENGLAND												
Maine	0	1	0	14	65	12	0	0	0	1	0	0
New Hampshire	0	0	0	4	5	6	0	0	0	0	0	0
Vermont	0	1	0	12	16	9	0	0	0	0	0	0
Massachusetts	0	1	0	187	392	345	0	0	0	0	1	1
Rhode Island	0	0	0	20	17	17	0	0	0	0	0	0
Connecticut	0	0	0	69	63	67	0	0	0	0	0	0
MIDDLE ATLANTIC												
New York	4	6	3	594	657	504	0	0	0	0	3	4
New Jersey	0	0	0	179	144	158	0	0	0	0	1	1
Pennsylvania	1	0	0	380	518	406	0	0	0	2	4	4
EAST NORTH CENTRAL												
Ohio	0	2	1	382	312	297	1	1	0	1	7	3
Indiana	0	0	0	56	122	82	0	0	0	2	1	2
Illinois	1	1	0	186	261	261	0	0	0	0	2	2
Michigan [3]	0	0	0	152	258	258	0	0	0	1	2	1
Wisconsin	1	1	1	122	221	221	0	0	0	0	0	0
WEST NORTH CENTRAL												
Minnesota	0	2	0	60	81	49	0	0	0	0	0	0
Iowa	3	0	0	46	39	39	0	0	1	4	0	0
Missouri	1	0	0	33	62	138	0	0	0	4	0	2
North Dakota	1	0	0	5	8	5	0	0	0	0	1	1
South Dakota	0	0	0	11	9	12	0	0	0	0	0	0
Nebraska	0	0	0	12	58	26	0	0	0	0	0	0
Kansas	1	0	0	35	91	63	0	0	0	0	3	2
SOUTH ATLANTIC												
Delaware	0	0	0	4	8	8	0	0	0	0	0	0
Maryland [3]	0	0	0	200	180	154	0	0	0	0	0	0
District of Columbia	0	0	0	14	35	18	0	0	0	1	1	0
Virginia	0	1	0	72	66	41	0	0	0	0	3	2
West Virginia	0	0	0	35	43	34	0	0	1	2	0	1
North Carolina	0	0	0	27	53	16	0	0	0	0	2	1
South Carolina	1	7	1	5	6	5	0	1	0	2	2	2
Georgia	0	0	0	2	20	19	0	0	0	6	3	4
Florida	17	1	2	3	8	4	0	0	0	3	0	1
EAST SOUTH CENTRAL												
Kentucky	1	0	1	14	48	48	0	0	0	0	3	3
Tennessee	0	2	0	12	44	44	0	1	0	2	2	3
Alabama	2	0	0	19	21	8	0	0	0	3	1	1
Mississippi [3]	0	2	2	5	13	5	0	0	0	1	0	3
WEST SOUTH CENTRAL												
Arkansas	1	0	0	10	10	7	0	0	0	2	2	2
Louisiana	1	0	0	7	9	3	0	0	0	2	4	5
Oklahoma	0	0	0	10	26	16	0	0	0	0	1	1
Texas	16	3	2	47	81	58	2	4	1	11	11	7
MOUNTAIN												
Montana	0	0	0	4	20	18	0	0	0	0	1	0
Idaho	0	0	0	9	10	10	0	0	0	0	0	1
Wyoming	0	0	0	8	8	16	0	0	0	1	0	0
Colorado	2	1	0	55	56	56	1	1	0	2	0	1
New Mexico	0	0	0	4	21	10	0	0	0	3	1	0
Arizona	0	0	0	10	21	9	0	0	0	0	0	0
Utah [2]	0	0	0	21	16	20	0	0	0	0	1	0
Nevada	0	0	0	0	0	2	0	0	0	0	0	0
PACIFIC												
Washington	0	0	0	18	68	31	0	0	0	0	1	1
Oregon	0	0	0	42	36	13	0	1	0	1	0	0
California	2	0	3	142	334	166	0	0	0	2	1	4
Total	56	32	28	3,358	4,660	3,963	4	9	24	59	65	86
18 weeks	729	648	436	66,503	103,420	75,724	193	198	419	956	1,114	1,376

[2] Period ended earlier than Saturday.

