PUBLIC HEALTH REPORTS

VOL. 53 OCTOBER 21, 1938 NO. 42

STUDIES ON IMMUNIZING SUBSTANCES IN PNEUMOCOCCI

VII. RESPONSE IN HUMAN BEINGS TO ANTIGENIC PNEUMOCOCCUS POLYSACCHARIDES, TYPES I AND II[1]

By LLOYD D. FELTON, *Senior Surgeon, United States Public Health Service*

In the prophylactic control of infectious diseases two reactions of the host are taken into consideration: First, the immunity response either to specific antigens, that is, active immunity, or to a lesser extent to serum of animals so immunized, passive immunity, and, second, the reaction to empirical procedures to increase the host's natural resistance. In the former, vaccination procedures for the prevention of infectious diseases are developments from the observations of Jenner, Pasteur, and other early workers in this field of bacteriology. Although the original concept of the mechanism of active immunity was production of a mild form of disease, such that resistance of the host was increased, this concept is being modified as a result of recent advances in our knowledge of antigens. Methods for the stimulation of active immunity have been of great prophylactic value in those diseases in which the immunity so induced is of long duration, as in smallpox, diphtheria, and tetanus, and, by repeated vaccination, also in those in which the immunity is of short duration, as in typhoid fever. Almost indiscriminately, immunization with specific antigens is the one method which has been widely employed for the prevention of all infectious diseases caused either by bacteria or by viruses, with results both uncertain and perhaps injurious, owing to incomplete knowledge of all factors involved.

[1] This is one of a series of studies carried out in part under a grant from the Influenza Commission of the Metropolitan Life Insurance Co. and in part under a grant from the Pneumonia Fund of Harvard and Johns Hopkins Universities. The work was done in the Department of Preventive Medicine and Hygiene, Harvard Medical School, and the Department of Pathology and Bacteriology, Johns Hopkins University.

Preceding papers in the series are:

I. Felton, L. D.: Active immunization of white mice by a nonpolysaccharide and probably non-protein-derivative of the pneumococcus. J. Immunol., 23: 405 (1932).

II. Felton, L. D.: Separation of the organism into acid soluble and acid insoluble fractions. J. Immunol., 27:379 (1934).

III. Felton, L. D., Kauffmann, G. and Stahl, H. J.: The precipitation of bacterial polysaccharides with calcium phosphate. Pneumococcus. J. Bact., 29: 149 (1935).

IV. Felton, L. D., Sutliff, W. D. and Steele, B. F.: Antigenic characteristics in man of certain products of the pneumococcus. Comparison with vaccine. J. Infect. Dis., 56: 101 (1935).

V. Felton, L. D. and Prescott, B.: The effect of alkalis on the immunizing properties of a type I pneumococcus polysaccharide. Bull. Johns Hopkins Hosp., 59: 114 (1936).

VI. Felton, L. D. and Kauffmann, G.: The essential immunizing antigen of types I and II pneumococci. Bull. Johns Hopkins Hosp., 62: 430 (1938).

Number VIII of the series follows the present paper in this issue of the Public Health Reports.

In addition to specifically induced immunity, natural resistance of the host obviously plays an important role in the control of infectious diseases. That this natural resistance varies in different individuals is well recognized. This seems particularly true in the case of pneumococcus infections. Although, at least during the pneumonia season, a very large percentage of the population have pneumococci in their throats almost constantly, yet in the United States only one in approximately 450 individuals contracts lobar pneumonia each year. The explanation for this relatively low incidence with such widespread distribution of infective agent is important for a better understanding of the disease. Is the individual who succumbs to pneumonia highly susceptible (natural or acquired susceptibility, temporary or permanent), and is another individual similarly exposed highly resistant and thus spared the serious infection? If such is shown to be the case, the study of the host factors—environmental conditions, hereditary characteristics, diet, and the like, especially in regard to the character of the defense mechanism—might reveal significant facts necessary for successful prophylaxis.

In this report the study is limited to the human host response to specific pneumococcus antigens. The antigen chosen was a highly antigenic form of the polysaccharide of the pneumococcus. It was used in preference to whole-cell vaccine, first because it was water-soluble and stable, and thus easily sterilized and standardized, and second, because it was thought that this antigen might possibly be superior to vaccine, giving a response similar to that in natural immunity. That is to say, by increasing the tolerance of the host for the polysaccharide, whether or not antibodies are produced, the threshold of infectivity might be raised and consequently the incidence of pneumonia decreased. That the presence of humoral antibody specifically increases resistance is well known. Whether or not the increased tolerance for a chemical substance, in this case polysaccharide of the pneumococcus, will raise the host resistance, awaits proof. Nevertheless the antigens used were standardized both by measurement of the degree of immunity conferred upon white mice and by the demonstration of serum antibodies in human beings following their use.

In studies on active immunization against pneumococcus infection, previous investigators have used the whole-cell vaccine, either stock or autogenous. The significant work of Lister (*1*), Cecil and Austin (*2*), and others has been briefly reviewed in our preliminary report (*3*). It is sufficient here to add to the list the extended survey reported by Lister and Ordman (*4*) of the use of autogenous vaccines in the mine workers of South Africa over a 24-year period, a continuation of Lister's earlier work. Although the apparently positive results of their study are encouraging, the inherent difficulties in such

a procedure render it impracticable for application to any large number of individuals.

It has long been recognized (Auld (*5*), Jobling and Strouse (*6*), Hirschfelder (*7*), and others) that a fractional part of the pneumococcus cell produces active immunity in experimental animals; but actual demonstration of similar results in human beings has been made only in the last decade. In 1929 and 1930 Francis and Tillett (*8*) observed that, when skin test doses of the different types of specific polysaccharide were used to indicate the presence or absence of antibody in pneumonia patients, there occurred a stimulation of antibody response of a type of pneumococcus different from the causative type in the disease. In 1932, Finland and Sutliff (*9*) reported further that, in normal individuals, the same doses of polysaccharide (even as small an amount as 0.01 mg) injected intradermally produced antibodies measurable by passive immunity experiments in white mice. After the publication by Avery and Goebel (*10*) of a description of acetyl polysaccharide which was antigenic for mice, Francis (*11*) tested both this acetylated and the deacetylated polysaccharide in human beings, again in skin test doses (three injections of 0.01 mg), with the result that both preparations were found to produce protective antibody in all individuals tested.

In the meantime, our work on the essential immunizing antigen (*12*) of the pneumococcus had shown that it was possible to isolate from the cell a fraction which contained more immunizing doses than the original dried organisms from which it was derived, at least as measured by the degree of active immunity developed in white mice. A preliminary study in human beings included a comparison of the antigenicity of such fractions with that of a vaccine made up of whole pneumococci (*3*). The response to the type-specific fractions was at least as great as that evoked by vaccine, but, in contrast to the type-specific nature of the latter, the antibodies stimulated by the various fractions were found for the most part to be non-type-specific.

Following our study, Finland and Dowling (*13*) reported the stimulation of protective antibody in the human subject by single and repeated skin test doses (0.01 to 0.05 mg) of cellular carbohydrate as prepared by Wadsworth and Brown (*14*). Contrary to our observations, in almost every instance a strictly type-specific antibody response was obtained.

The present study is a continuation of the investigation of the activity of the antigenic polysaccharide of the pneumococcus in human beings, and includes:

I. The antigens: (*a*) Outline of the methods of preparation of the polysaccharides; (*b*) some chemical and immunological characteristics; and (*c*) their suitability for human use;

II. Methods used for (*a*) preparing the solution for injection, (*b*) calculating the dose to be injected, (*c*) inoculation, and (*d*) testing of sera drawn before and after inoculation for protective antibodies in mice;

III. Results of injection of the antigen into humans with respect to (*a*) the type of reaction occurring with subcutaneous injection, (*b*) the specificity of response in children and adults, (*c*) the duration of the immunity as measured by the protective antibodies in serum, and (*d*) a comparison of the degree of immunity, similarly measured, conferred upon 281 individuals of age groups ranging from newborn to adults over 70 years of age.

I. THE ANTIGENS

METHOD OF PREPARATION

Several preparations of antigen were used in this study. The monovalent materials, the characteristics of which are given in table 1A, are representative preparations of specific polysaccharide. The polyvalent lots, shown in table 1B, were made by mixing the final products from several batches of media; hence the exact procedure of preparation cannot be given in detail in the present report. However, the general technique is based on the calcium phosphate method reported previously (*12c*). It is sufficient to say here that the purification procedure used in preparing the monovalent antigens has been solution of the crude product at 0° C. in concentrated HCl or in 1:1 H_2SO_4, and then precipitation with alcohol. Dialysis has given a purer type I product; and refluxing with chloroform has aided in removing residual protein from type II preparations. Details of these methods will be published subsequently.

CHEMICAL AND IMMUNOLOGICAL CHARACTERISTICS

The results of analysis of the monovalent samples are given in table 1A. In the case of the two type I preparations, nitrogen was much the same, the glucose and precipitin titer in number P167 were practically half those of P169, while active immunity was stimulated by each alike in dilution 1:50,000,000. Estimation of the amount of immune protein precipitated in various dilutions, using Heidelberger and Kendall's technique (*15*), showed that this activity of P167, the sample lower in glucose and precipitin titer, was almost twice that of P169. With the type II antigens P171 and P173, the nitrogen was low, the glucose number of one practically twice that of the other, as was also the precipitin titer, while the immunity endpoint was practically the

same, 1:100,000,000 dilution. However, P171, having a high glucose number, had a precipitin titer half that of P173, which had a low glucose number. The amount of protein precipitated from immune horse serum with these two type II preparations was practically the same. All preparations gave a negative test for glycogen. From the standpoint of antigenicity in mice, these four type-specific preparations showed no correlation between this property and either the glucose number, precipitin titer, or the amount of immune protein precipitated.

TABLE 1A.—*Monovalent antigens, types I and II*

Antigen		Nitrogen	Glucose number	Precipitin titer	Immunity in mice
Type	Number				
		Percent	*Percent*		
I	P167	3.30	18.38	1:1,280,000	1:50,000,000
I	P169	3.86	36.32	1:2,560,000	1:50,000,000
II	P171	.81	51.68	1:2,560,000	1:100,000,000
II	P173	1.44	27.60	1:5,000,000	1:100,000,000

Antigen	Immune precipitable nitrogen,[1] SSS dilutions								
	1:1,000	1:2,000	1:3,000	1:4,000	1:5,000	1:7,500	1:10,000	1:12,500	1:15,000
P167	0.392	0.370	0.370	0.370	0.314	0.262	0.258	0.254	0.195
P169	.152	.204	.204	.199	.181	.180	.181	.164	.158
P171	.448	.482	.400	.392	.400	.392	.396	.380	.384
P173	.430	.430	.444	.430	.392	.378	.328	.300	.294

[1] Amount of serum used contained 230 units of protective antibody.

TABLE 1B.—*Polyvalent antigens, types I and II*

Antigen		Year	Nitrogen	Glucose number	Precipitin titer	Immunity in mice
Type	No.					
			Percent	*Percent*		
I	15	1933–34	1.9	24.9	1:2,000,000	1:60,000,000
II					1:1,000,000	1:60,000,000
I	16	1934–35	6.7	13.7	1:3,000,000	1:50,000,000
II			1.0	63.8	1:4,000,000	1:50,000,000
I	160	1935–36	4.65	19.38	1:2,500,000	1:100,000,000
II			4.90	28.70	1:2,500,000	1:75,000,000
I	23	1936–37	4.22	14.40	1:5,000,000	1:50,000,000
II			.07	53.64	1:5,000,000	1:100,000,000
I	24	1936–37	1.86	49.98	1:2,500,000	1:100,000,000
II						1:100,000,000

The polyvalent antigens used were analyzed as shown in table 1B. Although the calcium phosphate method was used for initial precipitation, the antigens were purified by various methods in the search for one which would decrease the reaction-producing characteristics of the final product. Discussion of this point will be taken up later. From the standpoint of production of active immunity in white mice there

was little difference in these preparations when titrated against either type I or type II organisms, respectively. However, although nitrogen content was fairly constant, glucose number and precipitin titer varied significantly.

SUITABILITY FOR HUMAN USE

Our criteria for suitability of the antigen for human beings are (1) antigenicity and (2) freedom from reaction-producing substances.

It has been observed that all samples which are highly antigenic in mice also stimulate a response in human beings. Consequently the test for activity in mice proves an adequate test for suitability in man in regard to antigenicity. Although several instances have been found of samples without activity in mice which stimulated protective serum antibodies in human beings, it would be illogical to employ in human beings fractions which are nonantigenic for mice. More complete knowledge of the relationship between chemical constitution and antigenicity for human beings may make possible the isolation of an active antigen which can be standardized for human use by chemical analysis regardless of the response in laboratory animals.

While attempting to find a suitable animal for testing the reaction-producing properties of various antigens, it was found that on intravenous injection of some preparations mice apparently had a severe reaction from 2 to 4 hours later. At this time, Dr. H. B. Andervont (*16*) was testing the influence of the temperature at which the animal was held on the response to various products. He found that certain substances which were nontoxic for mice at room temperature, when injected intravenously in the same doses in mice held at 37.5° C., caused the death of the animals. In consequence, this technique was applied in testing various antigens which were found to be reaction-producers in human beings. The method was as follows: Mice were placed in a large wire cage to permit circulation of air and with an ample water supply, and were put in an incubator at 37.5° C. to remain overnight. Approximately 20 percent more than the required number were found necessary inasmuch as a certain number of mice succumb at this temperature. In the morning, enough for one sample were taken out at one time, injected in the tail vein with the specified amount and then replaced in the incubator at once. They were kept at room temperature for as short a time as possible. As a rule, three concentrations of the sample were injected in triplicate mice, 1, 2, and 4 mg each in 0.5 cc dose. Mice injected with toxic preparations generally died in 6 to 8 hours; occasionally others died in 18 hours. It is important to look for microorganisms in the heart blood of mice which die in 18 hours in order to rule out an intercurrent infection.

The specific antigens, type I numbers P167 and P169, and type II numbers P171 and P173, were tested in this manner using 5 mg as the largest dose. All mice, irrespective of amount injected, survived under the conditions of this test. When these lots were used in about 60 individuals, with an average of 15 persons to each preparation, no reactions occurred. The test was also run on lots Nos. 15 and 16 reported below with the result that with No. 15 all the mice injected remained alive during the 24-hour period of observation, whereas, with lot 16, a preparation which gave severe reaction in human beings in 2-mg dose, one mouse with 1 mg and all with 2 and 4 mg died. Of five other lots which have been tested in large numbers of human beings, the one which gave a rather severe reaction killed mice in 4-mg dose only. With the others, apparently without reaction in human beings, all mice lived following a dose of 4 mg. Whether or not this test will rule out all unsatisfactory antigen preparations awaits further trials. Nevertheless, in the antigens thus far employed in large groups of individuals, the test has proved a satisfactory measure of the suitability of the antigen with respect to untoward reaction. Needless to say, reactions due to sensitivity would not be eliminated by this mouse test.

II. METHODS

PREPARATION OF THE SOLUTION OF ANTIGENS

Antigens for use in human beings were dissolved in the following manner: With the monovalent antigen, 4 grams of type I (or type II) dried material were well moistened in physiological salt solution, and finally made up to 1,000 cc. Tricresol to make 0.2 percent concentration (or 0.4 percent phenol) was then added as preservative. The time required for making the solution of the antigen varied with the preparation, but did not exceed 4 hours at room temperature. Although at this stage the solution was generally clear, storage at 4° C. for 24 hours or longer rendered filtration easier. It was then passed through a medium Berkefeld or Mandler filter, tested for sterility and ampouled. With a polyvalent antigen, the same procedure was carried out, using 2 grams each of type I and type II material per liter instead of 4 grams of the specific type.

