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SICKNESS AMONG MALE INDUSTRIAL EMPLOYEES DURING THE THIRD QUARTER AND THE FIRST 9 MONTHS OF 1937 [1]

The data on the frequency of sickness and nonindustrial accidents lasting 8 consecutive calendar days or longer during the third quarter and the first 9 months of 1936 and 1937, presented in the accompanying tables, are derived from analyses of reports from 26 industrial sick-benefit organizations. The reports for the first 9 months of 1937 are based on an average of 183,748 male employees, 52 percent being employed in the iron and steel industry, 17 percent in public utilities, and 31 percent in industries producing chemicals, abrasives, plumbing fixtures, electrical equipment, paper, paper novelties, timepieces, hats, soap, and certain other products. The reporting establishments are located east of the Mississippi River and north of the Ohio and Potomac Rivers.

Considering the data for the first 9 months of 1937, as shown in table 1, the frequency of cases of sickness and nonindustrial accidents causing disability for 8 consecutive calendar days or longer was 104.4 per 1,000 men, as compared with 92.3 for the corresponding period of 1936, and 88.3 for the corresponding periods of the 5 years 1932–36. The influenza epidemic which occurred in the first quarter of the year was chiefly responsible for the excessive rate in 1937. The epidemic was reflected in the incidence of respiratory diseases during the first 9 months of 1937, the rate, 44.0, being 34 percent greater than the corresponding rate (32.8) for the previous year. More specifically, influenza and grippe showed a rate for the first 9 months of 1937 of 24.4, which was 65 percent greater than the corresponding rate (14.8) for 1936. Diseases of the pharynx and tonsils (5.6 cases per 1,000 men) was 14 percent in excess of the rate for 1936 (4.9), and 19 percent in excess of the rate for the period 1932–1936 (4.7). Diseases of the rheumatic group (particularly diseases of the organs of locomotion) showed a decrease of 8 percent, while infectious and parasitic diseases showed an increase of 23 percent; the former group was 7 percent below its 5-year average and the latter was 23 percent above its 5-year average.

[1] From the Division of Industrial Hygiene of the National Institute of Health, U. S. Public Health Service, Washington, D. C. The report for the second quarter and the first half of 1937 was published in the Public Health Reports for October 29, 1937 (*52*: 1523-1526).

TABLE 1.—*Frequency of disability lasting 8 calendar days or longer in the third quarter of 1937 compared with the same quarter of 1936, and in the first 9 months of 1937 as compared with the corresponding period of preceding years. (Male morbidity experience of industrial companies which reported their cases to the U. S. Public Health Service)* [1]

Diseases and disease groups which caused disability. (Numbers in parentheses are disease title numbers from the International List of the Causes of Death, fourth revision, Paris, 1929)	Annual number of disabilities per 1,000 men in—				
	Third quarter of—		First 9 months of—		
	1937	1936	1937	1936	5 years 1932–36
Sickness and nonindustrial injuries [2]	79.4	76.8	104.4	92.3	88.3
Nonindustrial injuries	13.3	13.6	11.6	11.8	11.6
Sickness [2]	66 1	63.2	92.8	80.5	76.7
Respiratory diseases	19.4	17.0	44.0	32.8	30.4
Bronchitis, acute and chronic (106)	2.9	2.7	4.7	4.8	3.7
Diseases of the pharynx and tonsils (115a)	4.5	4.2	5.6	4.9	4.7
Influenza and grippe (11)	5.3	4.4	24.4	14.8	14.7
Pneumonia, all forms (107–109)	1.5	.9	2.9	2.8	2.1
Tuberculosis of the respiratory system (23)	.9	.8	.8	.8	.9
Other respiratory diseases (104, 105, 110–114)	4.3	4.0	5.6	4.7	4.3
Nonrespiratory diseases	46.7	46.2	48.8	47.7	46.3
Diseases of the stomach, cancer excepted (117–118)	4.0	3.7	3.9	3.8	3.7
Diarrhea and enteritis (120)	2.2	1.8	1.5	1.4	1.2
Appendicitis (121)	4.5	4.7	4.6	4.4	3.9
Hernia (122a)	1.4	1.8	1.6	1.8	1.6
Other digestive diseases (115b, 116, 122b–129)	2.3	2.8	2.4	2.9	3.0
Rheumatic group, total	8.5	9.5	9.3	10.1	10.0
Rheumatism, acute and chronic (56, 57)	3.8	4.0	4.3	4.5	4.8
Diseases of the organs of locomotion (156b)	2.7	3.2	2.8	3.3	3.0
Neuralgia, neuritis, sciatica (87a)	2.0	2.3	2.2	2.3	2.2
Neurasthenia and the like (part of 87b)	1.2	1.0	1.1	1.1	1.1
Other diseases of the nervous system (78–85, part of 87b)	.9	1.1	1.0	1.2	1.3
Diseases of the heart and arteries, and nephritis (90–99, 102, 130–132)	3.3	3.3	4.0	3.8	3.9
Other genito-urinary diseases (133–138)	2.1	2.2	2.3	2.3	2.4
Diseases of the skin (151–153)	3.4	3.8	3.2	2.9	2.8
Infectious and parasitic diseases, except influenza (1–10, 12–22, 24–33, 36–44)	1.9	1.4	3.2	2.6	2.6
Ill-defined and unknown causes (200)	3.9	3.1	3.7	2.8	2.2
All other diseases (45–55, 58–77, 88, 89, 100, 101, 103, 154–156a, 157, 162)	7.1	6.0	7.0	6.6	6.6
Average number of males covered in the record	188,327	162,721	183,748	153,780	145,070
Number of companies	26	26	26	26	

[1] In 1937 and 1936 the same companies are included; the rates for the first 9 months of the years 1932 to 1936 include 21 of these companies, which employed an average of approximately 80 percent of the 145,070 men representing the sample average annual population for the 5-year period.
[2] Exclusive of disability from the venereal diseases and a few numerically unimportant causes of disability.

For the third quarter of 1937, the rate (79.4 cases per 1,000) for all sickness and nonindustrial accidents was 3 percent higher than for the same quarter of 1936 (76.8). With respect to particular diseases and disease groups, interest in the third quarter centers around influenza and grippe, pneumonia, infectious and parasitic diseases, and the rheumatic group, the first three showing percentage increases of 20, 67, and 36, respectively, and the last (particularly diseases of the organs of locomotion) a decrease of 11 percent.

The rate for pneumonia for the third quarter of 1937 was 1.5 cases per 1,000 men as compared with 0.9 for the same quarter of 1936, while the rates for the first 9 months of 1937 and 1936, 2.9 and 2.8

cases per 1,000, respectively, exceeded the rate (2.1) for the same period of the 5 years under consideration. The increases probably reflect the relatively large increase in the membership in the iron and steel industry, an industry whose workers are well known for their relatively high pneumonia rate. With respect to membership in the sick-benefit associations, table 2 shows for each of 3 quarters the percentage increase from 1936 to 1937 among the iron and steel workers, and among workers in all other industries; in the iron and steel industry there was an increase of 29.2 percent, while all other industries showed an increase of 10.4 percent. The pneumonia case rate among the iron and steel workers during the first 9 months of 1937 was 3.5 cases per 1,000, as compared with 2.2 for employees in other industries; this difference represents an excess of 59 percent in the instance of the iron and steel workers. Among other industrial workers the rate for the first 9 months of 1937 (2.2) was 8 percent less than for the same period of 1936 (2.4). The iron and steel workers experienced an increase of 13 percent in the first 9 months of 1937 (3.5) as compared with the same period of 1936 (3.1). Thus, the pneumonia rate among the iron and steel workers for the first 9 months of 1936 and 1937 is not only higher than the corresponding rate for the other workers, but the 9-month rate among the iron and steel workers is higher for 1937 than for the corresponding period of 1936.