[3] Including paratyphoid fever reported separately, as follows: Ohio 1; South Carolina 1; Georgia 6; Florida 2; Tennessee 1; Texas 2; Colorado 1; California 1.

Telegraphic morbidity reports from State health officers for the week ended May 11, 1946, and comparison with corresponding week of 1945 and 5-year median—Con.

Division and State	Whooping cough			Week ended May 11, 1946							
	Week ended—		Median 1941–45	Dysentery			Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever, endemic	Undulant fever
	May 11, 1946	May 12, 1945		Amebic	Bacillary	Unspecified					
NEW ENGLAND											
Maine	6	40	30								
New Hampshire		2	2								
Vermont	7	11	11								2
Massachusetts	137	158	158								1
Rhode Island	17	16	16				1				
Connecticut	40	53	51								
MIDDLE ATLANTIC											
New York	161	166	260	4	6						7
New Jersey	181	111	111				1				2
Pennsylvania	116	209	219								2
EAST NORTH CENTRAL											
Ohio	73	143	143								
Indiana	2	8	36		1						
Illinois	83	43	99		1						8
Michigan [2]	124	61	187		2						4
Wisconsin	84	41	134								6
WEST NORTH CENTRAL											
Minnesota	10	13	48	2							2
Iowa	33	3	18								2
Missouri	8	14	19			1					
North Dakota		1	7								
South Dakota		2	5								3
Nebraska		8	7				(*)				
Kansas	39	30	42								14
SOUTH ATLANTIC											
Delaware	5	1	1								
Maryland [2]	19	79	79			1		2			2
District of Columbia	8	7	19								
Virginia	110	58	65			35		3			1
West Virginia	51	5	16								
North Carolina	65	134	134					1			
South Carolina	44	57	62	4	26					1	
Georgia	12	17	28	1	1			1	2	6	2
Florida	15	7	12							3	
EAST SOUTH CENTRAL											
Kentucky	9	63	63		1						
Tennessee	8	29	41			2			1		
Alabama	23	21	51						1	11	2
Mississippi [2]									2	1	1
WEST SOUTH CENTRAL											
Arkansas	11	9	9	2							1
Louisiana	25	4	4	1					2		2
Oklahoma	7	29	29					3			
Texas	160	276	276	17	347	30				8	14
MOUNTAIN											
Montana	1	3	14								
Idaho	15	6	7					2			2
Wyoming	4		5						1		1
Colorado	56	37	37	1			1		0		
New Mexico	16	4	14								
Arizona	32	28	28			52					1
Utah [2]	19	44	43					1	1		1
Nevada		2	3								
PACIFIC											
Washington	28	26	35								1
Oregon	17	26	21								
California	84	471	431	3	1					(4)	6
Total	1,965	2,576	3,658	35	386	121	3	13	10	30	90
Same week, 1945	2,576			33	374	106	9	10	8	58	104
Average, 1943–45	2,800			26	369	74	7	[5] 16	17	[5] 50	
19 weeks: 1946	35,000			704	5,647	1,989	*156	42	339	857	1,553
1945	47,302			563	8,122	2,191	129	32	302	932	1,642
Average, 1943–45	52,767		[5] 73,019	536	5,436	1,456	183	[5] 54	272	[5] 792	

[2] Period ended earlier than Saturday.

[4] One case of louse-borne typhus fever reported in the U. S. Naval Hospital, San Diego, Calif., May 10, with onset on board ship Apr. 5, one day after leaving Yokosuka, Japan. Patient recovered.

[5] 5-year median, 1941–45.

Anthrax: Massachusetts, 1 case *Leprosy:* Florida, 1 case.

*Correction: Nebraska, week ended Apr. 27, encephalitis 2 cases (instead of 12).