CALCULATION OF DOSE

From experiments in mice, the zone of activity of an average polysaccharide preparation lies between 0.005 mg and 0.000005 mg. If the response in man may be calculated from the relative weights of men and mice, then the dose for an individual weighing 80 kg would be 4,000 times that for a 20-gram mouse, i. e., the zone in man might then be from $0.005 \times 4{,}000$ to $0.000005 \times 4{,}000$, or from 20 mg to 0.02

mg. For human use, calculation was made on the basis of 0.5 cc of a 1:1,000,000 dilution of antigen per 20-gram mouse. The comparable dose for a person weighing 80 kg would thus be 2 mg (0.0000005× 4,000=0.002 grams, or 2 mg). This dose is well below the theoretical inhibiting amount of 20 mg. Although this amount was used throughout the present study, with one exception noted below, it is not to be assumed that it is necessarily the optimum amount nor that a single injection is the best routine procedure.

INOCULATION PROCEDURE

For inoculation into human beings, this single injection of antigen containing 2 mg in 0.5 cc was made subcutaneously in the arm in the deltoid region. The response to the antigen was ascertained by measuring the protective antibodies in the serum 14 days after injection; that is, blood was withdrawn from the individual just before injection and 14 days afterwards. The serum separated aseptically from the first bleeding was stored in the icebox until the second serum was obtained. Both sera were then tested in a single experiment on one day with the same culture and with other conditions as nearly as possible identical. Triplicate mice were injected intraperitoneally with 0.1 cc of serum (0.5 cc of 1:5 dilution) followed immediately by a specified dose of virulent pneumococci. The culture dilutions varied logarithmically from 10 to 100,000 lethal doses of organisms of such virulence that 0.5 cc of 1:500,000,000 or 1:1,000,000,000 dilution killed mice in 36 to 60 hours. For the first titration, 10, 100, 1,000, and 10,000 lethal doses were employed. If all the mice survived, the test was repeated using larger doses of organisms. The endpoint was considered the greatest number of lethal doses against which at least two out of three mice were protected by 0.1 cc serum, i. e., providing all the mice survived in the next lower concentration of culture.

III. RESULTS IN HUMAN BEINGS

REACTIONS

It is well recognized that more or less severe reactions follow injection of the usual vaccine. The advantage of an antigen which is devoid of reaction-producing characteristics and yet is fully antigenic is obvious. Only two antigens, Nos. 15 and 16, are to be discussed in this respect. The effects of these antigens were studied in Civilian Conservation Corps volunteers. The results of their injection are shown in table 2. Antigen No. 15 in 2-mg dose, 1 mg each of type I and type II, was injected into 3,126 individuals. Of this number, 1,881 showed no reaction; 1,010 slight reaction, which means a local reaction without systemic symptoms; 214 moderate, a local reaction with slight malaise; and 21 severe, both local and systemic reactions

but not of sufficient degree to interfere with regular activity of the individual. In other words, this antigen appeared to be practically ideal.

TABLE 2.—*Reactions following injection*

Antigen number	Year	Number inoculated	Reactions				
			None	Slight	Moderate	Severe	
						Number	Percent
15	1933-34	3,126	1,881	1,010	214	21	0.7
16	1934-35	13,829	5,959	4,845	2,476	549	3.9

In the following year, however, when antigen No. 16 was used in 13,829 volunteers, a slightly different picture was obtained. In a preliminary test of this antigen on 15 individuals prior to its use in the large group, three suffered severe reactions. Inasmuch as one of the three individuals had received an injection of lot No. 15 the previous year, and the others had not, it was thought that the severity of his reaction might be due to sensitivity. However, as no untoward reaction has followed the inoculation each year since, the nonspecific toxic property of antigen No. 16 was undoubtedly responsible for the reaction.

Because of the severe reaction from the 2-mg dose of this antigen, 18 additional individuals were injected with one-half this dose. No severe reactions occurred. Now, the average fold increase of serum antibodies in the 15 individuals injected with the 2-mg dose with type I was 10,000 fold and with type II 4,000 fold; whereas with the 1-mg dose in 18 individuals, the increase with type I was 14,000 and with type II, it was 10,000 fold. In other words, although individual variation was great in response to a single injection of antigen, it would appear that the 1-mg dose stimulated antibody to at least the same degree as the 2-mg dose. For that reason, the smaller dose, containing 0.5 mg of each type, was used in the 13,829 volunteers. Because the number of individuals is four times that of the previous year, the results are perhaps more significant. Yet, inasmuch as some complaints were received of reactions sufficiently severe to interfere with regular activity for a day or more, and since there was an increase in the percentage of severe reactions from 0.7 percent (21 out of 3,126) with antigen No. 15 in the previous year to 3.9 percent (549 out of 13,829) with antigen No. 16, the half dose still contained either too much of a nonspecific toxic component or indeed a toxic form of SSS preparation.

From the foregoing data on the type of reaction obtained after injection of 1 or 2 mg of the active polysaccharide, it is apparent that the severity of the reaction is slight compared to that obtained from

many vaccines. The reactions which are of interest to us are the severe ones, because it has been our desire to use an antigenic substance as nearly as possible free from untoward reactions. Individual idiosyncrasies to various drugs, which, prior to the work of Landsteiner (*17*), were considered differences in tolerance, are well known. Landsteiner has demonstrated the possibility that these reactions may be due to a sensitivity to organic compounds of simple structure, which are otherwise nontoxic. In other words, proteins are not the only sensitizing agents. This raises the question as to how far the reaction to the polysaccharide antigen used may be due to a sensitized state of various individuals. The differences in the degree of reactions from the same dose of antigen would support this view. In a 4-year experiment, information has been accumulated from a second injection which has some bearing on this question. A total of 751 men received a second injection of 2 mg after an interval of 1 year; of this number 263 gave no reaction, 397 mild, 54 moderate, and 37 (4.9 percent) severe reactions. It is of importance to note that these 751 men were distributed in 36 different camps, but that the severe reactions occurred in only four of these camps. It is pertinent also that in these four camps all reactions, whether following first or second inoculations, were reported to be generally more severe than in the other camps. Thus the severe reactions in the 4.9 percent may be an expression of individual interpretation by the various camp physicians. Whether or not there is a slight increase in reaction in individuals who had a second dose (sensitivity reaction), the number who show a severe reaction is relatively low and would no doubt be at least as great with any active antigen employed. At no time, in the 61,000 individuals so far tested, have there been any reactions dangerous to life.

SPECIFICITY OF RESPONSE

All of the antigens used in this report were tested in mice for specificity, and the immunity produced was found to be homologous. The two following experiments are given to show the type of antibody response to type-specific lots No. 167 type I and No. 171 type II in children and adults. The actual titration protocols for children are given in tables 3A and 3B. One mg of the specific type I antigen was used instead of the 2 mg dose customarily used in adults. The technique described was otherwise exactly followed. It is evident that before inoculation none of the five children had antibodies detectable with five lethal doses of pneumococci, whereas afterward the same amount of serum protected against at least 5,000 lethal doses. In other words, all children from the ages of 2 to 9 years responded alike in the production of type I antibodies. These same sera were then tested with type II pneumococci, and in the serum before injection of antigen one child had sufficient type II antibody to protect mice

against five lethal doses of type II organisms, while the other four children were negative. In contrast, all the children after inoculation had antibodies sufficient to protect mice against 500 to 5,000 lethal doses of type II pneumococci. Thus, the type I antigen specific in mice produced in children almost as much type II as type I antibody.

TABLE 3A.—*Antibody response in children*

TYPE I ANTIGEN

Name	Age	Titration vs. Type I pneumococci								Titration vs. Type II pneumococci							
		Before injection				After injection				Before injection				After injection			
		Lethal doses								Lethal doses							
		5	50	500	5,000	5	50	500	5,000	5	50	500	5,000	5	50	500	5,000
W. H.	3	36	26	24	18	S	S	S	48	60	48	40	36	S	36	40	36
		36	36	24	22	S	S	S	S	S	48	48	36	S	40	S	36
		36	36	36	24	S	S	S	S	S	S	S	40	S	S	S	36
M. G.	2	25	25	22	18	36	S	S	S	36	36	24	24	S	S	S	S
		36	25	24	18	S	S	S	S	36	36	36	24	S	S	S	S
		36	S	24	24	S	S	S	S	36	36	36	36	S	S	S	S
M. C.	9	36	25	26	22	S	S	S	S	36	36	24	24	S	S	S	90
		36	36	26	24	S	S	S	S	36	36	24	24	S	S	S	S
		36	36	36	24	S	S	S	S	40	36	36	36	S	S	S	S
W. G.	8	36	36	22	18	S	S	S	S	36	36	24	24	S	60	36	36
		36	36	24	22	S	S	S	S	36	36	36	36	S	S	S	36
		36	40	26	24	S	S	S	S	36	36	36	36	S	S	S	36
D. B.	8	25	24	24	24	S	S	84	26	36	36	24	24	90	40	S	S
		36	26	24	25	S	S	S	S	36	36	36	24	S	S	S	S
		36	36	24	36	S	S	S	S	36	36	60	36	S	S	S	S

NOTE.—S indicates survival, and numbers refer to hours of survival of mice used in protection tests.

TABLE 3B.—*Antibody response in children*

TYPE II ANTIGEN

Name	Age	Titration vs. Type II pneumococci							Titration vs. Type I pneumococci								
		Before injection			After injection				Before injection	After injection							
		Lethal doses							Lethal doses								
		5	50	500	50	500	5,000	50,000	1	10	100	5	50	500	5,000	50,000	500,000
I. F.	12	36	24	18	S	S	S	S	36	36	20	36	36	36	20	------	------
		36	36	24	S	S	S	S	36	36	24	S	66	36	36	------	------
		S	36	24	S	S	S	S	36	S	24	S	S	36	36	------	------
B. B.	6	36	36	36	36	24	S	S	36	24	22	36	36	20	-----	------	------
		36	36	36	S	S	S	S	36	24	24	66	36	20	-----	------	------
		36	90	60	S	S	S	S	36	36	24	S	36	36	-----	------	------
J. L.	3	36	36	20	S	S	S	S	36	24	24	66	36	36	36	------	------
		90	36	20	S	S	S	S	36	24	24	90	36	36	36	------	------
		S	S	24	S	S	S	S	36	36	24	S	36	S	36	------	------
									5	50	500						
M. W.	5	36	24	24	S	S	S	S	36	36	----	36	36	24	36	------	------
		S	36	24	S	S	S	S	36	36	----	66	36	36	36	------	------
		S	36	36	S	S	S	S	36	----	----	90	40	36	36	------	------
D. Y.	7	36	36	24	S	36	24	S	36	24	36	S	S	S	-----	66	36
		36	36	36	S	S	S	S	36	24	36	S	S	S	-----	S	S
		S	36	36	S	S	S	S	S	36	S	S	S	S	-----	S	S

NOTE.—S indicates survival, and numbers refer to hours of survival of mice used in protection tests.

In the same way, type II antigen No. 171 was tested in five children. In all, the homologous antibody was stimulated to such degree that 0.1 cc of serum protected against 50,000 lethal doses of virulent organisms. However, when these sera were tested against type I organisms there was only one child of the five whose serum contained any activity against this heterologous type. In this child, the antibody was of exceedingly high titer; 0.1 cc protected against 500,000 lethal doses of type I pneumococci. To summarize, in children, type I antigen No. P167 stimulated antibodies against both type I and type II organisms, but the type II antigen No. 171, with one exception, was type-specific.

These antigens were then tested in adults in the same manner as that shown above with children. In five adults, aged 22 to 45 years, following the injection of 2 mg (instead of 1 mg as in children) there was an increase of the specific antibody titers in all individuals, and as in children this same type I antigen stimulated production of both type I and type II protective antibody. As seen from table 4A, there was, with the possible exception of M. P. and R. R. in whom the end-points of the sera were not obtained before injection (not sufficient sera for retest), an even better response from the specific type I antigen in the development of type II antibody than in that of type I antibody.

Four individuals, two for each of the type II specific antigens 171 and 173, were used to measure the antibody response in adults (table 4B). After injection with these antigens, both type I and type II antibodies were found present in the sera.

TABLE 4A.—*Antibody response in adults*

TYPE I ANTIGEN

Name	Age	Titration vs. Type I pneumococci					Titration vs. Type II pneumococci						
		Before injection		After injection			Before injection			After injection			
		Lethal doses					Lethal doses						
		10	100	1,000	10,000	100,000	5	50	500	500	5,000	50,000	500,000
G. F.	2†	36	36	S	36	66	S	36	36	S	S	S	S
		36	36	S	S	66	S	S	60	S	S	S	S
		36	36	S	S	S	S	S	S	S	S	S	S
M. P.	22	36	24	S	66	36	60	S	S	S	S	S	S
		36	36	S	S	36	S	S	S	S	S	S	S
		36	36	S	S	36	S	S	S	S	S	S	S
R. R.	45	36	36	S	S	36	90	S	S	S	S	S	S
		36	36	S	S	S	S	S	S	S	S	S	S
		36	36	S	S	S	S	S	S	S	S	S	S
S. I.	27	36	36	S	36	66	S	36	36	S	S	S	S
		36	36	S	S	S	S	S	36	S	S	S	S
		40	36	S	S	S	S	S	S	S	S	S	S
E. M.	35	24	36	S	S	36	36	24	24	S	S	S	60
		36	36	S	S	36	36	36	36	S	S	S	90
		36	36	S	S	66	36	S	S	S	S	S	90

NOTE.—S indicates survival, and numbers refer to hours of survival of mice used in protection tests.

TABLE 4B.—*Antibody response in adults*

TYPE II ANTIGEN

Name	Age	Titration vs. Type II pneumococci							Titration vs. Type I pneumococci				
		Before injection	After injection						Before injection	After injection			
		Lethal doses							Lethal doses				
		NO. 171											
		1	10	100	100	1,000	10,000	100,000	10	100	1,000	10,000	100,000
E. B.	50	-----	36	20	------	36	S	S	36	36	60	38	S
		-----	38	36	------	S	S	S	36	36	S	S	S
		-----	S	36	------	S	S	S	36	36	S	S	S
C. F.	31	-----	22	22	------	36	S	S	22	36	S	22	18
		-----	24	24	------	S	S	S	36	36	S	36	18
		-----	36	36	------	S	S	S	36	36	S	36	36
		NO. 173											
J. J.	55	36	36	------	S	36	36	--------	36	36	S	36	36
		36	36	------	S	S	60	--------	36	36	S	S	36
		36	36	------	S	S	S	--------	36	36	S	S	S
J. E.	24	36	36	------	S	66	S	--------	36	24	S	S	36
		36	36	------	S	S	S	--------	36	36	S	S	36
		S	36	------	S	S	S	--------	36	36	S	S	36

NOTE.—S indicates survival, and numbers refer to hours of survival of mice used in protection tests.

In addition, 10 individuals were injected with antigen type I P167 and 10 with 169. These antigens were chosen in order to make a comparison of antigenicity in chemically unlike materials; for 167 had a glucose number of 18 percent as compared with 36 percent in 169. Tests of the sera were made with type I organisms, and with type II organisms to determine the degree of heterologous response from the specific antigen. In these individuals the number of lethal doses against which 0.1 cc of serum would protect before the antigen was given was subtracted from the number afterwards, and the average was taken for the entire group of 10. With type I 167, the antibody on the average was increased to protect against an additional 17,000 doses, and the heterologous response on the test against type II showed an increase of 45,000. With 169, the average increase was 7,000; against type II it was 4,000. In other words, specific antigen 167, with a low glucose number, as tested on 10 individuals showed a significant superiority in regard to specific and to heterologous responses as compared to 169, the antigen with high glucose number and high precipitin titer. These results on human beings confirm those found in white mice, in that the degree of antigenicity does not parallel glucose number.

