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PREVALENCE OF POLIOMYELITIS

According to reports received from the State health authorities, a total of 143 cases of poliomyelitis was reported in the United States for the week ended July 15, 1939, as compared with 84 cases for the preceding week and with a 5-year median for the current week of 191 cases. Although a considerable increase is shown for the current week, the number of cases reported was only about 75 percent of the expectancy based on the median for the 5 preceding years.

There was no change in the situation in South Carolina, where 20 cases were reported (the same as for the preceding week), while North Carolina, Georgia, and Florida showed decreases. The number of cases in the East North Central States increased from 4 to 18, and in the West North Central group from none to 10. Nineteen States reported no cases. California reported 45 cases, as compared with 18 for the week ended July 8, but of these cases Los Angeles reported only 5 and San Francisco 1. Information regarding the distribution of the cases by other localities is not available.

DISABLING MORBIDITY AMONG EMPLOYEES IN THE SOAP INDUSTRY, 1930-34,[1] INCLUSIVE

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The present report dealing with sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer among workers in the soap industry covers the period 1930–34 and is derived from data transcribed from the sick benefit organization records of 10,833 members who were employed in 36 establishments. The basic data with respect to months of membership, cases and days of dis-

[1] From the Division of Industrial Hygiene, National Institute of Health, Washington, D. C. The supporting data of this report for the period January 1, 1930, to December 31, 1934, are drawn from material collected by the Occupational Morbidity and Mortality Study of the National Health Survey. The study was made possible by a grant from the Works Progress Administration in 1935. Bibliographic information concerning the reports prepared thus far is included in the list of references (*1–5*).

Readers interested in a description of soap making, useful in determining, among other things, the duties connected with the different occupations may consult reference *7*.

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ability, and deaths are summarized in the following table. It will be observed that the months of membership total 389,399. On the basis of continuous membership during the entire study period of 60 months, this would mean that there were at least 6,490 employees, but actually there were 10,833 employees, which results in an average membership of 36 months instead of 60 for the 5 years. Since the months of membership for the employees other than white are too small to be used for statistical purposes, the analysis will be based on the experience of white males and females.

Color and sex	Number of months of membership	Number of cases of disability	Number of days of disability	Number of deaths
Total	389,399	2,565	90,772	89
White:				
Male	336,015	2,129	75,490	84
Female	52,499	429	14,935	5
Colored:				
Male	668	7	256	----------
Unknown	217	----------	91	----------

Limitations of the data.—Membership in the sick benefit organization is compulsory, but excludes employees with initial salaries of $3,600 per year or over. There are no age limits for applicants for membership, but a physical examination is required. Benefits are refused for disabilities connected with the improper use of stimulants or narcotics, "immoral practices," venereal diseases, voluntary self-injury, unlawful acts, fighting, and maternity. There is a *waiting period* of 7 days, which means that payments are not made for the first 7 days of disability. Payments amounting to two-thirds of the weekly wages are paid for a *maximum benefit period* of 52 weeks in any one year in the event of one or more disabilities. Thereafter reduced payments are continuous.

The analysis is based on only those disabilities that occurred while a worker was a member of the sick benefit organization and these disabilities, furthermore, must have been eligible for benefits.

Since the various sick benefit organizations furnishing data to the Occupational Morbidity and Mortality Study had waiting periods and maximum benefit periods of different durations, certain principles were set down in order that the data for all organizations would be comparable. Thus, a standard waiting period of 7 days was adopted, since all of the cooperating sick benefit organizations considered in this series of reports have a waiting period of 7 days or less.

With respect to the standardization of the maximum benefit period, on the other hand, disabilities or cases which had a duration of 91 calendar days or longer were arbitrarily terminated at 91 days. Only disabilities which began during the study period and lasted 8 calendar days or longer were considered as cases. Disabilities which began before the study period started and lasted 8 calendar days or longer during the study period were not considered as cases, but all days of disability occurring during the study period were considered as days disabled. Known duration cases are those that began and terminated in recovery or death during the study period. Ended cases for calculating fatality rates consist of all disabilities which terminated either in death or recovery during the study period and disabilities which ended in death before the expiration of the waiting period.

Occupational grouping.—Since the number of months of membership for specific occupations was too small for separate analysis the occupations were arranged

into 11 groups for white male workers and into 3 groups for white female workers, as shown in table 1. For both sexes the group of office workers includes members working in similar environments who are presumably not subjected to the exposures in the plant. Process operators, males only, include mainly semiskilled workers who are engaged in making soap; although a large variety of materials is used, for example, fats, oils, lye, sal soda, glycerine, and other products, normally these workers are not exposed to such materials, since most of the processes are enclosed. The group consisting of soap handlers and process laborers is subjected to strenuous work. Soap handlers prepare the finished soap for the wrappers and packers; process laborers include equipment cleaners, as well as workers who supply the different materials required in processing, and general laborers who assist the process operators. Packing machine operators include both male and female workers who handle the finished soap. Warehouse laborers do strenuous work and are presumably not subjected to exposures in the plant. Laborers (not elsewhere classified) are unskilled workers who are not designated elsewhere in the table. This group is not homogeneous as to the type of work or exposure. Some of these laborers work inside and some outside the plant. The only characteristic which they have in common is the fact that they are unskilled. The remaining occupational groups listed in the table are self-explanatory.

TABLE 1.—*Specific occupations comprising each occupational group*

Occupational group	Specific occupations
WHITE MALES	
Office workers	Accountants, bookkeepers, cashiers, clerks, officials, and stenographers.
Salesmen	Commercial salesmen and sales-promotion men.
Foremen	Foremen in all departments.
Process operators	Amalgamators, crutchers, dryer operators, evaporator operators, filter-press operators, furnace men, hardening-machine operators, plodders, pump operators, refiners, roll operators soap boilers, still operators, and tower operators.
Soap handlers and process laborers (n. e. c.)[1].	Carry-offs, cutters, process laborers (except packing department laborers), pull-outs, setters, slabbers, stampers, and strippers.
Packing-machine operators.	Filling-machine operators, folders, packing-machine operators, sealers, and wrapping-machine operators.
Packing laborers	General laborers in the packing department, machinery cleaners, and truckers.
Warehouse laborers	Car loaders and unloaders, general warehouse laborers, stackers, and truckers.
Maintenance workers	Blacksmiths, carpenters, electricians, machinists, masons, mechanical helpers and laborers, mechanics, millwrights, oilers, painters, pipefitters and helpers, riggers and helpers, tank builders, tinners and helpers, welders and welders' helpers.
Laborers (n. e. c.)[1]	Ashmen, automobile washers, boiler cleaners, coal and coke handlers, and general laborers about plant and yard.
All others	Bakers, coopers and helpers, drivers, laboratory workers, licensed engineers and firemen, office and rest-room janitors, porters, railroad firemen and engineers, truck and tractor drivers, and watchmen.
WHITE FEMALES	
Office workers	Bookkeepers, cashiers, clerks, office machine operators, stenographers and typists, and telephone operators.
Packing-machine operators.	Filling-machine operators, sealers, wrapping- and packing-machine operators.
All others	Foreladies, janitors, laboratory workers, nurses, and restaurant help.

[1] Not elsewhere classified.

ANALYSIS OF THE DATA

Age distribution by occupational group.—For each occupational classification the percentage of workers in each age group, and the months of membership, by age group, are shown in table 2. In addition, are given the percentage distribution by age group for gainful white

male and female workers in the United States and the distribution for gainful male and female workers in the soap industry.

TABLE 2.—*Months of membership by age and sex according to occupational group, white employees in the soap industry, 1930–34, inclusive*

Occupational group	All known ages	Age in years					
		Under 25	25–34	35–44	45–54	55–64	65 and over
PERCENTAGE DISTRIBUTION							
	Males						
All gainful white workers in the United States [1]	*100.0*	*19.7*	*24.0*	*22.9*	*17.4*	*10.7*	*5.3*
All gainful workers in soap factories in the United States [1]	*100.0*	*22.3*	*27.0*	*22.9*	*16.2*	*8.5*	*3.1*
All occupations, present report	100.0	12.2	40.7	27.8	13.1	5.5	.7
Office workers	100.0	23.1	46.8	20.0	7.7	2.1	.3
Salesmen	100.0	7.6	47.2	33.8	8.9	2.4	.1
Foremen	100.0	5.9	35.8	34.0	16.0	7.1	1.2
Process operators	100.0	8.4	41.2	28.8	16.0	5.2	.4
Soap handlers and process laborers	100.0	8.6	44.2	29.3	13.6	3.3	1.0
Packing-machine operators	100.0	32.7	41.9	16.8	6.2	2.4	(2)
Packing laborers	100.0	17.2	43.9	23.5	10.1	5.0	.3
Warehouse laborers	100.0	8.5	36.4	33.2	17.2	4.4	.3
Maintenance workers	100.0	6.1	34.6	33.0	17.9	7.8	.6
Laborers (n. e. c.)	100.0	10.2	32.5	24.9	19.0	10.9	2.5
All others	100.0	17.6	34.9	20.6	13.9	10.9	2.1
	Females						
All gainful white workers in the United States [1]	*100.0*	*38.5*	*24.4*	*16.9*	*11.5*	*6.2*	*2.5*
All gainful workers in soap factories in the United States [1]	*100.0*	*54.6*	*26.0*	*11.7*	*5.6*	*1.7*	*.4*
All occupations, present report	100.0	42.0	37.9	13.4	5.3	1.4	(2)
Office workers	100.0	40.7	41.5	11.5	4.7	1.6	(2)
Packing-machine operators	100.0	54.0	34.3	9.6	2.1	----	----
All others	100.0	18.2	29.7	32.1	16.1	3.9	----
NUMBER OF MONTHS OF MEMBERSHIP							
	White males						
All occupations, present report	335,550	40,956	136,556	93,345	43,951	18,302	2,440
Office workers	47,254	10,891	22,137	9,471	3,622	970	163
Salesmen	50,872	3,889	23,993	17,212	4,545	1,199	34
Foremen	25,526	1,503	9,131	8,679	4,094	1,818	301
Process operators	38,095	3,194	15,702	10,974	6,071	1,993	161
Soap handlers and process laborers	26,681	2,308	11,788	7,812	3,637	878	258
Packing-machine operators	9,758	3,193	4,092	1,640	601	230	2
Packing laborers	22,951	3,946	10,077	5,397	2,316	1,154	61
Warehouse laborers	12,912	1,092	4,695	4,289	2,223	574	39
Maintenance workers	51,414	3,134	17,772	16,963	9,182	4,026	337
Laborers (n. e. c.)	13,605	1,384	4,422	3,383	2,591	1,488	337
All others	36,482	6,422	12,747	7,525	5,069	3,972	747
	White females						
All occupations, present report	52,470	22,050	19,900	7,032	2,765	717	6
Office workers	30,422	12,376	12,620	3,511	1,435	474	6
Packing-machine operators	15,795	8,534	5,422	1,516	323	----	----
All others	6,253	1,140	1,858	2,005	1,007	243	----

[1] Reference (*6*).
[2] Less than 0.1 of 1 percent.

Only in the age group 25–34 is the percentage of white male workers in this report (40.7) appreciably greater than the corresponding percentages given for the two other population groups. Summations show that the percentages of the gainful white male workers in the United States, the male workers in the soap industry and the white male workers in this study under 35 years of age are 43.7, 49.3, and 52.9, respectively. It is of interest to observe the percentage age distribution of white male office workers and of white male packing-machine operators. In the former group, 69.9 percent of the workers are under 35 years of age, while the corresponding percentage for the latter group is 74.6; these figures reflect the relatively high percentages of workers under 25 years of age. The two groups with the smallest percentage of workers under 35 years of age are foremen and maintenance workers with 41.7 and 40.7 percent, respectively.

A much larger percentage of female workers than of males are under 25 years of age, the ratio of the percentages being over 3 to 1. The percentages of workers under 35 years of age among all gainful white female workers in the United States, for female workers in the soap industry, and for white females in this study are 62.9, 80.6, and 79.9 percent, respectively. The proportion of workers in each 10-year age group after 34 years is nearly identical for gainful female workers in soap factories and white female workers covered in this report. In the occupational group of packing-machine operators 88.3 percent of the white female workers are under 35 years of age, as compared with 74.6 percent for white male workers.

Frequency of disabilities, by duration.—Table 3 shows by sex for two broad age groups the frequency of cases of disability of different durations. It will be noted that with respect to all durations the difference between the frequencies for the two age groups is very much greater among the males than among the females. Among both sexes, for the shortest durations, 8–14 days, there was a greater frequency among younger than among older persons, but for durations of 15 days and longer the cases in the older age groups showed greater frequencies, with the excess being most marked for the cases with longest duration.

At all ages and for all durations the rate for females was greater than that for males. For both age groups an increase in the length of case tended to make the position of females relatively more unfavorable. The difference between the male rate and the female rate was relatively less for all duration periods among persons aged 35 years and over than among persons under that age.

Selected indexes by age group and sex.—Table 4 gives certain indexes specific for age group and sex. For example, the annual number of cases per 1,000 males is shown to be 68.3 under 25 years of age and

211.5 at 65 years and over. Among males 35 years and over the rate rises with each succeeding age group. For females the small number of person-years of membership for the older age groups is apparently responsible for the irregularity in the trend of the rates.

TABLE 3.—*Frequency of sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer, by sex for the age groups under 35 years and 35 years and over, by known duration in calendar days, white employees in the soap industry, 1930–34, inclusive*

Duration of case in calendar days	Males		Females	
	Under 35 years	35 years and over	Under 35 years	35 years and over
	Annual number of cases per 1,000 persons			
All known durations	65.6	80.9	95.0	97.0
8–14	20.1	18.6	29.7	24.0
15–28	22.6	28.3	29.2	30.8
29–49	11.2	14.0	16.6	17.1
50–91	7.6	11.6	11.2	13.7
92 and over	4.1	8.4	8.3	11.4
	Number of cases of known duration [1]			
All known durations	970	1,065	332	85
8–14	298	245	104	21
15–28	334	372	102	27
29–49	165	184	58	15
50–91	112	153	39	12
92 and over	61	111	29	10
Number of person-years of membership	14,792.7	13,169.8	3,495.8	876.7

[1] Cases with onset during 1930–34, inclusive.

The annual number of days of disability per person under 25 years of age was 2.0 for males and 2.7 for females. It will be observed that the average number of days of disability increased more rapidly and at an earlier age for females than for males.

The average daily percentage of employees disabled was less than one until the age group 55–64 years was reached for males, while for females the percentage was over one in the age groups 25–34 years and 35–44 years.

Among the males, each case lasted, on the average, 35.5 days, and among the females 34.8 days. In the two age groups, under 25 years and 35–44 years, there was little difference between the sexes with respect to duration of case, but in the age group 25–34 years the cases among females averaged 5.8 days longer.

There were 84 deaths among males and 5 deaths among females, resulting in a mortality rate per 1,000 of 3.0 and 1.1, and a case fatality rate of 3.8 and 1.1 percent, respectively. Both rates for males showed a decided increase with age.

TABLE 4.—*Summary of selected morbidity and mortality indexes for different age groups, white male and female employees in the soap industry, 1930–34, inclusive*

Sex	All ages [1]	Age in years as of July 1, 1932					
		Under 25	25–34	35–44	45–54	55–64	65 and over
	Annual number of cases per 1,000 persons						
Male	76.0	68.3	66.0	75.6	92.3	114.1	211.5
Female	98.1	90.9	103.7	116.0	69.4	83.6	----
	Annual number of days of disability per person						
Male	2.70	2.01	2.12	2.70	3.44	5.81	9.95
Female	3.41	2.71	3.93	4.28	3.10	2.98	----
	Average daily percentage of employees disabled						
Male	0.7	0.6	0.6	0.7	0.9	1.6	2.7
Female	.9	.7	1.1	1.2	.9	.8	----
	Average number of days per case						
Male	35.5	29.5	32.1	35.7	37.3	50.9	47.0
Female	34.8	29.8	37.9	36.9	44.6	35.6	----
	Annual number of deaths per 1,000 persons						
Male	3.0	1.8	1.8	3.2	3.5	9.2	24.6
Female	1.1	1.6	1.2	----	----	----	----
	Percent of cases ending fatally						
Male	3.8	2.5	2.7	4.2	3.8	7.4	10.9
Female	1.1	1.8	1.1	----	----	----	----
	Number of cases beginning during 1930–34, inclusive						
Male	2,129	233	751	588	338	174	43
Female	429	167	172	68	16	5	----
	Number of calendar days of disability						
Male	75,490	6,874	24,096	21,010	12,603	8,856	2,023
Female	14,935	4,978	6,521	2,510	714	178	----
	Number of years of disability						
Male	206.8	18.8	66.0	57.6	34.5	24.3	5.5
Female	40.9	13.6	17.9	6.9	2.0	.5	----
	Number of person-years of membership						
Male	28,001.2	3,413.0	11,379.7	7,778.7	3,662.6	1,525.2	203.3
Female	4,374.9	1,837.5	1,658.3	586.0	230.4	59.8	.5
	Number of deaths						
Male	84	6	21	25	13	14	5
Female	5	3	2	----	----	----	----
	Number of ended cases during 1930–34, inclusive						
Male	2,184	239	770	600	339	188	46
Female	439	170	179	67	17	5	----

[1] Includes some of unknown age.

Frequency of disabilities by detailed diagnosis groups.—The annual number of cases per 1,000 persons is shown for each sex, by age group and diagnosis, in table 5. Considering only cases among males, it will be noted that there was a marked increase in frequency with age for certain specific diagnosis groups. This becomes more clear if rates are calculated for the six broad age groups rather than for the two groups as given in the table. Thus, rheumatic diseases, beginning with a rate of 1.5 for males under 25 years, rose in successive 10-year age periods as follows: 2.4, 8.1, 11.7, 17.0, and 44.3, the rate from the youngest to the oldest age group increasing more than 29 times. Diseases of the skin for the same period increased more than 16 times in frequency, while circulatory diseases increased 12 times. Respiratory diseases and digestive diseases did not fluctuate greatly until the oldest age group was reached. Infectious and parasitic diseases showed a greater frequency in the younger age groups; from a rate of 7.6 under 25 years, there was a continuous decline to 2.6 at 55–64 years. Diseases of the pharynx and tonsils and appendicitis likewise were less common in the older age groups.

For females it was not practicable to make a division into age groups other than under 35 years and 35 years and over. According to this division, a pronounced rise in rate with age is observed for nonindustrial injuries, diseases of the circulatory system, and diseases of the skin. A sharp decrease among older persons was noted for respiratory diseases, especially diseases of the pharynx and tonsils, and influenza and grippe. The same was also shown for appendicitis, and for infectious and parasitic diseases. In general the most decided changes with age among females followed the same trend as among males. Notable exceptions are the decline in the respiratory disease rate for older females and the failure of the rheumatic rate to show a rapid increase with age.