WEEKLY REPORTS FROM CITIES

City reports for week ended May 4, 1946

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

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland	0	0	------	0	-------	0	0	0	2	0	0	8
New Hampshire:												
Concord	0	0	------	0	2	0	0	0	0	0	0	------
Vermont:												
Barre	1	0	------	0	-------	0	0	0	0	0	0	------
Massachusetts:												
Boston	1	0	------	0	464	1	11	0	40	0	1	8
Fall River	0	0	------	0	204	0	0	0	5	0	0	1
Springfield	0	0	------	0	78	0	0	0	8	0	0	1
Worcester	0	0	------	0	324	0	7	0	4	0	0	32
Rhode Island:												
Providence	0	0	------	0	23	0	0	0	5	0	1	13
Connecticut:												
Bridgeport	0	0	------	0	2	1	0	0	1	0	0	------
Hartford	0	0	------	0	4	1	2	0	2	0	0	2
New Haven	0	0	------	0	-------	0	1	0	2	0	0	------
MIDDLE ATLANTIC												
New York:												
Buffalo	3	0	------	0	126	2	4	0	10	0	0	10
New York	10	2	7	0	1,481	3	72	1	287	0	0	34
Rochester	0	0	------	0	253	0	2	0	15	0	0	------
Syracuse	0	0	------	0	32	1	3	0	11	0	0	1
New Jersey:												
Camden	2	0	1	1	39	0	1	0	1	0	0	5
Newark	0	0	2	0	633	0	5	0	20	0	0	24
Trenton	0	0	------	0	59	0	2	0	5	0	0	2
Pennsylvania:												
Philadelphia	2	0	1	1	591	3	10	0	70	0	1	15
Pittsburgh	2	0	1	1	14	1	10	0	25	0	2	6
Reading	0	0	------	0	37	0	0	0	7	0	0	3
EAST NORTH CENTRAL												
Ohio:												
Cincinnati	3	0	------	0	58	1	8	0	9	0	0	3
Cleveland	0	0	2	0	141	1	7	0	54	0	0	23
Columbus	3	0	------	0	5	1	1	0	8	0	0	------
Indiana:												
Fort Wayne	0	0	------	0	2	0	1	0	3	0	0	------
Indianapolis	0	0	------	0	210	0	1	0	12	0	0	15
South Bend	0	0	------	0	6	0	0	0	5	0	0	------
Terre Haute	0	0	------	0	6	0	0	0	0	0	0	1
Illinois:												
Chicago	0	0	1	0	348	3	34	0	0	0	0	41
Springfield	0	0	------	0	5	0	3	0	3	0	0	------
Michigan:												
Detroit	0	0	------	1	325	3	15	0	52	0	2	49
Flint	1	0	------	0	4	0	3	0	5	0	0	1
Grand Rapids	0	0	------	0	206	0	1	0	10	0	0	2
Wisconsin:												
Kenosha	0	0	------	0	76	0	0	0	1	0	0	------
Milwaukee	0	0	------	0	1,982	0	7	0	24	0	0	30
Racine	0	0	------	0	60	0	0	0	8	0	0	------
Superior	0	0	------	0	1	0	0	0	0	0	0	------
WEST NORTH CENTRAL												
Minnesota:												
Duluth	0	0	------	0	4	0	0	0	0	0	0	5
Minneapolis	3	0	------	0	21	0	1	0	14	0	0	------
St. Paul	3	0	------	0	13	3	3	0	9	0	0	1
Missouri:												
Kansas City	0	0	------	1	7	0	7	1	2	0	0	------
St. Joseph	0	0	------	0	-------	0	0	0	1	0	0	------
St. Louis	2	0	1	0	127	3	4	1	9	0	0	4