TABLE 2.—*Average number of males covered in the records and the frequency of cases of pneumonia among all employees except those in the iron and steel industry and among iron and steel workers only, for the first 3 quarters of 1937, compared with similar periods of 1936*

Quarter	All except iron and steel employees		Iron and steel employees only		All except iron and steel employees	Iron and steel employees only
	1937	1936	1937	1936	Percentage changee 1936 to 1937	
	Average number of males covered					
First	86,036	77,379	89,512	68,322	+11.2	+31.0
Second	88,555	79,225	98,814	73,692	+11.8	+34.1
Third	88,240	81,525	100,087	81,196	+8.2	+23.3
First 9 months	87,610	79,376	96,138	74,403	+10.4	+29.2
	Annual number of cases of pneumonia per 1,000 men					
First	3.5	4.3	5.4	5.6	−18.6	−3.6
Second	1.9	2.2	3.4	3.2	−13.6	+6.2
Third	1.1	.9	1.9	1.0	+22.2	+90.0
First 9 months	2.2	2.4	3.5	3.1	−8.3	+12.9

STUDIES IN CHEMOTHERAPY

VII. SOME NEW SULPHUR COMPOUNDS ACTIVE AGAINST BACTERIAL INFECTIONS

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As a result of the original discovery of Prontosil by Domagk, and the subsequent development of sulfanilamide by Trefouel, Nitti, and Bovet, active investigation has been under way to obtain more effective compounds. The studies of Buttle, Gray, and Stephenson (*1*) and of Fourneau, Trefouel, Nitti, and Bovet (*2*) have been important contributions to the study of the relation of chemical structure to therapeutic action. Goissedet, Despois, Gaillot, and Mayer (*3*) developed the benzyl-aminobenzene sulfonamide ("Setazine") which is of slightly lower activity than sulfanilamide (*4*) but of very low toxicity (*5*). p-aminobenzene sulfonyl-sulfanilamide (di-sulfanilamide) was independently described by Gray, Buttle, and Stephenson (*6*), by ourselves (*4*), and in the German patent literature by Domagk (*7*). We found this compound approximately twice as active (by weight) as sulfanilamide when injected in oil subcutaneously, and also of very low toxicity. We obtained less favorable therapeutic results by mouth, although Domagk and the English investigators report it somewhat better than sulfanilamide administered orally. Domagk has recently reported on the use of di-sulfanilamide and its methyl and di-methyl derivatives in experimental staphylococcus infections (*7*).

HUMAN TOXICITY OF DI-SULFANILAMIDE [1]

Domagk refers to a report of O. Grutz (München. Med. Wchnschr. *84:* 1201 (1937)), who has employed di-sulfanilamide under the designation of D. B. 32, the methyl derivative (D. B. 87) and the di-methyl derivative (D. B. 90) in 36 cases of gonorrhea. Grutz employed 2 to 3 grams a day for 7 to 14 days. A high incidence of fever and dermatitis occurred as a result of therapy.

Some preliminary observations made upon 10 cases of gonorrhea indicate that, in human beings, toxic manifestations (fever, cyanosis, dermatitis) are as frequent from di-sulfanilamide as they are from sulfanilamide, if not more frequent. Furthermore, 4 cases of peripheral neuritis developed among these 10 individuals to whom di-sulfanilamide was administered. The dosage in each instance was 4.0 grams daily for 10 days.

[1] These studies were undertaken at this time because the drug was being distributed for clinical use from sources over which we had no control.

These observations are reported at this time to serve as an illustration of the care that must be taken in the introduction of a new drug. The acute toxicity of di-sulfanilamide to animals (*4*) is very low,[2] and in chronic toxicity studies 0.5 gram per kilo daily to rats for 30 days produced no demonstrable toxic effects. Effects upon human beings are not always predictable from animal experiments and the clinical use of a new drug should be preceded not only by a thorough pharmacological and toxicological study of the drug upon several species of animals, but also a careful study of its effects upon human beings under conditions where they can be closely observed for a considerable period of time.

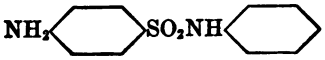
OTHER SULPHUR COMPOUNDS

An important development in the field of bacterial chemotherapy has been made by Buttle, Stephenson, Smith, and Foster (*8*), and by Fourneau, Trefouel, Nitti, and Bovet (*9*), who simultaneously reported upon the chemotherapeutic activity of diamino diphenylsulfone, dinitro diphenylsulfone, and the corresponding sulfides. These compounds were originally described by Fromm and Wittmann in 1908 (*10*), but their therapeutic action had not previously been explored. It has thus been demonstrated that neither the sulfonamide group nor the amino group is essential to therapeutic action. An entirely new series of chemical compounds is therefore subject to approach in the field of bacterial chemotherapy.

The present report deals with some new derivatives of the above compounds which we have prepared and studied.

SULFANILAMIDE DERIVATIVES

Buttle (*1*) first studied the anilide of sulfanilamide:



(X)

He reported it as active as sulfanilamide, although in our experience it has been about one-half as active (weight for weight). We have obtained three new compounds in this series by substitution in the para position (X) with COOH, NO_2, and NH_2.

The carboxy derivative, p-aminobenzene sulfonyl p-aminobenzoic acid, was of low toxicity but possessed little chemotherapeutic action against streptococci. The sodium salt was freely soluble in water.

The nitro derivative, sulfanil-p-nitroanilide, was two to three times as active as sulfanilamide by mouth or upon subcutaneous injection, in oil. However, it was approximately twice as toxic.

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[2] A recent report by O. W. Barlow (Proc. Soc. Exp. Biol. and Med., 37:315 (1937)) states that mice tolerate up to 40 grams per kilo without nervous symptoms. We have, however, been able to produce characteristic symptoms of paralysis, and in some cases death, in rabbits with 1 gram per kilo of di-sulfanilamide administered orally for from 5 to 8 days.

The amino derivative, sulfanil p-aminoanilide, was approximately two times as active as sulfanilamide against streptococci, and of about the same order of toxicity as sulfanilamide.

These three compounds were inferior to sulfanilamide against pneumococci.

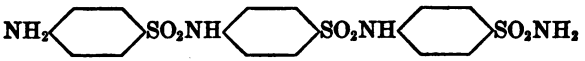
Two other (water soluble) derivatives of sulfanilamide, p-aminobenzene sulfonyl ethanolamine $NH_2C_6H_4SO_2NH{\cdot}C_2H_4OH$ and p-aminobenzene sulfonyl glycine $NH_2C_6H_4SO_2NH{\cdot}CH_2COOH$ were found to be of inferior activity.

DERIVATIVES OF DI-SULFANILAMIDE

The mono-sodium salt of di-sulfanilamide in water, injected subcutaneously, was found to be of increased toxicity and of lowered therapeutic activity.

The water soluble ethanolamine derivative $NH_2C_6H_4SO_2NH{\cdot}C_6H_4SO_2NH{\cdot}C_2H_4OH$ and glycine derivative $NH_2C_6H_4SO_2NH{\cdot}C_6H_4SO_2NH{\cdot}CH_2COOH$ were of low toxicity; the former was slightly less active than sulfanilamide, while the latter was decidedly inferior, against streptococci and pneumococci.

Following the procedure for obtaining di-sulfanilamide it is possible to obtain higher members of this series. By condensing sulfanilamide with p-acetyl aminobenzene sulfonyl p-aminobenzene sulfonyl chloride and subsequently deacetylating, the tri-sulfanilamide was prepared:



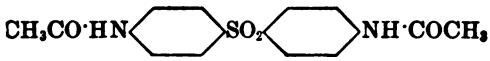
This compound, as well as its mono-sodium salt, was found to be of inferior action against streptococci and pneumococci.

SULFONE DERIVATIVES

Buttle (*8*) has reported that the diamino diphenylsulfone,

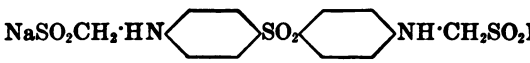
is approximately 100 times as active against streptococcal infections in mice as sulfanilamide, and 25 times as toxic. In our experiments, employing two virulent strains of streptococci (different from those used by Buttle), the diaminosulfone proved to be approximately 30 times as active (by weight) as sulfanilamide. Results with the toxicity of this compound given orally to mice have been in general agreement with those of Buttle. We have found the maximum tolerated dose for therapeutic purposes to be 0.1 gm per kilo (2 mg per 20 gm). The repeated administration of this dosage at daily intervals to infected mice often provokes symptoms of marked excitability.