While for all disabilities the female rate for ages under 35 years was 46 percent in excess of the corresponding male rate, and 17 percent in excess for ages 35 years and over, yet there were specific diagnosis groups where the opposite trend was observed. For pneumonia and hernia the rate for males was higher among both young and old persons. Indeed, no cases of hernia were reported among females. For males under 35 years the rate was greatly in excess for nonindustrial injuries and to a lesser extent for diseases of the teeth and gums, ulcer of the stomach or duodenum, and diseases of the circulatory system. Among males 35 years of age and older there was an excess in the rate for diseases of the pharynx and tonsils, acute and chronic bronchitis, respiratory tuberculosis, influenza and grippe, rheumatic diseases, and infectious and parasitic diseases. The excess in the rate for females was most pronounced for influenza and grippe and genitourinary diseases among the younger

TABLE 5.—*Frequency of sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer, by sex, for the age groups under 35 years and 35 years and over, according to detailed diagnosis groups, white employees in the soap industry, 1930–34, inclusive*

Diagnosis	Annual number of cases per 1,000 persons						Number of cases [1]					
	White males			White females			White males			White females		
	All ages	Under 35 years	35 years and over	All ages	Under 35 years	35 years and over	All ages [2]	Under 35 years	35 years and over	All ages [3]	Under 35 years	35 years and over
Total, all diagnoses	76.0	66.5	86.8	98.1	97.0	101.5	2,129	984	1,143	429	339	89
Nonindustrial injuries	8.0	7.2	9.0	4.8	2.9	12.5	225	106	119	21	10	11
Sickness	68.0	59.3	77.8	93.3	94.1	89.0	1,904	878	1,024	408	329	78
Respiratory diseases	27.8	26.8	28.9	40.3	43.2	27.4	779	397	381	176	151	24
Diseases of the pharynx and tonsils	5.7	7.6	3.5	9.6	11.8	1.1	159	113	46	42	41	1
Bronchitis, acute and chronic	2.2	1.5	3.1	2.7	2.9	2.3	63	22	41	12	10	2
Other diseases of the upper respiratory tract	1.8	1.8	2.0	3.2	2.6	4.6	52	26	26	14	9	4
Influenza, grippe	14.2	12.5	16.1	20.8	22.0	16.0	397	185	212	91	77	14
Pneumonia, all forms	1.7	1.3	2.0	1.2	1.1	1.1	47	20	27	5	4	1
Pleurisy	.9	1.0	.7	1.4	1.1	2.3	25	15	10	6	4	2
Respiratory tuberculosis	1.0	.9	1.1	1.2	1.4	-------	28	13	14	5	5	-------
Other respiratory diseases	.3	.2	.4	.2	.3	-------	8	3	5	1	1	-------
Digestive diseases	13.4	13.9	12.9	20.8	20.0	24.0	375	205	170	91	70	21
Diseases of the teeth and gums	.9	1.1	.6	.9	.8	1.2	24	16	8	4	3	1
Ulcer of the stomach or duodenum	1.4	.8	2.0	.9	.6	2.3	38	12	26	4	2	2
Other diseases of the stomach, cancer excepted	.9	.6	1.3	1.4	1.4	1.2	26	8	18	6	5	1
Diarrhea, enteritis	1.7	1.3	2.3	3.0	2.9	3.4	49	19	30	13	10	3
Appendicitis, with or without appendectomy	5.3	7.4	2.9	11.6	12.3	9.1	148	110	38	51	43	8
Hernia	1.3	1.3	1.3	-------	-------	-------	36	19	17	-------	-------	-------
Other digestive diseases	1.9	1.4	2.5	3.0	2.0	6.8	54	21	33	13	7	6
Nonrespiratory-nondigestive diseases	26.4	18.5	35.2	32.0	30.6	37.6	738	274	463	140	107	33
Diseases of the circulatory system	3.8	1.9	6.0	2.3	1.1	6.8	107	28	79	10	4	6
Genitourinary diseases	2.9	2.2	3.6	5.7	5.7	5.7	80	33	47	25	20	5
Rheumatic diseases	6.2	2.2	10.7	3.2	3.1	3.4	173	32	141	14	11	3
Diseases of the nervous system	1.9	1.9	1.8	4.6	4.3	5.7	53	29	24	20	15	5
Diseases of the skin	1.7	.9	2.6	1.6	.9	4.6	47	13	34	7	3	4
Other infectious and parasitic diseases	5.5	6.2	4.6	6.4	7.2	3.4	154	92	61	28	25	3
Other nonrespiratory-nondigestive diseases	4.4	3.2	5.9	8.2	8.3	8.0	124	47	77	36	29	7
Ill-defined or unknown diagnoses	.4	.1	.8	.2	.3	-------	12	2	10	1	1	-------
Number of person-years of membership	-------	-------	-------	-------	-------	-------	28,001.2	14,792.7	13,169.8	4,374.9	3,495.8	876.7

[1] See table 3, footnote 1.

[2] Includes 2 cases of unknown age.

[3] Includes 1 case of unknown age.

NOTE.—Of interest is the information available for the same period from a rubber manufacturing company which shows the following rates for white males of all ages: All diagnoses, 78.0; nonindustrial injuries, 14.5; respiratory diseases, 20.4 (the difference reflecting principally cases of influenza and grippe); digestive diseases, 14.4; nonrespiratory-nondigestive diseases, 27.8; and unknown diagnoses, 0.9. Specific diseases which had slightly higher rates than for the soap industry included diseases of the circulatory system, 4.5; rheumatic diseases, 7.4, and diseases of the skin, 2.5.

group, and appendicitis and diseases of the nervous system among those of all ages.

From the viewpoint of the four principal diagnosis groups, for all ages the position of females was most unfavorable for digestive diseases, with an excess in the rate of 55 percent, while for respiratory diseases there was an excess of 45 percent, and for nonrespiratory-nondigestive diseases an excess of 21 percent. Nonindustrial injuries were less common among females. The fact that maternity cases were not eligible for sickness benefits should be kept in mind when comparing rates for the sexes

Rates by occupation.—The frequency of disabilities for each sex, by occupation, is shown, among other things, in table 6 and the age-standardized frequency rates are shown graphically in decreasing order of magnitude in figure 1. It will be observed that the rates for males vary from 134.9 cases per 1,000 for soap handlers and process laborers to 31.8 for office workers. The rates for females, on the other hand, describe a narrower range, varying from 117.1 for packing-machine operators to 74.5 for office workers. Each of the 3 male occupations having standardized rates greater than 100 includes laborers, while occupations with the lowest rates include supervisory and white-collar workers. Packing-machine operators and process operators have rates nearest to that for all occupations (86.1).

TABLE 6.—*Frequency of sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer, annual number of days of disability per person, and average number of days per case, by occupational group and sex, white employees in the soap industry, 1930–34, inclusive*

Occupational group	Annual number of cases per 1,000 persons		Annual number of days of disability per person	Average number of days per case	Number of cases [2]	Number of calendar days of disability	Number of person-years of membership
	Crude	Standardized [1]					
	Males						
Soap handlers and process laborers	116.5	134.9	4.11	35.3	259	9,141	2,223.4
Laborers (n. e. c.)	117.3	126.7	4.35	37.1	133	4,937	1,133.7
Warehouse laborers	101.3	110.7	2.97	29.3	109	3,193	1,076.0
Maintenance workers	99.4	98.1	3.44	34.6	427	14,762	4,293.7
Packing laborers	93.0	93.5	3.46	37.2	178	6,618	1,914.7
Packing-machine operators	98.4	86.1	3.31	33.7	80	2,695	813.2
All occupations	*76.0*	*86.1*	*2.70*	*35.5*	*2,129*	*75,490*	*28,001.2*
Process operators	72.0	78.9	2.56	35.5	229	8,134	3,180.5
Salesmen	59.7	64.1	2.12	35.6	253	9,002	4,239.3
Foremen	48.3	59.3	2.01	41.6	103	4,288	2,132.2
Office workers	33.2	31.8	1.01	30.3	131	3,975	3,947.8
All others	74.5	78.2	2.87	38.5	227	8,745	3,046.7
	Females						
Packing-machine operators	138.2	117.1	5.26	38.1	182	6,933	1,316.9
All occupations	*98.1*	*93.1*	*3.41*	*34.8*	*429*	*14,955*	*4,374.9*
Office workers	75.3	74.5	2.35	31.2	191	5,955	2,536.9
All others	107.5	80.4	3.93	36.6	56	2,047	521.1

[1] Age standardized according to the total white gainfully employed workers in the United States (*6*).
[2] See table 3, footnote 1.

The annual number of days of disability per worker for males, as shown in table 6, will be observed to follow almost the same ranking by occupation as the standardized frequency rates, the highest being 4.35 days for laborers (not elsewhere classified) and the lowest being 1.01 days for office workers. On the other hand, the average number of days per case does not rank by occupation in the same order as the two rates just mentioned. Foremen, with comparatively infrequent disabilities, had the maximum average number of days per case of 41.6, while the minimum average number of days per case was 29.3 for warehouse laborers who had a high frequency rate.

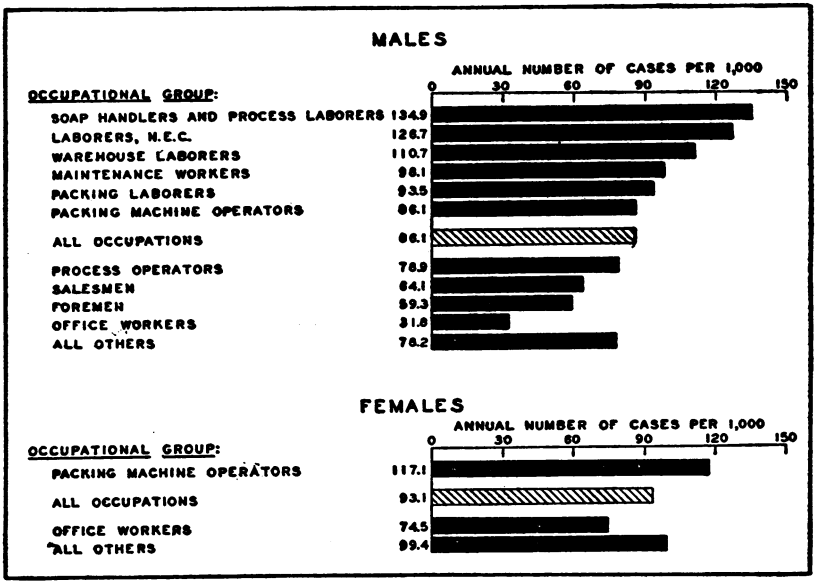

FIGURE 1.—Annual number of cases per 1,000 males and females, respectively, of sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer according to occupational group, white employees in the soap industry, 1930-34, inclusive. (The rates are age-standardized according to the total white gainfully employed workers in the United States.)

Frequency of disabilities by occupation, age, and broad diagnosis groups.—Table 7 shows for a twofold age division of each occupational group the frequency of disabilities by broad diagnosis groups. It is of interest to know the type of diagnosis which is relatively the most unfavorable for a particular occupation. A certain rate may be low with respect to all occupations, yet high from the viewpoint of the occupation itself. For males under 35 years of age the highest ratios of specific rate to the rate for all occupations were as follows: Nonindustrial injuries among soap handlers and process laborers, warehouse laborers, packing-machine operators, and process operators; respiratory diseases among laborers (not elsewhere classified) and maintenance workers; digestive diseases among salesmen, foremen,

TABLE 7.—*Frequency of sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer for each occupational group by age, under 35 years and 35 years and over, and ratio of specific occupational group to all occupations, according to broad diagnosis groups, white male and white female employees in the soap industry, 1930–34, inclusive*

Occupational group	All sickness and nonindustrial injuries [1]				Nonindustrial injuries				Sickness												Person-years of membership	
									Respiratory diseases				Digestive diseases				Nonrespiratory-nondigestive diseases					
	Annual number of cases per 1,000 members		Ratio to total		Annual number of cases per 1,000 members		Ratio to total		Annual number of cases per 1,000 members		Ratio to total		Annual number of cases per 1,000 members		Ratio to total		Annual number of cases per 1,000 members		Ratio to total			
	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over	Under 35 years	35 years and over
	White males																					
All occupations	66.5	86.8	1.00	1.00	7.2	9.0	1.00	1.00	26.8	28.9	1.00	1.00	13.9	12.9	1.00	1.00	18.5	35.2	1.00	1.00	14,792.7	13,169.8
Office workers	37.4	23.6	.56	.27	2.9	3.4	.40	.38	14.5	8.4	.54	.29	10.2	6.7	.73	.52	9.8	5.1	.53	.14	2,752.3	1,185.5
Salesmen	57.2	62.6	.86	.72	4.3	3.6	.60	.40	20.7	20.9	.77	.72	17.6	14.6	1.27	1.13	14.6	23.0	.79	.65	2,323.5	1,915.8
Foremen	30.5	61.2	.46	.71	4.5	6.4	.62	.71	7.9	13.7	.29	.47	9.0	11.3	.65	.88	9.1	29.8	.49	.85	886.2	1,241.0
Process operators	67.9	76.3	1.02	.88	8.9	15.0	1.24	1.67	25.4	23.1	.95	.80	10.8	6.9	.78	.53	22.2	31.3	1.20	.89	1,574.7	1,599.9
Soap handlers and process laborers	114.1	119.2	1.72	1.37	14.5	13.4	2.01	1.49	51.1	33.4	1.91	1.16	17.0	25.7	1.22	1.99	31.5	45.8	1.70	1.30	1,174.7	1,048.7
Packing-machine operators	95.5	106.7	1.44	1.23	14.8	19.4	2.06	2.16	37.9	63.1	1.41	2.18	16.5	9.7	1.19	.75	26.3	14.5	1.42	.41	607.1	206.1
Packing laborers	77.9	116.9	1.17	1.35	6.0	9.4	.83	1.04	33.4	40.3	1.25	1.39	12.0	17.5	.86	1.36	26.5	49.7	1.43	1.41	1,168.6	744.0
Warehouse laborers	105.8	97.7	1.59	1.13	24.9	11.8	3.46	1.31	35.2	38.7	1.31	1.34	18.7	11.8	1.35	.91	27.0	32.0	1.46	.91	482.2	563.8
Maintenance workers	82.1	110.9	1.23	1.28	8.0	8.6	1.11	.96	35.0	40.5	1.31	1.40	16.7	15.7	1.20	1.22	22.4	44.5	1.21	1.26	1,742.2	2,542.3
Laborers (n. e. c.)	101.3	129.3	1.52	1.49	10.3	12.3	1.43	1.37	47.6	47.7	1.78	1.65	18.6	9.2	1.34	.71	22.7	58.5	1.23	1.66	483.8	649.9
All others	55.1	96.3	.83	1.11	3.8	9.7	.53	1.08	24.4	29.1	.91	1.01	12.5	9.7	.90	.75	14.4	47.1	.78	1.34	1,597.4	1,442.8
	White females																					
All occupations	97.0	101.5	1.00	1.00	2.9	12.5	1.00	1.00	43.2	27.4	1.00	1.00	20.0	24.0	1.00	1.00	30.6	37.6	1.00	1.00	3,495.8	876.7
Office workers	71.1	92.9	.73	.92	1.9	17.7	.66	1.42	29.8	17.7	.69	.65	17.8	15.5	.89	.65	21.1	42.0	.69	1.12	2,083.0	452.2
Packing-machine operators	142.7	104.4	1.47	1.03	4.3	6.5	1.48	.52	67.9	26.1	1.57	.95	25.8	19.6	1.29	.82	44.7	52.2	1.46	1.39	1,163.0	153.2
All others	100.1	114.3	1.03	1.13	4.0	7.4	1.38	.59	40.0	44.2	.93	1.61	12.0	40.6	.60	1.69	44.1	22.1	1.44	.59	249.8	271.3

[1] Includes a small number of cases with ill-defined or unknown diagnosis.

and office workers; and nonrespiratory-nondigestive diseases among packing laborers. On the other hand, for males 35 years of age and over the highest ratios were for nonindustrial injuries among process operators; respiratory diseases among warehouse laborers, maintenance workers, and packing-machine operators; digestive diseases among soap handlers and process laborers, salesmen, foremen, and office workers; and nonrespiratory-nondigestive diseases among laborers (not elsewhere classified) and packing laborers. It will be observed that digestive diseases are in the most unfavorable position among persons of all ages who have low total frequency rates and are engaged in nonmanual occupations. Those who are engaged in strenuous manual labor and have high total rates are inclined to show an excess of nonindustrial injuries when young and of respiratory diseases when older.

The highest sickness rates among persons under 35 years were for respiratory diseases in 10 out of 11 occupational groups. In 8 occupational groups the second highest rates were for nonrespiratory-nondigestive diseases, and the third highest rates for digestive diseases. Among persons 35 years and over respiratory diseases held first place in 5 occupational groups and nonrespiratory-nondigestive diseases took first place in 6 occupational groups. Digestive diseases fell to third place in all but one group. The increasing absolute importance of nonrespiratory-nondigestive diseases among older people is clearly shown by these figures.

Included under the classification of nonrespiratory-nondigestive diseases there were some specific diseases which had much higher rates in certain occupations, as is shown in the following table giving the rate per 1,000 males. In each instance it will be noted that the frequency of a particular disease in certain occupations far exceeds the rate for the same disease in all occupations. Age apparently does not greatly influence the excess, which remains relatively the same among both the older and younger groups.

Diagnosis group	Occupational group	Annual number of cases per 1,000 males	
		Under 35 years	35 years and over
Circulatory diseases	Soap handlers and process laborers	3.4	13.3
	All occupations	1.9	6.0
Rheumatic diseases	Packing laborers	5.1	22.8
	Laborers (n. e. c.)	6.2	26.2
	All occupations	2.2	10.7
Skin diseases	Maintenance workers	2.3	5.5
	All occupations	.9	2.6

Rates by socio-economic class.—Table 8 and figure 2, which show the frequency of sickness and nonindustrial injuries by socio-economic class, reflect the influence of standards of living and of home condi-

tions more than a strictly occupational classification. Since the nonworking environment is of great importance with respect to the occurrence of disabilities, a classification which takes this into account will show definite gradations. Among males the different socio-economic classes arrange themselves as follows, when the corresponding frequency rates are written in order of increasing magnitude: clerks and salesmen, skilled workers and foremen, semiskilled workers, and un-

TABLE 8.—*Frequency of sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer by socio-economic class and sex according to broad diagnosis groups, annual number of days of disability per person, and average number of days per case by socio-economic class and sex, white employees in the soap industry, 1930–34, inclusive*

Diagnosis group	Males						Females			
	Total	Clerks and salesmen	Skilled workers and foremen	Semiskilled workers in manufacturing	Unskilled workers	All others	Total	Clerks	Semiskilled workers in manufacturing	All others
	Annual number of cases per 1,000 persons									
Total, all diagnoses [1]	76.0	50.5	72.5	89.4	102.5	59.8	98.1	74.6	136.6	109.1
Nonindustrial injuries	8.0	4.0	6.1	11.3	12.9	4.7	4.8	4.4	4.4	7.8
Sickness [1]	68.0	46.5	66.4	78.1	89.6	55.1	93.3	70.2	132.2	101.3
Respiratory diseases	27.8	17.9	24.9	33.9	39.1	20.9	40.3	28.1	60.6	44.8
Digestive diseases	13.4	13.6	12.5	13.2	15.4	10.1	20.8	16.8	26.3	25.3
Nonrespiratory-nondigestive diseases	26.4	14.9	28.5	30.6	34.4	23.7	32.0	24.9	45.3	31.2
	Annual number of days of disability per person									
Total, all diagnoses	2.70	1.69	2.69	2.99	3.66	2.36	3.41	2.31	5.27	3.81
	Average number of days per case									
Total, all diagnoses	35.5	33.5	37.2	33.4	35.7	39.5	34.8	31.0	38.6	34.9
	Number of cases [2]									
Total, all diagnoses [1]	2,129	367	460	427	721	154	429	186	187	56
Nonindustrial injuries	225	29	39	54	91	12	21	11	6	4
Sickness [1]	1,904	338	421	373	630	142	408	175	181	52
Respiratory diseases	779	130	158	162	275	54	176	70	83	23
Digestive diseases	375	99	79	63	108	26	91	42	36	13
Nonrespiratory-nondigestive diseases	738	108	181	146	242	61	140	62	62	16
	Number of calendar days of disability									
Total, all diagnoses	75,490	12,307	17,087	14,272	25,744	6,080	14,935	5,762	7,219	1,954
	Number of person-years of membership									
Total, all diagnoses	28,001.2	7,272.8	6,343.7	4,773.8	7,035.6	2,575.3	4,374.9	2,492.5	1,369.2	513.2

[1] Includes some cases of ill-defined or unknown diagnosis.
[2] See table 3, footnote 1.

skilled workers. From the first to the last class the rate more than doubled. A similar trend is apparent for each diagnosis group. There was relatively least difference for digestive diseases between the most favored and the least favored socio-economic class and most difference for nonindustrial injuries. The excess in the rate for skilled workers over white-collar workers was almost the same as the excess in the rate for unskilled over skilled. For semiskilled workers the rates were more nearly like those for the unskilled than the skilled.