City reports for week ended May 4, 1946—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL—continued												
Nebraska:												
Omaha	1	0	------	0	41	0	3	0	3	0	0	1
Kansas:												
Topeka	0	0	------	0	4	0	0	0	16	0	0	10
Wichita	0	0	1	1	133	0	3	0	5	0	0	1
SOUTH ATLANTIC												
Delaware:												
Wilmington	0	0	------	0	37	0	2	0	1	0	0	------
Maryland:												
Baltimore	7	0	1	1	469	0	6	0	30	0	1	15
Cumberland	0	0	------	0	1	0	0	1	3	0	0	------
Frederick	0	0	------	0	------	0	0	0	0	0	0	------
District of Columbia:												
Washington	0	0	------	0	384	0	4	0	13	0	0	12
Virginia:												
Lynchburg	0	0	------	0	41	0	0	0	0	0	0	------
Richmond	0	0	22	2	48	1	0	1	10	0	0	8
Roanoke	0	0	------	0	6	0	0	0	1	0	0	------
West Virginia:												
Charleston	0	0	------	0	3	0	0	0	2	0	0	------
Wheeling	2	0	------	0	------	0	2	0	0	0	0	20
North Carolina:												
Raleigh	0	0	------	0	22	0	1	0	0	0	0	------
Wilmington	0	0	------	0	17	0	1	0	0	0	0	------
Winston-Salem	0	0	------	0	32	0	0	0	2	0	0	3
South Carolina:												
Charleston	0	0	------	0	3	0	1	0	1	0	1	------
Georgia:												
Atlanta	1	0	1	1	26	0	3	0	1	0	0	1
Brunswick	0	0	------	0	4	0	0	0	0	0	0	3
Savannah	0	0	------	0	2	1	1	0	1	0	0	------
Florida:												
Tampa	1	0	------	0	27	0	1	0	1	0	0	4
EAST SOUTH CENTRAL												
Tennessee:												
Memphis	0	1	------	0	29	0	6	0	7	0	1	1
Nashville	0	0	------	1	2	0	3	0	3	0	0	4
Alabama:												
Birmingham	0	0	1	0	24	0	1	0	0	0	0	------
Mobile	0	0	------	1	2	0	0	0	0	0	0	------
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock	0	0	4	0	26	0	0	0	0	0	0	------
Louisiana:												
New Orleans	2	0	3	0	35	0	3	1	8	0	0	------
Shreveport	0	0	------	0	------	0	1	0	5	0	0	------
Texas:												
Dallas	1	0	------	0	45	0	3	0	2	0	1	------
Galveston	0	0	------	0	1	0	0	0	0	0	0	------
Houston	2	0	------	0	3	2	5	0	1	0	0	------
San Antonio	1	0	------	0	18	0	2	0	0	0	0	------
MOUNTAIN												
Montana:												
Billings	0	0	------	0	------	0	0	0	0	0	0	------
Great Falls	0	0	------	0	11	0	0	0	0	0	0	------
Helena	0	0	------	0	9	0	0	0	0	0	0	------
Missoula	0	0	------	0	4	0	0	0	0	0	0	------
Idaho:												
Boise	0	0	------	0	------	0	1	0	0	0	0	------
Colorado:												
Denver	5	0	------	0	706	0	3	4	12	0	0	14
Pueblo	0	0	------	0	42	0	0	0	1	0	0	------
Utah:												
Salt Lake City	0		------	1	115	0	2	0	4	0	0	6

City reports for week ended May 4, 1946—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza cases	Influenza deaths	Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
PACIFIC												
Washington:												
Seattle	3	0	------	1	74	0	3	0	0	2	0	3
Spokane	0	0	------	0	43	0	0	0	2	0	0	5
Tacoma	0	0	------	0	-------	0	0	0	0	0	0	------
California:												
Los Angeles	2	0	7	0	453	1	3	0	44	0	0	9
Sacramento	0	0	------	0	260	0	1	0	3	0	0	1
San Francisco	4	0	1	1	209	0	2	0	15	0	1	1
Total	68	3	57	15	11,384	33	293	10	946	2	12	462
Corresponding week, 1945	55	------	20	8	1,348	------	300	------	1,505	0	9	699
Average, 1941–45	59	------	73	[1] 22	[2] 6,312	------	[1] 375	------	1,573	0	14	966

[1] 3-year average, 1943–45.
[2] 5-year median, 1941–45.