It is therefore desirable to obtain derivatives of this highly active compound in which the toxicity will be lowered without corresponding decrease in therapeutic action. Fourneau, Trefouel, Nitti, and Bovet (*9*) have reported upon the diacetyl derivative:



They have found this compound tolerated in doses up to 10 grams per kilo when given orally to mice, while its activity against streptococci and pneumococci was 10 times as great as that of sulfanilamide.

We have prepared the formaldehyde sulfoxylate derivative of the diaminosulfone:



This compound is of interest in that it is a highly active preparation which is freely soluble in water and can be injected subcutaneously without apparent signs of irritation.

We have also prepared the corresponding formaldehyde bisulfite derivative of diamino diphenylsulfone and found it to possess surprisingly little chemotherapeutic activity.

Comparative studies have been carried out on mice on the toxicity and therapeutic activity of the diamino diphenylsulfone and its diacetyl and diformaldehyde sulfoxylate derivatives. Two virulent strains of streptococci, and three strains of pneumococci, types I, II, and III, were employed.

Toxicity studies upon normal mice revealed that the diaminosulfone caused death in 2 of 3 mice from 0.25 gm per kilo given orally. With a dosage of 0.2 gm per kilo symptoms of excitability occurred, with 10 percent mortality; 0.15 gm per kilo caused some excitability and spasticity but no fatalities.

With the formaldehyde sulfoxylate derivative, 3 gm per kilo subcutaneously was tolerated without appreciable symptoms; 4.0 gm per kilo caused 44 percent mortality; while 6 gm caused 66 percent mortality. The only symptom prior to death was respiratory distress. A comparison of the acute toxicities of these two compounds is shown in the following table:

Drug	Dosage, gm per kilo	Number of mice	Mortality
			Percent
Diamino diphenylsulfone	0.15	5	0
	.20	10	10
	.25	3	75
	.50	3	100
Formaldehyde sulfoxylate sulfone	2.0	7	0
	3.0	7	0
	4.0	9	44.4
	6.0	3	66.6

The sulfoxylate derivative is very sensitive to weak acids, and we have found it more toxic when administered orally, probably as a result of decomposition in the acid gastric contents.

Four grams per kilo of the acetyl derivative given orally were tolerated without symptoms. We have had insufficient material to test the toxicity further.

Comparative studies were made in mice infected with streptococcus No. 1685, an erysipelas strain, and strain No. 995, isolated from human septicemia (Lancefield group A strains). The number of organisms injected intraperitoneally (0.5 cc 10^{-6} dilution of broth culture) represented approximately 100 lethal doses. The results are shown in table 1 and in figures 1 and 2. It is seen that the following doses represent approximately equal activity:

	Gm per kilo
Diaminodiphenyl sulfone	0.025
Diacetyl diamino diphenylsulfone	.2
Diformaldehyde sulfoxylate diamino diphenylsulfone	.2
Sulfanilamide	.75

TABLE 1.—*Streptococcus 1685*

Drug	Therapy	Deaths in days										Mortality
		1	2	3	4	5	6	7	8	9	10	
												Percent
Sulfanilamide	1 gm per kilo, orally, 4 days	---	---	---	---	---	---	3	---	---	---	26.6
	0.5 gm per kilo, orally, 4 days	---	8	---	---	---	2	---	---	---	1	73.3
Di-sulfanilamide	1 gm per kilo, orally, 4 days	1	6	1	---	---	3	---	---	---	1	80
	0.5 gm per kilo, orally, 4 days	---	5	1	---	1	3	3	1	---	1	100
Diamino diphenylsulfone.	0.05 gm per kilo, orally, 4 days	[1] 1	1	---	---	---	1	1	---	---	1	28.5
	0.025 gm per kilo, orally, 4 days	---	5	1	---	---	---	2	1	---	---	60
Diacetyl diamino diphenylsulfone.	0.5 gm per kilo, orally, 4 days	2	2	1	---	3	---	---	1	---	---	60
	0.2 gm per kilo, orally, 4 days	1	4	---	---	2	---	---	---	---	2	60
Diformaldehyde sulfoxsulfone.	0.5 gm per kilo, s. c., 4 days	---	1	---	1	---	---	2	1	1	---	40
	0.2 gm per kilo, s. c., 4 days	---	3	2	---	---	1	2	1	---	---	60
Controls	None	15	---	---	---	---	---	---	---	---	---	100
		Streptococcus 995										
Sulfanilamide	1 gm per kilo, orally, 2 days	---	---	1	---	1	2	1	---	---	---	33.3
	0.5 gm per kilo, orally, 2 days	---	---	---	2	4	2	1	---	1	---	66.6
Di-sulfanilamide	1 gm per kilo, orally, 2 days	---	---	---	2	2	3	1	2	---	---	66.6
	0.5 gm per kilo, orally, 2 days	---	---	1	6	3	3	---	---	---	---	86.6
Diamino diphenyl-sulfone.	0.05 gm per kilo, orally, 2 days	---	---	---	---	---	1	1	3	3	---	53.3
	0.025 gm per kilo, orally, 2 days	---	---	1	---	1	3	2	---	---	---	46.6
Diacetyl sulfone	0.5 gm per kilo, orally, 2 days	---	---	---	1	---	2	1	1	---	---	33.3
	0.25 gm per kilo, orally, 2 days	---	---	---	---	2	3	---	1	---	1	46.6
Diformaldehyde sulfoxsulfone.	0.5 gm per kilo, s. c., 2 days	---	---	---	1	1	1	1	1	2	1	53.3
	0.25 gm per kilo, s. c., 2 days	[1] 1	---	---	---	---	5	2	---	---	---	50.0
Controls	None	10	3	2	---	---	---	---	---	---	---	100.0

[1] Death not due to streptococcal infection.

Comparative action of compounds against 2 strains of streptococci. 0.5 cc of 10^{-6} broth culture of organisms intraperitoneally. Therapy within ½ hour and repeated daily as indicated. 15 mice in each group.

Di-sulfanilamide was approximately one-half as active as sulfanilamide when given orally. It must be remembered that this relationship is reversed when these two drugs are injected subcutaneously in oil (4).

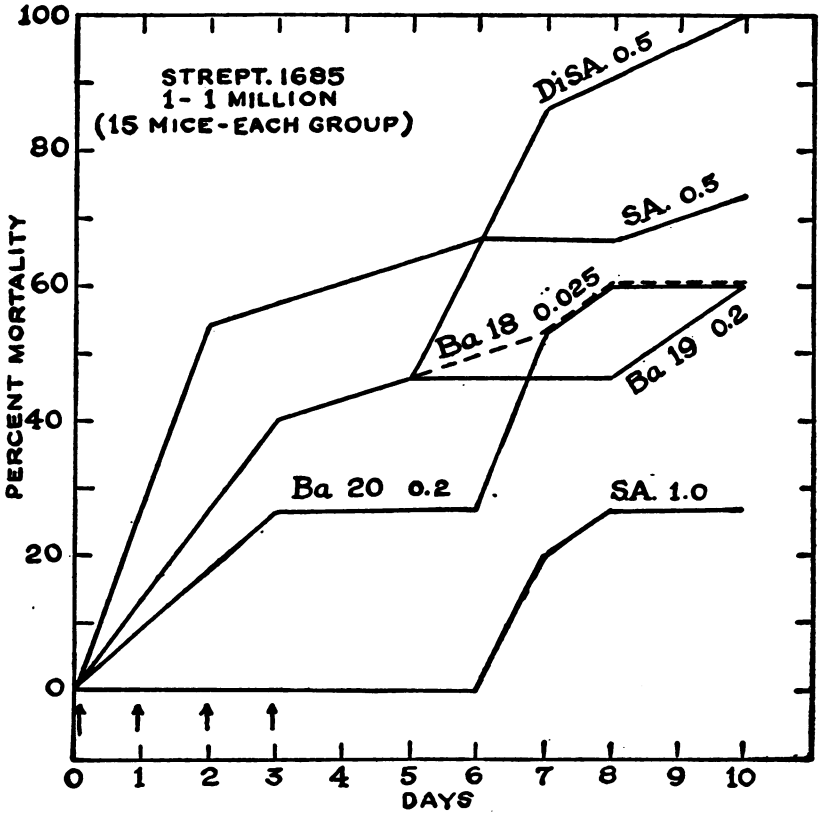


FIGURE 1.—Comparative action of compounds against streptococcus No. 1685 infection in mice. Dosage in grams per kilo is shown on curves and time of administration is indicated by arrows. S. A.=sulfanilamide. DiS.A.=di-sulfanilamide. Ba 18=diamino diphenylsulfone. Ba 19=diacetyl diamino diphenylsulfone. Ba 20=diformaldehyde sulfoxylate diamino diphenylsulfone (see table 1).