DURATION OF THE IMMUNITY

Although the duration of antibodies found in convalescents from lobar pneumonia has been studied, little work has been done on duration in normal individuals following vaccination. The most recent is that of Ferguson (*18*) in three individuals after four (or five) injections of pneumococcus vaccine over a period of 15 (or 21) days. These individuals still had antibodies in their sera 1 year after vaccination. No specific experiment in our study has been planned to estimate duration of the antibodies from a single injection of the antigen. Yet over a period of 4 years the sera from 35 individuals have been tested 1 year after injection of this antigen. Eighteen, or 51 percent, still contained at least tenfold more type I antibodies, and 27, or 77 percent, in the case of type II, than were found before injection. However, since the smallest number of lethal doses used in testing was that represented in 0.5 cc of 1:10,000,000 dilution of pneumococcus culture, which would contain from 10 to 100 lethal doses, the total number of individuals who had any antibody in their sera after 1 year may not be represented in the 51 percent who showed type I and the 77 percent who showed type II antibodies.

RESPONSE IN DIFFERENT AGE GROUPS

The curve picturing the incidence and mortality rate of lobar pneumonia shows definitely a peak under 1 year of age, a minimum from 5 to 15, and a more or less gradual increase in the older age groups. It is for this reason that an attempt has been made to ascertain the immunity responses of the different age groups to the antigens here employed. It should be emphasized, that, although all the antigens used in this study were active, a single preparation was not used throughout. Indeed, all the antigens of tables 1A and 1B were used without discrimination as to age of the subject. The majority were injected with polyvalent types I and II polysaccharide solution. The age groups include male and female newborn babies, babies under 1 year, and groups varying in decades from 1 to 9 to 70 to 79 years.

In the first group, blood from four prospective mothers was tested along with blood from the cord and from the baby at delivery. Blood from two of the mothers was tested without inoculation of the antigen, and two after the injection of 2 mg of the antigen 20 days prior to the birth of the child. The blood from the two not inoculated, the cord blood, and the baby's blood were taken immediately after delivery. The babies were then inoculated with 1 mg of type I P167 and blood was taken again after 14 days. Briefly, the tests for antibody in all these serum specimens gave negative results. On

the other hand, the second serum of the two mothers injected 20 days prior to delivery in 0.1 cc dose protected against 5,000 lethal doses of type I culture. In contrast, in these two cases neither the serum from the cord blood nor from the baby contained any detectable antibody. Although no definite conclusions can be drawn from the study of this small group, the results indicate that the pneumococcus antibody is not transferred from the mother to the embryo, at least during the last stage of embryonic development.

In addition, eight infants ranging in age from 3 weeks to 10 months were tested for the response to 1 mg of antigen type I 167. As usual the blood was taken before the antigen was administered and again after 14 days. No protective antibodies against either type I or type II cultures were found in this group following the use of the antigen. The fact that infants vary in their response to antigenic substances is well known. Sutliff and Finland (*19*) have shown this peculiarity with pneumococcus, and more recently Davies (*20*), using immunological tests other than mouse protection, has made the same observation with type I cellular carbohydrate (Wadsworth and Brown (*14*)). Our observations are a confirmation of the refractoriness of the human baby to pneumococcus antigen.

In contrast to the negative results obtained in the age group 1 year and younger, antibody response occurred in the higher brackets irrespective of age. The results of the study of 281 and 276 individuals are given in tables 5A and 5B, for type I and type II, respectively. Column 3 gives the number of subjects who showed measurable antibodies before injection, column 5 the fold increase in serum antibody titer after inoculation of the group, and column 6 the number of fold increase in those without antibodies before injection. These results indicate a greater increase in antibody titer in those who previously had no serum antibodies against pneumococcus. The fold increase was estimated in each case by subtracting the activity before inoculation, in terms of lethal doses of pneumococci protected by 0.1 cc of serum, from the activity after inoculation. Unfortunately, the different age groups are not composed of the same number of individuals. As a consequence, significant deductions cannot be made in regard to the comparative antibody response in the different age brackets. Although the morbidity curve at different age groups indicates that a lowering of resistance may be due to inability of the host to respond to a specific antigen, and thus shows a higher incidence in older age brackets, until a larger number of individuals is tested in the various age groups the only safe conclusion to be drawn from our observations is that antibody response occurs in all age groups from 2 to 79 years. As can be seen from table 5B, this is also true in regard to type II.

TABLE 5A.—*Response of individuals in different age groups to pneumococcus antigen*

RESULTS OF TYPE I TITRATIONS

Age	Number of individuals	Original sera protective antibodies present		Average increase in protective antibody in terms of lethal doses	
		Number	Percent	Sera with antibodies	Sera without antibodies
Under 1	8				0
1-9	6				1,000
10-19	53	14	26.4	401	1,921
20-29	112	18	16.0	429	8,483
30-39	51	5	9.8	242	2,177
40-49	25	4	16.0	257	31,192
50-59	12	1	8.3	1,000	3,920
60-69	7				3,160
70-79	7	1	14.2	1,000	3,370
Total	281	43	15.3		

TABLE 5B.—*Response of individuals in different age groups to pneumococcus antigen*

RESULTS OF TYPE II TITRATIONS

Age	Number of individuals	Original sera protective antibodies present		Average increase in protective antibody in terms of lethal doses	
		Number	Percent	Sera with antibodies	Sera without antibodies
Under 1	8				0
1-9	3	1	33.3	100	10,000
10-19	49	7	14.2	600	6,419
20-29	115	23	20.0	266	12,234
30-39	54	12	22.2	550	19,351
40-49	16	4	25.0	300	3,766
50-59	18				21,335
60-69	8	2	25.0	500	8,350
70-79	5	2	40.0	100	6,700
Total	276	51	18.5		

In tables 5A and 5B is given the average increase in antibody response in different age groups from a single injection of antigen; but this leaves out of consideration individual variations. That experimental animals vary greatly in their ability to produce antibody to bacterial antigens and toxins is well known. In tables 6A and 6B the individual responses of the various age groups, for type I and type II, are tabulated to show the degree of variation in response to the antigen as measured by serum antibodies. It is to be emphasized again that the same antigen was not used in all individuals. However, all antigens were effective in white mice in approximately the same dose.

Conclusions drawn from these observations are that 0.1 cc of serum protected mice against cultures varying from 0 to 100,000 lethal doses. The highest percentage of individuals lies in the 1,000 lethal dose column. However, the number that failed to respond in type I was 6 out of 230 individuals, and with type II, 2 out of 217 individuals.

It cannot be said at present whether this failure to respond was due to the antigen or to the inability of the individuals to manufacture pneumococcus antibody, or whether this is a temporary state of these individuals or, indeed, represents a defective immunological mechanism. This much is certainly true, that there is a very great difference in individual response. This fact emphasizes a possible influence which may affect the incidence of the disease. At present it is a mere assumption that high degree of susceptibility and high incidence rate are found among individuals who do not readily respond to this pneumococcus antigen. Yet the number of individuals who failed to respond, at least in this group, is relatively much higher than the number attacked by pneumonia in the general population. This assumption may be logical; however proof can be ascertained only by study of a large number of individuals over a period of years.

TABLE 6A.—*Number of individuals showing variation in protective activity in 0.1 cc serum*

TYPE I

Age	Total		Individuals with no protective antibody in original sera											
			Number						Percent					
	Number	Percent	Lethal doses						Lethal doses					
			0	10	100	1,000	10,000	100,000	0	10	100	1,000	10,000	100,000
1-9	6	2.6	----	----	----	6	----	----	----	----	----	----	----	----
10-19	39	16.9	----	1	9	24	5	----	----	2.6	23.0	61.0	12.8	----
20-29	94	40.8	3	11	13	46	15	6	3.2	11.7	13.8	48.9	16.0	6.3
30-39	46	20.0	1	7	11	19	8	----	2.2	15.0	23.5	41.0	17.0	----
40-49	21	9.0	1	4	----	5	5	6	4.8	19.0	----	23.8	23.8	29.0
50-59	11	4.8	1	2	1	3	4	----	9.0	18.0	9.0	27.0	36.0	----
60-69	7	3.0	----	2	1	2	2	----	----	28.4	14.2	28.4	28.4	----
70-79	6	2.6	----	2	2	----	2	----	----	33.3	33.3	----	33.3	----
Total	230	----	6	29	37	105	41	12	2.6	12.6	16.0	45.7	17.8	5.2

TABLE 6B.—*Number of individuals showing variation in protective antibody in 0.1 cc serum*

TYPE II

Age	Tcta		Individuals with no protective antibody in original sera											
			Number						Percent					
	Number	Percent	Lethal doses						Lethal doses					
			0	10	100	1,000	10,000	100,000	0	10	100	1,000	10,000	100,000
1-9	2	0.9	----	----	----	----	2	----	----	----	----	----	----	----
10-19	42	19.3	----	1	6	19	15	1	----	2.4	14.2	45.2	35.7	2.4
20-29	92	42.4	----	6	15	44	18	9	----	6.5	16.3	47.8	19.5	9.7
30-39	42	19.3	----	6	7	12	10	7	----	14.2	16.6	28.4	24.0	16.6
40-49	12	5.5	1	----	2	5	4	----	8.3	----	16.6	41.5	33.3	----
50-59	18	8.4	1	2	----	4	8	3	5.5	11.0	----	22.0	44.0	16.6
60-69	6	2.8	----	----	1	----	5	----	----	----	16.6	----	83.3	----
70-79	3	1.4	----	----	1	----	2	----	----	----	33.3	----	66.6	----
Total	217	----	2	15	32	84	64	20	.9	6.9	14.7	38.6	29.4	9.2

The observations of Blake (*21*) some years ago in measuring agglutinins to rough pneumococci in a relatively large number of individuals support a similar inference. He found that 80 percent of the individuals tested possessed agglutinins for rough pneumococci. Deductions drawn by him were to the effect that most individuals in the general population are immune to pneumococcus infection and that the relationship between antibody content and morbidity is reciprocal. Although the number of individuals who actually have protective antibody, from our observations, is much smaller than was found to have agglutinins against rough pneumococci, nevertheless the data are as yet insufficient to show a relationship either between agglutinin titer, or variation in protective antibody, and the morbidity or mortality rate of pneumonia.

DISCUSSION

The question arises as to whether the antigen used in this experiment is the same as the classical soluble specific substance of Heidelberger and Avery (*22*) or the new preparation isolated by recent methods of Avery and Goebel (*10*), and Heidelberger and others (*23*). The product is similar in that the amount of protein precipitated from antipneumococcus horse serum is approximately that obtained by Heidelberger, and in that the antigenicity for mice is of the same degree. However, it is pertinent that neither the type I nor the type II antigenic polysaccharide used by us contained acetyl groups. True, in some preparations vacuum distillation after acid hydrolysis yields an organic acid; but in all tests carried out this acid has been shown not to be acetic acid. This subject will be taken up in detail in another publication.

Another point of difference is the lack of correlation between antigenicity and glucose number in our preparations, and also the lower glucose numbers. One preparation of type I has been described which showed no glucose after hydrolysis and was still antigenic, both for type I and type II, in mice. In human beings the two preparations P167 with low glucose number and P169 with high number revealed significant difference antigenically; for P167 showed greater activity as to both specific and heterologous antibody stimulation than was the case with P169. In a measure this is a confirmation of the work in mice, and may point to an antigen of universal characteristics, a common denominator of the pneumococcus species.

The heterologous response in human beings has been quite consistent, with the exception that the type II preparations tested were largely specific in children. In adults, however, all these preparations gave specific and heterologous response. These observations are at variance with the report of Finland and Dowling (*13*) in which they observed a specific response to the cellular carbohydrate of Wads-

worth and Brown (*14*). There are perhaps two significant differences in our experiments. Our preparations contained no phosphorus, while in those used by Finland and Dowling this element was found in varying amounts. Second, the single dose of 2 mg was a larger quantity than the sum of their repeated doses. Yet at present there is no adequate answer for these differences in antigenic response. Our observations tend to support the existence of varied forms of the polysaccharide as measured by the difference in immunological response.

The response to the polysaccharide antigen occurred irrespective of age above 1 year and with the exceptions given above. However, the important consideration is the observed variation in different individuals. This marked difference may be due to improper methods of immunization, to the use of an unsatisfactory antigen, or indeed may be the actual measure of the ability of any individual to respond to this or perhaps any other pneumococcus antigen. It is thus conceivable that the method of study, although expensive, may make it possible to determine individuals susceptible to pneumococcus infections and thus point to a possible method of prevention. For if susceptible individuals are ones who give little or no response to a pneumococcus antigen, the problem of prevention can be narrowed to a relatively small group. Consequently, efforts may be concentrated on the relatively small number of susceptible individuals with perhaps greater promise of successful prevention than in work on the entire population. However, it must first be determined whether or not these persons who fail to respond are really susceptible. To ascertain this a large group should be followed for a period of years, after their antigenic response is known.

Of the two methods of approach for the prophylaxis of pneumococcus infections, active immunity or building up the natural resistance, the former is the better known. However, there are many obstacles in general application. The main one is, as has already been observed, the short duration of immunity, necessitating frequent inoculations. Nevertheless, our information is incomplete as to the exact duration in which the resistance of the host is sufficiently increased to influence the morbidity rate. The excellent work of Colonel Siler and staff at the Army Medical School on typhoid vaccination (*24*), in which they are measuring the duration of antibodies following a series of injections of typhoid vaccine, would indicate that a measurable amount of antibody is present in the serum of those vaccinated for 1 year or more. In other words, since typhoid vaccination has been shown to be of great prophylactic value, especially in the Army where vaccination is repeated twice at an interval of 3 years, the possibility exists that a resistant state continues not only over this 3-year period, but perhaps for a still longer interval of time.

Whether or not vaccination with the antigen here reported, or any other, will give a duration of immunity similar to that shown with typhoid vaccine awaits demonstration. The use of the polysaccharide antigen has been continued over a period of 5 years during which time 61,000 individuals have been inoculated. The results of this study will be published in a following paper. The number is small in view of the short duration of observation of each volunteer. Nevertheless, results are promising and would indicate the possible value of this antigen, especially in high concentrations of population from different geographic areas, such as Army, Navy, or concentration camps of different kinds, in other words, as an emergency procedure. The antigen used would be particularly well adapted for such use, inasmuch as it is a dry, stable product which can be prepared ahead of time and made ready for injection on very short notice. Considerable success has been obtained also in individuals in whom repeated attacks of lobar pneumonia have occurred. This would indicate that those individuals known to be susceptible may be immunized by the polysaccharide antigen or some other vaccine. Nevertheless, if there has been a definite prophylactic value apparently demonstrated, it is not to be inferred that the attempt to immunize the general population should at this time be advocated. But rather efforts should be directed toward developing means for measuring susceptible individuals, with subsequent procedures to increase their resistance specifically with an immunizing agent or perhaps to enhance their natural immunity.

SUMMARY AND CONCLUSIONS

Some chemical and immunological characteristics are given of fractions of pneumococci which are antigenic both in mice and in human beings. It is shown that there is a significant variation in glucose number from that of the polysaccharide of Heidelberger and Avery, and yet the antigenic activity in mice and human beings is as great as that of preparations approaching the chemical analysis of SSS as given by Heidelberger.

The occasional untoward reactions in humans following injection of 2-mg doses of some preparations of antigen have been discussed. One method of purification to eliminate these has been given, namely, treatment with either concentrated HCl or 1 : 1 H_2SO_4 at 0° C. In addition, a test is described for white mice which apparently determines the presence of reacting substances, and consequently may be used to assure antigen suitable for injection without reactions in human beings.