Anthrax.—Cases: Philadelphia 1.
Dysentery, amebic.—Cases: New York 2; Chicago 3; St. Louis 2; Baltimore 1; San Antonio 1; Los Angeles 2.
Dysentery, bacillary.—Cases: Buffalo 1; New York 5; Detroit 2; Memphis 1; San Francisco 1.
Dysentery, unspecified.—Cases: Cincinnati 1; San Antonio 21.
Rocky Mountain spotted fever.—Cases: Atlanta 1.
Tularemia.—Cases: Memphis 1.
Typhus fever, endemic.—Cases: New York 1; Savannah 1; Little Rock 1; New Orleans 3; Shreveport 1; Houston 1.

Rates (annual basis) per 100,000 population, by geographic groups, for the 89 cities in the preceding table (estimated population, 1943, 34,366,400)

	Diphtheria case rates	Encephalitis, infectious, case rates	Influenza case rates	Influenza death rates	Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Poliomyelitis case rates	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
New England	5.2	0.0	0.0	0.0	2,878	7.8	54.9	0.0	180	0.0	5.2	170
Middle Atlantic	8.8	0.9	5.6	1.4	1,511	4.6	50.5	0.5	209	0.0	1.4	46
East North Central	4.3	0.0	1.8	0.6	2,089	5.5	49.3	0.0	118	0.0	1.2	100
West North Central	18.1	0.0	4.0	4.0	704	12.1	42.2	4.0	119	0.0	0.0	44
South Atlantic	18.0	0.0	39.2	6.5	1,834	3.3	36.0	3.3	108	0.0	3.3	108
East South Central	0.0	5.9	5.9	11.8	336	0.0	59.0	0.0	59	0.0	5.9	30
West South Central	17.2	0.0	20.1	0.0	367	5.7	40.2	2.9	46	0.0	2.9	0
Mountain	39.7	0.0	0.0	7.9	7,045	0.0	47.7	31.8	135	0.0	0.0	159
Pacific	14.2	0.0	12.7	3.2	1,643	1.6	14.2	0.9	101	3.2	1.6	30
Total	10.3	0.5	8.7	2.3	1,732	5.0	44.6	1.5	144	0.3	1.8	70

PLAGUE INFECTION IN SANTA BARBARA AND VENTURA COUNTIES, CALIF.

Plague infection was reported under date of May 2 to have been proved, on May 1, in a pool of 128 fleas from 9 ground squirrels, *C. beecheyi*, shot 1 mile south of Buellton, Santa Barbara County, Calif. Under date of May 2 plague infection was reported proved, on April 30, in tissue from 4 rats, *R. alexandrinus*, trapped ½ mile south and 2 miles east of Santa Paula, Ventura County, Calif., and on May 1 in

a pool of 90 fleas from the same rats; also, under date of May 8, proved on May 6, in tissue from 1 ground squirrel, *C. beecheyi*, shot at the same location.

SMALLPOX IN SAN FRANCISCO, CALIF., AND SEATTLE, WASH.

Week ended May 11, 1946

No new case of smallpox was reported in either San Francisco or Seattle during the week, leaving the totals for the States at 13 for California (9 in San Francisco—6 with origin in the city, 3 with origin outside the United States), and 59 cases in Washington State (50 in Seattle and King County). One additional death from smallpox was reported in the Seattle area during the week, bringing the total deaths to date in that area to 17 (15 in Seattle and King County, 2 in Everett).

TERRITORIES AND POSSESSIONS

Hawaii Territory

Plague (in ectoparasites).—Plague infection was proved positive on April 13, 1946, in a pool of 54 fleas and 15 lice collected from 7 rats and 22 mice trapped on March 28, 1946, in District 14BA, Island of Maui, T. H.