From the above observations the following tentative comparison can be made, employing the therapeutic index as representing

$$\frac{\text{Maximum tolerated dose}}{\text{Minimum effective dose}}.$$

It must be emphasized that these comparisons should be established on several species of animals before they can be accepted as a probable index of the behavior in human beings. It must also be pointed out that the animal toxicity of sulfanilamide and related compounds has not revealed certain manifestations, such as fever, dermatitis,

cyanosis, and hematological changes, which have been encountered in human beings.

	Therapeutic index
Sulfanilamide (oral administration) $\left\{\begin{matrix}\text{MTD } 2.5 \\ \text{MED } 0.75\end{matrix}\right\}$	3.3
Di-sulfanilamide (oral administration) $\left\{\begin{matrix}\text{MTD } 8.0 \\ \text{MED } 1.6\end{matrix}\right\}$	5.0
Diamino diphenylsulfone (oral administration) $\left\{\begin{matrix}\text{MTD } 0.15 \\ \text{MED } 0.025\end{matrix}\right\}$	6.0
Formaldehyde sulfoxylate sulfone (subcutaneous administration) $\left\{\begin{matrix}\text{MTD } 3.0 \\ \text{MED } 0.2\end{matrix}\right\}$	15.0
Diacetylsulfone (oral administration) $\left\{\begin{matrix}\text{MTD } >4 \\ \text{MED } 0.2\end{matrix}\right\}$	>20

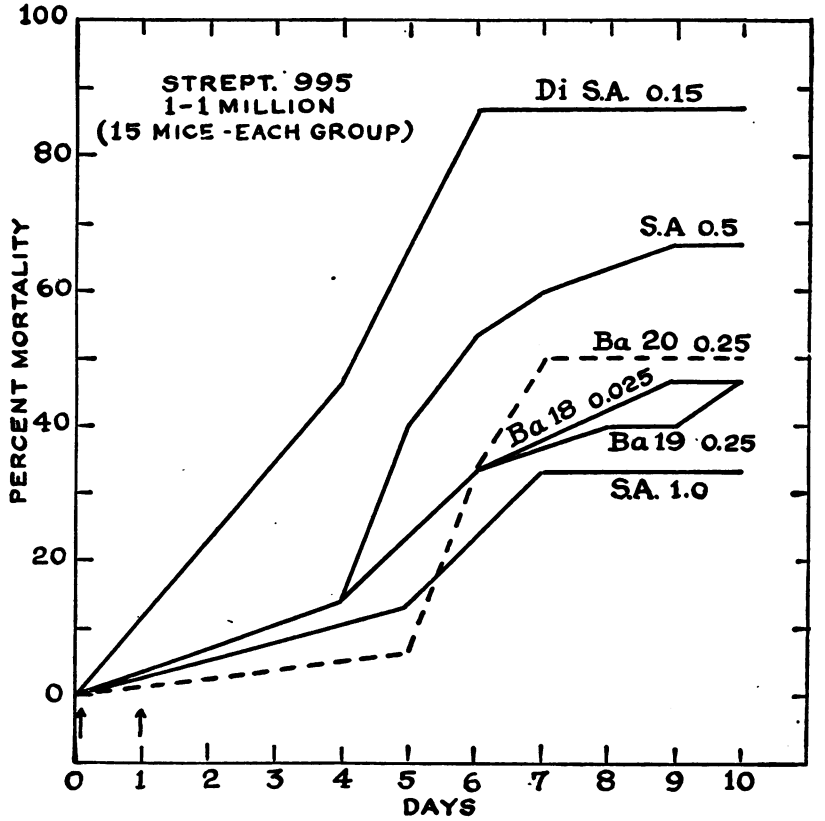


FIGURE 2.—Comparison of compounds against streptococcus No. 995. (For interpretation see figure 1 and table 1.)

EXPERIMENTS ON PNEUMOCOCCI

A number of tests have been made on pneumococci for the purpose of comparing these compounds. Some results are shown in table 2.

Buttle has reported in preliminary experiments (*8*) that the diamino sulfone is superior to sulfanilamide in pneumococcal infections, while

Fourneau (*9*) finds the diacetyl derivatives 10 times as effective as sulfanilamide.

Our experiences indicate that the diamino sulfone as well as its diacetyl and sulfoxylate derivatives are all superior to sulfanilamide. However, we have encountered variations in effectiveness between the three organisms (types I, II, and III) that make comparison difficult. Upon the Type I organism the diamino sulfone was most effective, while the diacetyl derivative was least active. Upon types II and III organisms no appreciable differences were observed among the three compounds. It is believed that these variations represent strain rather than type differences.

TABLE 2.—*Pneumococcus, Mulford Type I, 10^{-6}*

Drug	Therapy	Number of mice	Deaths in days										Mortality
			1	2	3	4	5	6	7	8	9	10	
													Percent
Diamino diphenylsulfone.	0.1 gm per kilo, orally, 5 days	10	---	---	---	3	1	---	1	---	---	---	50
Diacetylsulfone	1.0 gm per kilo, orally, 4 days	10	---	2	5	3	---	---	---	---	---	---	100
Diformaldehyde sulfox. sulfone.	1 gm per kilo, s. c., 5 days	10	---	---	1	5	---	1	1	1	---	1	100
Sulfanilamide	1 gm per kilo, orally, 4 days	10	---	1	6	---	2	1	---	---	---	---	100
Controls	None	10	6	4	---	---	---	---	---	---	---	---	100
	Pneumococcus Mulford II 10^{-6}												
Diamino diphenylsulfone.	0.1 gm per kilo, orally, 4 days	10	---	---	1	1	1	2	3	---	1	1	100
Diacetylsulfone	1.0 gm per kilo, orally, 4 days	10	---	---	1	---	---	---	2	2	---	2	70
Diformaldehyde sulfox. sulfone.	1.0 gm per kilo, s. c., 4 days	10	---	2	---	---	---	1	1	2	2	2	100
Sulfanilamide	1.0 gm per kilo, orally, 4 days	10	---	---	2	---	1	3	---	3	---	1	100
Controls, 10^{-6}	None	10	7	3	---	---	---	---	---	---	---	---	100
10^{-7}	None	2	2	---	---	---	---	---	---	---	---	---	100
10^{-8}	None	2	1	1	---	---	---	---	---	---	---	---	100
	Pneumococcus, Mulford III, 10^{-6}												
Diamino diphenylsulfone.	0.01 gm per kilo, orally, 4 days	10	1	---	---	1	7	---	---	---	---	---	90
Diacetylsulfone	1.0 gm per kilo, orally, 4 days	10	---	1	1	2	4	1	---	---	---	---	90
Diformaldehyde sulfox. sulfone.	1 gm per kilo, s. c., 4 days	10	---	---	2	3	4	1	---	---	---	---	100
Sulfanilamide	1 gm per kilo, orally, 4 days	10	---	2	7	1	---	---	---	---	---	---	100
Controls, 10^{-6}	None	10	8	2	---	---	---	---	---	---	---	---	100
10^{-7}	None	2	2	---	---	---	---	---	---	---	---	---	100
10^{-8}	None	2	---	2	---	---	---	---	---	---	---	---	100

Comparative action of compounds against pneumococci. 0.5 cc of broth culture (10^{-6} dilution) intraperitoneally. Therapy within ½ hour, and repeated daily as indicated.