A type I antigen, shown to be specific for white mice, produced antibodies in children against type II of almost as high a titer as against type I organisms. Conversely, one preparation of specific type II antigen stimulated type I antibody in only one of five children tested.

In adults, these same specific antigens produced heterologous immunity; type I antigen stimulated type II antibodies as well as type I, and type II antigen stimulated type I as well as type II antibodies.

Test was made of two samples of type I specific antigen in 10 individuals each; the essential difference between the antigens was the variation in glucose number. The one having approximately one-half the glucose number of the other produced greater antibody response of both homologous and heterologous type.

A test of 35 individuals 1 year after injection of 2 mg of polyvalent antigen showed the presence of type I serum antibody in 51 percent and of type II antibody in 77 percent of the group.

A total of 281 individuals varying in age from birth to 79 years has been inoculated and tested for serum antibodies against type I and 276 against type II pneumococci. By actual test 15 percent of the group had type I antibodies in the serum before injection and 18.5 percent had type II. From two mothers who had been immunized before delivery there was no transfer of the antibody to the baby. All babies under 1 year and six adults in the type I group and two in the type II series showed no antibodies either before or after the injection. All others, following a single injection of 2 mg of antigen, showed an increase, although varying in amount, of serum antibodies against both type I and type II pneumococci. A marked variation in response to the antigen as judged by serum antibody content was observed in different individuals.

ACKNOWLEDGMENTS

This experiment was carried out with the cooperation of many individuals. All in reality are considered collaborators in the investigation. It is indeed a pleasure to express my appreciation for their whole-hearted spirit of cooperation, without which such a study would have been impossible. The field study was done through the help of Col. G. M. Ekwurzel and staff, at the Army base in Boston, on a group of volunteers from the Civilian Conservation Corps enrollees in Massachusetts camps. The observations on children were made possible through the cooperation of Dr. L. E. Holt and staff of the Harriet Lane Home for Invalid Children, Johns Hopkins Hospital. The study on infants and mothers was carried out through the help of Dr. A. U. Christie, Johns Hopkins Hospital. Additional tests in human beings were carried out through the help of Drs. W. R. Cameron and P. F. Prather of Hagerstown, Md. For aid in the preparation of the antigen and testing of the sera indebtedness is acknowledged to Miss Gladys Kauffmann, Miss Helene J. Stahl, Benjamin Prescott, and C. Albert Loeb. For a great part of the material necessary for preparation of the polysaccharide and the sera for testing,

appreciation is expressed to Mr. Stanley D. Beard of the Lederle Laboratories, and Dr. John Reichel of the Mulford Laboratories of Sharp & Dohme.

REFERENCES

(1) Lister, F. S.: An experimental study of prophylactic inoculation against pneumococcal infection in the rabbit and in man. So. African Inst. Med. Res., No. 8; p. 231 (1916).

(2) Cecil, R. L., and Austin, J. H.: Results of prophylactic inoculation against pneumococcus in 12,519 men. J. Exp. Med., 28: 19 (1918).

(3) Felton, L. D., Sutliff, W. D., and Steele, B. F.: Antigenic characteristics in man of certain products of the pneumococcus. J. Inf. Dis., 56: 101 (1935).

(4) Lister, F. S., and Ordman, D.: The epidemiology of pneumonia on the Witwatersrand goldfields and the prevention of pneumonia and other allied acute respiratory diseases in native labourers in South Africa by means of vaccine. So. African Inst. Med. Res., No. 37 (1935).

(5) Auld, A. G.: Remarks on the morphology and chemical products of the diplococcus pneumoniae, and some results of vaccination. Brit. Med. J., 1: 775 (Mar. 27, 1897).

(6) Jobling, J. W., and Strouse, S.: Studies on ferment action. V. Immunization with proteolytic cleavage products of pneumococci. J. Exp. Med., 16: 860 (1912).

(7) Hirschfelder, J. O.: The production of active and passive immunity to the pneumococcus with a soluble vaccine. J. Am. Med. Assoc., 59: 1373 (1912).

(8) Francis, T., and Tillett, W. S.: Cutaneous reactions in pneumonia. The development of antibodies following the intradermal injection of type-specific polysaccharide. J. Exp. Med., 52: 573 (1930).

(9) Finland, M., and Sutliff, W. D.: Specific cutaneous reactions and circulating antibodies in the course of lobar pneumonia. I. Cases receiving no serum therapy. J. Exp. Med., 54: 637 (1931).

(10) Avery, O. T., and Goebel, W. F.: Chemoimmunological studies on the soluble specific substances of pneumococcus. I. The isolation and properties of the acetyl polysaccharide of pneumococcus type I. J. Exp. Med., 58: 731 (1933).

(11) Francis, T.: Antigenic action of the specific polysaccharide of pneumococcus type I in man. Proc. Soc. Exp. Biol. and Med., 31: 493 (1934).

(12) (a) Felton, L. D.: Active immunization of white mice by a non-polysaccharide and probably non-protein derivative of the pneumococcus. J. Immunol., 23: 405 (1932).

(b) Felton, L. D.: Studies on the immunizing substances in pneumococci. II. Separation of the organism into acid soluble and acid insoluble fractions. J. Immunol., 27: 379 (1934).

(c) Felton, L. D., Kauffmann, G., and Stahl, H. J.: The precipitation of bacterial polysaccharides with calcium phosphate. Pneumococcus. J. Bact., 29: 149 (1935).

(d) Felton, L. D., Sutliff, W. D., and Steele, B. F.: Antigenic characteristics in man of certain products of the pneumococcus. Comparison with vaccine. J. Inf. Dis., 56: 101 (1935). (See *ref.* (3).)

(e) Felton, L. D., and Prescott, B.: Studies on the immunizing substances in pneumococci. V. The effect of alkalis on the immunizing properties of a type I pneumococcus polysaccharide. Bull. Johns Hopkins Hosp., 59: 114 (1936).

(f) Felton, L. D., and Kauffmann, G.: Studies on the immunizing substances in pneumococci. VI. The essential immunizing antigen of types I and II pneumococci. Bull. Johns Hopkins Hosp., 62: 430 (1938).

(13) Finland, M., and Dowling, H. F.: Cutaneous reactions and antibody response to intracutaneous injections of pneumococcus polysaccharides. J. Immunol., 29: 285 (1935).

(14) Wadsworth A. B., and Brown, R. J.: Chemical and immunological studies of the pneumococcus. III. Cellular carbohydrate fractions. J. Immunol., 24: 349 (1933).

(15) Heidelberger, M., and Kendall, F. E.: The precipitin reaction between type III pneumococcus polysaccharide and homologous antibody. II. Conditions for quantitative precipitation of antibody in horse sera. III. A quantitative study and a theory of the reaction mechanism. J. Exp. Med., 61: 559, 563 (1935).

(16) Andervont, H. B.: Personal communication.
(17) Landsteiner, K.: Serological and allergic reactions with simple chemical compounds. New Eng. J. Med., 215: 1199 (1936).
(18) Ferguson, D.: Studies of active pneumococcus immunity. III. The duration of type I pneumococcus immunity. U. S. Naval Med. Bull., 33: 219 (1935).
(19) Sutliff, W. D., and Finland, M.: Antipneumococcic immunity reactions in individuals of different ages. J. Exp. Med., 55: 837 (1932).
(20) Davies, J. A. V.: The response of infants to inoculation with type I pneumococcus carbohydrate. J. Immunol., 33: 1 (1937).
(21) Blake, E. G.: Address at Harvard Alumni meeting, 1927.
(22) Heidelberger, M., and Avery, O. T.: The soluble specific substance of pneumococcus. J. Exp. Med., 38: 73 (1923); and others to date.
(23) Heidelberger, M., Kendall, F. E., and Scherp, H. W.: The specific polysaccharides of types I, II, and III pneumococcus. A revision of methods and data. J. Exp. Med., 64: 559 (1936).
(24) Siler, J. F.: Personal communication.

STUDIES ON IMMUNIZING SUBSTANCES IN PNEUMOCOCCI

VIII. REPORT ON FIELD TESTS TO DETERMINE THE PROPHYLACTIC VALUE OF A PNEUMOCOCCUS ANTIGEN[1]

By Col. G. M. Ekwurzel and Lieut. Col. J. S. Simmons, *Medical Corps, United States Army*, Louis I. Dublin, *third Vice-President and Statistician, Metropolitan Life Insurance Co.*, and Lloyd D. Felton, *Senior Surgeon, United States Public Health Service*

This report presents an analysis of the results obtained in a series of field tests with a pneumococcus antigen active for both mice and men, prepared by Felton. The description of the antigen used is given in the preceding report (*1*). The antigen is polysaccharide in nature and is similar in chemical characteristics to the classical polysaccharide of Heidelberger and Avery. Yet, unlike their original preparations, but like those of Schiemann and Casper (*2*), the antigen is fully active. Again, it is different from the polysaccharide described recently by Avery and Goebel (*3*) in that no evidence is found to indicate the presence of an acetyl group. The present work was undertaken on the use of a soluble, readily sterilized antigen, which was found not only to be an active polysaccharide but, from actual test in white mice, was also found to contain as many, or more, immunizing doses as the original organisms from which it was derived. The antigen used was polyvalent, consisting of equal portions of type I and type II so that each 0.5 cc contained 1 mg of each type of polysaccharide. The technique of injection and the study of the antibody response are given in the previous paper (*1*).

The field tests were organized under the supervision of one of us (Colonel Ekwurzel) on volunteers of the Civilian Conservation Corps, first in New England and later on the west coast. Five tests in all

[1] This is one of a series of studies carried out in part under a grant from the Influenza Commission of the Metropolitan Life Insurance Company, and in part under a grant from the Pneumonia Fund of Harvard University and of Johns Hopkins University. This study was conducted in the Civilian Conservation Corps Camps of New England and the west coast.

Preceding papers of this series are listed in the preceding article.

were made to establish the efficacy of the antigen, the last two tests being conducted on a large scale with carefully planned controls. The results presented here are necessarily of a preliminary character and are to be confirmed by further experiments.

In the winter of 1933–1934, through Colonel Ekwurzel, who was then surgeon of the Army First Corps Area, Boston, Mass., an opportunity was given to inoculate 3,126 Civilian Conservation Corps enrollees in November and to observe them until April. Prior to the use of the antigen, it was tested in both mice and human beings. In addition, the sera of 188 individuals were tested before inoculation, 1 month after, 3 months after, and 1 year after inoculation. The results indicated that all individuals tested showed the presence of protective antibodies against both type I and type II for the first month, 97 percent 3 months after inoculation, and 65 percent 1 year afterwards. No pneumonia occurred in the inoculated group (3,126) while eight cases were reported in the noninoculated group of about 9,000.

In the next year (1934–35), beginning in November, 14,000 volunteers in the Civilian Conservation Corps camps were inoculated and observed together with 12,000 controls. Because of an unexpected turnover in the personnel in April, a follow-up system was instituted to extend the period of observation from April to June 15. In all, cards were sent to 15,000 individuals, of whom about half were inoculated and half noninoculated, asking for information in regard to the occurrence or nonoccurrence of pneumonia subsequent to their discharge from the camps. Any pneumonia reported was confirmed through the physician in charge of the case. During the period from November to June 15, there were reported 13 cases of lobar pneumonia in the inoculated group, with no deaths, and 23 cases in the control group, with 2 deaths. Most of the pneumonias were unclassified in regard to type. However, in the inoculated group there was reported one type II case, and in the controls there were two of type I and one type II.

In the winter of 1935–36 the third test was made with 15,000 inoculated enrollees and 18,000 controls. The period of observation extended from December 1, 1935, to March 31, 1936. Not all of these enrollees were under observation for the entire 4 months' period. Altogether there were reported 18 cases of pneumonia in the inoculated group and 39 cases in the control group. On the basis of enrollees in the camps on December 31, 1935, the case rate was 2.25 per 1,000 in the control group. Among the 14,881 men inoculated, the case rate was 1.21 per 1,000. There were five pneumonia deaths in the control group and only one in the inoculated group. No type I or type II cases were found in the inoculated groups, as compared with six of each type in the controls.

The results of the third test were promising, but in the absence of systematic records it was impossible, for this experiment, to compute rates on the proper basis, namely, with respect to the exact number of lives exposed and the duration of their exposure to infection. For this reason arrangements were made to conduct the next experiment along lines that would provide a more rigorous basis for comparing pneumonia incidence in the control and in the inoculated groups. As the outcome of these arrangements the fourth and fifth tests were conducted by the use of a card record for each individual, whether inoculated or acting as a control. These two tests were carried out during the winter of 1936–37 in the west coast camps and in the New England camps of the Civilian Conservation Corps. The experiment in the west coast camps was conducted under the supervision of Col. G. M. Ekwurzel, surgeon of the Army Ninth Corps Area, Presidio of San Francisco, while the experiment in the New England camps was supervised by Col. Herbert G. Shaw, surgeon, and Lt. Col. James Stevens Simmons, assistant to the surgeon of the First Corps Area, Army base, Boston, Mass. The records obtained from the two areas were tabulated and analyzed in the Statistical Bureau of the Metropolitan Life Insurance Co., under the immediate direction of Mr. Mortimer Spiegelman to whom much credit is due.

NATURE AND TREATMENT OF THE DATA

PERIOD OF OBSERVATION

In the New England camps the period of observation began December 1, 1936, and terminated May 15, 1937. All enrollees in the New England camps were traced from the beginning of the period of observation, or from date of enrollment, if it fell within that period, to the termination of the period of observation, or to prior date of discharge. The control experience included, in addition to the individuals expressly selected for control (i. e., not inoculated), for each inoculated enrollee, the period lapsing from the initial date of observation to the date of inoculation.

The west coast experiment had no fixed initial date of observation applying to the group as a whole, but instead, the initial date of observation was reckoned separately for each of the 312 companies in which enrollees were inoculated, the initial date of observation being taken as the date on which the first of the men in the company received the antigen. The period of observation ended on April 30, 1937. Men enrolled after the initial date of observation were not included in the experiment. All enrollees present at the first date of observation were traced from that date to the termination of the period of observation or to prior discharge.

EXPOSURE TO RISK OF INFECTION

In considering a group of persons exposed to risk of infection for a period of time, evidently the total opportunity for infection is proportional both to the number of persons and to the length of time each is exposed. It is, therefore, proportional to the product of the number of persons and the number of days each is exposed during the period considered. When this product is divided by 365 the result obtained is the "years of life exposed to risk of infection."

The experiment in the New England camps was based upon a total of 25,234 enrollees of whom 10,740 were inoculated. These enrollees were exposed for a total of 8,395.7 years of life during the period of observation. Of this total, the inoculated experience constituted 3,453.4 years of life and the control experience 4,942.3 years of life. The latter includes 752.1 years of life contributed by inoculated enrollees from their initial date of observation to the date of inoculation.

The west coast experiment included 45,022 enrollees who were exposed for a total of 8,558.4 years of life. The 18,494 inoculated enrollees in this experiment were exposed for 3,461.2 years of life. The control experience totalled 5,097.2 years of life, of which 127.6 represented the period elapsed from date of initial observation to date of inoculation among those who received antigen.

AGE DISTRIBUTION

Table 1 presents, in summary form, the data discussed in the preceding paragraphs, and presents in addition the distribution of the men by broad age groups. As was to be expected, the subjects of this experiment were essentially a youthful group, 80 percent being under 25 years of age. This percentage was practically the same for the New England and the west coast camps, and did not vary appreciably between the control and inoculated groups. There was also a considerable number of enrollees at ages 40 and over, resulting from the admission of World War veterans to the camps.