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—April 13, 1946.—During the week ended April 13, 1946, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox		2		132	192	22	26	15	56	445
Diphtheria		3	3	13	9	1				29
Dysentery, bacillary				2						2
Encephalitis, infectious								1		1
German measles				22	31	1		13	12	79
Influenza		521			30	3			38	592
Measles		160	16	662	1,150	21	1	68	14	2,092
Mumps				65	195	75	16	46	67	464
Poliomyelitis								1		1
Scarlet fever	2	4	2	72	94	14	1	8	6	203
Tuberculosis (all forms)		13	2	144	67	23	11	21	27	308
Typhoid and paratyphoid fever				6	3					9
Undulant fever				5	2					7
Venereal diseases:										
Gonorrhea	11	17	13	126	157	48	30	40	97	539
Syphilis	3	17	3	148	114	14	12	7	32	350
Other forms									1	1
Whooping cough		51		100	65	4		10	13	243

CUBA

Habana—Communicable diseases—4 weeks ended April 27, 1946.—During the 4 weeks ended April 27, 1946, certain communicable diseases were reported in Habana, Cuba, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Chickenpox	7		Scarlet fever	2	
Diphtheria	16		Tuberculosis	12	2
Malaria	1		Typhoid fever	23	2
Measles	4				

Provinces—Notifiable diseases—4 weeks ended April 20, 1946.—During the 4 weeks ended April 20, 1946, cases of certain notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Rio	Habana[1]	Matanzas	Santa Clara	Camaguey	Oriente	Total
Cancer	4	25	12	9	3	15	68
Chickenpox		10	4		2	6	22
Diphtheria	1	11				1	13
Hookworm disease	1	17					18
Leprosy		4	1	1	1		7
Malaria	8	2		2	4	92	108
Measles		2			4	15	21
Poliomyelitis					1	2	3
Scarlet fever		2					2
Tuberculosis	12	43	25	74	25	34	213
Typhoid fever	21	42	9	32	20	38	162
Whooping cough					2		2

[1] Includes the city of Habana.

NORWAY

Notifiable diseases—December 1945.—During the month of December 1945, cases of certain notifiable diseases were reported in Norway as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis	9	Mumps	99
Diphtheria	553	Pneumonia (all forms)	2,792
Dysentery, unspecified	14	Poliomyelitis	36
Encephalitis, epidemic	3	Rheumatic fever	205
Erysipelas	493	Scabies	6,006
Gastroenteritis	4,139	Scarlet fever	523
Gonorrhea	667	Syphilis	106
Hepatitis, epidemic	847	Tuberculosis (all forms)	356
Impetiga contagiosa	4,177	Typhoid fever	7
Influenza	3,144	Typhus fever	2
Malaria	2	Whooping cough	3,018
Measles	5,595		

WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

From medical officers of the Public Health Service, American consuls, International Office of Public Health, 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]

NOTE.—Since many of the figures in the following tables are from weekly reports, the accumulated totals are for approximate dates.

Place		January–February 1946	March 1946	April 1946—week ended—			
				6	13	20	27
ASIA							
Burma	C	22	99	26			
Rangoon	C	1	1				
Ceylon	C					[1] 3	
China:							
Fukien Province	C		1				
Hupeh Province	C	[2] 52	28		3		
Hunan Province	C		1				
Kwangtung Province	C						[3] 21
Canton	C	73	229	164		64	
India	C	3,930	5,302	3,056			
Calcutta	C	294	361	79	149	128	78
Chittagong	C	2			1		
Madras	C	2					
Indochina (French): Cochin-china	C		18			[4] 298	
Chaudok	C		10			[4] 9	
Mytho	C		6			[4] 26	
Saigon-Cholon	C					[4] 8	
Thailand (Siam)	C	1,279					
Bangkok	C	308					

[1] Suspected.
[2] Deaths.
[3] For the month of April 1946.
[4] For the period April 11–20, 1946.