Our results with the sulfones show that, although marked prolongation of life is brought about in pneumococcal infections, few animals permanently survive as a result of therapy. Similar results with sulfones have been reported by Domagk (*7*). Those sulfone derivatives of low toxicity and more marked action are of greater promise than sulfanilamide against pneumococci, but at their present degree of effectiveness it would seem preferable to consider their use chiefly

in conjunction with serum therapy, where a synergism has been shown to exist (*11*, *12*).

DINITRO SULFONES

As previously mentioned, Buttle and coworkers found the dinitrodiphenyl sulfone to be as active as sulfanilamide, while Fourneau described a preparation (M. P. 238° C.) 10 times as active; Fourneau makes mention of the existence of different isomers of this compound.

The original compound described by Fromm and Wittmann (*10*) melted at 282° C. Following the method of Fromm and Wittmann, a compound of the same melting point was obtained, and in addition some other fractions whose melting points were as follows: 250°, 252°, 305°, and 325° C. All of these preparations possessed only feeble activity against streptococci and pneumococci. The inactivity of our preparations may signify that they are different isomers from those investigated by Buttle and by Fourneau. Further work is required to clarify this phase of the problem.

SUMMARY

Some new derivatives of sulfanilamide and di-sulfanilamide have been prepared and tested against streptococci and pneumococci. Only one compound in this group proved to be slightly superior to sulfanilamide, the sulfanil p-amino-anilide. It has been confirmed that much more favorable results are obtained with di-sulfanilamide when it is injected in oil than when given orally. By mouth di-sulfanilamide has a therapeutic index only twice as good as sulfanilamide.

Comparative studies of toxicity and chemotherapeutic action have been carried out in mice on the diamino diphenylsulfone, first studied by Buttle and coworkers, the acetyl derivative of this compound introduced by Fourneau and coworkers, and the formaldehyde sulfoxylate derivative first prepared by us.

The diamino diphenylsulfone was found to be approximately 30 times as active against streptococci as sulfanilamide, but its high toxicity makes its therapeutic index only two times as favorable.

The formaldehyde sulfoxylate derivative on subcutaneous injection has a therapeutic index approximately five times as good as sulfanilamide orally. This compound is of interest in that it is the first water soluble preparation that we have obtained with high therapeutic activity.

The acetyl derivative possesses a therapeutic index more than six times as high as sulfanilamide against streptococcal infections in mice.

Against pneumococcal infections in mice these three sulfones are all superior to sulfanilamide. However, in mice the action is still considerably less marked than against streptococci; and, while marked

prolongation of life can be achieved, few animals permanently survive pneumococcal infections as a result of therapy.

REFERENCES

(1) Buttle, G. A., Gray, W. H., and Stephenson, D.: Protection of mice against streptococcal and other infections by p-aminobenzene sulfonamide and related substances. Lancet, I: 1286 (1936).

(2) Fourneau, E., Trefouel, J., Nitti, F. and Bovet, D.: Chemotherapie des infections streptococciques par les dérivés du p-aminophenylsulfamide. Compt. rend. Soc. de biol., 122: 258, 652 (1936).

(3) Goissedet, P., Despois, R., Gaillot, P. and Mayer, R.: De l'action du radical sulfamide sur l'infection streptococcique experimentale de la souris. Compt. rend. Soc. de biol., 121: 1082 (1936).

(4) Rosenthal, S. M., Bauer, H., and Branham, S. E.: Studies in chemotherapy. IV. Comparative studies of sulfonamide compounds in experimental pneumococcus, streptococcus, and meningococcus infections. Pub. Health Rep., 52: 662 (1937).

(5) Halpern, B. N., and Mayer, R. L.: Toxicité expérimentale comparée de quelques substances antistreptococciques. Presse méd., 45: 747 (1937).

(6) Gray, W. H., Buttle, G. A., and Stephenson, D.: Derivatives of p-aminobenzenesulfonamide in the treatment of streptococcal infection in mice. Biochem. J., 31: 724 (1937).

(7) Domagk, G.: Weitere Untersuchungen uber die chemotherapeutische Wirkung Sulfonamidhaltiger Verbindungen bei bakteriellen Infektionen. Klin. Wchnschr., 41: 1412 (1937).

(8) Buttle, G. A., Stephenson, D., Smith, S., and Foster, G. E.: Treatment of streptococcal infections in mice with 4:4′ diamino-diphenylsulfone. Lancet, I: 1331 (1937).

(9) Fourneau, E., Trefouel, J., Nitti, F., and Bovet, D.: Action antistreptococcique des dérivés sulfures organiques. Compt. rend. Acad. d. sc., 204: 1763; 205: 299 (1937).

(10) Fromm, E., and Wittmann, J.: Derivate des p-nitrothiophenols. Berichte der Deutsch. Chem. Gesellsch., 41: 2264 (1908).

(11) Gross, P., and Cooper, F. B.: p-aminobenzenesulfonamide and antipneumococcal serum therapy in Type I pneumococcal infections of rats. Proc. Soc. Exper. Biol. & Med., 36: 535 (1937).

(12) Branham, S. E., and Rosenthal, S. M.: Studies in chemotherapy. V. Sulfanilamide, serum, and combined drug and serum therapy in experimental meningococcus and pneumococcus infections in mice. Pub. Health Rep., 52: 685 (1937).

RECENT DEVELOPMENTS IN OUR KNOWLEDGE OF PLAGUE TRANSMISSION *

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Over 30 years have elapsed since the Indian Plague Commission demonstrated that fleas acted as the transmitting agents of bubonic plague. Since then, many investigators have attempted to implicate other blood-sucking parasites, such as bed bugs, lice, and ticks, as vectors of this disease. Thus far there is no evidence to indicate that any insect except the flea is of any importance in the natural dissemination of plague. Most of the work of the Indian Plague Commission was conducted with fleas of the genus *Xenopsylla*. The Commission also investigated the ability of other species to trans-

*Read before the health officers section, League of California Municipalities, San Jose, Calif., Sept. 15, 1937.

mit plague, some of which failed entirely to act as vectors, such as the oriental cat fleas. Regardless of these negative findings there has developed a widespread belief that the bites of practically all fleas that have fed on plague-infected animals are very likely to transmit the disease. Some workers claim that plague transmission by fleas is purely a mechanical process, and so they believe that practically all species of fleas are about equally involved as vectors. However, if one compares the epizootics and epidemics of plague that have occurred throughout the world during the present pandemic, it will be noted that the persistence and the severity of infection have varied greatly according to climatic conditions, which, in turn, have a great influence in determining the prevalence of different species of fleas found on domestic rats, but little effect on the human susceptibility to plague or the extent of the rat population of cities.

That the intensity of plague epidemics is not regulated by the total number of fleas present on rats of a community but rather by the species of fleas with which the rats are infested is well illustrated by the course of the outbreaks in San Francisco, Calif., and Guayaquil, Ecuador. Flea surveys at these two places show that the rats of San Francisco average over 7 fleas per animal, or about 2 more than found on rats at Guayaquil, yet there were only 278 cases of plague reported in the former city in the course of 7 years while there was an average of 364 cases per annum at Guayaquil during the 22 years that the infection was continuously present. Only one species of rodent flea *Xenopsylla cheopis* was found on rats of the South American city while three species, *Nosopsyllus fasciatus*, *Xenopsylla cheopis*, and *Ctenopsyllus segnis*, were present on the San Francisco rats. The *cheopis* index of the latter city was only about half that of Guayaquil, which probably accounts for the mild type of the epidemic at San Francisco. If *fasciatus*, the most prevalent of the three flea species in San Francisco were as efficient a vector of plague as *cheopis*, the California outbreak would have been much more severe. In this connection it may be stated that, insofar as is known, plague epidemics have never occurred in communities where *fasciatus* existed alone and were not associated with *cheopis*.

During the past year an experimental investigation was begun at the Public Health Service laboratory in San Francisco to determine as nearly as possible the infectibility of fleas found on rats and wild rodents when fed on plague-infected guinea pigs and also their ability to transmit the disease to other guinea pigs during the act of feeding. Some interesting observations regarding plague-infected fleas have already been made, but this type of experiment requires a large amount of data before positive conclusions can be formulated; therefore such statements as are made in this paper are only impressions gained from the study thus far, and some of them may have to be modified

later. Only eight species of fleas have been used in the experiments, three from rats, and five from wild rodents. It is hoped that other fleas will be available for investigation during the coming winter months.