The females fell chiefly into two socio-economic classes, clerks and semiskilled workers. The latter had a rate 83 percent in excess of the

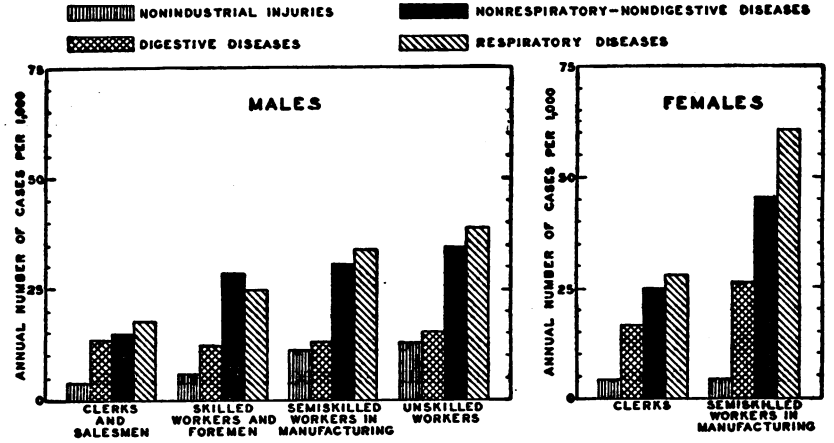

FIGURE 2.—Annual number of cases per 1,000 males and females, respectively, of sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer by socio-economic class, according to broad diagnosis group, white employees in the soap industry, 1930-34, inclusive.

former for all diagnosis groups, although the rates for nonindustrial injuries were the same; the excess for respiratory diseases was 116 percent, and for nonrespiratory-nondigestive diseases 82 percent.

According to table 8 the annual number of days of disability per worker for males varied from 1.69 for clerks and salesmen to 3.66 for unskilled workers. The rate for females, which was 26 percent greater than that for males for all classes, was 76 percent greater for semiskilled workers.

For males the average number of days per case does not follow so regular a trend. Unskilled workers had disabilities lasting longer than did clerical or semiskilled workers, but for skilled workers and foremen the average length of case was greater than for the other three groups. Probably this rate was influenced by the fact that the group of skilled workers and foremen included a large proportion of older persons, whose disabilities tend to last longer than those of younger persons.

For female clerks the duration of cases was shorter than for male clerks and salesmen. The reverse was observed for semiskilled workers in manufacturing, where the cases among females were longer by an average of 5.2 days.

SUMMARY

This report deals with sickness and nonindustrial injuries causing disability lasting 8 calendar days or longer among persons engaged in the soap industry. The annual number of cases per 1,000 was 76.0 for males and 98.1 for females, while the annual number of days of disability per person was 2.70 and 3.41, respectively. The average number of days per case was 35.5 among males and 34.8 among females.

Age-standardized frequency rates by occupation among males ranged from 31.8 for office workers to 134.9 for soap handlers and process laborers. High rates were associated with strenuous manual labor, and low rates with white-collar and supervisory occupations. In some occupations certain diagnosis groups showed rates much above the average for all occupations.

According to socio-economic class for males, clerks and salesmen had the lowest frequency rate, followed in order of increasing magnitude by skilled workers and foremen, semiskilled workers in manufacturing, and unskilled workers. Similarly, with respect to females, semiskilled workers in manufacturing showed a higher frequency rate than clerks.

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STUDIES IN CHEMOTHERAPY

IX. ANTIBACTERIAL ACTION OF SOME AROMATIC ARSENIC, SULFUR, AND NITRO COMPOUNDS

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Since the original discovery of Prontosil by Domagk many compounds have been investigated for chemotherapeutic activity. Studies have been directed both to obtaining more effective derivatives and to investigating the relation of chemical structure to therapeutic action. Tréfouël, Nitti, and Bovet first demonstrated the antistreptococcal action of sulfanilamide (p-aminobenzene sulfonamide) and later reported upon a large series of compounds related to it (*1*, *2*). Other contributions include those of Buttle, Gray, and Stephenson (*3*, *14*, *15*), Fourneau et al. (*4*, *5*), Goissedet et al. (*6*), Gley (*7*), Girard (*8*), Bauer and Rosenthal (*9*), Mayer and Oechslin (*10*), Mietzsch (*11*), Whitby (*12*), Crossley, Northey, and Hultquist (*13*). Significant knowledge concerning the effects of position in the benzene ring and of substitutions or replacements of the amino or sulfonamide radical has been gained from such studies.

The discovery of the antibacterial activity of the diphenyl-sulfones, sulfides, disulfides, and sulfoxides (Buttle (*14*, *15*), Fourneau et al. (*16*), Gley (*7*) and Girard (*8*)) marked the first active compounds that did not contain sulfonamide groups.

Active compounds previously described have practically all been sulfur derivatives. While Levaditi (*17*) found that hydroquinone and 4,4′-dioxyazobenzene possess some activity, this action was limited to the "toxi-infection" of the meningococcus and gonococcus in mice, and perhaps related to an antiendotoxic effect under these conditions. Kolmer, Brown, and Raiziss (*20*) have reported upon the activity of 2-amino-5-iodopyridine in suppurative streptococcal lesions in rabbits.

TECHNIQUE

All experiments were carried out upon albino mice. The drugs were administered by mouth or subcutaneously, usually in one-half of the maximum tolerated dose (M. T. D.). The M. T. D. was accepted as the maximum single dose of the drug that killed not more than 10 percent of the animals. Therapy was begun within one-half hour after inoculation of the organisms, and repeated at daily intervals for several doses. Subcutaneous injections of insoluble compounds were made in 0.1 cc. of olive oil. Acid solutions were neutralized with sodium bicarbonate prior to administration.

In the present study the therapeutic index, derived from the ratio of the maximum tolerated dose to the minimum effective dose, as

defined below, is only a rough approximation; it is intended to represent only a qualitative appraisal of activity to be employed for purposes of comparison, and not a final coefficient of curative power.

It has become evident (*18*, *19*) that toxicity varies considerably from one species to another, and also that the acute toxicity is no reliable indication of the amount of drug which will be tolerated on repeated administration. Another source of difficulty is the variation in therapeutic activity that is experienced from one experiment to another and from one strain of organism to another. The minimum effective dose (M. E. D.) is also conditioned by the length of treatment, the route of administration, the period of observation, and the percentage of survivals taken to represent an effective dose. Even when these factors are standardized, considerable variation in results occurs. The activity of compounds in relation to one another is more constant. In studying a large series of compounds it is desirable to have some basis of comparison; the information obtained under the conditions of our experiments is of value for a preliminary comparison. For our present purposes the survival of one-third to two-thirds of the animals for 10 days was taken as a measure of a minimum effective dose. The results of several experiments were considered in the determination of the M. E. D.

Two highly virulent strains of hemolytic streptocci were employed. Eighteen-hour peptone broth cultures containing rabbit blood were diluted in broth 10^{-6}, and 0.5 cc. was inoculated intraperitoneally. This represented 100 to 1,000 lethal doses of the organisms. Similar tests were carried out with two strains of type I pneumococcus.

RESULTS WITH ARSENIC COMPOUNDS

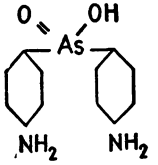
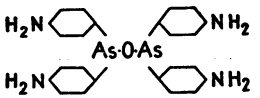
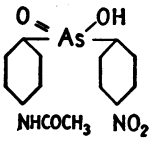
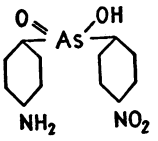
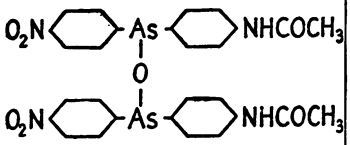
We have investigated a series of compounds structurally similar to some active sulfur compounds, but differing in that the sulfur was replaced by tri- or pentavalent arsenic. Fourneau, Tréfouël, Nitti, and Bovet (*4*) have replaced the sulfonamide radical of sulfanilamide by NH_2, CN, SO_3H, AsO_3H_2 and $CONH_2$, and in each instance the antistreptococcal action was abolished. Tréfouël, Nitti, and Bovet (*2*) also prepared a series of arsenic benzene derivatives containing amino or substituted amino groups (including azo compounds), all of which were inactive.

The toxicity for mice of the arsenic compounds used in this study is shown in table 1. The trivalent arsenicals all possessed irritant properties, as shown by local induration at the site of the injection.

No active arsenic compounds structurally analogous to sulfanilamide were obtained. 4-Aminophenyl and 4-nitrophenyl arsonic acid were inactive. Tryparsamide was inactive although it was tolerated in mice in doses up to 1.0 gm. per kilo (tables 4 and 5).

The sulfur compounds most active against streptococci are 4,4′-diaminodiphenylsulfone and the corresponding nitroamino derivative. We have found 4,4′-diaminodiphenylarsinic acid (Ba 25) and the corresponding arsyloxide (Ba 28) devoid of action. However, 4-nitro-4′-aminodiphenylarsinic acid (Ba 30) showed some activity both by mouth and upon subcutaneous injection (tables 2, 3, and 5).

TABLE 1.—*Preliminary study of acute toxicity for mice of some arsenic and sulfur compounds*

Compound	Number of mice	Dose (gm. per kilo)	Route	Mortality (percent)
Ba 25 	8	0.05	S. C.	0
	8	.125	S. C.	25
	8	.25	S. C.	100
	10	.15	Oral	0
	10	.3	Oral	0
	5	.05	I. V.	0
	5	.1	I. V.	0
Ba 28 	5	0.01	S. C. (4) [1]	0
	5	.025	S. C. (4)	0
	10	.05	S. C.	70
	10	.10	S. C.	100
Ba 29 	5	0.05	S. C.	0
	5	.1	S. C.	0
	5	.25	S. C.	80
	5	.5	S. C.	100
	10	.25	Oral	0
	6	.5	Oral	0
	5	1.0	Oral	40
Ba 30 	5	0.025	S. C.	20
	5	.05	S. C.	0
	5	.10	S. C.	100
	5	.25	Oral (2)	0
	5	.5	Oral (2)	100
Ba 31 	10	0.025	S. C. (oil)	0
	16	.05	S. C.	0
	5	.1	S. C.	40
	5	.2	S. C.	40
	5	.025	Oral	80
	5	.05	Oral	100

[1] Figures in parentheses represent repetition of dosage on successive days.

TABLE 1.—*Preliminary study of acute toxicity for mice of some arsenic and sulfur compounds*—Continued

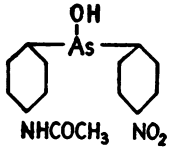
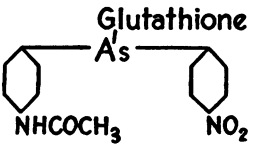
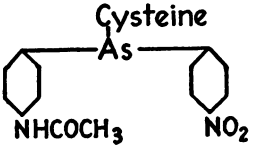
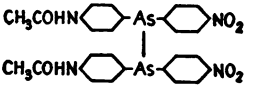
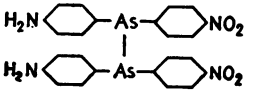
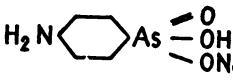
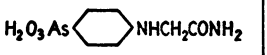
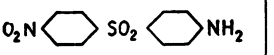
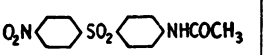
Compound	Number of mice	Dose (gm. per kilo)	Route	Mortality (percent)
Ba 31b 	5	0.025	S. C. (oil)	0
	5	.05	S. C.	0
	10	.1	S. C.	10
	5	.25	S. C.	20
Ba 33 	5	0.025	S. C.	0
	5	.05	S. C.	0
	5	.075	S. C.	40
	5	.10	S. C.	80
	5	.25	S. C.	100
Ba 34 	5	0.0125	S. C.	0
	13	.025	S. C.	77
	6	.05	S. C.	100
Ba 42 	5	0.025	S. C.	0
	5	.05	S. C.	0
	5	.10	S. C.	80
Ba 46 	5	0.10	S. C. (oil)	0
	5	.20	S. C.	0
	6	.4	S. C.	33
Ba 49 	5	0.05	S. C. (oil)	0
	5	.10	S. C.	40
	5	.25	S. C.	100

TABLE 1.—*Preliminary study of acute toxicity for mice of some arsenic and sulphur compounds*—Continued

Compound	Number of mice	Dose (gm. per kilo)	Route	Mortality (percent)
Atoxyl 	10 5	0.25 .5	S. C. S. C.	10 60
Tryparsamide 	5 5	1.0 2.0	S. C. S. C.	0 40
Ba 35 	5 5 5	0.25 .50 1.0	Oral Oral Oral	0 20 80
				N
Ba 36 	5 5 5 6	0.5 1.0 2.0 4.0	Oral Oral Oral Oral	0 0 0 33
Ba 37 	5 5 5	0.5 1.0 2.0	Oral Oral Oral	0 0 0

Acetylation of 4-nitro-4′-aminodiphenylarsinic acid (Ba 29) caused an increase of antistreptococcal action and at the same time a decrease in toxicity of one-half. When administered in amounts close to the tolerated dose, curative effects, with a certain percentage of permanent survivors, could be obtained. This favorable effect of acetylation of arsenic compounds has several counterparts in the field of trypanocidal and spirillocidal derivatives (i. e., arsacetin). By mouth the activity of Ba 29 was approximately the same as equal doses of sulfanilamide, but on subcutaneous injection it was more active.

The corresponding trivalent arsenic derivative was obtained both as an anhydride, 4,4′′-dinitro-4′,4′′′-diacetyldiamino-tetraphenylarsyl-oxide (Ba 31), and as a hydroxy compound, 4-nitro-4′-acetylamino-diphenylarsylhydroxide (Ba 31b). Both forms were approximately twice as active and twice as toxic as the pentavalent compound. Curative effects were seen with 0.025 to 0.05 gm. per kilo (0.5 to 1 mg. per 20-gm. mouse). They were insoluble and were administered

TABLE 2.—*Comparative activity of some asymmetric arsenic and sulfur compounds against streptococcal infections in mice*

Number	Compound	Dosage	Number of mice	Deaths in days												Mortality (percent)	Organism
				1	2	3	4	5	6	7	8	9	10	11–14	15–21		
Ba 29	4 - acetylamino - 4′ - nitrodiphenylarsinic acid	0.015×2 days subcutaneous. 0.01×2 days subcutaneous.	20	9	8	1	1	----	----	----	----	----	----	1	1	95	Streptococcus No. 995, 10^{-6}.
Ba 31	4, 4″ - dinitro - 4′, 4‴ - diacetyldiaminotetraphenylarsyloxide	0.015×2 days subcutaneous. 0 01×2 days subcutaneous.	20	5	5	4	----	1	2	----	----	----	----	1	1	95	
Ba 35	4, 4′-aminonitro diphenylsulfone	0.015×2 days subcutaneous. 0.01×2 days subcutaneous.	20	2	1	----	----	----	2	----	3	----	3	3	3	85	
	Sulfanilamide	0.4×2 days subcutaneous. 0.3×2 days subcutaneous.	20	2	2	----	----	----	4	----	1	----	1	3	2	75	
	Controls	----	18	13	3	----	----	----	----	----	1	----	----	----	----	95	
Ba 29	4 - acetylamino - 4′ - nitrodiphenylarsinic acid.	0.025×4 days subcutaneous.	20	3	2	1	----	3	1	3	----	----	----	1	----	70	Streptococcus No. 995, 10^{-6}.
Ba 30	4-amino-4′-nitrodiphenylarsinic acid	----do----	20	9	1	1	3	----	----	3	----	----	----	----	1	90	
Ba 31	----	----do----	20	4	----	4	1	3	----	2	1	----	----	1	3	95	
Ba 31b	4 - acetylamino - 4′ - nitrodiphenylarsyloxide.	----do----	20	5	5	2	----	----	----	2	----	----	----	----	1	75	
Ba 34	Glutathione derivative of Ba 31	0.01×4 days subcutaneous.	20	5	4	----	1	1	2	2	----	1	1	----	1	90	
Ba 35	4-amino-4′-nitrodiphenylsulfone	0.025×4 days subcutaneous.	20	----	----	1	----	----	----	1	5	----	1	3	3	70	
	Sulfanilamide	0.4×4 days subcutaneous.	20	19	----	----	2	1	3	2	2	1	4	4	1	100	
	Controls	----	20	----	----	----	----	----	----	----	----	----	----	1	----	100	
Ba 29	----	0.05×2 days subcutaneous. 0.05×2 days oral	10 10	----	6 6	2 4	1	----	----	----	----	----	----	----	----	90 100	Streptococcus No. 1685, 10^{-6}.
Ba 31	----	0.05×2 days subcutaneous.	20	----	----	3	6	4	3	1	1	----	----	----	1	95	
	Controls	----	20	20	----	----	----	----	----	----	----	----	----	----	----	100	
Ba 31	----	0.05×1 day subcutaneous. 0.25×1 day subcutaneous.	20	----	----	2	6	2	4	----	1	----	1	1	----	85	Streptococcus No. 1685, 10^{-6}.
	Sulfanilamide	0.15×1 day subcutaneous. 0.015×1 day subcutaneous.	20	----	1	3	9	6	----	----	----	----	----	----	----	95	
	Controls	----	18	15	3	----	----	----	----	----	----	----	----	----	----	100	
Ba 34	Glutathione derivative of Ba 31	0.015×2 days subcutaneous. 0.01×2 days oral	20	1	----	----	----	----	2	4	----	----	2	----	----	45	Strepto coccus No. 1685, 10^{-6}
Ba 35	4-amino-4′-nitrodiphenylsulfone	0.03×2 days oral 0.02×2 days oral	20	1	1	----	----	----	5	1	----	1	1	----	----	50	
Ba 36	4-acetylaminonitrodiphenylsulfone	0.03×2 days oral 0.02×2 days oral	20	----	1	----	----	----	6	1	1	1	----	----	1	55	

Ba 37	4 - acetylamino - 4′ - nitrodiphenyl-sulfoxide.	0.03×2 days oral	20	10	18	1											95		
	Controls	0.02×2 days oral	20	16	4												100		
Ba 34		0.015×2 days subcutaneous.	12						2	1		1	1	1	1	1	75	Streptococcus 1685, 10^{-6}.	No.
		0.01×2 days subcutaneous.																	
Ba 34		0.01×4 days subcutaneous.	15	3	7			1	1	1							86		
Ba 37		0.2×2 days oral	15		3	1			2	1	3						66		
		0.15×2 days oral																	
	Sulfanilamide	0.5×2 days oral	15		1	2			1			1		1			40		
		0.38×2 days oral																	
	Controls		15	15													100		
Ba 34	Glutathione derivative of Ba 31	0.0125×4 days subcutaneous.	15	1		1	1	2			1	1					46	Streptococcus 1685, 10^{-6}.	No.
Ba 42	Cysteine derivative of Ba 31	0.025×4 days subcutaneous.	15	1	5	2	1	1			1		1				80		
	Controls		15	11	4												100		

subcutaneously in olive oil. The toxicity of the anhydride was greater orally than subcutaneously, differing in this respect from other compounds in this series.