PLAGUE

[C indicates cases; P, present]

Place		January–February 1946	March 1946	April 1946—week ended— 6	13	20	27
AFRICA							
Algeria	C		2				
Bechuanaland	C		[1] 10				
Belgian Congo	C	2					
British East Africa:							
Kenya	C	7			5	1	
Uganda	C	7					1
Egypt	C	11	15	5	6	8	7
Alexandria	C	6	8	1	2	4	7
Ismailiya	C		4	4	4	4	
Port Said	C	1					
Suez	C	4	3				
Madagascar	C	80	35		[2] 4		
Union of South Africa	C					1	
ASIA							
Burma	C	20	256	62			
Rangoon	C	2	22	11			
China:							
Chekiang Province	C	52		64	3		
Fukien Province	C	[3] 298	200				
Foochow	C		96				
Kwangtung Province	C			1			
Yunnan Province	C		11				
India	C	5,768	2,573	876			
Manchuria	C		[4] 52				
Mukden	C		[4] 39				
Palestine	C	12	1				
Thailand (Siam)	C	15					
EUROPE							
Great Britain: Malta	C	1	1				
Portugal: Azores	C	[5] 10					
SOUTH AMERICA							
Bolivia:							
Santa Cruz Department	C	12					
Tarija Department—Plague-infected rats		P					
Ecuador: Loja Province	C		6				
Peru:							
Lambayeque Department	C	1	7				
Lima Department	C	15	3				
OCEANIA							
Hawaii Territory: Plague-infected rats[6]		4					

[1] For the period Jan. 1 to Mar. 13, 1946.
[2] For the period Apr. 1–10, 1946.
[3] Deaths reported for the period Feb. 1 to Mar. 6, 1946.
[4] Pneumonic plague.
[5] Includes 2 cases of pneumonic plague.
[6] Plague infection was also proved positive on Feb. 5, 1946, in a pool of 29 rats and on Apr. 13, 1946, in a pool of 54 fleas and 15 lice collected from 7 rats and 22 mice.

SMALLPOX

[C indicates cases; P, present]

Place		January-February 1946	March 1946	April 1946—week ended— 6	13	20	27
AFRICA							
Basutoland	C	6					
Belgian Congo	C	[1] 345	[1] 232	[1] 125			
British East Africa:							
Kenya	C	208	94	31		6	16
Nyasaland	C	44	12		19	60	
Tanganyika	C	783	713				
Uganda	C	101	141	10	12		
Cameroon (French)	C	27	13			[2] 18	
Dahomey	C	288	521			[2] 97	
Egypt	C	83	33	16	17		
French Equatorial Africa	C	84	28				
French Guinea	C	88	279			[2] 165	
French West Africa: Dakar District	C	14	16			[2] 7	
Gambia	C	1	1				
Gold Coast	C	526	67	9			
Ivory Coast	C	193	111			[2] 166	
Libya	C	30	7	2	2	5	1
Morocco (French)	C	914	349			[2] 189	
Morocco (Int. Zone)	C	79	50				
Nigeria	C	1,599	[3] 715				
Niger Territory	C	169	77			[2] 61	
Rhodesia:							
Northern	C	186	30	1	4		
Southern	C		1				
Senegal	C	12	51		[4] 5		
Sierra Leone	C	161	89	16			
Sudan (Anglo-Egyptian)	C	2	11		6		
Sudan (French)	C	1,087	456			[2] 118	
Togo (French)	C	27	20			[2] 84	
Tunisia	C	27	3				
Union of South Africa	C	71	P	P			P
ASIA							
Arabia	C					1	
Burma	C	74	344	138			
Ceylon	C	261	48	13	10		
China	C	165	154			[2] 93	
India	C	20,046	8,878				
Indochina (French):							
Cochinchina	C	12	50		[4] 13		
Laos	C	9					
Iran	C	3	4				
Iraq	C	2		1		2	
Japan	C	495					
Palestine	C		1				[5] 1
Syria and Lebanon	C		7				
Thailand (Siam)	C	7,271					
Turkey (See Turkey in Europe).							
EUROPE							
Czechoslovakia	C	24					
France	C	6	7				
Gibraltar	C	[5] 1					[5] 1
Great Britain:							
England and Wales	C	[6] 9	[6] 13	[6] 7	[5] 1	1	
Scotland	C		[6] 2				
Greece	C		96	16		1	
Italy	C	164	16			[2] 31	
Portugal	C	5	9		1	2	1
Turkey	C	7	3				1
NORTH AMERICA							
Canada	C	2					
Guatemala	C	51					
Honduras	C		3				
Mexico	C	93	37				
SOUTH AMERICA							
Argentina	C	50					
Bolivia	C	109					
Brazil	C	[1] 10	[1] 1				
Colombia	C	195	20				
Ecuador	C	6	3				
Peru	C	23					
Uruguay	C	9					
Venezuela	C	[1] 318	[1] 78				
OCEANIA							
Hawaii Territory	C		[7] 1				