By housing each flea in a separate test tube it has been possible to keep a complete individual history chart. In attempting to infect a flea with plague, only one feeding on an infected animal was allowed in most of the experiments. Fleas were fed on the sick guinea pigs just a few hours before the latter were expected to die, as plague septicemia seldom occurs as early as 48 hours before death of a guinea pig. Of 270 fleas fed on guinea pigs at a time when the blood was capable of infecting fleas, 66 were later proved to harbor virulent organisms. Three methods are available for determining whether or not fleas are plague infected: First, by the transmission of the disease by feeding on experimental animals; second, by inoculating experimental animals with the dead fleas; and third, by inoculation with flea feces. The latter procedure is the most important in detecting plague-infected fleas when they are alive.

As might be expected, *Xenopsylla cheopis* were found to be much more susceptible to plague infection than any of the other fleas tested, as 32, or 66 percent, of those fed on infected guinea pigs were later found to harbor the plague bacillus, while only 21 percent of all the other fleas were so infected. In one group of 19 *cheopis*, 79 percent were infected by one feeding on septicemic blood. Four species, *Nosopsyllus fasciatus* from rats, *Diamanus montanus* and *Hoplopsyllus anomalus* from California ground squirrels, and fleas from desert antelope ground squirrels all showed approximately the same degree of susceptibility to plague infection, as about 25 percent of them harbored virulent organisms. An even smaller number, only 10 percent, of mouse fleas, *Ctenopsyllus segnis*, and fleas from *Peromyscus* (white-footed mice) were infected, while it was impossible to demonstrate any infection among 24 *Oropsylla idahoensis* used in the experiments. The latter fleas were obtained from *Citellus beldingi* nests. They are frequently found associated with other fleas on ground squirrels in several States and have been found in regions where plague foci exist. These experimental findings on the susceptibility of fleas to plague infection after feeding on an infected host seem to warrant the conclusion that the proportion of fleas that will subsequently harbor the plague bacillus will vary according to the species involved.

Our attempts to transmit plague by feeding fleas on infected animals and then on healthy ones were entirely futile during the first 2 months of the experiments, although many of the fleas were found to be plague infected. The results were so constantly negative that the personnel engaged in the work began to question the theory that plague was transmitted by the bites of fleas. It was not until the rat fleas,

Xenopsylla cheopis, were included in the study that positive results were obtained.

During the last half of the work, 20 guinea pigs died of plague following the bites of fleas; 16 were infected by *cheopis;* 2 by *fasciatus;* and one each was infected by *Diamanus montanus* and *Hoplopsyllus anomalus*. With the exception of *cheopis* and *Diamanus*, there were not sufficient numbers of infected fleas of each species to justify definite conclusions regarding their abilities to transmit plague when feeding. Only 9 of the 32 infected *cheopis* transmitted the infection; one of them infected 5 animals, of which 3 were infected on 3 successive days, while another infected 3 guinea pigs in 1 day. Had the infected *cheopis* been allowed to feed more frequently, they would have caused many more infections, because when one of these fleas is capable of transmitting plague it will infect an animal practically every time it inserts its proboscis. Although only two guinea pigs were infected by *fasciatus*, the transmissions followed the bites of 2 fleas out of only 5 known to have been infected, which makes a higher percentage of vectors among the *fasciatus* infected than among the *cheopis*. Both of these *fasciatus* were given opportunities to feed on days following that on which their bites were infectious, but neither one would attempt to feed again, thus differing markedly from the much more voracious *cheopis*. As only one of 12 infected *Diamanus montanus* transmitted the disease, it would appear that these fleas are much less efficient vectors of plague than either *cheopis* or *fasciatus*.

In 1914, Bacot and Martin reported that the plague bacillus multiplied in such large masses in the proventriculus of infected fleas that the esophagus became blocked so that blood could not enter the stomach and that, in the attempts of such fleas to feed, blood carrying bacilli was regurgitated and injected back into the host. In every case in which flea bites were infectious during last winter's experiments, except the one transmission by *Hoplopsyllus anomalus*, it was observed that, although the feeding period was longer than normal, or several attempts were made to feed, blood did not enter the stomachs of the fleas. Infected fleas that did not show this evidence of blockage never transmitted plague. In other words, the bites of plague-infected fleas are innocuous as long as blood can freely enter their stomachs. Even some of the fleas with blockage of the stomach did not transmit plague, as 12 of the *cheopis* were observed to be unable to obtain blood, but only 9 of them were vectors. It is possible that, owing to their weakened physical condition at the time when they attempted to feed, their efforts were not strong enough to cause regurgitation.

All *Xenopsylla cheopis* that transmitted plague showed evidence of obstruction to the stomach between the 9th and 26th days after ingesting infected blood. Those that were kept at a temperature of

over 70° F. became blocked earlier than those kept at a mean temperature of 60° F. and so it would appear possible that increased temperatures hasten the multiplication of the plague organism in the proventriculus of *cheopis*. A much longer period elapsed after infection of all other species of fleas before their bites were infectious. *Hoplopsyllus anomalus* did not infect until the 35th day, *Nosopsyllus fasciatus* not until the 55th and 70th days, respectively, and *Diamanus montanus* not until the 84th day. During the interval between their infection and the time when they infected guinea pigs, the 2 *fasciatus* fed 39 times and the *Diamanus montanus* 25 times, securing blood in a normal manner. During the course of the experiments, 25 infected fleas from wild rodents fed 150 times without infecting guinea pigs. From these laboratory experiments it would appear that *cheopis* develop blockage earlier and more readily than do other fleas, which would tend to make them much more dangerous vectors of plague.

During the experiments only two fleas, both *cheopis*, infected guinea pigs on days following the one on which their bites were first infectious. One of them infected animals during a 2-day period and the other over an interval of 10 days; this latter flea was kept at a mean temperature of 60° F. Insofar as these observations go, it would seem that the bites of most plague-infected fleas are infectious for a very short time, probably not more than 1 or 2 days.

The average length of life of the 32 plague-infected *cheopis* was only 16 days, and with one reaching the maximum of 36 days. Under the conditions of these experiments uninfected *cheopis* may live for months; therefore plague is apparently a fatal infection to these fleas. Starvation due to blockage was not the only factor involved in causing their deaths, as many of them died within 4 days of the time they secured blood in a normal manner, while uninfected *cheopis* under observation at the laboratory at the same time would voluntarily starve from 12 to 20 days between normal feedings on human blood.

As regards the effects of plague on other species of fleas, all died within a short time after blockage; but when obstruction did not occur, and prior to its development, some of them survived long periods without any apparent bad effects from the plague organisms in their gastro-intestinal tracts. Plague-infected fleas from *Peromyscus* and desert antelope ground squirrels survived for as long as 35 and 58 days, respectively, or about as long as they could be expected to live under laboratory conditions. These findings indicate that plague-infected fleas, with the exception of *cheopis*, may at times live for months, possibly long enough to carry the infection through the months that rodents are hibernating.

One rather interesting feature in connection with this study was the fact that all of the fleas which transmitted plague were females.

It cannot be positively stated that the bites of male fleas are never infectious, but the fact that 7 of the *cheopis* and 9 of the other fleas were plague-infected males and failed to infect guinea pigs is suggestive at least that male fleas do not readily act as vectors when feeding. None of the male *cheopis* showed evidence of blockage of the stomach, and they survived infection an average of only 14 days, indicating that plague undoubtedly shortened their existence. Two of them died immediately after obtaining blood in a normal manner or under conditions that were never observed among fleas that were uninfected.