The soluble glutathione (Ba 34) and cysteine (Ba 42) derivatives [1] of Ba 31 and Ba 31b were prepared. The glutathione derivative was twice as toxic and four times as active as the parent compound. Curative effects against streptococci could be shown with 0.01 to 0.015 gm. per kilo (0.2 to 0.3 mg. per 20-gm. mouse). This represents an activity equal to that of the highly active sulfones. Although the toxicity of the cysteine derivative was less, therapeutic activity was diminished to a greater extent than toxicity (tables 2 and 5).

By further reduction of 4-nitro-4′-aminodiphenylarsinic acid and its acetyl derivative, two arsines were prepared, Ba 46 and Ba 49. As in the case of the arsinic acid, the acetyl derivative was more active and less toxic than the deacetylated compound. The acetylated derivative (Ba 46) was highly insoluble and was poorly absorbed from the site of its subcutaneous injection in oil. Curative effects were seen with 0.1 gm. per kilo, while it was tolerated in twice this dosage (tables 4 and 5).

The activity of the arsenic compounds was characterized by a limited range of dosage. Therapeutic effects which were pronounced with a given dose diminished rapidly when the dose was decreased.

All of the arsenic compounds in this series were tested against a virulent strain of pneumococcus type I, but no appreciable activity was observed with any of them.

The following arsenic compounds were also tested against *Trypanosoma equiperdum* infection in mice: Ba 25, Ba 28, Ba 29, Ba 30, Ba 31, and Ba 42. Only Ba 42 (cysteine derivative) possessed some trypanocidal action, bringing about prolongation of life but no permanent survival when given in one-half the maximum tolerated amount for 3 doses at intervals of 3 days.

SULFUR COMPOUNDS

Included for comparative purposes are those sulfur compounds analogous to the arsenic derivatives in this series (table 2). With the exception of 4-nitro-4′-acetylaminodiphenylsulfone, they have been previously investigated.

4,4′-Diaminodiphenylsulfone is among the most active compounds against streptococcal infections in mice (*14*, *16*, *21*, *22*). 4-Nitro-4′-aminodiphenylsulfone has been found to be of equal activity and toxicity (*5a*, *15*). Our results are in general agreement with these findings; approximately 0.025 to 0.03 gm. per kilo (0.5 to 0.6 mg. per 20-gm. mouse) represented an effective dose. 4-Nitro-4′-acetylamino-

[1] The chemical structure of these derivatives has not yet been established.

TABLE 3.—*Antistreptococcal action of some arsenic compounds administered orally to mice*

Number	Compound	Dosage (gm. per kilo)	Number of mice	Deaths in days												Mortality (percent)	Organism
				1	2	3	4	5	6	7	8	9	10	11-14	15-21		
Ba 29	4-acetylamino-4'-nitrodiphenylarsinic acid.	0.15×3 days	20	1	----	3	3	2	1	1	1	----	1	1	------	70	Streptococcus No. 1685, 10^{-6}.
Ba 30	4-amino-4'-nitrodiphenylarsinic acid	do	20	----	11	2	1	2	2	1	----	----	----	------	------	95	
Ba 25	4, 4'-diaminodiphenylarsinic acid	do	20	20	----	----	----	----	----	----	----	----	----	------	------	----------	
	Controls		20	20	----	----	----	----	----	----	----	----	----	------	------	----------	
Ba 29		0.15×4 days	20	6	3	1	2	----	1	1	----	1	----	1	------	80	Streptococcus No. 995, 10^{-6}.
Ba 30		do	20	6	3	3	1	1	----	----	----	2	----	------	------	80	
Ba 25		do	20	16	3	1	----	----	----	----	----	----	----	------	------	100	
	Sulfanilamide	do	20	1	1	3	4	1	2	2	2	----	----	1	------	85	
	Controls:																
	10^{-6}		20	12	4	3	----	----	1	----	----	----	----	------	------	100	
	10^{-5}		4	1	----	----	----	1	1	----	----	----	----	------	------	75	
Ba 29		0.15×3 days	20	4	4	1	1	2	3	1	1	----	----	1	------	90	Streptococcus No. 995, 10^{-6}.
Ba 30		do	20	4	7	3	4	----	1	1	----	----	----	------	------	100	
Ba 25		do	20	10	3	1	1	1	2	1	----	----	----	------	------	95	
	Sulfanilamide	do	20	----	1	----	1	----	3	7	----	2	1	1	------	80	
	Controls:																
	10^{-6}		20	10	4	3	3	----	----	----	----	----	----	------	------	100	
	10^{-5}		4	2	2	----	----	----	----	----	----	----	----	------	------	100	
Ba 29		0.15×4 days	20	4	4	3	2	3	2	----	----	----	----	------	------	90	Streptococcus No. 1685, 10^{-6}.
Ba 30		do	20	5	8	3	2	2	----	----	----	----	----	------	------	100	
Ba 25		do	20	17	3	----	----	----	----	----	----	----	----	------	------	100	
	Sulfanilamide	do	20	----	9	----	----	----	6	----	----	----	1	------	------	80	
	Controls:																
	10^{-6}		20	17	2	----	----	----	----	----	----	----	----	------	------	95	
	10^{-5}		5	5	----	----	----	----	----	----	----	----	----	------	------	100	

TABLE 4.—*Comparative antistreptococcal activity of some arsenic and sulfur compounds*

Number	Compound	Dosage, S. C. (gm. per kilo)	Number of mice	Deaths in days												Mortality (percent)	Organism
				1	2	3	4	5	6	7	8	9	10	11–14	15–21		
Ba 46	4, 4''-diacetyldiamino-4', 4'''-dinitrotetraphenyldiarsyl.	0.1×2 days	15	1	1	----	2	----	4	----	1	----	1	1	1	80	Streptococcus No. 995, 10^{-6}.
		0.05×1 day															
	Sulfanilamide	0.5×2 days	15	----	----	2	1	1	2	1	2	----	----	------	1	66	
		0.25×1 day															
	Controls	----------	15	11	4	----	----	----	----	----	----	----	----	------	------	100	
Ba 46	----------	0.035×3 days	20	10	4	3	----	----	----	1	----	----	----	------	------	90	Streptococcus No. 995, 10^{-6}.
Ba 49	Deacetylated Ba 46	do	20	16	3	1	----	----	----	----	----	----	----	------	------	100	
	Controls	----------	20	18	2	----	----	----	----	----	----	----	----	------	------	100	
Ba 46	----------	0.05×3 days	15	2	6	1	3	----	----	1	----	1	----	1	------	100	Streptococcus No. 1685, 10^{-6}.
	Controls	----------	15	15	----	----	----	----	----	----	----	----	----	------	------	100	
Ba 33	4-nitrophenylarsonic acid	0.05×1 day	20	18	2	----	----	----	----	----	----	----	----	------	------	100	Streptococcus No. 1685, 10^{-6}.
	Tryparsamide	1.0×1 day	20	17	3	----	----	----	----	----	----	----	----	------	------	100	
		0.5×1 day															
	Atoxyl	0.2×1 day	20	16	4	----	----	----	----	----	----	----	----	------	------	100	
		0.1×1 day															
	Controls	----------	20	16	4	----	----	----	----	----	----	----	----	------	------	100	
Ba 35	4-amino-4'-nitrodiphenylsulfone	0.0125×4 days (oral)	20	2	5	3	1	1	4	1	----	----	----	------	------	85	Streptococcus No. 1685, 10^{-6}.
Ba 18	4, 4'-diaminodiphenylsulfone	do	20	3	4	4	----	1	----	----	----	2	1	------	1	80	
	Controls	----------	20	16	3	1	----	----	----	----	----	----	----	------	------	100	
Ba 18	----------	0.03×3 days (oral)	20	1	3	3	1	1	4	1	----	----	----	1	------	75	Streptococcus No. 995, 10^{-6}.
Ba 35	4-amino-4'-nitrodiphenylsulfone	do	20	3	2	2	4	1	2	1	----	----	1	------	1	85	
Ba 36	4-acetylamino-4'-nitrodiphenylsulfone	do	20	3	5	1	3	1	----	2	----	----	1	------	------	85	
	Controls	----------	10	5	3	----	1	----	----	----	----	----	1	------	------	100	

TABLE 5.—*Summary of the toxicity and therapeutic activity against streptococci of some arsenic and sulfur compounds (drugs administered subcutaneously unless otherwise stated)*

Number	Compound	M. T. D., gm. per kilo	M. E. D. (streptococcus) gm. per kilo	Therapeutic index
Ba 25	4,4'-diaminodiphenylarsinic acid	0.05	None	0
Ba 25	4,4'-diaminodiphenylarsinic acid (oral)	.3	do	0
Ba 28	4,4',4'',4'''-tetraaminotetraphenylarsyloxide	.025	do	0
Ba 29	4-acetylamino-4'-nitrodiphenylarsinic acid	.1	0.1	1
Ba 29	4-acetylamino-4'-nitrodiphenylarsinic acid (oral)	.5	0.15–0.25	2
Ba 30	4-amino-4'-nitrodiphenylarsinic acid	.05	Slight	<1
Ba 30	4-amino-4'-nitrodiphenylarsinic acid (oral)	.25	do	<1
Ba 31	4',4'''-diacetyldiamino-4,4''-dinitrotetraphenylarsyloxide	.05	0.05	1
Ba 31b	4-acetylamino-4'nitrodiphenylarsylhydroxide	.05	0.05	1
Ba 34	Glutathione derivative of Ba 31b	.025	0.0125	2
Ba 42	Cysteine derivative of Ba 31	.05	0.025–0.05	1–2
Ba 46	4,4''-diacetyldiamino-4',4'''-dinitrotetraphenyldiarsyl	.2	0.1	1–2
Ba 49	4,4''-diamino-4',4'''-dinitrotetraphenyldiarsyl	.05	Slight	<1
Ba 33	4-nitrophenyl arsonic acid	.05	None	0
	Atoxyl	.25	do	0
	Tryparsamide	1.0	do	0
		(oral)		
	Sulfanilamide	2.5	0.4–0.75	3.3–6
Ba 18	4,4'-diaminodiphenylsulfone	.15	0.025	6
Ba 35	4-amino-4'-nitrodiphenylsulfone	.25	0.03	8
Ba 36	4-acetylamino-4'-nitrodiphenylsulfone	2.0–3.0	0.03	70–100
Ba 19	4,4'-diacetyldiaminodiphenylsulfone	[1] >8.0	0.2	>40
Ba 37	4-acetylamino-4'-nitrodiphenylsulfoxide	>2.0	0.2	>10

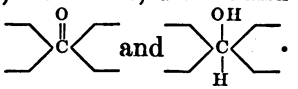
[1] The low acute toxicity of this compound is deceptive since it is only partially absorbed from the alimentary canal. This may also apply to the oral toxicity of other compounds in this series.

diphenylsulfoxide was less active. It is of interest that the corresponding diaminodiphenyl arsenic compounds were inactive while the nitroamino compounds were active.

The favorable effect of acetylation upon the therapeutic action of the 4-nitro-4′-aminodiphenyl arsenic compounds was not to be anticipated from the results with sulfur compounds. Acetylation of sulfanilamide reduces its activity to a trace. Acetylation of 4,4′-diaminodiphenylsulfone reduces its activity several fold, although toxicity is decreased to an even greater extent. Incomplete absorption from the alimentary tract is a factor in the decreased toxicity of this compound (*9*, *21*, *22*).

Our results with the asymmetric arsenic compounds led us to study the acetylated derivative of 4-nitro-4′-aminodiphenylsulfone. Our results in mice indicate that acetylation of this compound does not diminish its antistreptococcal activity while it does bring about a decrease in toxicity to approximately one-tenth of the free compound (tables 2, 4, and 5). This derivative possesses a very high therapeutic index against streptococcal infections in mice; while variation in absorption and excretion might account for some of the decrease in toxicity, the fact that the therapeutic activity is not decreased makes this observation of significance. Results in pneumococcal infections in mice were much less marked, and showed no appreciable superiority over the other sulfones in this series.

AROMATIC NITRO AND AMINO COMPOUNDS

Experiments were carried out with a series of 4,4′-diamino,-dinitro and -nitroamino compounds possessing the linkages  and . In spite of the relatively low toxicity of these compounds no therapeutic activity was observed against streptococcal or pneumococcal infections in mice. These compounds, the benzophenones, and benzhydrols represent a replacement of arsenic or sulfur by carbon.

At the suggestion of one of us (E. E.) some simple nitro- and nitrosobenzene derivatives were investigated. Some activity against pneumococcus infections in mice was observed with p-nitro-benzoic acid.[2] This compound was more toxic than sulfanilamide but with maximum tolerated doses a prolongation of life was observed which was as great as or greater than the effect of similar doses (by weight) of sulfanilamide. Only rarely, however, did survival occur as a result of therapy. The toxicity by mouth was less than that upon subcutaneous injection, and greater prolongation of life could be obtained by oral administration (tables 6 and 7).

[2] Since this was written a report of the antistreptococcal and antipneumococcal action of p-nitrobenzoic acid and some esters by R. L. Mayer and C. Oechslin has appeared (Compt. Rend. Soc. Biol., 130:211 (1939)).

TABLE 6.—*Toxicity and antibacterial activity of some benzophenones, benzhydrols, nitro and amino benzoic acids and related compounds*

Compound	M. T. D., gm. per kilo	Route	Activity
4,4'-dinitrodiphenylmethane	2.0	S. C. (oil)	0
4,4'-dinitrobenzophenone [1]	1.5	S. C. (oil)	0
4-amino-4'-nitrobenzophenone [1]	1.5	S. C. (oil)	0
4,4'-diaminobenzophenone [1]	.5	Oral	0
4,4'-tetramethyldiaminobenzophenone	2.0	S. C. (oil)	0
4,4'-diaminobenzhydrol [1]	.5	S. C. (oil)	0
4,4'-diaminobenzhydrol [1]	1.0	Oral	0
4,4'-tetramethyldiaminobenzhydrol	1.0	Oral	0
2-nitrobenzoic acid	0.5	S. C., oral	0
3-nitrobenzoic acid	.5	S. C., oral	0
4-nitrobenzoic acid	.5	S. C.	[2] Moderate
4-nitrobenzoic acid	1.0	Oral	[2] Moderate
1,3,5-trinitrobenzoic acid	.3	S. C.	0
4-nitrobenzamide	1.0	S. C. (oil)	[2] Trace
4-nitrobenzhydrazide	.03	S. C. (oil)	0
4-nitrosobenzoic acid [1]	.08	S. C.	0
4-hydroxylaminobenzoic acid [1]	.5–1.0	S. C.	0
4-aminobenzoic acid	4.0	S. C.	0
4-aminobenzoic acid	2.0–4.0	Oral	0
4,4'-azoxybenzoic acid [1]	.5–1.0	S. C.	0
4,4'-azoxybenzoic acid [1]	1.0	Oral	0
4,4'-azobenzoic acid [1]	.2	S. C.	0
4,4'-azobenzoic acid [1]	.5	Oral	0
4-nitrobenzaldehyde	.5	S. C. (oil)	[2] Moderate
4-nitrobenzaldehyde	1.0	Oral	[2] Moderate
4-nitrobenzal bromide	1.0	S. C. (oil)	[2] Moderate
4-nitrobenzal bromide	.5–1.0	Oral	[2] Moderate
4-nitrobenzyl chloride	.5	S. C. (oil)	[2] Slight
4-nitrobenzyl chloride	.5–1.0	Oral	[2] Slight
4-nitrotoluene	1.0	Oral	[2] Moderate
4-nitroaniline	1.0	Oral	0
4-nitrodiphenylamine	.5–1.0	S. C. (oil)	0
4-nitroacetanilide	.5	S. C. (oil)	0
4-nitrophenylglycine	.5	S. C.	0
1-nitro-3-methoxyphenol	.5	S. C.	0
1-nitro-4-methoxyphenol (4-nitroanisol)	2.0	S. C. (oil)	0
1,4-dinitrobenzene	.05	Oral	0
4-nitrodiphenyl	2.0	S. C. (oil)	0
4,4'-dinitrodiphenyl	2.0	S. C. (oil)	0
4,4'-dinitroaminoazobenzene	1.0	S. C., oral	0
4,4'-dinitrodiphenyl ether	1.0	S. C. (oil)	0
4-nitrosophenol sodium	0.125	S. C.	0
4-nitrosodimethylaniline	.025	S. C. (oil)	0
4-nitrosodiphenylamine	.05	S. C. (oil)	0
Diphenyl nitrosoamine	.5	S. C. (oil)	0
Diphenyl nitrosoamine	1.0	Oral	0

[1] Prepared by H. B.
[2] Prolongation of life, especially against pneumococcus.

4-Nitrobenzoic acid differed from compounds of the sulfur and arsenic series in that activity was less marked upon streptococcal than upon pneumococcal infections. With maximum doses some prolongation of life was observed but the effect was much weaker than that obtained with similar doses of sulfanilamide.

Experiments were also carried out upon a series of compounds related to 4-nitrobenzoic acid. Substitution of the COOH group by CHO, CH_3 or $CHBr_2$ did not greatly affect the activity; 4-nitrobenzyl chloride (CH_2Cl) was less active (tables 6 and 7).