AVERAGE DURATION OF OBSERVATIONS

The average period of time during which the enrollees were exposed to risk of infection while under observation was relatively short. On an average, each inoculated enrollee in the New England camps was under observation for 117.4 days after his inoculation; for those who were not inoculated the average duration of exposure was 105.5 days. In the west coast camps, the average duration was even less, being 68.3 days for those inoculated and 68.4 for those not inoculated. The shorter average durations for the west coast camps arose from two circumstances. In the first place, the inoculation of enrollees in the west coast camps could not be started until January 1937 because of a

technical difficulty in the commercial laboratory where the antigen was being prepared. (It will be recalled that the initial date of observation in the New England camps was December 1, 1936.) Secondly, the west coast observations terminated April 30, a half-month earlier than in the New England camps. As a result of the short periods of observation and the large proportion of enrollees at ages when pneumonia incidence is relatively low, the pneumonia cases that occurred were few in number, as will be shown later. The same circumstance also made it impossible to ascertain what effect the lapse of time had on the immunizing power of the antigen.

TABLE 1.—*Number of enrollees and years of life exposed to risk of infection, for the control and inoculated groups (New England Civilian Conservation Corps camps, from Dec. 1, 1936, to May 15, 1937; west coast Civilian Conservation Corps camps, from initial date of observation in January or February 1937 to Apr. 30, 1937* [1])

Group	Total	Age			
		Under 20	20–24	25–49	50 and over[2]
NEW ENGLAND CAMPS					
	Number of enrollees				
Total	25,234	13,745	6,889	4,076	524
Control	14,494	7,980	3,540	2,597	377
Inoculated	10,740	5,765	3,349	1,479	147
	Years of life exposed				
Total	8,395.68	4,289.09	2,479.06	1,445.46	182.07
Control[3]	4,942.32	2,463.68	1,391.43	954.06	133.15
Inoculated	3,453.36	1,825.41	1,087.63	491.40	48.92
WEST COAST CAMPS					
	Number of enrollees				
Total	45,022	17,940	18,171	7,747	1,164
Control	26,528	10,711	10,368	4,556	893
Inoculated	18,494	7,229	7,803	3,191	271
	Years of life exposed				
Total	8,558.44	3,300.36	3,494.15	1,523.17	240.76
Control[3]	5,097.22	1,992.03	2,019.55	901.86	183.78
Inoculated	3,461.22	1,308.33	1,474.60	621.31	56.98

[1] The initial date of observation was reckoned separately for each of the 312 companies in which enrollees were inoculated, being taken as the date on which the first of the men in the company received the antigen.
[2] Including those of unknown age.
[3] This includes the years of life exposed by inoculated enrollees from initial date of observation to date of inoculation.

The low average duration of observation for the two experiments was primarily a natural consequence of the short time elapsing from the initial to terminal dates of observation. But another contributing factor of great importance was the rate of turnover among the enrollees. Of all the enrollees who were included in the experiments, 45 percent in the west coast camps and 30 percent in the New England camps left camp before the period of observation terminated. With such large proportions of enrollees lost to observation before the closing dates of the experiment, the desirability of a follow-up system becomes patent, for without such follow-up it is not known to what extent the results obtained would be modified by any differential in pneumonia incidence between those in control groups and those in the inoculated groups after they passed out of the range of observation. However, facilities were not available for installing an adequate follow-up system by which the number of pneumonia cases developing in the interval elapsing from date of discharge to the closing date of observation might be ascertained. Data regarding the movement of enrollees into and out of the camps will be found in table 2.

TABLE 2.—*Movement of enrollees into and out of Civilian Conservation Corps camps during period of observation (New England camps from Dec. 1, 1936, to May 15, 1937; west coast camps from January or February 1937 to Apr. 30, 1937* [1])

	Total	Inoculated	Control
	New England camps		
In camp on Dec. 1, 1936	17,193	[2] 9,500	7,693
Enrollees, Dec. 1, 1936, to May 15, 1937	8,041	[3] 1,240	6,801
Total under observation	25,234	10,740	14,494
Discharges, Dec. 1, 1936, to May 15, 1937	7,477	3,511	3,966
In camp on May 15, 1937	17,757	7,229	10,528
	West coast camps		
In camp at start of experiment	45,022	[4] 18,494	26,528
Subsequent discharges prior to Apr. 30, 1937	20,296	8,004	12,292
In camp on Apr. 30, 1937	24,726	10,490	14,236

[1] The initial date of observation was reckoned separately for each of the 312 companies in which enrollees were inoculated, being taken as the date on which the first of the men in the company received the antigen.
[2] Most of these were inoculated at a subsequent date.
[3] Inoculation was not necessarily given on date of enrollment.
[4] Most of these were inoculated near the start of the experiment.

DISTRIBUTION OF EXPOSURE BY CALENDAR MONTHS

The seasonal characteristic of pneumonia would appreciably affect a comparison of the incidence of the disease between the control and inoculated groups if the exposure to risk for each calendar month were not distributed similarly in the two groups. This factor is also to be considered when the pneumonia incidence in the New England camps is compared with that in the west coast camps. Table 3 shows the

distribution of the "years of life exposed to risk" by calendar months for the inoculated and control groups in the New England and west coast camps.

TABLE 3.—*Distribution of years of life exposed to risk of infection by calendar months within the periods of observation, for control and inoculated groups (New England Civilian Conservation Corps camps from Dec. 1, 1936, to May 15, 1937; west coast Civilian Conservation Corps camps from initial date of observation in January or February 1937 to Apr. 30, 1937* [1])

Month	New England camps			West coast camps		
	Total	Inoculated	Control	Total	Inoculated	Control
	Years of life exposed					
Total	8,395.68	3,453.36	4,942.32	8,558.44	3,461.22	5,097.22
December	1,460.16	233.68	1,226.48			
January	1,628.78	696.93	931.85	282.23	99.29	182.94
February	1,530.57	766.64	763.93	2,761.71	1,082.12	1,679.59
March	1,627.20	837.36	789.84	3,413.03	1,393.96	2,019.07
April	1,409.35	619.04	790.31	2,101.47	885.85	1,215.62
May	739.62	299.71	439.91			
	Percent distribution					
Total	100.00	100.00	100.00	100.00	100.00	100.00
December	17.39	6.77	24.82			
January	19.40	20.18	18.85	3.30	2.87	3.59
February	18.23	22.20	15.46	32.27	31.27	32.95
March	19.38	24.25	15.98	39.88	40.27	39.61
April	16.79	17.92	15.99	24.55	25.59	23.85
May	8.81	8.68	8.90			

[1] The initial date of observation was reckoned separately for each of the 312 companies in which enrollees were inoculated, being taken as the date on which the first of the men in the company received the antigen.

It will be noted first of all, that, in the New England camps, only 6.8 percent of the total exposure of the inoculated group occurred during the month of December, whereas 24.8 percent of the control exposure was concentrated in that month. On the other hand, the inoculated group had larger proportions of total exposure than the control group in the period from January through April. The high incidence of control exposure to risk in December as compared to that of the inoculated group arises from the fact that the period of observation began the first of that month, whereas inoculation was started later in the month.

In the west coast camps the distribution of the years of life exposed to risk by calendar months did not vary appreciably between the inoculated and control groups. The low proportion of total exposure in January is a result of the delay in the receipt of the antigen until late in the month. It will be recalled, in this connection, that observations in the west coast camps were begun only when the inoculations were started. Because of the shorter period of observation in the west

coast camps than in the New England camps, the "years of life exposed to risk" in the former were more heavily concentrated in February, March, and April.

GEOGRAPHIC DISTRIBUTION OF ENROLLEES

It is noted, in connection with the west coast camps, that the camp at Havre, Mont., experiences the lowest temperatures in the United States. Camps in southern California have almost perpetual summer. Altitudes vary from about 6,000 feet to sea level. Many camps are in mountain forests, others in alkali deserts. These wide differences in geographic location and in climate contrasted strongly with the situation in New England camps, where all enrollees were subjected to practically the same climatic conditions.

SELF-SELECTION OF VOLUNTEERS

Sight must not be lost of the fact that the inoculations were given on a voluntary basis. It is possible that this may have had some effect on the results, for there are two contradictory considerations that may be involved. In the first place, there is the chance that many of those who volunteered for inoculation belonged to that healthy class of persons which takes care of its health. Or, on the other hand, the volunteers may contain many who felt themselves susceptible to respiratory conditions which they would like to avoid. In the absence of definite information regarding these considerations, it is here assumed that the self-selection of volunteers for inoculation did not materially affect the results.

DESCRIPTION OF RESULTS

NUMBER OF PNEUMONIA CASES AND DEATHS

In the New England camps there were altogether 51 cases of pneumonia during the period of observation; 36 of these were in the control group and 15 in the inoculated group. Only three enrollees died of pneumonia during this period; two of these were in the control group and one was inoculated. It may be worth noting that the latter individual, who was 48 years old, had been inoculated only the day before he was hospitalized with lobar pneumonia. The two men in the control group who died were 18 and 43 years of age, respectively.

In the west coast camps there were 86 cases of pneumonia, of which only six were inoculated. There were eight pneumonia deaths in the control group and none among the inoculated. Of the eight deaths, six were of enrollees between the ages of 16 and 23; one was 44 and the other 65 years old.

DISTRIBUTION OF PNEUMONIA CASES BY TYPE

Typing facilities were more adequate in the New England camps than in the west coast camps. The relative frequency of the different types of pneumonia is shown in tables 4 and 5 for the New England and west coast camps, respectively. It will be observed that none of the inoculated cases in the New England camps was determined as either of type I or type II, the very types for which this antigen was prepared. This seems to indicate that the antigen may be particularly effective for these types. However, in four inoculated cases the type was, unfortunately, not determined, and in the west coast camps three of the six cases among the inoculated enrollees were of types I or II, the remaining being again undetermined in type. The degree of specificity of the vaccine for types I and II, therefore, remains in doubt.

TABLE 4.—*Incidence of pneumonia cases by type in a control group and in a group inoculated with pneumococcus antigen (New England Civilian Conservation Corps camps, from Dec. 1, 1936, to May 15, 1937)*

Causative agent	Both groups			Inoculated			Control		
	All pneumonias	Lobar pneumonia	Broncho-pneumonia	All pneumonias	Lobar pneumonia	Broncho-pneumonia	All pneumonias	Lobar pneumonia	Broncho-pneumonia
All cases	51	37	14	15	13	2	36	24	12
Undetermined	16	8	8	4	3	1	12	5	7
Streptococcus	1		1				1		1
Pneumococcus	34	29	5	11	10	1	23	19	4
Type I	5	5					5	5	
Type II	2	1	1				2	1	1
Type III	2	2					2	2	
Type IV	10	9	1	3	3		7	6	1
Type V	3	2	1	1	1		2	1	1
Type VII	3	2	1	3	2	1			
Type VIII	2	2		1	1		1	1	
Type IX	1	1		1	1				
Type XVI	1	1					1	1	
Type XVII	1	1					1	1	
Type XIX	1	1		1	1				
Type XXVII	1	1					1	1	
Types III and VIII	1	1		1	1				
Types III and X	1		1				1		1

TABLE 5.—*Incidence of pneumonia cases by type in a control group and in a group inoculated with pneumococcus antigen (west coast Civilian Conservation Corps camps, from initial date of observation in January or February 1937 to Apr. 30, 1937* [1])

Type	Total	Inoculated	Control
All cases	86	6	80
Undetermined	33	3	30
I	35	2	33
II	10	1	9
I and II	2		2
III	1		1
IV	4		4
VII	1		1

[1] The initial date of observation was reckoned separately for each of the 312 companies in which enrollees were inoculated, being taken as the date on which the first of the men in the company received the antigen.

It would appear from a comparison of the control data that there was a larger proportion of type I and type II pneumonias in the west coast camps than in the New England camps. Here again the validity of the observation must necessarily be qualified by the large proportion of pneumonia of undetermined type. The heavy concentration of type IV pneumonias in the New England camps may be due largely to a confusion in classification between the specific type IV and the old group IV which included all types other than I, II, or III.

TIME ELAPSED FROM INOCULATION TO ONSET OF DISEASE, AND DURATION OF DISEASE AMONG INOCULATED CASES

The pneumonia cases among inoculated enrollees were too few to warrant any extensive analysis of the relation between duration since inoculation and incidence of the disease. However, for purposes of record there is shown in table 6 the number of days elapsing from inoculation to onset of pneumonia for each case. The date of onset was taken as the date of admission to a hospital or the date of diagnosis where it is stated. In this connection it should be kept in mind that the west coast experiment ran for a shorter period than the New England experiment.

TABLE 6.—*Analysis of pneumonia cases among inoculated enrollees, showing, for each case, the age, type of pneumonia, and duration from date of inoculation to onset of the disease* [1] *(New England Civilian Conservation Corps camps from Dec. 1, 1936, to May 15, 1937; west coast Civilian Conservation Corps camps from date of initial observation in January or February 1937 to Apr. 30, 1937* [2]*)*

Age of patient	Type of pneumonia	Number of days from inoculation to onset of disease
NEW ENGLAND CAMPS		
27	III and VIII	1
48	IV	1
17	VII	6
18	(3)	7
20	IV	13
22	VII	14
18	XIX	21
17	V	48
47	(3)	54
19	VII	60
19	VIII	66
18	IX	89
38	(3)	125
21	IV	126
22	(3)	126
WEST COAST CAMPS		
18	I	3
27	I	37
30	(3)	64
20	II	74
20	(3)	76
18	(3)	89

[1] The date of onset was taken as the date of admission to a hospital or the date of diagnosis where it is stated.

[2] The initial date of observation was reckoned separately for each of the 312 companies in which enrollees were inoculated, being taken as the date on which the first of the men in the company received the antigen.

[3] Not determined.

Insufficient data and too few cases were available to study the effect of inoculation upon duration of the pneumonia. Factors which would have to be considered in this connection are the type of pneumonia and serum treatment.

PNEUMONIA INCIDENCE RATE IN THE NEW ENGLAND CAMPS

The pneumonia incidence rate in the total control experience of New England enrollees was found to be 7.28 cases per 1,000 years of life; the corresponding figure for those inoculated was only 4.34 cases per 1,000 years of life, the pneumonia incidence in the control group thus being 168 percent of that in the inoculated group. Such a difference as this could be expected to occur as a mere accident of sampling only 9 times in 100 trials. In this experiment the odds are therefore just about 10 to 1 that the difference observed is definitely due to the effect of inoculation.

When the data are analyzed with regard to age, it is found that in the age group under 20 years the case incidence of pneumonia was 10.15 per 1,000 years of life in the control group and 3.83 per 1,000 years of life in the inoculated group. Although there were only 7 cases among those inoculated and 25 in the controls, this difference is statistically significant.

In the age group 20 to 24 years, the pneumonia incidence rates were 5.03 and 3.68 per 1,000 years of life in the control and inoculated groups, respectively. The cases were too few (total 11) to warrant any positive conclusion.

Although pneumonia incidence in the age group 25 to 49 years among those inoculated was actually higher than in the control group, the rates being 8.14 and 4.19 per 1,000 years of life respectively, the cases in each group were too few in number to attach any importance at present to this reverse finding.

The pneumonia case incidence rates cited above will be found in table 7.

PNEUMONIA INCIDENCE RATE IN THE WEST COAST CAMPS

The pneumonia incidence among west coast inoculated enrollees was 1.73 cases per 1,000 years of life exposed to risk of infection. In the control experience the pneumonia incidence was 15.69 cases per 1,000 years of life exposed, the rate being about nine times that of the inoculated group. In the New England camps, the corresponding ratio was only 1.68.