Prior to the discovery that fleas may transmit plague when blood is regurgitated because of obstruction of the stomach, the most widely accepted theory of the mechanism by which fleas transmit the disease was one advanced by the Indian Plague Commission. According to this theory, the hosts, both human beings and rodents, were infected when the plague organisms present in the fecal deposits of infected fleas were rubbed into the minute wounds made by the insects' bites. Laboratory experiments have confirmed this theory to the extent that it has been possible to infect animals by rubbing infected feces into the skin at the site of flea bites. It is rather doubtful that man, who acts only as a temporary host for rodent fleas, is very frequently infected in this manner, as fleas seldom deposit feces when feeding and the reactions following the bites of rodent fleas rarely cause itching. On the other hand, it is difficult to understand how it is possible for the natural rodent hosts to escape infection when harboring fleas that are depositing infected feces on their skins over long periods of time. It would seem that the virulent organisms present in the feces would eventually gain access to the body through abrasions or be scratched or forced into the skin by the teeth of the animals in their efforts to rid themselves of parasites.

That virulent bacilli may be constantly present for long periods of time in the feces of plague-infected fleas was well illustrated by one of the *Diamanus montanus* used in the laboratory. This flea survived infection nearly 3 months, and during the last 2 months of its life its feces were inoculated into nine guinea pigs at about weekly intervals. All nine of the animals died of plague, but the guinea pig into which the dead flea itself was injected completely recovered after a short illness.

Fecal inoculation tests that have been conducted thus far seem to indicate that virulent bacteria are more constantly present in the feces of some species of fleas than in others. Plague followed every inoculation of feces deposited by infected *Diamanus montanus*, while less than one-third of the fecal inoculations of *fasciatus* gave positive reactions. Even the feces of infected fleas from desert antelope ground squirrels were found to be twice as infectious as those of *fasciatus*. Out of four fecal tests of an infected flea from *Peromyscus*,

one was followed by plague. The feces of *cheopis* gave positive reactions, but these fleas did not survive long enough to determine whether or not the results would be constant for any great length of time. Insofar as this study has gone, it would appear that when the plague bacillus once becomes established in the gastrointestinal tract of a flea, it continues to exist there until the death of the flea.

In connection with this subject it may be stated that the fecal deposits of different fleas vary in frequency and bulk. *Diamanus montanus* and *fasciatus* were observed to defecate more frequently and in greater amounts than other fleas, some of which did not deposit feces oftener than once every 2 or 3 days. It would seem that the infectiousness of flea feces might depend on two factors—first, the regularity with which virulent organisms are excreted, and, second, the frequency and amount of the fecal deposits. Our observations would indicate that plague-infected California ground squirrel fleas, *Diamanus montanus*, meet these specifications to a greater degree than do any of the other fleas studied.

According to statements in the literature on plague, the virulence of the organism is reduced by its habitat in the gastrointestinal tract of fleas, but our observations do not entirely support these ideas. Several guinea pigs infected by the bites of fleas died in less than 4 days, and the autopsy findings indicated a much greater degree of virulence than is usually evident when guinea pigs die of plague induced in them by other means. Animals infected by the bites of *cheopis* died more quickly than those infected by other fleas, but there was not a sufficient number of the latter infections to indicate that these findings had any particular significance. Inoculations of infected flea feces gave practically the same results as the use of infected tissues or cultures. In a way, the organisms excreted in the feces seemed to be somewhat more virulent than those remaining in the gastrointestinal tracts of the fleas that deposited the feces, as several guinea pigs into which the bodies of fleas were inoculated did not develop infection or recovered from a mild attack, while the feces of the same fleas caused death of other animals. These findings were the only ones indicating that virulence of the plague bacillus might be somewhat reduced in the stomach of fleas.

There has been considerable comment and speculation in recent years regarding the possibility that plague contracted from wild rodents was more likely to cause the pneumonic type of infection than that contracted from domestic rats. In regard to the localization of plague in the lungs it has been found that, since the use of flea inoculation to locate sylvatic plague foci and inoculations made in the course of experiments with infected fleas, autopsy examinations conducted at the Public Health Service laboratory in San Francisco have demonstrated more constant involvement of the lungs than was ever

observed to follow the use of tissue or cultures. When the source of the organisms has been the gastrointestinal tracts of fleas, the macroscopical lesions of the lungs have been as common as those of the spleen. Lung pathology follows injections of the plague bacilli that have resided in domestic rat fleas just as frequently as the inoculations of organisms from wild rodent fleas. It therefore appears that plague bacilli which have developed in fleas are very prone to produce pathological lesions in the lungs of guinea pigs.

Besides the probable dissemination of plague among wild rodents through the agency of bites and infected feces, there are two other ways by which the infection may be spread. It is possible that plague sometimes follows the killing of parasites with the teeth, and the cannibalistic habits of some wild rodents undoubtedly account for a certain amount of plague infection among them. However, it is believed that plague epizootics will always be more widespread and severe when the transmission is caused by fleas that readily infect their hosts when feeding.

From the slight information now available regarding plague-infected fleas, it is possible to gain some idea regarding the reasons why plague outbreaks in different parts of the world have varied considerably. In the warm localities, where *Xenopsylla cheopis* are the only rat fleas found, plague epizootics have frequently had a tendency to subside rather quickly, or in accordance with the experimental observation that plague-infected *cheopis* do not survive very long and therefore cannot carry the infection over great intervals. As the bites of infected *cheopis* may readily transmit plague, the human incidence of infection will usually be rather high where these fleas are abundant.

In colder climates, where the *cheopis* infestation is low but *fasciatus* is present in relatively large numbers, plague outbreaks may be prolonged, with few human cases. The plague epizootic at Seattle offers an extreme example of this type of outbreak. Here plague smoldered slowly among the rats for 10 years, with only three human cases officially reported. Experiments show that *fasciatus* are only slightly susceptible to infection by the plague bacillus, but when infected they may carry the infection for 2 or more months before transmitting it, and so they are apparently capable of prolonging rat epizootics where they are associated with *cheopis*.

The unusually low human incidence of plague from wild rodent sources during the widespread dissemination of the sylvatic epizootics over the western part of the United States can hardly be explained unless it is considered that the parasites involved are rather inefficient vectors as compared with those responsible for domestic rat epizootics

and the associated human epidemics. In the many years that sylvatic plague has existed in the United States, only about 40 human cases have been reported whose source of origin has been ascribed to wild rodents. Many of these cases have been infected by direct contact with the wild rodents and not through the agency of parasites, while the history of other cases indicates that they were infected by exposure to domestic rats. Just how many of these cases were caused by bites of infected fleas is a matter of conjecture, possibly less than half of them.

In California the ground squirrels harbor many more fleas than are ever found on domestic rats. These fleas will attack man when sufficiently starved, but not as readily as rat fleas. A field worker recently reported that, in a very short time, he had collected about 2,000 fleas from the mouths of ground squirrel burrows. This indicates the enormous number of fleas to which an individual may be exposed when walking through ground-squirrel infested fields. Such exposure must have commonly occurred in areas where epizootics have been in progress with very few, if any, cases of human plague developing.

Laboratory observations also support the idea that ground squirrel fleas do not readily transmit plague when feeding. For instance, 11 *Diamanus montanus* collected from *Citellus beecheyi* in San Mateo County, Calif., that were known to harbor the plague bacillus in their gastrointestinal tracts, fed a total of 66 times on guinea pigs with only one bite being infectious. It is possible that more wild rodents contract plague from infected flea feces, cannibalism, and by eating infected fleas than by the bites of fleas. The fact that it has been possible to obtain a large number of positive guinea pig inoculations from pooled specimens of fleas collected from several different rodent hosts, which showed no evidence of being infected themselves, yet which harbored infected fleas, strongly suggests that these infected insects may feed on their hosts without infecting them. If this is true of rodents, one would not expect that human infection would very often follow bites of wild rodent fleas.

In conclusion, it may be said that both epidemiological data and laboratory experiments indicate that the extent to which plague is transmitted depends upon the species of fleas involved. Those fleas which are most susceptible to plague infection of the gastrointestinal tract and to the bacterial obstruction of the esophagus are the most dangerous vectors. As long as the flow of blood to the stomach is not blocked, infected fleas may feed on their hosts without their bites being infectious; but there seems to be danger of infection from the virulent organisms present in the feces of all plague-infected fleas.