Substitution of COOH by $CONH_2$ (4-nitrobenzamide) decreased activity to a trace; substitution by $CONH.NH_2$ (4-nitrobenzhydrazide) abolished activity, but only small doses could be given because of toxicity. Replacement of the COOH group by NO_2 (1-4-dinitroben-

TABLE 7.—*The action of 4-nitrobenzoic acid and related compounds upon pneumococcal infections in mice*

Compound	Dosage (gm. per kilo)	Number of mice	Deaths in days										Mortality (percent)	Organism
			1	2	3	4	5	6	7	8	9	10		
4-nitrobenzoic acid	0.5 x 2 days oral 0.25 x 2 days oral	15	1	1	2	10	----	----	----	----	----	----	93	Pneumococcus Mulf. I, 10^{-5}
Do	0.5 x 1 day S. C 0.25 x 3 days S. C	15	----	5	3	6	1	----	----	----	----	----	100	
Sulfanilamide	0.5 x 2 days oral 0.25 x 1 day oral	15	1	11	3	----	----	----	----	----	----	----	100	
Controls		15	5	10	----	----	----	----	----	----	----	----	100	
4-nitrobenzoic acid	0.5 x 2 days oral 0.3 x 2 days oral	15	----	3	3	7	2	----	----	----	----	----	100	Pneumococcus Mulf. I, 10^{-6}
Do	0.5 x 1 day S. C 0.3 x 3 days S. C	15	6	5	2	----	2	----	----	----	----	----	100	
Sulfanilamide	0.5 x 2 days oral 0.3 x 2 days oral	15	4	9	1	1	----	----	----	----	----	----	100	
Controls		15	8	7	----	----	----	----	----	----	----	----	100	
4-nitrobenzoic acid	0.5 x 3 days S. C	20	8	2	10	----	----	----	----	----	----	----	100	Pneumococcus Lederle I, 10^{-6}
Sulfanilamide	0.5 x 3 days S. C	20	----	4	9	3	3	----	----	----	----	----	100	
Controls		20	18	2	----	----	----	----	----	----	----	----	100	
4-nitrobenzoic acid	0.75 x 1 day oral 0.5 x 2 days oral	12	----	5	7	----	----	----	----	----	----	----	100	Pneumococcus Lederle I, 10^{-6}
4-nitrobenzaldehyde	0.5 x 2 days oral	15	----	5	9	1	----	----	----	----	----	----	100	
Controls		15	8	7	----	----	----	----	----	----	----	----	100	
4-nitrobenzal bromide	0.5 x 2 days oral	15	2	4	7	2	----	----	----	----	----	----	100	Pneumococcus Lederle I, 10^{-6}
4-nitrobenzyl chloride	0.25 x 2 days oral	15	6	7	2	----	----	----	----	----	----	----	100	
Controls		15	15	----	----	----	----	----	----	----	----	----	----	
4-nitrobenzoic acid	0.3 x 3 days oral	15	----	5	9	1	----	----	----	----	----	----	100	Pneumococcus Lederle I, 10^{-6}
4-nitrobenzyl chloride	0.3 x 3 days oral	15	2	12	1	----	----	----	----	----	----	----	100	
Controls		15	12	3	----	----	----	----	----	----	----	----	100	
4-nitrotoluene	0.5 x 2 days oral 0.25 x 1 day oral	15	5	6	2	2	----	----	----	----	----	----	100	Pneumococcus Lederle I, 10^{-6}
Do	0.25 x 1 day S. C	15	5	9	1	----	----	----	----	----	----	----	100	
4-nitrobenzoic acid	0.25 x 1 day oral	10	1	7	1	----	1	----	----	----	----	----	100	
Controls		15	12	3	----	----	----	----	----	----	----	----	100	

zene), NH_2 (4-nitroaniline), $NH.CH_2COOH$ (4-nitrophenylglycine), $NH.C_6H_5$ (4-nitrodiphenylamine), $NH.COCH_3$ (4-nitroacetanilide), $O.CH_3$ (4-nitroanisol), C_6H_5 (4-nitrodiphenyl), or AsO_3H_2 (4-nitrophenylarsonic acid) abolished activity in tolerated doses. The inactivity of the benzophenones and benzhydrols has already been referred to (table 6).

Reduction of the nitro group of 4-nitrobenzoic acid abolished activity. Various stages of reduction were represented by 4-nitroso-, azoxy-, azo-, hydroxylamino-, and aminobenzoic acid, all of which were inactive.

Mayer and Oechslin (*10, 23*) have investigated the various products of oxidation of the amino group of sulfanilamide. Their series included the corresponding 4-nitro-, 4-nitroso-, azoxy-, azo-, 4-hydroxylamino-, and 4-aminobenzenesulfonamide. They report activity for all members of the series except the azo compound; 4-nitrobenzenesulfonamide was more active but also more toxic than the amino derivative (sulfanilamide). The benzoic acid derivatives differ, therefore, from the sulfonamide series in that activity has been observed only for the nitro compound.

Changes of the position in the benzene ring to ortho- and meta-nitrobenzoic acid destroyed activity. 1-3-5-Trinitrobenzoate was also inactive.

Other related compounds, all inactive, were 1-nitro-3-methoxyphenol, 4-nitrosophenol sodium, 4,4′-dinitroaminoazobenzene, 4-nitrosodiphenylamine, diphenylnitrosoamine, 4-nitrosodimethylaniline, 4,4′-dinitrodiphenyl, 4,4′-dinitrodiphenyl ether (table 6).

DISCUSSION

The interest in the compounds reported in this paper lies in the relationship of their structure to their antibacterial action. Chemotherapeutic activity of two different types of compounds containing no sulfur also affords new possibilities of chemical approach to the problem. Some of the arsenic compounds with a structure corresponding to the highly active diphenyl sulfur compounds were found to possess a high degree of activity, thus giving evidence that sulfur is not essential to therapeutic action. However, of the active arsenic compounds so far obtained, the toxicity has been such that the effective dose closely approaches the toxic dose.

Acetylation of the 4-nitro-4′-aminodiphenylarsinic acid did not diminish therapeutic activity, although it did decrease toxicity. This was also true for the corresponding arsine, as well as the asymmetric 4-nitro-4′-aminodiphenylsulfone. This is evidence that a nitro group in certain structural arrangements may be more important than a free amino group. Other evidence to this effect was shown in that 4-nitro-4′-aminodiphenylarsinic acid (Ba 30) was active while the correspond-

ing diamino compound (Ba 25) was inactive. Likewise, some antibacterial activity was found for p-nitrobenzoic acid and related compounds, while the corresponding p-amino derivative, although of lower toxicity, was devoid of activity. Buttle and co-workers (*15*) reported a trace of antistreptococcal action for 4,4′-dinitrodiphenylmethane, while the amino compound was inactive. In our experiments no appreciable activity was observed with the former compound.

The difficulties, however, must be pointed out in separating the activity of a certain radical from that of the rest of the molecule. As examples may be cited the facts that the diaminodiphenylarsinic compounds are inactive while the corresponding sulfur compounds are active; 4-aminobenzoic acid is inactive while 4-aminophenylsulfonamide is active; 4-nitrophenylsulfonamide is more active than the amino compound but 4,4′-dinitrodiphenylsulfone is less active than 4,4′-diaminodiphenylsulfone.

Mayer (*10*) found p-nitrobenzenesulfonamide five times as active as the amino compound (sulfanilamide), while p-hydroxylaminobenzene sulfonamide was highly bactericidal *in vitro* but only slightly active in the body. Mayer suggested (*23*) that the hydroxylamino compound is the active derivative formed from sulfanilamide in the body; he explained its slight action *in vivo* on a basis of its rapid oxidation at the site of injection.

In our experiments any reduction of the nitro group of 4-nitrobenzoic acid abolished activity. While the greater toxicity of the nitroso compound might have reduced the tolerated dose to where no effect was obtained, this would not account for the inactivity of the hydroxylamino, the amino, the azoxy, and the azo derivatives. The importance of the carbonyl (CO) group in the para position is also seen in that only those compounds containing this or a closely related group were active.

SUMMARY

Two new types of chemical compounds have been found to possess antibacterial properties.

(a) The asymmetric 4-nitro-4′-aminodiphenylarsinic acid and corresponding arsyloxide and arsine were active against streptococcal infections in mice. Acetylation increased activity and lowered toxicity but the effective doses were close to the toxic doses. The symmetric 4,4′-diaminodiphenylarsinic acid and arsyloxide were inactive.

(b) 4-Nitrobenzoic acid, the aldehyde, 4-nitrobenzal bromide, 4-nitrobenzyl chloride and 4-nitrotoluene possessed some activity, particularly against pneumococcal infections in mice.

The various reduction products of 4-nitrobenzoic acid were inactive, as were likewise the symmetric and asymmetric benzophenones and benzhydrols, and a series of other nitro and nitroso compounds.

Some sulfur compounds were included for their comparative activity. It was found that acetylation of 4-nitro-4'-aminodiphenylsulfone decreased its toxicity without decreasing its antistreptococcal activity. This compound possesses a very high therapeutic index against streptococcal infections in mice.

The fact that antibacterial properties have been demonstrated for some asymmetric arsenic compounds containing a nitro group, and also for some simple aromatic nitro compounds, demonstrates the importance of the nitro group and also that sulfur is not essential to therapeutic activity.

Chemical Supplement

By HUGO BAUER

4,4'-Diaminodiphenylarsinic acid (Ba 25) was prepared according to L. Benda (*24*) and F. L. Pyman and W. C. Reynolds (*25*).

4,4',4'',4'''-Tetraaminotetraphenylarsyloxide (Ba 28) was prepared by reduction of 4,4'-diaminodiphenylarsinic acid in hydrochloric acid solution by means of sulfur dioxide, employing iodine as a catalyst. The tetrahydrochloride thus obtained yielded the free amino compound in fine needles upon treatment with ammonia. Melting range 85–90° C.

4-Nitro-4'acetylaminodiphenylarsinic acid (Ba 29).—This compound was formed by the action of diazo-p-nitroaniline upon p-acetylaminophenylarsinoxide in a dilute solution of acetic acid. The colorless needles melted at 258° C. Analysis: $C_{14}H_{13}O_5N_2As$. Calculated As 20.58 percent; found As 20.43 percent.

4-Nitro-4'-aminodiphenylarsinic acid (Ba 30).—The corresponding acetyl compound was deacetylated by heating with concentrated hydrochloric acid. Yellow needles. M. P. 239° C. Analysis: $C_{12}H_{11}O_4N_2As$. Calculated As 23.26 percent; found As 23.61 percent.

4,4''-Dinitro-4',4'''-diacetyldiaminotetraphenylarsyloxide (Ba 31).—4-Nitro-4'-acetylaminodiphenylarsinic acid was reduced with sulfur dioxide and a trace of iodine in a mixture of glacial acetic acid and hydrochloric acid. The compound was precipitated with water and crystallized from benzene. The pale yellow needles contained benzene of crystallization. Melting range 95–99° C. Analysis: $C_{28}H_{24}O_7N_4As_2+2C_6H_6$. Calculated As 17.97 percent; found As 18.28 percent.

4-Nitro-4'-acetylaminodiphenylarsylhydroxide (Ba 31b).—The corresponding arsyloxide (Ba 31) was dissolved in a solution of dilute sodium hydroxide and dilute acetic acid was added. The hydroxide crystallized in colorless needles which showed no sharp melting point, but softened at about 70° C. Analysis: $C_{14}H_{13}O_4N_2As$. Calculated As 21.53 percent; found As 20.89 percent.

4-Nitrophenylarsonic acid (Ba 33).—For preparation see H. Bart (*26*).

4,4''-Dinitro-4',4'''-diacetyldiaminotetraphenylarsyloxide+glutathione (Ba 34).—Equal parts of the components were dissolved in a small amount of alcohol along with a little water, and warmed to about 40° C. for 5 minutes. The mixture was evaporated in a vacuum desiccator.

4-Nitro-4'-acetylaminodiphenylarsylhydroxide+cysteine (Ba 42).—A mixture of the components containing an excess of cysteine was prepared as described for the glutathione preparation. The resulting product was not further investigated chemically.

4,4''-Dinitro-4',4'''-diacetyldiaminotetraphenyldiarsyl (Ba 46).—4-Nitro-4'-acetylaminodiphenylarsinic acid in an acetone solution was reduced with hypophosphorous acid containing a trace of potassium iodide. Yellow powder. Analysis: $C_{28}H_{24}O_8N_4As_2$. Calculated As 22.63 percent; found As 22.65 percent.

4,4''-Dinitro-4',4'''-diaminotetraphenyldiarsyl (Ba 49).—The reduction of 4-nitro-4'-aminodiphenylarsinic acid was made with hypophosphorous acid in the presence of potassium iodide. Orange powder. Analysis: $C_{24}H_{20}O_4N_4As_2$. Calculated As 25.92 percent; found 25.22 percent.

4-Nitro-4'-aminodiphenylsulfone (Ba 35).—The acetyl derivative (Ba 36) was deacetylated by heating with a mixture of equal parts of concentrated hydrochloric acid and alcohol for one-half hour. The hydrochloride thus obtained yielded the free base upon treatment with ammonia; it was recrystallized from alcohol. Yellow needles, M. P. 172° C. Analysis: $C_{12}H_{10}O_4N_2S$. Calculated S 11.53 percent; found S 11.67 percent. (See Buttle et al. (*15*).)

4-Nitro-4'-acetylaminodiphenylsulfone (Ba 36).—4-Nitro-4'-aminodiphenylsulfide (F. Kehrmann and E. Bauer (*27*)) was acetylated. Ten gm. of the acetyl compound were dissolved in 100 cc. of glacial acetic acid, 5 cc. of 30 percent hydrogen peroxide added, and the mixture boiled for one-half hour. Following the addition of water the solution was cooled. Nine gm. of yellowish crystals which separated out were recrystallized from alcohol. M. P. 223° C. Analysis: $C_{14}H_{12}O_5N_2S$. Calculated S 10.01 percent; found 10.13 percent.

4-Nitro-4'-acetylaminodiphenylsulfoxide (Ba 37).—Sixty gm. of 4-nitro-4'-acetylaminodiphenylsulfide were dissolved in 600 cc. of glacial acetic acid, 27 cc. of 30 percent hydrogen peroxide added, and the mixture heated at 100° C. for 3 hours. Upon addition of water crystals separated which were recrystallized from alcohol. Thirty-nine gm. of yellowish needles were obtained which melted at 212° C. Analysis: $C_{14}H_{12}O_4N_2S$. Calculated S 10.54 percent; found 10.53 percent.

4,4'-Dinitrobenzophenone (Ba 48).—For preparation see W. Staedel (*28*).

4,4'-Diaminobenzophenone (Ba 50).—For preparation see W. Staedel and E. Sauer (*29*).

4-Nitro-4'-aminobenzophenone (Ba 55).—This compound, not previously described, was prepared by partial reduction of 4, 4'-dinitrobenzophenone with alcoholic ammonium sulfide. Orange needles crystallized from alcohol. M. P. 179° C. Analysis: $C_{13}H_{10}O_3N_2$. Calculated N 11.57 percent; found 11.65 percent.

4, 4'-Diamino benzhydrol (Ba 51).—For preparation see H. Wichelhaus (*30*).

4-Hydroxylaminobenzoic acid (Ba 54).—4-Nitrobenzoic acid, in the form of its barium salt, was reduced with zinc dust in the presence of ammonium chloride, according to the method of E. Bamberger and F. L. Pyman (*31*). White needles were obtained with no melting point, but which showed decomposition beginning at about 170–175° C. This compound reduced Fehling's solution at room temperature.

Analysis: $C_7H_7O_3N$. Calculated N 9.15 percent; found 8.85 percent.

4-Nitrosobenzoic acid (Ba 53).—4-Hydroxylaminobenzoic acid was oxidized with ferric chloride; a yellow amorphous precipitate was formed. With diphenylamine sulfuric acid reagent a deep red color is produced. The compound has been described previously by F. I. Alway (*32*).

p-Azoxybenzoic acid (Ba 45).—*p-Azobenzoic acid* (Ba 44). For preparation see G. Bachrach and R. Weinstein (*33*).

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VARIETIES OF MEXICAN TYPHUS STRAINS

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In 1929 one of us (*1*) isolated two strains of typhus from patients during a short-lived epidemic occurring in a village near Mexico City. The strains failed to produce the characteristic scrotal swelling reaction with the regularity observed by Mooser (*2*) in his Mexican strains. One of the strains produced scrotal reaction in two guinea pigs out of 26 serial transfers, the other one showed no scrotal reaction in 25 generations; then by transfer into human lice by the Weigl method and inoculation of the ground lice into guinea pigs, the swelling of the scrotum was established with regularity for a few generations before discontinuing the strain. The isolation of nonorchitic strains in Mexico, before the report of Neil in 1917 and the studies of Mooser in 1928, seems to have been the rule, because the descriptions conform with those of Nicolle in his first communications. The discovery of Dyer, Rumreich, and Badger (*3*), in rat fleas, and by Mooser, Castaneda, and Zinsser (*4*), in the brains of rats of a rickettsial disease similar to the Wilmington and Mooser strains of typhus, was taken as a proof that the New World typhus has a murine origin. The nonorchitic strains isolated in Mexico were considered by Nicolle (*5*) as intermediates between the murine and the Old World typhus.

In 1934, Mooser, Varela, and Pils (*6*) obtained 5 nonorchitic strains from patients during a typical epidemic of typhus. In accordance with the opinion of Nicolle, these authors applied the name "epidemic" to their strains and also considered them as intermediates between murine and Old World typhus. They established a subdivision of the Mexican typhus, separating it into "endemic" and "epidemic" strains, corresponding to murine and Europeanlike strains, respectively.

During the past 2 years the typhus incidence in Mexico City has been low if we compare it with previous years. From the cases brought to the General Hospital we isolated several strains of typhus which we consider sufficiently interesting to describe in the present paper.

METHODS AND MATERIALS

Forty-six patients in whom a diagnosis of typhus fever was established by clinical and serological data, were bled from the 4th to the 13th day of the disease and 5 cc. of this blood was injected by intraperitoneal route into a rat in each case We used rats for the first animal transfer following the experience of Mooser, who obtained better results with these animals than by direct inoculation into guinea pigs. Most of the rats were killed from the fifteenth to the twentieth day after the injection; a few were killed later. The

brains were emulsified in saline and injected into male guinea pigs, which were observed daily in order to note the appearance of fever or the scrotal reactions. When the inoculated guinea pigs developed febrile reactions suggestive of the typhus infection, the animals were killed and the brain emulsions transferred to new guinea pigs, usually on the 5th day of the fever. The animals were castrated under ether anesthesia when scrotal swelling was found, and the tunica vaginalis was first smeared for microscopical examination and then washed with salt solution and the washings were injected intraperitoneally into new guinea pigs. Part of the guinea pig brain not used for inoculation was fixed and stained for the study of typhus lesions. The newly isolated strains were submitted to cross-immunity tests, the recovered animals being reinoculated with tunica washings from guinea pigs infected with our "L" orchitic strain.

All strains in which the diagnosis of typhus was established by the finding of rickettsiae in the tunica, typhus lesions in the brain, and by cross-immunity tests were discontinued. Some other strains were lost after one or two transfers in guinea pigs, the last of which did not present fever or swelling but showed immunity when reinoculated with the orchitic "L" strain. The results were considered negative when no fever or swelling was observed in the guinea pigs injected with rat brain and the animals developed typhus fever when reinoculated with the "L" strain. The investigation of the survival of the strain in mice through successive transfers was made in a manner similar to that followed by Savoor and Velasco (7). Tunica or brain emulsions from guinea pigs infected with the strain to be tested were injected in amounts of 2 cc. into three mice by intraperitoneal route and transfers were made at 10-day intervals from mice to mice and into one guinea pig.