Although the results in the west coast camps strongly confirm the findings in the New England camps, a comparison of the case rates brings out differences between the two experiments. By referring to table 8 it will be seen that among inoculated enrollees, those in the

TABLE 7.—*Pneumonia incidence in a control group, compared with that in a group inoculated with pneumococcus antigen (New England Civilian Conservation Corps camps from Dec. 1, 1936, to May 15, 1937; west coast Civilian Conservation Corps camps from date of initial observation in January or February 1937 to Apr. 30, 1937* [1])

Group	Age period				
	Total	Under 20	20–24	25–49	50 and over[2]
CASES PER 1,000 YEARS OF LIFE EXPOSED					
	New England				
Control	7.28±1.21	10.15±2.02	5.03	4.19	
Inoculated	4.34±1.12	3.83±1.45	3.68	8.14	
Difference	2.94±1.72	6.32±2.66	1.35	−3.95	
	West coast				
Control	15.69±1.74	19.58±3.10	13.37	11.09	22.07
Inoculated	1.73±.71	[3]	[3]	[3]	[3]
Difference	13.96±2.20				
NUMBER OF CASES					
	New England				
Total	51	32	11	8	
Control	36	25	7	4	
Inoculated	15	7	4	4	
	West coast				
Total	86	41	29	12	4
Control	80	39	27	10	4
Inoculated	6	2	2	2	

[1] The initial date of observation was reckoned separately for each of the 312 companies in which enrollees were inoculated, being taken as the date on which the first of the men in the company received the antigen.
[2] Including those of unknown age.
[3] Number of cases insufficient for the computation of a rate.

NOTE.—Standard errors are shown only in those instances where the numbers of cases involved were large enough to warrant the computation.

New England camps had a pneumonia incidence rate fully 2.5 times as great as those in the west coast camps. On the other hand, when the control experience is compared, the rate in the New England camps was about half that of the west coast camps. These differences were observed even when the case rates in the two experiments were compared for their common calendar period, February through April (table 8).

The magnitude of the differences in the case incidence rates between the New England and west coast camps is such that it requires explanation. Three considerations arise in connection with the figures for the inoculated group:

1. Is there any reason to believe that the quality of the antigen used in the New England camps differed from that of the antigen

used in the west coast camps? In other words, the possibility should be considered that the same standard of antigen was not used in the two experiments. Possibly the observed difference may have been due to the fact that the antigen for the west coast camps was rushed there and used at the earliest possible date after manufacture.

2. It has already been shown that the duration of observations for the inoculated cases was 117.4 days in the New England camps and 68.3 days in the west coast camps. Since the pneumonia incidence rate was greater in the experiment with the longer duration, there must also be considered the possibility that the immunizing effect of the antigen wears off rapidly with lapse of time.

3. The use of the antigen, which is presumably specific for pneumonia types I and II, should lower the case incidence of the disease most in the areas where these types would ordinarily be most prevalent. To the extent that the rather incomplete data of tables 4 and 5 may be accepted as evidence, the indications are that types I and II were relatively more prevalent in the west coast camps, where the case incidence in the inoculated group is lower than in the New England camps.

TABLE 8.—*Pneumonia case incidence per 1,000 years of life exposed in a control group, compared with that in a group inoculated with pneumococcus antigen (New England and west coast Civilian Conservation Corps camps for their entire periods of observation, winter of 1936–37, and for their common period of observation, February through April 1937* [1])

Group	New England camps (1)	West coast camps (2)	Ratio (1) to (2)
	Entire periods of observation [1]		
Control	7.28	15.69	0.5
Inoculated	4.34	1.73	2.5
	Common period of observation, February through April		
Control	6.83	13.23	0.5
Inoculated	4.50	1.49	3.0

[1] New England period of observation: Dec. 1, 1936 to May 15, 1937. West coast period of observation: The initial date of observation was reckoned separately for each of the 312 companies in which enrollees were inoculated, being taken as the date on which the first of the men in the company received the antigen; observations terminated Apr. 30, 1937.

None of the influences here noted can be evaluated, so that the difference in the case rates between inoculated enrollees in the New England camps and those in the west coast camps cannot be definitely accounted for.

Turning now to a comparison of the control experiences in the two experiments, it appears that much of the higher case incidence rate in the west coast camps as compared with that in the New England

camps may be accounted for by an outbreak of pneumonia in California during the period from January through April.[3] An examination of the pneumonia case records in this connection was particularly interesting. It was found that 10 out of the 80 cases in the control experience, and one of the six cases in the inoculated experience arose among enrollees located at Three Rivers, Calif. Moreover, all but one of these cases became ill some time between January 22, and February 6. During the same time interval four additional cases, all controls, were found in localities near Three Rivers, one in Dunlop and three in Springville. In contrast to this concentration of pneumonia cases in these localities, only 1,148 enrollees were located there, or 2.5 percent of the total number in the west coast experiment; 456 of these enrollees were inoculated.

THE INCIDENCE OF RESPIRATORY CONDITIONS OTHER THAN PNEUMONIA

An analysis was made of the New England records to ascertain whether the antigen has any effect on the incidence of respiratory conditions other than pneumonia. The results obtained were not positive. Enrollees in the inoculated group lost from duty an average of 4.22 days per 1,000 days exposed to risk of infection; the figure for those in the control group was not much different, namely, 4.38 days per 1,000 days. The difference between these two figures, namely, 0.16 days per 1,000, is barely twice its standard error and is thus on the borderline of statistical significance. Further analysis by age and calendar month failed to disclose any consistent tendency in the data; in some instances the figure for the control experience was higher than for the inoculated experience, while in others the situation was reversed, as will be seen by examination of the data given in table 9. Other factors that lessen the value of these findings are the many cases with respiratory conditions where the duration of the illness was not stated and the cases for which it is not stated whether the condition occurred before or after inoculation. In the case of the inoculated experience, the duration was not stated for 2.4 percent of the cases reporting a respiratory illness other than pneumonia; moreover, for 4.5 percent of the inoculated enrollees reporting a respiratory illness resulting in days lost from duty, it was not stated whether the illness occurred before inoculation or afterwards. In the control experience, the duration of illness was not stated for 4.9 percent of the enrollees reporting a respiratory condition resulting in days lost from duty.

[3] This statement is based upon a comparison of provisional pneumonia mortality data for January through April 1937, obtained from the weekly reports of the United States Public Health Service and from monthly State health reports, with corresponding data for the previous year.

TABLE 9.—*Incidence of respiratory conditions other than pneumonia in a control group and in a group inoculated with pneumococcus antigen, both groups being classified by age and calendar month (New England Civilian Conservation Corps camps, from Dec. 1, 1936, to May 15, 1937)*

Age period (all calendar months)	Days lost from duty per 1,000 days exposed		Calendar month (all ages)	Days lost from duty per 1,000 days exposed	
	Inoculated	Control		Inoculated	Control
Total	4.22	4.38	Total	4.22	4.38
Under 20	4.80	5.05	December	1.68	3.87
20–24	3.79	3.68	January	10.04	9.34
25–29	2.77	3.45	February	5.32	5.87
30–39	2.60	2.66	March	2.36	2.21
40–49	4.44	4.22	April	1.41	1.90
50 and over	2.91	5.00	May	.84	1.06

NOTE.—Duration not stated for 2.4 percent of inoculated cases reporting days lost from duty because of a respiratory illness other than pneumonia; corresponding figure for control cases, 4.9 percent. In 4.5 percent of the inoculated cases with respiratory illness, it was not stated whether the illness occurred before or after inoculation.

The absence of any positive finding from the New England records as to the effect of the antigen on respiratory conditions other than pneumonia made it appear inadvisable to conduct a similar analysis on the west coast records. This decision was also influenced by the uncertain quality of the records as far as this phase of the inquiry is concerned.

SUMMARY

The observations arising from experiments with a pneumococcus antigen, as prepared by Felton, in the New England and west coast Civilian Conservation Corps camps during the winter of 1936–37 may be summarized as follows:

1. An analysis of the records of the present experiments which takes into account not only the numbers exposed to risk of infection, but also the length of time they were so exposed, suggests that the antigen may be effective in reducing the case incidence of pneumonia. In the New England camps the pneumonia incidence rate was 4.34 cases per 1,000 years of life in the inoculated group as compared with 7.28 per 1,000 years of life in the control group. The corresponding figures for the west coast camps are 1.73 and 15.69 per 1,000 years of life, respectively. Thus the findings of the 1936–37 experiments are consistent with the impressions gained from the other preliminary experiments. Taking all the experiments together, it appears that this or a similar antigen may prove to be a useful tool for the control of pneumonia incidence. However, this statement must be qualified by the two considerations set forth under (2) and (3) below. It should be mentioned, incidentally, that there were too few deaths upon which to base any conclusions regarding the effect of the antigen on the case fatality from pneumonia.

2. The present experiments provide no indication as to the length of time for which the inoculations of antigen may influence the pneumonia morbidity rates. It was observed that the pneumonia incidence rate among inoculated enrollees was higher in the New England camps, where the average period of observation was 117.4 days, than in the west coast camps, where the average period was 68.3 days. However, it is quite likely that the difference in the case incidence rates between the inoculated enrollees of the two camps may result from other factors than merely the difference in duration of the period of observation.

3. There is some indication that the antigen may be most effective for adolescents and that it loses its effectiveness with advancing age. It was found in the New England camps that, at ages under 20, the pneumonia incidence rate in the control group was 2.7 times that in the inoculated group; at ages 20 to 24, the ratio was 1.4; and at ages 25 to 49, the inoculated enrollees actually experienced a higher rate than the control group. However, the numbers of cases at the ages over 20 were too few to give much reliability to the rates. These findings could not be confirmed by the observations in the west coast camps, where there were only six pneumonia cases in the inoculated group.

4. There was no satisfactory evidence found to show that the antigen will lower the incidence of respiratory conditions other than pneumonia. Enrollees in the inoculated group in the New England Civilian Conservation Corps camps lost from duty an average of 4.22 days per 1,000 days exposed to risk of infection, while the corresponding figure for the group not inoculated was 4.38 days per 1,000 exposed. Although the difference between these two figures is on the borderline of statistical significance, there were many cases for which the duration of illness was not stated, and so the value of these results becomes somewhat uncertain.

RECOMMENDATIONS FOR FURTHER INVESTIGATION

The results of the present surveys indicate the need for additional investigations in regard to the extent and the duration of the immunity against pneumonia and possibly other respiratory diseases conferred by the pneumococcus antigen used at various age groups. In any future investigations, it is highly desirable to carry the observations for two or more winters on the same group of individuals. An attempt should also be made to determine whether the antigen influences the duration or severity of clinical cases of pneumonia, taking into account the type of infection and serum treatment. Such future investigations should be on an adequate sample of the population at large before a definite recommendation for or against the general application of the antigen can be safely given.

ACKNOWLEDGMENTS

We wish to acknowledge our gratitude to Maj. Gen. C. R. Reynolds, Surgeon General, United States Army, for his approval of the experiment and of publication of this preliminary study; to Col. H. G. Shaw, surgeon, Medical Corps, United States Army, for his generous spirit of cooperation; to Col. R. A. Kelser, Veterinary Corps, United States Army, and Lt. Col. F. M. Fitts, Medical Corps, United States Army for material aid; and also to the medical officers of the Civilian Conservation Corps of the First and Ninth Corps Areas.

REFERENCES

(1) Felton, Lloyd D.: Studies on immunizing substances in pneumococci. VII. Response in human beings to antigenic pneumococcus polysaccharides, types I and II. Pub. Health Rep., 53: 1855–1877 (1938).
(2) Schiemann, O., and Casper, W.: Sind die spezifisch präcipitablen Substanzen der 3 Pneumokokkentypen Haptene? Ztschr. f. Hyg. u. Infekt., 108: 220 (1927-28).
(3) Avery, O. T., and Goebel, W. F.: Chemoimmunological studies on the soluble specific substances of pneumococcus. I. The isolation and properties of the acetyl polysaccharide of pneumococcus type I. J. Exp. Med., 58: 731 (1933).

ASBESTOSIS AMONG WORKERS IN THE ASBESTOS TEXTILE INDUSTRY

Asbestosis, a lung disease caused by long-continued inhalation of asbestos dust, was the principal physical defect found on medical examination of 541 men and women employed (or recently employed) in three asbestos textile factories, according to a report recently issued by the Public Health Service.[1] The primary effect of asbestos dust seems to be the initiation of fine, interstitial, pulmonary fibrosis, which was not observed to progress as far as the nodular stage. This fibrosis was observed in post-mortem examinations of three former asbestos workers. During life, lung fibrosis can be detected by X-ray examination. The more important symptoms of asbestosis are progressive dyspnoea, variable cough which sometimes raises blood-streaked sputum, and loss of weight.

The processes that produce dust in asbestos textile factories were studied and recommendations for dust control are incorporated in the report. Enough dust counts (242) were made in all parts of these factories so that the dust exposure of each worker could be estimated. The percentage of persons in different occupational groups who were affected by asbestosis or any of its symptoms varied with the average dust concentration to which they were subjected and with their length of employment. The only cases of asbestosis, three in number, found in exposures to concentrations below 5 million particles

[1] Pub. Health Bull. No. 241. "A Study of Asbestosis in the Asbestos Textile Industry." By Waldemar C. Dreessen et al. Govt. Printing Office, Wash., D. C. 20 cents.

per cubic foot were diagnosed as doubtful; well-established cases occurred at higher concentrations.

It appears from these data that, if asbestos dust concentrations in the air breathed are kept below this limit, new cases of asbestosis would not appear. Methods of control are already available which will protect workers from this disease.

DEATHS DURING WEEK ENDED OCTOBER 1, 1938

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

	Week ended Oct. 1, 1938	Corresponding week, 1937
Data from 88 large cities of the United States:		
Total deaths	[1] 7,673	[2] 7,857
Average for 3 prior years	[2] 7,382	
Total deaths, first 39 weeks of year	316,977	341,046
Deaths under 1 year of age	[1] 501	[2] 489
Average for 3 prior years	[2] 516	
Deaths under 1 year of age, first 39 weeks of year	20,597	22,025
Data from industrial insurance companies:		
Policies in force	68,322,230	69,912,986
Number of death claims	11,194	12,491
Death claims per 1,000 policies in force, annual rate	8.5	9.3
Death claims per 1,000 policies, first 39 weeks of year, annual rate	9.3	9.9

[1] Data for 87 cities.
[2] Data for 86 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.

In these and the following tables, a zero (0) indicates a positive report and has the same significance as any other figure, while leaders (----) represent no report, with the implication that cases or deaths may have occurred but were not reported to the State health officer.