[1] Alastrim.
[2] For the period Apr. 1–20, 1946.
[3] For the week ended Mar. 2, 1946.
[4] For the period Apr. 1–10, 1946.
[5] Imported.
[6] Includes imported cases.
[7] Off-shipping.

TYPHUS FEVER *

[C indicates cases; P, present]

Place		January–February 1946	March 1946	April 1946—week ended—			
				6	13	20	27
AFRICA							
Basutoland	C	1	1				
Belgian Congo [1]	C	902	478	50			
British East Africa: Kenya	C	9	3	1			
Egypt	C	598	316	28	44		
Eritrea	C	90	95	28	8	34	
Libya	C	10	12		1	2	1
Morocco (French)	C	914	717			[2] 488	
Morocco (Int. Zone)	C	3	20	9			
Morocco (Spanish)	C	1					
Nigeria	C	13	6				
Sierra Leone [1]	C	2	1				
Tunisia [1]	C	65	61		[3] 36		
Union of South Africa [1]	C	52	P	P			P
ASIA							
Arabia [4]	C	1					
China	C	11	10	2		1	
India	C	58	4	178			
Indochina (French)	C		2				
Iran	C	32	36				
Iraq	C	17	25	16	7	3	9
Japan	C	128					
Palestine [4]	C	12					
Syria and Lebanon	C	30	11	10	6		4
Trans-Jordan	C	1	10	3			
Turkey (See Turkey in Europe).							
EUROPE							
Austria	C	17	8	1			
Bulgaria	C	200	267	35		37	
Czechoslovakia [1]	C	327	136	29			
France	C	8					
Germany	C	763	980	28	9	14	
Great Britain: Malta [4]	C	7					
Greece [1]	C	56	30	5	5	108	
Hungary	C	189	128	51	58	51	
Italy	C	6					
Netherlands	C	15					
Poland	C	1,200	519	106	67	50	
Portugal	C	1	1				
Rumania	C	568	1,021	613			
Spain	C		1		1		
Turkey	C	403	271		66	60	35
NORTH AMERICA							
Costa Rica [4]	C	21		4	3		6
Cuba [4]	C	3	1				
Guatemala	C	120					
Jamaica [4]	C	8	4				
Mexico	C	217	127				
Panama (Republic)	C	1					
Puerto Rico [4]	C		2	4	1	5	
Virgin Islands [4]	C	1					
SOUTH AMERICA							
Argentina	C	1					
Bolivia	C	36					
Colombia	C	27					
Ecuador [1]	C	169	87				
Paraguay	C	1					
Peru	C	52					
Venezuela [1]	C	22	15				
OCEANIA							
Australia [4]	C	[3] 33	9				
Hawaii Territory [4]	C	12	3	1			

*Reports from some areas are probably murine type, while others probably include both murine and louse-borne types.

[1] Includes cases of murine type.
[2] For the period Apr. 1–20, 1946.
[3] For the period Apr. 1–10, 1946.
[4] Murine type.

YELLOW FEVER

[C includes cases; D, deaths]

Place		January–February 1946	March 1946	April 1946—week ended—			
				6	13	20	27
AFRICA							
Nigeria: Ibadan	C					[1] 1	
SOUTH AFRICA							
Bolivia: Santa Cruz Department	D	[1] 39	[1] 1				
Colombia: Caqueta Territory	D		1				
Venezuela:							
Tachira State	C	2	2				
Trujillo State	C	3	1				
Zulia State	C	4					

[1] Suspected.

×