In staining the smears of the tunica vaginalis and preparing brain sections for the search for typhus lesions we followed the methods described in our previous publications.

ISOLATION OF TYPHUS STRAINS FROM PATIENTS

From October 1936 to January 1938, 69 patients suffering from typhus fever were admitted to the General Hospital of Mexico City. No attempts were made to isolate typhus strains from cases arriving after the thirteenth day of the disease.

In table 1 is indicated the monthly distribution of typhus patients admitted to the service, the number of cases suitable for rat inoculation, the strains of typhus isolated after transfer to guinea pigs, and those which were lost by premature death of the rats from intercurrent infections or because the guinea pigs did not react to the rat brain inoculation. Forty-six of these cases were bled for rat inocula-

tion, from which 20 typhus strains were recovered and many of these were established in guinea pigs for several generations. Disregarding the 8 cases lost by premature death of the rats, the table shows that from 38 cases of typhus, in more than 50 percent the disease was successfully transferred to laboratory animals by the rat to guinea pig method.

TABLE 1.—*Strains isolated from typhus patients*

Month	Typhus cases admitted to the hospital	Cases transferred into rats	Rats lost before ready for transfer into guinea pigs	Guinea pigs which were negative to inoculation	Number of typhus strains obtained in guinea pigs
1936					
October	4	2	0	1	1
November	1	1	0	0	1
December	1	1	0	0	1
1937					
January	3	2	0	1	1
February	6	3	0	2	1
March	4	3	1	1	1
April	1	1	0	0	1
May	3	2	0	2	0
June	2	1	1	0	0
July	6	3	1	2	0
August	9	8	0	3	5
September	9	4	0	2	2
October	5	3	1	1	1
November	5	4	3	1	0
December	3	3	1	1	1
1938					
January	7	5	0	1	4
Total	69	46	8	18	20

PROPERTIES OF 20 MEXICAN TYPHUS STRAINS

The data concerning the typhus strains from 20 patients is summarized in table 2. It was apparent that the severity of the disease had no influence on its transmission to laboratory animals. Most of the strains were obtained before the tenth day of the disease, and in two cases 1 or 2 days later. No attempts were made after the thirteenth day. The transfer of the infection from rats to guinea pigs was characterized by the appearance of fever, and with strain "L" and in cases 13, 28, and 42 a more or less pronounced swelling of the scrotum was also apparent, which only in strain "L" remained a constant feature of the infection. However, in strain No. 42 the scrotal reaction reappeared in some of the subsequent transfers. Of the remaining strains, nonorchitic in the first transfer, No. 5 became orchitic and the swelling was transmitted for several generations by using tunica washings or brain emulsions for the inoculations. Several strains were lost accidentally or by inapparent typhus infections; others were carried for a sufficient number of transfers to be classified according to their clinical features.

Considering the scrotal swelling as a constant sign of the murine type of typhus we may say that from our 20 strains 2 were murinelike,

because the local reaction was transmitted in from 11 to 112 generations. One of these strains was discontinued in order to save animals, but the other one is still going on and has been successfully used in the elaboration of typhus vaccine and typhus antiserum. Eight strains were lost by inapparent typhus infection after one to six transfers. Of these Nos. 3, 7, and 28 showed one or two scrotal reactions, but the majority of the inoculated animals showed no swelling. The remaining 10 strains were characterized by the Europeanlike course of the infection. However, the scrotal reaction was not infrequent and in many cases lasted as long as in murine strains, which may be accounted for by the considerable doses of inoculum injected, reaching at times one half of a brain into one single guinea pig. In these Europeanlike strains the microscopic examination of the tunica when the scrotal swelling appeared very rarely showed rickettsia bodies.

Strains No. 42, 44, and 45 were transferred from 11 to more than 25 generations, many of the animals showing the scrotal reaction; but this was not easily transferred from tunica material, and with the exception of No. 42, in which three successive swellings were observed, this sign was never produced consecutively. Furthermore, in one instance, X-rayed rats were inoculated with strain 42 and rickettsiae were found in the tunica of such animals, but the inoculation into guinea pigs of the rat tunica washings failed to produce the scrotal swelling.

TABLE 2.—*Varieties of Mexican typhus strains*

Serial number of strain	Date of admission of the patient	Course of the disease	Day of rat inoculation	Transfers into guinea pigs	Guinea pigs inoculated	Guinea pigs with scrotal reaction and fever	Guinea pigs with fever only	Type of the strain	Observations
2	Oct. 27, 1936	Grave	8th	112	250	250	0	Murine	"L" strain used for the preparation of vaccine.
3	Nov. 13, 1936	Fatal	8th	3	4	3	1	Intermediate	Slight unilateral scrotal reaction. Discontinued.
4	Dec. 6, 1936	do	11th	5	6	1	4	European	Last transfer was inapparent.
5	Jan. 2, 1937	do	10th	13	13	11	2	Murine	Discontinued.
7	Feb. 8, 1937	Mild	10th	6	6	2	3	Intermediate	Last transfer was inapparent.
11	Mar. 28, 1937	do	10th	6	6	0	5	European	Do.
13	June 28, 1937	do	8th	3	3	1	1	(?)	Do.
22	Aug. 18, 1937	Grave	10th	7	7	1	6	European	Lost accidentally.[1]
24	Aug. 25, 1937	do	11th	6	6	0	6	do	Do.[1]
25	Aug. 31, 1937	Mild [2]	9th	7	7	0	7	do	Do.[1]
26	do	do.[2]	4th	8	8	0	8	do	Lost by intercurrent infection.
27	do	do.[2]	9th	11	11	1	10	do	Do.
28	Sept. 5, 1937	do	7th	5	5	1	4	(?)	Lost accidentally.[1]
31	Sept. 28, 1937	do	7th	2	2	0	1	(?)	Last transfer was inapparent.
32	Oct. 9, 1937	Fatal	8th	1	1	0	0	(?)	Inapparent infection proved by immunity test.
39	Dec. 3, 1937	Mild	8th	1	1	0	0	(?)	Do.
42	Jan. 11, 1938	do	12th	27	53	10	43	European	Nonorchitic strain No. 42.
44	Jan. 20, 1938	do	9th	17	18	4	14	do	Discontinued.
45	Jan. 21, 1938	do	9th	11	12	2	10	do	Do.
46	Jan. 24, 1938	Fatal	9th	2	2	0	1	(?)	Last transfer was inapparent.

[1] An accident occurred in the animal room which resulted in the loss of several guniea pigs, including those inoculated with strains 22, 24, 25, and 28.

[2] These patients were members of the same family.

BRAIN LESIONS

A search for brain lesions in guinea pigs infected with both orchitic and nonorchitic strains showed that the orchitic strain "L" had little tendency to produce typhus lesions in the brain as compared with nonorchitic strains. The animals were killed on the seventh, eleventh, and sixteenth days, and the lesions were usually found on the eleventh day. Eight nonorchitic strains studied showed brain lesions when the animals were killed on the eleventh to the sixteenth day. The lesions were particularly numerous in strain 42, which we have kept as representative of the Mexican nonorchitic strains.

A systematic study of the brain lesions is now being conducted in a manner similar to that followed by Lillie, Dyer, and Armstrong (*8*).

TRANSFER OF MEXICAN NONORCHITIC STRAINS THROUGH MICE

Since Nicolle and Laigret (*9*) and Laigret and Jadin (*10*) found that Old World typhus was lost by successive transfers in rats and mice, while murine strains were easily kept in these animal species, we found it interesting to test our nonorchitic strains in mice. Strains No. 27, 42, 44, and 45 were inoculated into mice and transferred from mice to mice for three or four generations. The guinea pigs that were injected in order to detect the presence of typhus infection showed that these strains were lost from the second to the third transfer from mice to mice. These experiments show that there is an additional similarity between our nonorchitic strains and the Old World typhus.

VACCINATION EXPERIMENTS AGAINST MEXICAN ORCHITIC AND NONORCHITIC STRAINS

One of our orchitic strains has been used for the preparation of vaccines by methods recommended by Zinsser and Castaneda (*11*). The vaccines contained about 5,000 million rickettsiae per cubic centimeter and have been tested in guinea pigs subsequently inoculated with the homologous strain. This vaccine has been used in this laboratory in 14 workers who have been in close contact with typhus strains. Of these workers one developed a short febrile reaction 1 month after vaccination which, because of the characteristic serologic reaction (*12*), we suspect was an accidental typhus infection.

Recently, a careful study of the vaccine was made in our laboratories by Veintemillas (*13*), who demonstrated that the Mexican vaccine was capable of protecting guinea pigs with a single dose of 1 cc. of formalinized rickettsiae given subcutaneously. Partial protection was obtained by injection of ½, ¼, and even ⅛ cc. The vaccinated animals were tested with the "L" strain used for the preparation of the vaccine. In the same series of experiments Vientemillas observed that guinea

pigs vaccinated with one single dose of vaccine and tested with the nonorchitic strain No. 42 developed typical Europeanlike typhus, exactly as did the nonvaccinated controls. This failure to protect

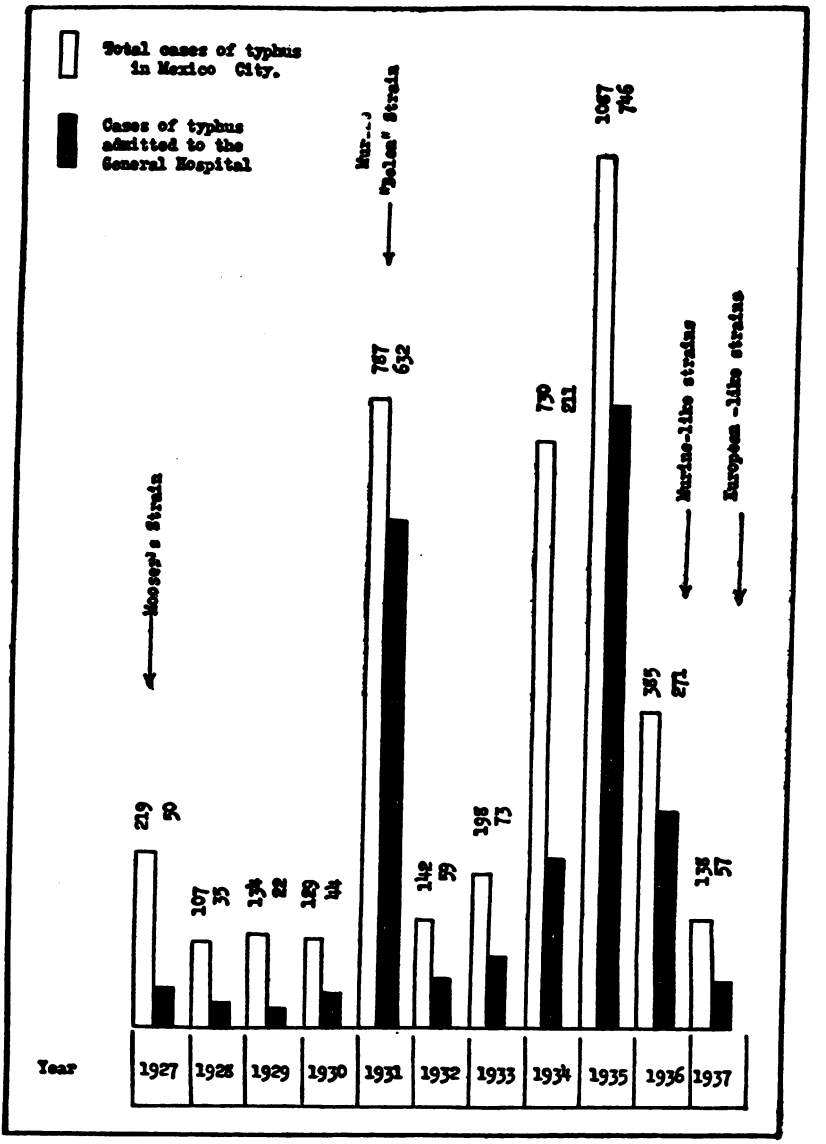

FIGURE 1.

guinea pigs with Mexican vaccine against Mexican nonorchitic strains with doses which were effective against the homologous "L" murine-like typhus shows another property which belongs to the European strains. However, the treatment of guinea pigs with three or four doses of vaccine at 5-day intervals afforded complete protection against strain No. 42.

DISCUSSION

The incidence of typhus fever in the city of Mexico during the 16 months of observation to which we have referred in this paper, was lower than in comparative periods of time in previous years. The number of cases admitted to the General Hospital at an average of 4.5 per month, with a maximum of 9 and a minimum of 1, gives a fair idea of the total monthly incidence in this city. Figure 1 shows the incidence of typhus registered from 1927 to 1937 in Mexico City and suburbs, and in black columns are recorded those admitted to the Hospital. Whether the cases registered from October 1936 to January 1938 may be considered endemic or as a long standing epidemic of low case rate, we are not in a position to discuss, but it is evident that the typical outburst of an epidemic of typhus did not occur within this period of time. The isolation of various strains of typhus which presented great differences from one another corroborates the hypothesis that typhus fever in Mexico is constantly starting from a murine origin and then, by the influence of man-to-man adaptation, undergoes transformation towards the European type. Many strains may revert to the original murine type, but others retain the newly acquired characteristics. This theory, which has been repeatedly sustained by Zinsser, Mooser, Nicolle, and ourselves, is illustrated in table 3. Some of the known strains of typhus are indicated with their relative positions between the murine and European types.

TABLE 3

Strain	Neil-Mooser reaction	Type of the strain
Breinl strain	Incidental	Typical European typhus.
Tunisian typhus	do	European.
"Boston" (Zinsser and Castaneda, 1933).	Not observed	Do.
Strains No. 42, 44, and 45	Frequent	Do.
"Zinacatepec" (Mooser, Varela, and Pils, 1934).	Reverted to orchitic typhus [1]	Intermediates.
"J" strain (Castaneda, 1930)	do.[2]	Do.
No. 7	Spontaneously reverted	Do.
"L" strain	Constant	Murine.
American sporadic strains (Maxcy, 1929).	do	Do.
Mooser strain (1928)	do	Do.
Dyer's flea strains (1931)	do	Do.
"Belen" strains (Mooser, Castaneda, and Zinsser, 1931).	do	Typical murine typhus.

[1] The infected animals were inoculated daily in the peritoneum with guinea pig blood.
[2] The strain was transferred through human lice and then recovered in guinea pigs.

One of the most important differences between European and Mexican typhus was that found by Zinsser and Castaneda (*14*) in their cross-immunization experiments. The observation in our laboratory, by Veintemillas (*13*), of similar differences in the protective power of the vaccine against orchitic and nonorchitic Mexican strains is a valuable contribution, because it suggests that the immunological differences are only quantitative. We believe, so far, that it is

premature to consider that the Mexican vaccine is insufficient to protect against the European typhus, as such opinions are based mainly on the relatively short experimental data of Zinsser and Castaneda (*14*). Certain other work in this line cannot be given serious consideration, owing to the low antigenic value of the vaccines with which it was made. The necessity of using rich vaccines is emphasized by the fact, already mentioned, that the vaccine protects better against Mexican orchitic than against Mexican nonorchitic strains, unless we assume that No. 42 is an imported strain.

In regard to the subdivision of Mexican typhus into "endemic" and "epidemic" based on the clinical aspects of the guinea-pig infection, we believe that such designations are not correct. Typical murine-like strains have been found during epidemic periods, and on the other hand our Europeanlike strains were isolated during a non-epidemic period.

SUMMARY

From October 1936 to January 1938, 69 cases of typhus were admitted to the General Hospital of Mexico City. Of these cases, 46 were bled for inoculation into rats and then guinea pigs were inoculated with the brains of those rats which survived 15 to 30 days after injection. Eight rats died from intercurrent infection before they were ready for transfer, but the 38 remaining animals produced in guinea pigs 20 typhus strains. Two of these strains showed the characteristics of the murine typhus; 8 were lost by inapparent infection, but some showed the scrotal reaction after one or more transfers into guinea pigs; and the remaining 10 strains were nonorchitic, showed numerous brain lesions, could not be kept in mice for more than two transfers and had some minor immunological differences from the orchitic strains. These properties correspond to the European type of typhus, but it is our opinion that such strains were not imported.

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ORNITHODOROS PARKERI: DISTRIBUTION AND HOST DATA; SPONTANEOUS INFECTION WITH RELAPSING FEVER SPIROCHETES[1]

By GORDON E. DAVIS, *Bacteriologist, Rocky Mountain Laboratory, United States Public Health Service*

During the past 5 years, the argasid tick, *Ornithodoros parkeri*, described by Cooley (*1*) in 1936, has been collected in Wyoming, Montana, Utah, Washington, and Colorado. Specimens from three collection areas have been found spontaneously infected with relapsing fever spirochetes. It is the only known likely tick vector of this disease in the first four of these States and in the part of Colorado from which it has been collected, but it has not thus far been positively identified with human infection.

DISTRIBUTION AND HOST DATA

All known distribution and host data of this tick are given in table 1. The determinations were made by Entomologist R. A. Cooley of the Rocky Mountain Laboratory.

These data, for the most part, represent chance observations incident to field work on other problems, a fact which suggests that this tick may be much more generally distributed in the regions indicated.

Since rodent burrows appear to be the usual habitat of this tick, and since it engorges rapidly like most other species of its genus, the finding of even a few specimens on rodents may be indicative of a considerable burrow infestation locally. This has proved true wherever the finding of *parkeri* infested rodents has been followed up by an extensive examination of rodent burrows, as in the Poison Spider Creek collection area in Natrona County, Wyo., and in the area 10 miles northeast of Dillon in Beaverhead County, Mont.

[1] Contribution from the Division of Infectious Diseases, National Institute of Health, Rocky Mountain Laboratory, Hamilton, Mont.