Cases of certain diseases reported by telegraph by State health officers for the week ended Oct. 8, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median

Division and State	Diphtheria				Influenza				Measles			
	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median
NEW ENG.												
Maine	6	1	1	1	----	----	----	----	49	8	5	5
New Hampshire	0	0	0	0	----	----	----	----	----	----	1	1
Vermont	0	0	0	0	----	----	----	----	----	----	5	3
Massachusetts	7	6	1	5	----	----	----	----	42	36	19	27
Rhode Island	0	0	0	2	----	----	----	----	----	----	4	----
Connecticut	6	2	6	0	3	1	3	2	27	9	3	5
MID. ATL.												
New York	4	11	22	22	[1] 6	[1] 9	[1] 10	[1] 8	18	45	65	65
New Jersey	17	14	7	9	19	16	8	8	13	11	34	19
Pennsylvania	10	20	23	51	----	----	----	----	17	34	228	49
E. NO. CEN.												
Ohio	36	47	25	50	----	----	----	3	4	5	72	29
Indiana	84	56	17	48	6	4	37	27	3	2	18	15
Illinois	21	31	23	32	6	9	12	12	12	18	57	12
Michigan [2]	18	17	17	17	1	1	----	1	58	54	24	24
Wisconsin	2	1	4	5	50	28	17	17	118	66	22	22
W. NO. CEN.												
Minnesota	12	6	9	10	2	1	1	1	114	58	3	5
Iowa	12	6	4	13	65	32	1	1	20	10	3	2
Missouri	25	19	30	44	13	10	39	35	4	3	53	18
North Dakota	15	2	0	3	37	5	----	----	539	73	1	3
South Dakota	30	4	0	3	----	----	----	----	30	4	----	2
Nebraska	19	5	3	3	----	----	----	----	8	2	----	1
Kansas	25	9	4	12	17	6	4	1	11	4	1	4
SO. ATL.												
Delaware	20	1	0	0	----	----	----	----	----	----	2	2
Maryland [2]	47	15	7	9	6	2	3	4	43	14	3	3
Dist. of Col.	58	7	4	11	----	----	----	----	33	4	1	----
Virginia [2]	179	93	64	64	129	67	----	----	15	8	9	9
West Virginia	45	16	34	68	25	9	8	12	3	1	11	5

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Oct. 8, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Diphtheria				Influenza				Measles			
	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median
SO. ATL.—continued												
North Carolina [3 4]	268	173	107	112	6	4	5	5	161	108	31	11
South Carolina [4]	117	42	18	18	654	235	93	171	3	1	4	4
Georgia [4]	100	59	35	40	30	18						
Florida	28	9	20	10	3	1					8	3
E. SO. CEN.												
Kentucky	100	56	31	60	36	20	6	6	9	5	33	13
Tennessee [4]	87	48	34	64	50	28	12	12	4	2	21	2
Alabama [4]	83	46	44	45	34	19	30	9	23	13		1
Mississippi [3 5]	82	32	15	23								
W. SO. CEN.												
Arkansas	81	32	25	25	66	26	15	5	3	1	4	
Louisiana [4]	59	24	8	18	2	1	4	4	12	5		2
Oklahoma	59	29	23	21	86	42	32	26	8	4	7	1
Texas [4]	45	53	48	48	97	115	170	61	8	9	20	13
MOUNTAIN												
Montana	10	1	1	1	19	2			522	54	10	10
Idaho	11	1	0	0	11	1	5	1	32	3	10	
Wyoming	0	0	0	0					444	20	2	1
Colorado	78	16	4	6					39	8	10	10
New Mexico	37	3	3	6				1	457	37	8	8
Arizona	25	2	0	2	392	31	24	16	25	2		2
Utah [3]	0	0	0	0			12		70	7	81	4
PACIFIC												
Washington	0	0	1	3					47	15	6	34
Oregon [3]	25	5	1	2	25	5	13	19	36	7	6	8
California	29	34	17	27	9	11	15	18	143	169	17	55
Total	43	1,054	740	1,147	37	759	579	506	39	939	922	682
40 weeks	19	19,307	17,719	23,599	61	49,948	277,409	143,529	785	765,503	246,318	345,309

Division and State	Meningitis, meningococcus				Poliomyelitis				Scarlet fever			
	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median
NEW ENG.												
Maine	0	0	0	0	0	0	10	3	55	9	0	11
New Hampshire	0	0	0	0	0	0	2	1	0	0	1	5
Vermont	0	0	0	0	0	0	2	1	136	10	10	5
Massachusetts	0	0	1	1	0	0	7	7	67	57	76	76
Rhode Island	0	0	1	1	0	0	0	0	23	3	19	12
Connecticut	3	1	1	0	3	1	6	5	60	20	29	26
MID. ATL.												
New York	2	5	6	4	0.8	2	43	43	42	104	145	145
New Jersey	0	0	0	0	0	0	9	9	24	20	43	41
Pennsylvania	0.5	1	6	4	6	11	18	12	65	127	188	211
E. NO. CEN.												
Ohio	2.3	3	0	0	2.3	3	7	10	110	142	126	229
Indiana	0	0	0	1	6	4	4	3	125	83	124	97
Illinois	0.7	1	3	3	2	3	37	23	129	195	159	161
Michigan [3]	2.2	2	4	1	2.2	2	26	16	244	226	243	117
Wisconsin	0	0	0	1	4	2	15	6	151	85	66	102

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Oct. 8, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Meningitis, meningococcus				Poliomyelitis				Scarlet fever			
	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median
W. NO. CEN.												
Minnesota	0	0	0	0	6	3	17	4	104	53	54	39
Iowa	2	1	3	0	4	2	18	4	78	38	44	42
Missouri	0	0	1	1	1.3	1	20	2	55	42	133	55
North Dakota	0	0	0	0	0	0	0	1	148	20	12	12
South Dakota	0	0	0	0	8	1	1	2	151	20	11	14
Nebraska	0	0	0	0	0	0	11	1	19	5	2	12
Kansas	0	0	4	0	2.8	1	19	2	271	97	113	65
SO. ATL.												
Delaware	0	0	0	0	0	0	0	0	180	9	4	4
Maryland [2]	3	1	2	2	0	0	2	2	43	14	32	34
Dist. of Col.	0	0	0	0	8	1	1	2	58	7	9	8
Virginia [2]	0	0	4	1	4	2	1	4	66	34	35	58
West Virginia	6	2	0	0	2.8	1	4	5	240	86	79	79
North Carolina [3] [4]	4	3	1	1	1.5	1	3	1	130	87	68	68
South Carolina [4]	2.8	1	0	0	2.8	1	0	0	31	11	4	7
Georgia [4]	0	0	0	0	3	2	0	0	34	20	39	17
Florida	6	2	0	0	0	0	2	0	16	5	0	1
E. SO. CEN.												
Kentucky	1.8	1	1	1	0	0	0	5	118	66	37	75
Tennessee [4]	1.8	1	2	2	5	3	1	4	123	68	32	69
Alabama [4]	1.8	1	0	0	1.8	1	3	0	49	27	19	19
Mississippi [2] [3]	0	0	1	0	0	0	10	0	44	17	25	15
W. SO. CEN.												
Arkansas	0	0	2	0	0	0	7	0	51	20	21	7
Louisiana [4]	0	0	0	0	0	0	4	1	29	12	11	9
Oklahoma	0	0	0	1	0	0	15	2	68	33	29	13
Texas [4]	0	0	1	1	1.7	2	29	1	61	72	52	32
MOUNTAIN												
Montana	0	0	0	0	0	0	0	0	174	18	10	19
Idaho	0	0	0	0	0	0	2	0	11	1	11	5
Wyoming	0	0	0	0	0	0	0	1	266	12	12	5
Colorado	0	0	2	1	10	2	15	0	141	29	15	16
New Mexico	0	0	1	0	0	0	0	0	37	3	18	14
Arizona	0	0	0	0	0	0	0	0	51	4	3	5
Utah [2]	0	0	1	0	0	0	2	1	100	10	33	12
PACIFIC												
Washington	0	0	1	0	0	0	11	5	69	22	22	33
Oregon [3]	0	0	0	0	0	0	2	2	213	42	18	23
California	0	0	0	1	0.8	1	17	18	81	96	102	128
Total	1	26	49	49	2.1	53	403	290	88	2,181	2,338	2,462
40 weeks	2.4	2,363	4,548	4,548	1.4	1,407	8,127	6,054	148	146,338	174,922	174,922

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough	
	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases
NEW ENG.										
Maine	0	0	0	0	18	3	5	2	110	18
New Hampshire	0	0	0	0	0	0	1	0	0	0
Vermont	0	0	0	0	27	2	8	0	463	34
Massachusetts	0	0	0	0	0	0	6	3	95	81
Rhode Island	0	0	0	0	8	1	0	0	184	24
Connecticut	0	0	0	0	12	4	3	2	132	44

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Oct. 8, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough	
	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases	Oct. 9, 1937, cases	1933–37 median	Oct. 8, 1938, rate	Oct. 8, 1938, cases
MID. ATL.										
New York	0	0	0	0	8	19	25	25	142	354
New Jersey	0	0	0	0	4	3	7	8	195	162
Pennsylvania	0	0	0	0	13	26	29	31	111	217
E. NO. CEN.										
Ohio	0	0	0	0	12	16	17	34	38	49
Indiana	5	3	1	1	17	11	1	11	12	8
Illinois	3	5	0	1	11	17	16	27	228	344
Michigan [2]	0	0	1	0	6	6	9	17	163	151
Wisconsin	4	2	6	1	4	2	5	5	517	290
W. NO. CEN.										
Minnesota	0	0	3	0	2	1	1	1	63	32
Iowa	0	0	0	1	8	4	11	11	45	22
Missouri	0	0	9	1	9	7	20	20	13	10
North Dakota	0	0	15	1	37	5	2	3	258	35
South Dakota	0	0	0	0	8	1	1	1	0	0
Nebraska	0	0	0	0	15	4	0	0	8	2
Kansas	11	4	0	0	6	2	5	5	45	16
SO. ATL.										
Delaware	0	0	0	0	0	0	0	2	20	1
Maryland [2]	0	0	0	0	31	10	11	11	78	25
Dist. of Col	0	0	0	0	25	3	1	1	42	5
Virginia [2]	0	0	0	0	27	14	17	17	60	31
West Virginia	0	0	0	0	14	5	10	16	56	20
North Carolina [3] [4]	0	0	0	0	9	6	14	16	161	108
South Carolina [4]	0	0	0	0	25	9	3	15	89	32
Georgia [4]	0	0	0	0	10	6	10	11	19	11
Florida	0	0	0	0	3	1	2	0	41	13
E. SO. CEN.										
Kentucky	0	0	0	0	52	29	16	37	59	33
Tennessee [4]	0	0	7	0	13	7	22	30	49	27
Alabama [4]	0	0	0	0	16	9	10	10	70	39
Mississippi [2] [3]	0	0	1	0	18	7	9	7	------	------
W. SO. CEN.										
Arkansas	0	0	0	0	41	16	24	9	13	5
Louisiana [4]	0	0	0	0	29	12	11	11	46	19
Oklahoma	4	2	16	1	31	15	22	17	4	2
Texas [4]	0	0	0	0	19	23	56	38	55	65
MOUNTAIN										
Montana	68	7	7	0	68	7	3	3	223	23
Idaho	11	1	6	1	11	1	0	1	32	3
Wyoming	0	0	0	1	0	0	0	0	44	2
Colorado	10	2	4	1	10	2	11	8	73	15
New Mexico	0	0	4	0	111	9	13	14	111	9
Arizona	25	2	0	0	38	3	0	2	152	12
Utah [2]	0	0	0	0	20	2	1	1	271	27
PACIFIC										
Washington	9	3	8	2	28	9	3	2	116	37
Oregon [3]	5	1	1	0	5	1	1	3	10	2
California	3	3	7	1	6	7	13	17	100	118
Total	1	35	90	33	14	347	455	623	106	2,577
40 weeks	13	12,967	8,374	5,517	12	11,624	12,221	14,074	171	167,172

[1] New York City only.
[2] Period ended earlier than Saturday.
[3] Rocky Mountain spotted fever, week ended Oct. 8, 1938, 4 cases, as follows: Virginia, 1; North Carolina, 1; Mississippi, 1; Oregon, 1.
[4] Typhus fever, week ended Oct. 8, 1938, 59 cases, as follows: North Carolina, 3; South Carolina, 10; Georgia, 20; Tennessee, 1; Alabama, 16; Louisiana, 1; Texas, 8.

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	Meningitis, meningococcus	Diphtheria	Influenza	Malaria	Measles	Pellagra	Poliomyelitis	Scarlet fever	Smallpox	Typhoid and paratyphoid fever
July 1938										
Alaska	0	0	16				0	0	0	0
August 1938										
Alaska	0	0	1				0	0	0	0
Wisconsin	6	7	56	1	333		27	169	1	15
September 1938										
Arkansas	0	104	81	1,082	24	97	1	35	0	104
Connecticut	3	2	10		20		8	48	0	22
Delaware	1	4			2		1	11	0	3
Maine	1	7	4		34		2	12	0	11
Michigan	3	35	1	21	154		14	547	5	57
Missouri	2	61	35	74	18		3	118	3	81
Pennsylvania	7	65		3	115		25	371	0	91
Tennessee	4	106	87	379	21	14	2	99	3	75
West Virginia	9	58	48		10		1	144	0	104

July 1938

	Cases
Alaska:	
Chickenpox	3
Septic sore throat	1
Tularaemia	2
Whooping cough	9

August 1938

	Cases
Alaska:	
Chickenpox	3
Whooping cough	12
Wisconsin:	
Chickenpox	130
Encephalitis	4
Mumps	118
Septic sore throat	25
Tularaemia	2
Undulant fever	7
Whooping cough	1,843

September 1938

	Cases
Anthrax:	
Delaware	1
Michigan	1
Chickenpox:	
Arkansas	10
Connecticut	37
Delaware	5
Maine	37
Michigan	111
Missouri	9
Pennsylvania	171
Tennessee	8
West Virginia	10
Conjunctivitis, infectious:	
Connecticut	1
Dysentery:	
Arkansas (amoebic)	6
Arkansas (bacillary)	14
Connecticut (bacillary)	28
Michigan (amoebic)	5
Michigan (bacillary)	54
Missouri (amoebic)	53
Pennsylvania (bacillary)	27
Tennessee (amoebic)	3
Tennessee (bacillary)	23

September 1938—Continued

	Cases
Encephalitis, epidemic or lethargic:	
Connecticut	1
Michigan	1
Missouri	15
Pennsylvania	2
German measles:	
Connecticut	5
Maine	7
Michigan	20
Pennsylvania	16
Hookworm disease:	
Arkansas	1
Impetigo contagiosa:	
Tennessee	21
Jaundice, epidemic:	
Michigan	1
Lead poisoning:	
Maine	1
Mumps:	
Arkansas	6
Connecticut	57
Delaware	5
Maine	24
Michigan	82
Missouri	24
Pennsylvania	318
Tennessee	11
West Virginia	2
Ophthalmia neonatorum:	
Arkansas	1
Pennsylvania	4
Tennessee	3
Puerperal septicemia:	
Tennessee	2
Rabies in animals:	
Arkansas	14
Connecticut	2
Michigan	1
Missouri	2
Rabies in man:	
Michigan	1
Rocky Mountain spotted fever:	
Arkansas	1
Missouri	2

September 1938—Continued

	Cases
Septic sore throat:	
Arkansas	32
Connecticut	9
Michigan	9
Missouri	15
Tennessee	8
Tetanus:	
Arkansas	2
Connecticut	1
Michigan	2
Tennessee	1
Trachoma:	
Arkansas	9
Missouri	41
Pennsylvania	1
Tennessee	5
Tularaemia:	
Arkansas	4
Missouri	2
Tennessee	4
Typhus fever:	
Tennessee	3
Undulant fever:	
Arkansas	4
Connecticut	6
Delaware	1
Maine	5
Michigan	7
Missouri	3
Pennsylvania	6
Vincent's infection:	
Maine	5
Michigan	10
Tennessee	2
Whooping cough:	
Arkansas	59
Connecticut	190
Delaware	34
Maine	90
Michigan	1,243
Missouri	67
Pennsylvania	999
Tennessee	94
West Virginia	134

WEEKLY REPORTS FROM CITIES

City reports for week ended Oct. 1, 1938

This table summarizes the reports received weekly from a selected list of 140 cities for the purpose of showing a cross section of the current urban incidence of the communicable diseases listed in the table.