TABLE 1.—*Host, source, and locality data of collections of* Ornithodoros parkeri

Accession No.	State	Locality	Date	Host animal or source	Ticks collected
10711	Wyoming	Poison Spider Creek 40 miles southwest of Casper, Natrona County.[1]	June 7-23, 1934	*Citellus* sp.	1 nymph.
10716				do	Do.
10718				*Lepus* sp.	Do.
10719				*Cynomys* sp.	3 nymphs.
10722				*Citellus* sp.	1 nymph.
11254	do	do.[2]	July 27-29, 1935	Burrow of *Citellus* sp.	44 nymphs and adults.
11259				do	16 larvae, nymphs, and adults.
11260				Burrow and nest of *Citellus* sp.	44 nymphs and adults.
11284	do	30 miles north of Rock Springs, Sweetwater County.[2]	Aug. 5, 1936	*Citellus* sp.	1 nymph.
13756	do	18 miles north of Rock Springs, Sweetwater County.[2]	Aug. 6, 1937	Burrow of *Citellus* sp.	13 nymphs, 1 adult.
13757				do	3 nymphs.
13759				do	4 nymphs.
14840	do	North of Rawlins, Carbon County.[1]	July 13, 1938	*Citellus* sp.	1 larva, 1 nymph.
14112			July 14, 1938	Burrow of *Citellus* sp.	16 nymphs, 2 adults.
14113			do	From sand under sage brush near burrow of 14112.	2 nymphs.
14139	do	16 miles north of Rock Springs, Sweetwater County.[1]	July 23, 1938	Burrow of *Citellus* sp.	7 adults.
14140				do	1 nymph.
14141				do	3 adults.
14142				do	1 nymph.
14143				do	1 adult.
13791	do	11 miles south of Rock Springs, Sweetwater County.[1]	do	*Mustela* sp.	11 larvae.
13816				Burrow of *Citellus* sp.	1 nymph.
13812				do	2 nymphs.
13813				do	9 nymphs, 1 adult.
15230	do	Sweetwater County.[1]	Aug. 24, 1938	2 *Cynomys leucurus*	1 nymph.
12302A	Utah	Wayne County.[1]	Aug. 12, 1936	*Citellus* sp.	6 larvae.
12260A		Washington County.[1]	Aug. 11-13, 1936	do	1 larva, 2 nymphs.
15407	do	Uintah County.[1]	Aug. 3, 1938	8 *Cynomys leucurus*	1 nymph.
10143	Washington	Near Yakima,[4] Yakima County	June 22, 1934	*Sylvilagus* sp.	Do.
15341	Colorado	Moffat County.[1]	June 16, 1938	5 *Cynomys leucurus*	Do.
12601	Montana	10 miles northeast of Dillon, Beaverhead County.[3]	June 19, 1936	*Citellus richardsoni*	6 specimens.
12602			do	do	7 specimens.
12603			do	5 *Citellus richardsoni*	14 specimens.
———				Burrow of *C. richardsoni*	3 specimens.
———			June 22, 1936	Burrow and nest of *C. richardsoni*	38 specimens.
———			Aug. 1, 1936	Nest of *C. richardsoni*	11 specimens.
———			Sept. 8, 1936	do	44 specimens.
12793			Oct. 31, 1936	Burrow and nest of *C. richardsoni*	6 specimens.
12794			do	do	2 specimens.
12795			do	do	46 specimens.
12630			July 7, 1936	14 *C. richardsoni*	2 specimens.

12613	do	10 miles south of Cameron, Madison County [2]	June 25, 1936	*C. richardsoni*	1 nymph, 1 adult.
12611	do	15 miles south of Cameron, Madison County [2]	do	*Citellus* sp	3 larvae, 4 adults.
13223	do	10 miles south of Dillon, Beaverhead County [3]	May 28, 1937	*Peromyscus* sp	1 larva.

[1] Collected by Bacteriologist Gordon E. Davis, Rocky Mountain Laboratory.
[2] Collected by Laboratory Assistant E. W. Malone, Rocky Mountain Laboratory.
[3] Collected by Assistant Parasitologist W. L. Jellison, Rocky Mountain Laboratory.
[4] Collected by Medical Entomologist Cornelius B. Philip, Rocky Mountain Laboratory.
[5] Collected by field crew operating under Surgeon C. R. Eskey, in charge of the Plague Laboratory, San Francisco, Calif.

Less extensive follow-ups have also resulted in locating tick-infested burrows. For example, a return trip of 150 miles was made to an area where a ground squirrel infested with an engorged larva and an early nymph had been shot. Twenty ticks were collected. Two were found in the sand under a sagebrush not far from a burrow, 16 immature forms were in the burrow near its opening, and a ♀ and ♂ were found at the end of a 16-foot excavation of the burrow through sun-baked prairie clay. In another instance a number of rodents had been taken during a 75-mile across-country drive. Late in the day they were examined for parasites. A weasel yielded 11 partially engorged larvae. On a return trip to the location where the weasel was shot, 13 late nymphs and adults were recovered from 3 ground-squirrel burrows.

Experience suggests that the simplest way of determining the local presence or absence of this tick in a given locality is by the examination (screening may be necessary) of earth pulled out of animal burrows by means of a scraper attached to the end of a rod several feet long.

As shown in table 1, this species has been found feeding on ground squirrels, a jack rabbit, a cottontail rabbit, prairie dogs, a weasel, and a white-footed mouse. This suggests that it is by no means highly selective in its choice of hosts.

In the laboratory it feeds readily on white mice, white rats, guinea pigs, monkeys, and man. The following four feeding experiments on man are recorded.

FEEDING OF *O. PARKERI* ON HUMAN VOLUNTEER

On July 8, 1938, male No. 65 was allowed to engorge on the forearm of a human volunteer. It attached readily, engorged completely, and at end of 14 minutes detached voluntarily. No sensation was felt by the volunteer. The following morning there was a red area 4 mm. in diameter at the site of attachment. There was no itching.

On July 11, 1938, male No. 32 was allowed to engorge on the forearm of the volunteer. It attached readily, engorged completely, and at end of 12 minutes detached voluntarily. No sensation nor itching was felt. A deep red area about 3 mm. in diameter occurred in 1 hour, which enlarged to 5 mm. in 6 hours.

Male No. 31 was allowed to engorge on the forearm. It attached readily, engorged completely, and at end of 15 minutes detached voluntarily. There was no sensation. In 6 hours, a deep red area 3 mm. in diameter appeared.

On July 15 all of the above areas were still red and indurated, considerably elevated, and crateriform with necrotic centers. There was some itching. Healing was gradual.

On Sept. 12, 1938, a second stage nymph, No. 39, was placed on the back of the hand where it attached at once. It engorged com-

pletely in 23 minutes and detached voluntarily. There was no sensation. A hemorrhagic area 2 mm. in diameter was present.

On Sept. 13 there was intense itching during night. On Sept. 23 a small scab was removed.

SPONTANEOUS INFECTIONS WITH SPIROCHETES

Six strains of spirochetes have been recovered from ticks representing three of the collection areas, four from the northern part and one from the southern part of Sweetwater County, Wyo., and one from Beaverhead County, Mont. The ticks from Natrona County, Wyo., the one specimen from Washington, and those from Utah and Colorado were received in alcohol and could not be tested.

These strains are easily maintained in white mice and white rats. In the latter, one strain was carried through 180 transfers. In guinea pigs they produce clinical relapses at which times spirochetes are present in the peripheral blood. Thus far they have not produced febrile periods in rhesus monkeys.

POSSIBLE RELATIONSHIP OF *O. PARKERI* SPIROCHETES TO HUMAN INFECTION

Of the several States in which *O. parkeri* occurs, no case of relapsing fever has been reported from Wyoming and none from the part of Colorado in which *parkeri* was collected. A case occurring near Salt Lake City, Utah, in July 1928, was attended by Dr. H. G. MacNeil, then of that city. Tollefsen (*3*) has reported two cases treated at the Veterans' Facility Administration, Walla Walla, Wash. No satisfactory data have been obtained concerning their points of origin. One apparently was infected at some point in Montana in the early summer of 1927, the other somewhere in Washington in the early fall of 1932.

Since *O. parkeri* is the only known likely transmitting agent of relapsing fever in these two States and since it has been shown that this tick is spontaneously infected with spirochetes which produce a relapsing fever in guinea pigs, it is at least open to suspicion as a transmitting agent to man.

REFERENCES

(*1*) Cooley, R. A.: *Ornithodoros parkeri*, a new species on rodents. Pub. Health Rep., **51**: 431–433 (1936).
(*2*) Parker, R. R., Philip, Cornelius B., Davis, Gordon E., and Cooley, R. A.: J. Econ. Ent., **30**: 51 (1937).
(*3*) Tollefsen, A. D.: Relapsing fever. Med. Bul. Vet. Admin., **12**: 84–85 (July 1935).
(*4*) Annual reports of the Surgeon General, U. S. Public Health Service, for 1936, 1937, and 1938.

162189°—39——4

DEATHS DURING WEEK ENDED JULY 1, 1939

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

	Week ended July 1, 1939	Corresponding week, 1938
Data from 88 large cities of the United States:		
Total deaths	7,369	7,580
Average for 3 prior years	[1] 7,515	
Total deaths, first 26 weeks of year	229,356	221,808
Deaths under 1 year of age	519	519
Average for 3 prior years	[1] 512	
Deaths under 1 year of age, first 26 weeks of year	13,571	13,811
Data from industrial insurance companies:		
Policies in force	67,166,768	69,248,240
Number of death claims	11,326	11,389
Death claims per 1,000 policies in force, annual rate	8.8	8.6
Death claims per 1,000 policies, first 26 weeks of year, annual rate	11.1	9.7

[1] 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 July 8, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median

Division and State	Diphtheria				Influenza				Measles			
	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median
NEW ENG.												
Maine	0	0	0	0	.....	.....	1	.....	91	15	13	21
New Hampshire	0	0	0	0	.....	.....	.....	.....	91	9	31	31
Vermont	0	0	0	0	.....	.....	.....	.....	1,448	108	30	30
Massachusetts	6	5	0	5	.....	.....	.....	.....	425	361	232	232
Rhode Island	0	0	1	0	.....	.....	.....	.....	420	55	3	20
Connecticut	0	0	1	2	3	1	2	1	448	151	20	78
MID. ATL.												
New York	4	10	21	28	[1]1	[1]1	[1]1	[1]1	295	738	1,299	1,299
New Jersey [2]	7	6	8	10	.....	.....	7	2	26	22	207	442
Pennsylvania	4	7	28	30	.....	.....	.....	.....	43	85	630	630
E. NO. CEN.												
Ohio	8	11	8	11	4	5	.....	2	10	13	246	387
Indiana	9	6	4	7	6	4	.....	7	6	4	131	67
Illinois [2]	14	21	25	35	2	3	4	5	14	21	177	326
Michigan [3]	1	1	6	7	.....	.....	.....	.....	99	94	714	260
Wisconsin	0	0	2	2	14	8	10	10	380	216	855	821
W. NO. CEN.												
Minnesota	4	2	1	1	2	1	.....	.....	60	31	135	40
Iowa [2]	8	4	0	2	.....	.....	.....	.....	205	101	122	13
Missouri	4	3	14	14	.....	.....	6	11	5	·	36	36
North Dakota	0	0	1	1	58	8	1	.....	110	15	41	1
South Dakota	8	1	1	2	.....	.....	.....	.....	225	30	0	5
Nebraska	0	0	1	2	.....	.....	.....	.....	23	6	29	14
Kansas	0	0	3	5	.....	.....	.....	.....	34	12	31	31

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended July 8, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Diphtheria				Influenza				Measles			
	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median
SO. ATL.												
Delaware	0	0	1	1					79	4	2	5
Maryland [2 3 4]	12	4	1	3	9	3	1	1	52	17	44	44
Dist. of Col	0	0	2	3					380	47	12	20
Virginia [2 4]	19	10	26	6	36	19			240	128	151	89
West Virginia	8	3	4	4	3	1	11	5	11	4	49	49
North Carolina [3 4]	4	3	5	6	1	1	6		54	37	337	127
South Carolina [4]	11	4	10	1	303	111	90	53	19	7	100	18
Georgia [4]	18	11	9	3	7	4			17	10	0	
Florida [4]	0	0	5	5	9	3			39	13	10	9
E. SO. CEN.												
Kentucky	5	3	2	4	10	6	3	3	7	4	45	53
Tennessee	7	4	7	5	12	7	8	8	72	41	46	35
Alabama [4]	16	9	9	9	7	4	10	3	69	39	42	25
Mississippi [3 4]	15	6	3	4								
W. SO. CEN.												
Arkansas	7	3	4	3	15	6	10	3	25	10	45	5
Louisiana [4]	15	6	11	11	24	10	9	9	27	11	4	5
Oklahoma	2	1	4	4	8	4	27	12	16	8	17	17
Texas [4]	12	14	13	17	28	34	90	60	82	99	40	86
MOUNTAIN												
Montana	0	0	0	0	19	2			421	45	0	8
Idaho [3]	0	0	1	0					71	7	1	3
Wyoming [3]	0	0	1	1					393	18	3	3
Colorado [3 5]	39	8	12	3	48	10			67	14	55	59
New Mexico	0	0	2	2				1	124	10	5	13
Arizona	25	2	0	1	331	27	11	6	25	2	17	15
Utah [3 3]	20	2	7	0	10	1			457	46	97	36
PACIFIC												
Washington	9	3	0	1					1,600	519	11	69
Oregon	10	2	1	1	15	3	7	6	169	34	14	14
California	18	22	27	24	7	9	11	14	394	481	394	394
Total	8	197	292	292	14	296	326	275	151	3,746	6,523	6,523
27 weeks	15	10,424	12,479	13,385	262	149,771	44,016	102,548	506	338,261	745,983	651,646

Division and State	Meningitis, meningococcus				Poliomyelitis				Scarlet fever			
	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median
NEW ENG.												
Maine	0	0	0	0	0	0	2	1	24	4	8	8
New Hampshire	0	0	0	0	0	0	0	0	10	1	2	2
Vermont	0	0	0	0	0	0	2	0	13	1	6	2
Massachusetts	2.4	2	0	0	0	0	1	1	51	43	95	74
Rhode Island	0	0	0	0	0	0	0	0	46	6	6	6
Connecticut	3	1	0	0	3	1	0	0	36	12	23	23
MID. ATL.												
New York	1.6	4	2	11	1.6	4	1	6	43	108	141	212
New Jersey [3]	0	0	0	1	1.2	1	0	1	61	51	31	41
Pennsylvania	2.5	5	2	4	0	0	0	0	65	128	122	177

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended July 8, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Meningitis, meningococcus				Poliomyelitis				Scarlet fever			
	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median
E. NO. CEN.												
Ohio	0.8	1	2	2	0	0	1	1	31	40	89	100
Indiana	0	0	0	0	0	0	1	1	18	12	30	28
Illinois [2]	0	0	1	5	0	0	2	2	51	78	133	190
Michigan [3]	1.1	1	1	1	4	4	0	0	94	89	135	135
Wisconsin	0	0	0	0	0	0	1	1	100	57	46	87
W. NO. CEN.												
Minnesota	0	0	1	0	0	0	0	0	29	15	25	39
Iowa [2]	0	0	1	0	0	0	2	0	32	16	18	23
Missouri	0	0	0	0	0	0	1	1	10	8	30	25
North Dakota	7	1	0	1	0	0	0	0	15	2	5	5
South Dakota	8	1	0	0	0	0	0	0	45	6	3	9
Nebraska	0	0	1	1	0	0	0	0	15	4	5	9
Kansas	2.8	1	0	0	0	0	0	1	61	22	25	25
SO. ATL.												
Delaware	0	0	0	0	0	0	0	0	39	2	2	2
Maryland [2 3 4]	0	0	0	0	0	0	0	0	15	5	12	15
Dist. of Col	0	0	0	0	0	0	0	0	24	3	5	7
Virginia [2 4]	4	2	1	3	1.9	1	0	1	21	11	11	11
West Virginia	0	0	0	1	0	0	0	1	38	14	10	18
North Carolina [2 4]	2.9	2	1	2	9	6	1	1	19	13	17	15
South Carolina [4]	5	2	1	1	55	20	0	0	0	0	6	2
Georgia [4]	1.7	1	0	0	17	10	1	1	7	4	8	4
Florida [4]	3	1	1	1	12	4	0	0	3	1	1	1
E. SO. CEN.												
Kentucky	5	3	1	2	1.7	1	1	1	12	7	12	14
Tennessee	0	0	3	3	4	2	0	1	26	15	13	11
Alabama [4]	0	0	5	1	4	2	5	4	16	9	11	7
Mississippi [3 4]	5	2	0	0	2.5	1	3	0	18	7	7	5
W. SO. CEN.												
Arkansas	0	0	0	1	0	0	0	0	5	2	2	2
Louisiana [4]	0	0	0	0	0	0	0	0	10	4	8	4
Oklahoma	0	0	2	1	6	3	1	1	8	4	9	8
Texas [4]	0	0	0	1	3	4	0	2	14	17	41	26
MOUNTAIN												
Montana	0	0	0	0	0	0	0	0	56	6	0	9
Idaho [2]	0	0	0	0	0	0	0	0	10	1	0	2
Wyoming [2]	0	0	0	0	22	1	0	0	0	0	2	7
Colorado [2 5]	0	0	1	0	0	0	0	0	39	8	18	18
New Mexico	0	0	0	0	0	0	0	0	37	3	9	7
Arizona	0	0	1	0	12	1	1	1	12	1	4	4
Utah [2 3]	0	0	0	0	0	0	0	0	89	9	10	10
PACIFIC												
Washington	0	0	0	1	0	0	0	0	43	14	13	14
Oregon	0	0	0	0	0	0	1	0	25	5	11	11
California	1.6	2	0	2	15	18	4	8	43	53	63	79
Total	1.3	32	28	78	3	84	32	156	37	921	1,283	1,550
27 weeks	1.8	1,205	1,926	3,708	1.3	877	580	1,071	165	111,719	131,647	158,823

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended July 8, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough		
	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38, median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases	1934–38 median	July 8, 1939, rate	July 8, 1939, cases	July 9, 1938, cases
NEW ENG.											
Maine	0	0	0	0	18	3	2	1	24	4	24
New Hampshire	0	0	0	0	0	0	0	0	20	2	0
Vermont	0	0	0	0	13	1	0	0	483	36	16
Massachusetts	0	0	0	0	6	5	1	1	82	70	92
Rhode Island	0	0	0	0	0	0	0	0	99	13	30
Connecticut	0	0	0	0	0	0	4	1	113	38	79
MID. ATL.											
New York	0	0	0	0	2	4	5	7	165	413	406
New Jersey [3]	0	0	0	0	1	1	3	3	264	222	237
Pennsylvania	0	0	0	0	2	4	5	13	235	462	211
E. NO. CEN.											
Ohio	10	13	3	1	5	7	13	10	79	103	156
Indiana	24	16	16	3	7	5	7	7	128	86	15
Illinois [3]	1	2	11	4	5	7	13	12	150	229	292
Michigan [3]	0	0	2	0	1	1	2	5	128	121	300
Wisconsin	2	1	3	9	0	0	2	2	450	256	185
W. NO. CEN.											
Minnesota	10	5	5	5	0	0	1	2	41	21	30
Iowa [2]	41	20	16	10	6	3	0	1	55	27	11
Missouri	12	9	10	4	5	4	17	14	22	17	58
North Dakota	0	0	13	3	15	2	0	0	110	15	13
South Dakota	53	7	6	4	0	0	0	0	0	0	14
Nebraska	0	0	2	4	0	0	0	0	76	20	3
Kansas	0	0	0	0	3	1	4	5	53	19	123
SO. ATL.											
Delaware	0	0	0	0	0	0	0	0	138	7	7
Maryland [2 3 4]	0	0	0	0	0	0	6	6	126	41	36
Dist. of Col.	0	0	0	0	0	0	2	1	234	29	4
Virginia [2 4]	0	0	0	0	66	35	31	16	489	261	242
West Virginia	3	1	0	0	24	9	1	8	24	9	64
North Carolina [2 4]	0	0	1	0	16	11	29	19	164	112	282
South Carolina [4]	0	0	0	0	96	35	26	21	246	90	208
Georgia [4]	2	1	0	0	42	25	44	38	81	49	75
Florida [4]	0	0	0	0	6	2	1	1	18	6	16
E. SO. CEN.											
Kentucky	0	0	4	2	40	23	28	26	36	21	56
Tennessee	0	0	0	0	58	33	29	24	125	71	83
Alabama [4]	0	0	2	0	11	6	19	19	92	52	39
Mississippi [3 4]	0	0	0	0	30	12	13	15			
W. SO. CEN.											
Arkansas	0	0	0	0	40	16	17	17	45	18	36
Louisiana [4]	0	0	0	0	56	23	15	15	29	12	46
Oklahoma	12	6	3	0	40	20	4	16	6	3	9
Texas [4]	0	0	2	4	36	43	82	61	58	70	261
MOUNTAIN											
Montana	47	5	33	18	28	3	1	2	47	5	0
Idaho [3]	61	6	2	2	0	0	1	0	122	12	0
Wyoming [3]	0	0	0	0	0	0	0	0	65	3	3
Colorado [3 5]	0	0	0	2	10	2	4	2	246	51	27
New Mexico	0	0	2	0	25	2	7	7	161	13	29
Arizona	0	0	2	0	25	2	3	3	98	8	49
Utah [2 3]	0	0	0	0	10	1	2	0	546	55	66
PACIFIC											
Washington	6	2	19	11	15	5	0	1	25	8	19
Oregon	0	0	26	3	5	1	0	2	35	7	41
California	11	13	10	3	3	4	6	6	70	85	215
Total	4	107	193	112	14	361	450	450	132	3,272	4,208
27 weeks	12	8,379	12,130	5,685	6	4,164	4,748	4,748	157	105,049	115,995

[1] New York City only.
[2] Rocky Mountain spotted fever, week ended July 8, 1939, 17 cases as follows: New Jersey, 1; Illinois, 2; Iowa, 1; Maryland, 2; Virginia, 4; North Carolina, 2; Idaho, 1; Wyoming, 1; Colorado, 1; Utah, 2.
[3] Period ended earlier than Saturday.
[4] Typhus fever, week ended July 8, 1939, 50 cases as follows: Maryland, 1; Virginia, 2; North Carolina, 4; South Carolina, 2; Georgia, 12; Florida, 2; Alabama, 9; Mississippi, 1; Louisiana, 5; Texas, 12.
[5] Colorado tick fever, Colorado, 2 cases.