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								
Data for 90 cities:											
5-year average	174	81	21	129	351	522	3	340	81	894	----
Current week [1]	154	57	16	247	348	453	2	296	66	1,300	----
Maine:											
Portland	0	----	0	0	2	0	0	0	0	2	20
New Hampshire:											
Concord	0	----	0	0	0	0	0	0	0	0	9
Manchester	0	----	0	0	0	0	0	0	0	0	14
Nashua	0	----	0	0	0	1	0	1	0	0	14
Vermont:											
Barre	----	----	----	----	----	----	----	----	----	----	----
Burlington	0	----	0	0	0	0	0	0	0	0	10
Rutland	0	----	0	0	0	0	0	0	0	0	10
Massachusetts:											
Boston	1	----	0	2	13	8	0	6	1	11	210
Fall River	0	----	0	0	1	1	0	1	0	0	35
Springfield	0	----	0	6	0	1	0	0	0	5	37
Worcester	0	----	0	0	6	1	0	2	0	6	47
Rhode Island:											
Pawtucket	0	----	0	0	0	1	0	0	0	0	18
Providence	0	----	0	0	3	2	0	0	0	8	49
Connecticut:											
Bridgeport	0	----	0	0	1	1	0	0	0	1	29
Hartford	1	----	0	0	1	0	0	0	0	1	27
New Haven	0	2	0	1	4	0	0	0	1	15	35
New York:											
Buffalo	0	----	0	1	6	11	0	0	0	14	119
New York	13	2	1	19	57	21	0	70	14	260	1,302
Rochester	0	----	0	8	5	0	0	2	0	2	60
Syracuse	0	----	0	0	3	3	0	0	0	15	34
New Jersey:											
Camden	1	----	0	0	1	3	0	1	0	3	31
Newark	1	2	0	2	3	1	0	9	1	46	84
Trenton	1	----	0	0	3	0	0	0	0	6	31
Pennsylvania:											
Philadelphia	2	2	1	6	14	22	0	23	4	85	450
Pittsburgh	3	1	1	0	11	10	0	9	1	15	134
Reading	8	----	0	0	3	2	0	1	0	9	23
Scranton	0	----	----	1	----	0	0	----	0	4	----
Ohio:											
Cincinnati	9	----	1	0	5	11	0	6	0	16	124
Cleveland	1	3	1	2	10	17	0	4	1	65	164
Columbus	3	2	2	2	4	5	0	5	0	3	90
Toledo	0	1	0	1	6	3	0	7	0	10	72
Indiana:											
Anderson	0	----	0	0	3	1	0	0	0	4	16
Fort Wayne	0	----	0	0	4	2	0	0	0	0	21
Indianapolis	4	----	0	0	17	13	0	1	1	5	117
South Bend	0	----	0	0	1	2	0	1	0	2	18
Terre Haute	4	----	0	0	0	4	0	0	1	0	22
Illinois:											
Alton	0	----	0	0	0	1	0	0	0	0	3
Chicago	10	7	1	8	31	59	0	34	3	256	619
Elgin	0	----	0	1	1	0	0	0	0	0	8
Moline	0	----	1	0	0	1	0	1	0	1	4
Springfield	0	----	0	0	1	2	0	1	0	2	19
Michigan:											
Detroit	12	1	0	7	8	46	0	14	0	124	233
Grand Rapids	0	----	0	2	1	16	0	0	0	2	26
Wisconsin:											
Kenosha	0	----	0	1	0	0	0	0	0	2	9
Madison	0	----	----	0	----	2	0	----	0	1	5
Milwaukee	0	----	0	2	1	28	0	2	0	112	90
Racine	0	----	0	0	0	4	0	0	0	18	11
Superior	0	----	0	0	0	2	0	0	0	8	5

[1] Figures for Barre, Vt., estimated; report not received.

City reports for week ended Oct. 1, 1938—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								
Minnesota:											
Duluth	0		0	0	0	0	1	0	0	8	30
Minneapolis	1		1	8	3	5	0	2	1	16	95
St. Paul	0		0	23	6	3	0	1	0	8	63
Iowa:											
Cedar Rapids	0			0		2	0		0	3	
Davenport	0			0		1	0		0	0	
Des Moines	0		0	1	0	3	0	0	0	0	35
Sioux City	0			2		5	0		0	3	
Waterloo	5			0		4	0		0	0	
Missouri:											
Kansas City	2		0	0	8	5	0	1	0	2	102
St. Joseph	0		0	0	2	1	0	0	0	1	17
St. Louis	4		0	1	4	24	0	9	2	12	367
North Dakota:											
Fargo	0		0	50	0	2	0	0	0	0	10
Grand Forks	0			0		0	0		0	0	
Minot	2		0	2	0	1	0	0	0	0	8
South Dakota:											
Aberdeen	3			0		0	0		0	0	
Nebraska:											
Lincoln	0			1		1	0		0	0	
Omaha	0		0	1	1	1	0	2	0	0	47
Kansas:											
Lawrence	0	3	0	0	1	0	0	0	0	0	4
Topeka	0		0	1	1	4	0	0	0	2	19
Wichita	0		0	0	4	4	0	0	0	1	34
Delaware:											
Wilmington	3		0	0	1	1	0	1	0	1	24
Maryland:											
Baltimore	1	2	0	8	12	5	0	9	0	12	223
Cumberland	0		0	0	0	0	0	0	0	0	8
Frederick	0		0	0	0	0	0	0	0	0	3
Dist. of Col.:											
Washington	4	2	2	3	4	8	0	10	5	17	137
Virginia:											
Lynchburg	7		0	0	0	1	0	0	1	2	9
Norfolk	0		0	0	2	2	0	1	1	2	33
Richmond	1		0	1	2	5	0	2	1	0	39
Roanoke	1		0	0	1	2	0	0	4	1	23
West Virginia:											
Charleston	0		0	0	1	2	0	0	1	0	20
Huntington	0			0		1	0		0	0	
Wheeling	0		0	2	1	1	0	0	0	0	11
North Carolina:											
Gastonia	0			0		1	0		0	0	
Raleigh	0		0	0	0	0	0	0	0	0	11
Wilmington	1		0	0	2	0	0	0	0	0	10
Winston-Salem	5		0	1	1	3	0	1	0	1	12
South Carolina:											
Charleston	0	6	0	0	0	0	0	1	0	0	12
Florence	1		0	0	0	0	0	0	0	0	17
Greenville	0		0	0	0	0	0	0	0	0	11
Georgia:											
Atlanta	4	15	0	0	2	6	0	6	0	4	91
Brunswick	0		0	0	0	2	0	0	0	0	1
Savannah	1	1	0	0	0	1	0	1	1	2	25
Florida:											
Miami	0		0	0	1	0	0	0	1	1	19
Tampa	0		0	0	1	2	0	1	0	0	17
Kentucky:											
Ashland	5		0	0	0	0	0	0	0	0	8
Covington	0		0	0	0	0	0	0	0	0	15
Lexington	0		0	0	1	1	0	0	0	0	18
Louisville	0		0	0	3	0	0	2	0	0	68
Tennessee:											
Knoxville	3		1	0	2	4	0	1	0	0	30
Memphis	4		1	0	2	6	0	4	0	9	65
Nashville	0		1	0	0	2	0	1	1	3	65
Alabama:											
Birmingham	3	4	0	0	3	2	0	2	0	0	65
Mobile	0		0	0	1	0	0	3	0	0	22
Montgomery	4	2		1		2	0		0	0	
Arkansas:											
Fort Smith	0			0		1	0		0	0	
Little Rock	1		1	0	0	0	0	0	0	0	2

City reports for week ended Oct. 1, 1938—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								
Louisiana:											
Lake Charles	0		0	0	0	0	0	1	0	1	2
New Orleans	6	1	1	21	18	0	0	8	8	5	156
Shreveport	2		0	0	5	1	0	1	1	0	36
Oklahoma:											
Oklahoma City	1	3	0	0	1	2	0	0	0	0	39
Tulsa	0			0		5	0		0	0	
Texas:											
Dallas	2	1	0	0	3	14	0	2	1	0	58
Fort Worth	2		0	0	1	7	0	1	0	0	35
Galveston	0		0	0	6	0	0	0	0	0	22
Houston	2		0	0	3	4	0	7	2	1	69
San Antonio	0		0	0	2	1	0	4	0	0	38
Montana:											
Billings	0		0	0	0	0	0	1	1	2	11
Great Falls	0		0	0	0	1	0	0	1	0	5
Helena	0		0	0	0	1		0	0	0	3
Missoula	0		0	0	0	0	0	0	0	0	7
Idaho:											
Boise	0		0	0	0	1	0	0	0	0	5
Colorado:											
Colorado Springs	0		0	0	0	1	0	0	0	5	10
Denver	7		1	5	2	7	0	3	1	8	72
Pueblo	0		0	0	1	0	0	0	0	2	9
New Mexico:											
Albuquerque	0		0	0	2	1	0	1	0	0	12
Utah:											
Salt Lake City	0		0	1	0	0	0	1	0	12	28
Washington:											
Seattle	0		0	0	1	1	0	4	0	4	117
Spokane	0		0	0	2	0	0	0	0	2	25
Tacoma	0		0	0	1	2	1	0	0	3	23
Oregon:											
Portland	0		0	2	2	6	2	0	0	1	52
Salem	0			0		4	0		0	0	
California:											
Los Angeles	14	2	0	3	11	18	0	10	5	14	307
Sacramento	0		0	5	1	0	0	0	0	0	26
San Francisco	4	1	0	44	9	4	0	6	1	20	175

State and city	Meningitis, meningococcus		Poliomyelitis cases	State and city	Meningitis, meningococcus		Poliomyelitis cases
	Cases	Deaths			Cases	Deaths	
Rhode Island:				Alabama:			
Providence	0	0	1	Birmingham	0	0	1
New York:				Montgomery	0	0	1
New York	1	0	3	Louisiana:			
Pennsylvania:				New Orleans	1	0	0
Philadelphia	0	0	10	Oklahoma:			
Illinois:				Oklahoma City	0	0	1
Chicago	1	1	2	Texas:			
Michigan:				Houston	0	1	0
Detroit	0	0	1	California:			
Maryland:				Los Angeles	0	0	1
Baltimore	2	1	0				

Encephalitis, epidemic or lethargic.—Cases: New York, 2; Minneapolis, 2; St. Louis, 1; Lawrence, 1; Denver, 1; Spokane, 1.

Pellagra.—Cases: Washington, 1; Birmingham, 2; Mobile, 2; Fort Smith, 1.

Typhus fever.—Cases: Charleston, S. C., 5; Savannah, 3; Miami, 1; Tampa, 1; Mobile, 1; Dallas, 1; Houston, 2. Deaths: Charleston, S. C., 1.

FOREIGN AND INSULAR

CANADA

Provinces—Communicable diseases—2 weeks ended September 24, 1938.—During the 2 weeks ended September 24, 1938, cases of certain communicable diseases were reported by the Department of Pensions and National Health of Canada, as follows:

Disease	Prince Edward Island	Nova Scotia [1]	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan [2]	Alberta	British Columbia	Total
Cerebrospinal meningitis					1					1
Chickenpox			4	29	78	17	18	11	120	277
Diphtheria		5	6	112	6	7	14			150
Dysentery					31					31
Erysipelas				7	6	2	1	3	1	20
Influenza		10			31	3			9	53
Lethargic encephalitis			1			1				2
Measles		10		35	48	9	3	3	8	116
Mumps					13	16	4	10	7	50
Paratyphoid fever					8			1		9
Pneumonia					11				2	13
Poliomyelitis				3	6	22	4	11	2	48
Scarlet fever	1	14	24	94	109	38	29	29	26	364
Trachoma							1		4	5
Tuberculosis	3	10	9	74	91	3	13	6	25	234
Typhoid fever		2	15	60	20	4	8	11	7	127
Undulant fever				4	4			1		9
Whooping cough		2		110	359	51	2	4	60	588

[1] For 2 weeks ended Sept. 28, 1938.
[2] For the period ended Sept. 10, 1938, the report from Saskatchewan should read 4 cases of poliomyelitis, instead of 5 cases, and 1 case of smallpox.

CUBA

Habana—Communicable diseases—4 weeks ended September 24, 1938.—During the 4 weeks ended September 24, 1938, certain communicable diseases were reported in Habana, Cuba, as follows:

Disease	Cases	Deaths
Diphtheria	8	
Malaria	[1] 24	1
Tuberculosis	14	5
Typhoid fever	[1] 23	3

[1] Includes imported cases.

94359°—38——4

Provinces—Notifiable diseases—4 weeks ended September 17, 1938.—During the 4 weeks ended September 17, 1938, cases of certain notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Rio	Habana	Matanzas	Santa Clara	Camaguey	Oriente	Total
Cancer	1	2	1	14		2	20
Chickenpox					1		1
Diphtheria		10	4	2		2	18
Hookworm disease				1		10	11
Leprosy		1		1		4	6
Malaria	48	31	9	34	21	33	176
Measles		1					1
Poliomyelitis	1					1	2
Rabies	1						1
Scarlet fever		2					2
Tuberculosis	19	43	32	20	27	33	174
Typhoid fever	26	85	24	53	25	49	262
Whooping cough		2					2

FINLAND

Communicable diseases—August 1938.—During the month of August 1938, cases of certain communicable diseases were reported in Finland, as follows:

Disease	Cases	Disease	Cases
Diphtheria	124	Poliomyelitis	72
Dysentery	8	Scarlet fever	299
Influenza	519	Typhoid fever	16
Lethargic encephalitis	1	Undulant fever	5
Paratyphoid fever	92		

ITALY

Communicable diseases—4 weeks ended July 17, 1938.—During the 4 weeks ended July 17, 1938, cases of certain communicable diseases were reported in Italy, as follows:

Disease	June 20-26	June 27-July 3	July 4-10	July 11-17
Anthrax	22	31	31	36
Cerebrospinal meningitis	19	21	29	14
Chickenpox	338	259	267	124
Diphtheria	317	340	304	316
Dysentery	39	41	61	55
Hookworm disease	57	45	59	90
Lethargic encephalitis	2	3	2	
Measles	2,313	2,083	1,859	1,559
Mumps	173	142	127	176
Paratyphoid fever	61	92	122	125
Pellagra	44	29	25	15
Poliomyelitis	47	46	44	42
Puerperal fever	29	16	21	24
Rabies	1		1	
Scarlet fever	223	222	210	165
Typhoid fever	354	452	768	818
Undulant fever	135	102	115	114
Whooping cough	630	477	600	628

YUGOSLAVIA

Communicable diseases—4 weeks ended September 11, 1938.—During the 4 weeks ended September 11, 1938, certain communicable diseases were reported in Yugoslavia, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Anthrax	92	7	Poliomyelitis	18	3
Cerebrospinal meningitis	10	3	Scarlet fever	185	1
Diphtheria	487	27	Sepsis	8	
Dysentery	447	36	Tetanus	56	18
Erysipelas	184	7	Typhoid fever	691	43
Favus	5		Typhus fever	5	
Paratyphoid fever	72	1	Weil's disease	7	3

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

NOTE.—A table giving current information of the world prevalence of quarantinable diseases appeared in the PUBLIC HEALTH REPORTS for September 30, 1938, pages 1759–1773. A similar cumulative table will appear in future issues of the PUBLIC HEALTH REPORTS for the last Friday of each month.

Cholera

China.—During the week ended October 1, 1938, cases of cholera were reported in China as follows: Canton, 5; Hong Kong, 7; Macao, 7; Shanghai, 113.

Chosen (Korea).—During the week ended September 24, 1938, 11 cases of cholera with 7 deaths were reported in Chosen (Korea).

Plague

Tunisia—Tunis.—During the week ended October 15, 1938, 1 case of bubonic plague was reported in Tunis, Tunisia.

Yellow Fever

Colombia—Cundinamarca Department—Medina.—On August 21, 1938, 2 cases of yellow fever with 1 death were reported in Medina, Cundinamarca Department, Colombia.

Gold Coast—Tamale.—During the week ended October 8, 1938, 1 fatal case of yellow fever was reported in Tamale, Gold Coast.

Ivory Coast—Dedougou.—During the week ended October 8, 1938, 1 fatal case of yellow fever was reported in Dedougou, Ivory Coast.