ROCKY MOUNTAIN SPOTTED FEVER

Cases of Rocky Mountain spotted fever, which were formerly reported from only a limited area in certain Western States, have in recent years been reported in increasing numbers from Eastern and Central States. The average percent of the total number of cases reported in recent years has been about 29 percent in the New England, Middle Atlantic, and South Atlantic States, combined, and about 5 percent in the Central States.

Reports for previous years indicate that, while cases are reported in every month of the year, February is the month of fewest cases, the season of increased prevalence beginning early in March or possibly in February in the Mountain States, and in late April or early May in the Eastern States. The peak appears to be reached in June in the West and in July in the East. Comparatively few cases are reported after July in the Western States, but cases continue to be reported in considerable numbers in the Eastern States until the middle of September, and in decreasing numbers to the end of the year.

The accompanying table shows, for the current year, by 4-week periods, the number of cases of Rocky Mountain spotted fever reported to the Public Health Service by the health officers of the various States, beginning immediately after the seasonal quiescence of the disease. Similar tables will continue to be published throughout the season of prevalence.

Cases reported by States for 4-week periods, February 26 to July 15, 1939

State	Feb. 26 to Mar. 25	Mar. 26 to Apr. 22	Apr. 23 to May 20	May 21 to June 17	June 18 to July 15
New York				3	3
New Jersey				4	8
Pennsylvania				6	3
Ohio				3	2
Indiana				2	1
Illinois			1	1	5
Iowa			1	10	9
Missouri				1	
Delaware				3	
Maryland			7	13	11
District of Columbia			2	2	2
Virginia			1	13	10
North Carolina				3	13
Georgia					1
Tennessee			1		3
Montana	[1] 2	2	8	5	2
Idaho		4	7	4	5
Wyoming		3	14	16	5
Colorado		2	3	9	4
Utah		2	5	5	6
Washington		2	3	2	
Oregon		9	16	7	2

[1] 1 other case was reported in Montana as occurring in February, exact date not given.

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
March 1939										
New Hampshire	0	2	----	----	2	----	0	28	0	0
North Carolina	8	67	749	12	5,189	13	0	204	1	14
April 1939										
New Hampshire	0	0	----	----	52	----	0	21	0	----
May 1939										
New Hampshire	0	0	----	----	12	----	0	14	0	0
June 1939										
Arkansas	4	9	87	626	89	101	4	17	15	52
Connecticut	1	3	7	----	2,205	----	1	114	6	9
Missouri	0	24	1	2	23	----	0	133	46	18

March 1939

	Cases
New Hampshire:	
Chickenpox	9
Mumps	26
Whooping cough	10
North Carolina:	
Chickenpox	644
Dysentery (amoebic)	1
German measles	52
Septic sore throat	9
Tularaemia	2
Typhus fever	1
Undulant fever	2
Vincent's infection	7
Whooping cough	1,393

April 1939

	Cases
New Hampshire:	
Chickenpox	15
Mumps	28
Whooping cough	10

May 1939

	Cases
New Hampshire:	
Chickenpox	5
Mumps	15
Whooping cough	2

June 1939

	Cases
Chickenpox:	
Arkansas	59
Connecticut	234
Missouri	79
Conjunctivitis, infectious:	
Connecticut	7
Dysentery:	
Arkansas (amoebic)	80
Arkansas (bacillary)	118
Connecticut (bacillary)	3
Missouri (bacillary)	1
German measles:	
Arkansas	4
Connecticut	9
Hookworm disease:	
Arkansas	1
Missouri	1
Mumps:	
Arkansas	66
Connecticut	278
Missouri	196
Ophthalmia neonatorum:	
Arkansas	1
Missouri	1
Puerperal septicemia:	
Arkansas	3
Rabies in animals:	
Arkansas	26

June 1939—Continued

	Cases
Rocky Mountain spotted fever:	
Missouri	1
Septic sore throat:	
Arkansas	28
Connecticut	25
Missouri	6
Tetanus:	
Arkansas	1
Connecticut	1
Missouri	2
Trachoma:	
Arkansas	15
Missouri	58
Trichinosis:	
Arkansas	1
Tularaemia:	
Arkansas	15
Missouri	1
Undulant fever:	
Arkansas	11
Connecticut	11
Missouri	2
Whooping cough:	
Arkansas	97
Connecticut	307
Missouri	76

WEEKLY REPORTS FROM CITIES

City reports for week ended July 1, 1939

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	128	37	16	2,673	358	850	10	377	53	1,289	------
Current week	79	23	9	1,383	236	436	9	330	42	1,301	------
Maine:											
Portland	0	------	0	0	0	1	0	1	0	0	24
New Hampshire:											
Concord	0	------	0	0	1	0	0	0	0	0	5
Manchester	0	------	0	0	1	0	0	0	0	0	23
Nashua	0	------	0	1	0	0	0	0	0	0	8
Vermont:											
Barre	0	------	------	0	------	0	0	------	0	0	------
Burlington	0	------	------	7	0	0	0	0	0	4	2
Rutland	0	------	0	0	0	0	0	0	0	0	9
Massachusetts:											
Boston	0	------	0	98	11	14	0	8	2	16	186
Fall River	0	------	0	1	0	1	0	2	0	1	24
Springfield	0	------	0	4	1	0	0	0	0	0	29
Worcester	0	------	0	18	2	1	0	1	0	19	41
Rhode Island:											
Pawtucket	0	------	0	5	0	2	0	2	0	0	------
Providence	0	------	0	53	2	4	0	1	0	16	61
Connecticut:											
Bridgeport	0	------	0	7	1	0	0	0	0	1	30
Hartford	1	------	0	6	2	0	0	0	1	10	48
New Haven	0	------	0	67	0	3	0	0	0	12	41
New York:											
Buffalo	0	------	0	35	9	18	0	7	0	15	128
New York	9	1	2	129	44	52	0	73	5	117	1,178
Rochester	0	------	0	42	4	3	0	0	0	2	63
Syracuse	0	------	0	80	1	0	0	0	0	98	51
New Jersey:											
Camden	0	------	0	0	0	3	0	0	0	11	20
Newark	0	------	0	2	0	13	0	1	------	64	73
Trenton	0	------	0	0	2	6	0	1	0	0	31
Pennsylvania:											
Philadelphia	2	2	2	31	13	18	0	29	1	126	394
Pittsburgh	1	1	1	2	4	8	0	7	1	32	125
Reading	0	------	0	0	2	0	0	2	0	0	20
Scranton	0	------	------	1	------	2	0	------	0	5	------
Ohio:											
Cincinnati	6	1	------	2	------	39	0	------	2	29	110
Cleveland	0	6	0	3	4	20	0	9	0	54	155
Columbus	0	1	1	8	1	1	0	2	0	5	80
Toledo	0	------	0	20	2	10	4	3	0	42	75
Indiana:											
Anderson	0	------	0	0	0	0	0	0	0	4	5
Fort Wayne	1	------	0	0	0	3	0	2	0	0	24
Indianapolis	1	------	0	3	2	4	0	2	1	48	88
Muncie	0	------	0	0	0	1	0	1	0	0	8
South Bend	0	------	0	0	1	0	0	0	0	11	14
Terre Haute	0	------	1	0	1	0	0	2	0	0	23
Illinois:											
Alton	0	------	0	0	0	0	0	0	0	0	3
Chicago	15	------	0	10	14	56	0	38	2	109	630
Elgin	0	------	0	1	0	0	0	1	0	2	9
Moline	0	------	0	0	0	0	0	0	0	0	10
Springfield	0	------	0	0	1	0	0	0	0	18	20
Michigan:											
Detroit	4	------	0	30	7	52	0	9	1	101	222
Flint	0	------	0	7	0	6	0	0	0	1	35
Grand Rapids	0	------	0	2	1	10	0	0	0	1	27
Wisconsin:											
Kenosha	0	------	0	0	0	0	0	0	0	4	4
Madison	0	------	0	15	1	1	0	0	0	8	21
Milwaukee	0	------	0	1	6	18	0	1	0	24	68
Racine	0	------	0	3	0	2	0	0	0	14	18
Superior	0	------	0	0	0	0	0	0	0	0	9

City reports for week ended July 1, 1939—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	2	0	0	0	0	0	1	29
Minneapolis	0	------	0	15	1	1	0	1	0	11	94
St. Paul	0	------	0	5	2	3	0	1	1	17	62
Iowa:											
Cedar Rapids	0	------	--------	3	-------	0	0	-------	0	0	--------
Davenport	0	------	--------	0	-------	0	10	-------	0	0	--------
Des Moines	0	------	0	5	0	3	3	0	6	2	40
Sioux City	0	------	--------	0	-------	1	0	-------	0	0	--------
Waterloo	0	------	--------	4	-------	0	0	-------	0	0	--------
Missouri:											
Kansas City	0	------	0	1	1	5	0	7	1	1	90
St. Joseph	1	------	0	0	3	0	0	0	0	0	30
St. Louis	1	------	0	1	4	6	2	5	3	30	215
North Dakota:											
Fargo	0	------	0	0	0	1	0	0	0	2	2
Grand Forks	0	------	--------	0	-------	0	0	-------	0	0	--------
Minot	0	------	0	0	0	0	0	0	0	0	10
South Dakota:											
Aberdeen	0	------	--------	5	-------	0	25	-------	0	0	--------
Sioux Falls	0	------	0	0	0	5	0	0	0	0	7
Nebraska:											
Lincoln	0	------	--------	4	-------	0	0	-------	0	19	--------
Omaha	0	------	0	2	2	1	0	4	0	0	58
Kansas:											
Lawrence	0	------	0	0	1	0	0	0	0	0	6
Topeka	0	------	0	1	0	1	0	0	0	2	9
Wichita	0	------	0	1	0	2	0	0	0	2	28
Delaware:											
Wilmington	0	------	0	1	0	1	0	0	0	0	24
Maryland:											
Baltimore	1	------	0	14	2	3	0	11	0	44	153
Cumberland	0	------	0	0	0	0	0	0	0	2	11
Frederick	0	------	0	0	0	1	0	0	0	0	2
District of Col.:											
Washington	4	------	0	77	4	2	0	10	0	29	147
Virginia:											
Lynchburg	2	------	0	13	2	0	0	1	1	22	11
Norfolk	0	------	0	0	0	1	0	0	0	0	18
Richmond	0	------	0	22	3	0	0	1	1	0	43
Roanoke	0	------	0	0		1	0	0	0	0	17
West Virginia:											
Charleston	0	------	0	0	1	0	0	0	1	0	8
Huntington	0	------	--------	0	-------	0	0	-------	0	0	--------
Wheeling	0	------	0	3	0	1	0	0	1	1	18
North Carolina:											
Gastonia	0	------	--------	0	-------	0	0	-------	0	0	--------
Raleigh	0	------	0	0	1	0	0	0	0	8	16
Wilmington	0	------	0	0	1	0	0	0	0	1	14
Winston-Salem	0	------	0	0	0	0	0	1	0	3	18
South Carol'na:											
Charleston	0	------	0	0	1	1	0	1	2	0	27
Florence	0	------	0	0	1	0	0	1	0	0	8
Greenville	0	------	0	0	0	0	0	0	0	0	12
Georgia:											
Atlanta	0	3	1	0	·	2	0	3	0	0	84
Brunswick	0	------	0	0	0	0	0	0	1	0	3
Savannah	1	2	0	0	8	0	0	1	0	11	30
Florida:											
Miami	0	2	1	0	3	0	0	3	0	3	34
Tampa	0	------	0	15	0	0	0	1	0	1	20
Kentucky:											
Ashland	0	------	0	0	1	0	0	0	0	0	7
Covington	0	------	0	1	2	0	0	0	0	0	12
Lexington	0	------	0	0	1	0	0	1	0	0	20
Louisville	1	------	0	1	3	3	0	4	0	14	74
Tennessee:											
Knoxville	0	------	1	1	2	1	0	2	1	4	30
Memphis	0	------	0	0	4	4	0	8	2	71	76
Nashville	0	------	0	1	3	0	0	5	2	11	55
Alabama:											
Birmingham	0	------	0	0	1	0	0	5	0	1	59
Mobile	0	------	0	0	0	0	0	2	0	0	15
Montgomery	0	------	--------	0	-------	1	0	-------	0	2	--------

City reports for week ended July 1, 1939—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								
Arkansas:											
Fort Smith	0			0		0	0		0	0	
Little Rock	0		0	0	1	0	0	2	1	0	3
Louisiana:											
Lake Charles	1		0	0	0	0	0	0	0	0	8
New Orleans	2		0	11	7	4	0	9	2	1	141
Shreveport	0		0	0	6	0	1	4	3	0	46
Oklahoma:											
Oklahoma City	0	3	0	0	3	1	0	2	0	0	43
Tulsa	0			1		3	1		0	0	
Texas:											
Dallas	2		0	14	1	0	0	1	0	0	57
Fort Worth	0		0	5	2	4	0	0	0	0	24
Galveston	0		0	0	3	0	0	0	0	0	11
Houston	1		0	1	7	1	0	3	3	4	77
San Antonio	1		1	0	2	0	0	7	0	0	64
Montana:											
Billings	0		0	1	2	0	0	0	0	0	13
Great Falls	0		0	36	0	0	0	0	0	0	16
Helena	0		0	1	1	0	0	0	0	0	4
Missoula	0		0	0	0	0	0	1	0	0	7
Idaho:											
Boise	0		0	0	1	0	0	0	0	0	9
Colorado:											
Colorado Springs	0		0	0	1	4	0	1	0	1	9
Denver	8		0	11	2	6	0	2	0	10	62
Pueblo	4		0	3	0	0	0	1	0	6	8
New Mexico:											
Albuquerque	0		0	0	0	0	0	2	0	0	8
Utah:											
Salt Lake City	0		0	4	2	1	6	0	0	26	39
Washington:											
Seattle	0		0	286	1	1	0	6	0	5	93
Spokane	0		0	21	1	1	0	0	0	0	21
Tacoma	0		0	9	2	0	0	0	0	0	22
Oregon:											
Portland	1		0	7	2	2	0	2	0	4	69
Salem	0			5		0	0		0	0	
California:											
Los Angeles	4	6	0	145	6	27	0	19	0	17	282
Sacramento	5		0	16	0	1	0	1	0	0	20
San Francisco	2		0	6	3	2	0	8	1	2	130

State and city	Meningitis, meningococcus		Poliomyelitis cases	State and city	Meningitis, meningococcus		Poliomyelitis cases
	Cases	Deaths			Cases	Deaths	
New York:				South Carolina:			
New York	1	0	0	Charleston	0	0	8
New Jersey:				Georgia:			
Camden	0	0	1	Atlanta	0	0	1
Ohio:				Tennessee:			
Cincinnati	1	0	0	Nashville	0	0	1
Michigan:				Arkansas:			
Detroit	0	0	1	Fort Smith	1	0	0
North Carolina:				California:			
Wilmington	1	0	0	Los Angeles	0	0	3
				San Francisco	0	1	0

Pellagra.—Cases: Boston, 1; Baltimore, 3; Lynchburg, 1; Atlanta, 1; Savannah, 4; New Orleans, 2; Dallas, 1.

Typhus fever.—Cases: New York, 2; Charleston, S. C., 1; Brunswick, 1; Mobile, 1; Montgomery, 1.—Deaths: Atlanta, 1.

FOREIGN AND INSULAR

CANADA

Provinces—Communicable diseases—Week ended June 17, 1939.—During the week ended June 17, 1939, 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	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Cerebrospinal meningitis			1	1	2					4
Chickenpox		2		77	215	43	15	19	60	431
Diphtheria		5		32		3		1		41
Dysentery				1	1					2
Influenza		7			3		1		47	58
Lethargic encephalitis									1	1
Measles		5	1	754	720	50	14	6	20	1,570
Mumps				21	74	35		2	9	141
Pneumonia		3			18				6	27
Poliomyelitis				1	1					2
Scarlet fever		2	16	40	80	15	6	14	9	182
Smallpox							1			1
Tuberculosis	3	2	12	88	50	6		3		164
Typhoid and paratyphoid fever		2		15	2	1	1	1	1	23
Whooping cough		7		84	81	9	18	9	51	259

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 June 30, 1939, pages 1182-1194. 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 July 1, 1939, cholera was reported in China as follows: Hong Kong, 97 cases; Macao, 95 cases.

Iran—Sistan Region—Zabol.—During the week ended July 1, 1939, 10 cases of cholera were reported in Zabol, Sistan Region, Iran.

Plague

Brazil.—During the month of March 1939, plague was reported in Brazil as follows: Alagoas State, 11 cases, 3 deaths; Bahia State, 1 case; Pernambuco State, 5 cases, 2 deaths.

Peru.—During the month of May 1939, plague was reported in Peru as follows: Lambayeque Department, 1 case; Libertad Department, Trujillo city, 3 cases; Piura Department, 7 cases, 1 death.

Smallpox

Society Islands—Tahiti—Papeete.—During the week ended July 8, 1939, 12 suspected cases of smallpox with 1 death were reported in Papeete, Tahiti, Society Islands.

Yellow Fever

Brazil—Para State—Capanema.—On May 23, 1939, 1 death from the jungle type of yellow fever was reported in Capanema, Para State, Brazil.

Colombia—Department of Antioquia—Caracoli.—On May 29, 1939, 1 death from yellow fever was reported in Caracoli, Department of Antioquia, Colombia.