DEATHS DURING WEEK ENDED DEC. 25, 1937

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

	Week ended Dec. 25, 1937	Corresponding week, 1936
Data from 86 large cities of the United States:		
Total deaths	8,631	8,548
Average for 3 prior years	9,049	
Total deaths, first 51 weeks of year	437,067	438,469
Deaths under 1 year of age	509	530
Average for 3 prior years	569	
Deaths under 1 year of age, first 51 weeks of year	27,897	28,191
Data from industrial insurance companies:		
Policies in force	69,971,632	68,974,371
Number of death claims	12,424	10,869
Death claims per 1,000 policies in force, annual rate	9.3	8.2
Death claims per 1,000 policies, first 51 weeks of year, annual rate	9.7	9.7

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) is to be interpreted to mean that no cases or deaths occurred, while leaders (.....) indicate that cases or deaths may have occurred although none was reported.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended Jan. 1, 1938, and Jan. 2, 1937

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937
New England States:								
Maine	4	-----	6	3	35	8	1	0
New Hampshire	-----	-----	-----	-----	103	1	0	0
Vermont	-----	-----	-----	-----	179	-----	0	0
Massachusetts	3	5	-----	-----	96	654	2	2
Rhode Island	-----	1	-----	-----	-----	45	0	0
Connecticut	6	1	6	18	9	157	0	1
Middle Atlantic States:								
New York	42	28	[1] 17	[1] 487	189	220	12	6
New Jersey	20	13	20	26	675	278	2	4
Pennsylvania	39	50	-----	-----	3,330	59	5	5
East North Central States:								
Ohio	60	56	35	48	448	24	8	8
Indiana	26	21	35	322	88	5	0	1
Illinois	36	59	29	455	1,299	22	1	9
Michigan	23	41	3	12	647	41	1	2
Wisconsin	7	7	29	164	223	23	0	0
West North Central States:								
Minnesota	1	6	-----	7	7	21	1	0
Iowa	5	2	7	45	15	4	0	1
Missouri	50	23	67	189	1,644	8	2	2
North Dakota	2	-----	-----	-----	1	3	1	0
South Dakota	1	-----	1	9	-----	3	1	0
Nebraska	-----	2	-----	-----	4	2	1	2
Kansas	8	10	4	13	53	4	1	0
South Atlantic States:								
Delaware [2]	-----	2	-----	2	2	82	0	0
Maryland [2]	6	9	22	25	11	164	3	1
District of Columbia	5	5	4	3	8	11	0	2
Virginia	34	25	-----	-----	163	67	3	13
West Virginia	12	13	22	64	43	9	3	6
North Carolina [2]	35	61	18	46	558	38	2	5
South Carolina	3	3	311	400	249	13	0	0
Georgia [2]	10	17	-----	77	-----	-----	0	0
Florida [2]	30	11	2	4	23	1	3	12
East South Central States:								
Kentucky	6	15	22	57	127	9	5	32
Tennessee	25	25	120	108	251	31	1	5
Alabama [2]	17	19	371	121	41	2	11	7
Mississippi [2]	22	7	-----	-----	-----	-----	1	0

See footnotes at end of table.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended Jan. 1, 1938, and Jan. 2, 1937—Continued

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937
West South Central States:								
Arkansas	22	5	192	46	64	----	0	0
Louisiana [2]	8	15	47	23	----	14	3	1
Oklahoma [4]	15	3	114	72	----	3	4	4
Texas [3]	45	55	444	362	23	127	2	5
Mountain States:								
Montana	----	3	----	282	2	3	0	0
Idaho [2]	----	2	5	30	6	89	0	3
Wyoming	----	----	----	300	----	3	0	2
Colorado	6	5	----	----	96	7	1	2
New Mexico	8	4	5	15	61	1	0	0
Arizona	2	----	99	65	2	50	0	0
Utah [2]	4	----	----	----	57	80	0	1
Pacific States:								
Washington	7	5	----	2	4	17	0	0
Oregon	1	----	21	47	15	6	1	0
California	40	58	38	44	48	42	1	5
Total	696	692	2,107	3,993	10,899	2,451	83	149
52 weeks	27,892	28,771	292,271	160,030	302,242	284,033	5,390	7,411

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid and paratyphoid fevers		Whooping cough
	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938
New England States:									
Maine	0	0	20	11	0	0	1	0	56
New Hampshire	0	0	17	17	0	0	0	0	8
Vermont	0	0	2	3	0	0	0	0	16
Massachusetts	0	0	252	176	0	0	3	0	89
Rhode Island	0	0	18	37	0	0	0	0	25
Connecticut	0	0	69	51	0	0	0	2	24
Middle Atlantic States:									
New York	1	0	449	610	0	35	9	4	253
New Jersey	0	1	114	125	0	0	3	2	117
Pennsylvania	1	0	430	530	0	0	6	11	210
East North Central States:									
Ohio	0	4	332	380	1	8	4	5	110
Indiana	0	0	134	194	69	7	1	2	12
Illinois	4	4	566	437	44	2	3	12	76
Michigan	4	1	564	520	0	0	1	11	200
Wisconsin	1	0	170	228	1	12	0	1	103
West North Central States:									
Minnesota	2	0	98	111	47	12	1	1	24
Iowa	0	0	141	84	19	12	0	3	15
Missouri	1	3	255	174	36	41	11	6	169
North Dakota	0	0	18	65	7	21	0	0	13
South Dakota	1	0	30	33	3	0	0	0	9
Nebraska	1	0	33	43	0	1	0	2	3
Kansas	0	2	233	270	7	21	1	1	47
South Atlantic States:									
Delaware [2]	0	0	14	12	0	0	1	0	5
Maryland [2]	0	0	35	68	0	0	5	3	46
District of Columbia	0	0	15	15	0	0	1	0	8
Virginia	0	1	67	38	0	0	9	7	85
West Virginia	0	1	44	41	0	0	1	5	12
North Carolina [3]	0	0	53	56	0	0	8	4	192
South Carolina	0	1	2	5	0	0	1	1	14
Georgia [3]	0	1	19	13	0	0	1	2	22
Florida [3]	1	2	20	12	0	0	4	0	4

See footnotes at end of table.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended Jan. 1, 1938, and Jan. 2, 1937—Continued

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid and paratyphoid fevers		Whooping cough
	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938	Week ended Jan 2, 1937	Week ended Jan. 1, 1938	Week ended Jan. 2, 1937	Week ended Jan. 1, 1938
East South Central States:									
Kentucky	1	1	55	49	0	0	0	1	32
Tennessee	3	0	36	44	5	0	2	2	35
Alabama [2]	1	1	10	19	6	0	4	5	6
Mississippi [2]	4	2	15	19	0	0	2	2	----
West South Central States:									
Arkansas	3	1	46	4	5	0	10	3	38
Louisiana [2]	0	0	15	14	0	0	6	12	7
Oklahoma [4]	0	0	42	16	3	4	1	4	4
Texas [3]	0	1	75	75	2	0	9	11	142
Mountain States:									
Montana	0	0	16	71	10	24	3	2	34
Idaho [2]	0	0	21	19	34	17	0	3	60
Wyoming	0	0	27	28	1	1	0	0	5
Colorado	1	1	31	25	8	1	0	1	4
New Mexico	0	0	12	24	0	0	4	5	15
Arizona	0	0	14	7	0	0	2	0	9
Utah [2]	0	0	100	19	0	0	0	0	10
Pacific States:									
Washington	0	1	40	36	11	5	0	1	73
Oregon	0	0	37	44	6	22	1	0	10
California	5	4	171	215	20	5	10	14	179
Total	35	33	4,977	5,087	345	251	129	151	2,630
52 weeks	9,451	4,506	223,425	232,990	11,110	7,547	15,059	14,661	----

[1] New York City only.
[2] Week ended earlier than Saturday.
[3] Typhus fever, week ended Jan. 1, 1938, 32 cases, as follows: North Carolina, 2; Georgia, 15; Florida, 2; Alabama, 8; Texas, 5.
[4] Figures for 1937 are exclusive of Oklahoma City and Tulsa.

SUMMARY OF MONTHLY REPORTS FROM STATES

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

State	Meningococcus meningitis	Diphtheria	Influenza	Malaria	Measles	Pellagra	Poliomyelitis	Scarlet fever	Smallpox	Typhoid fever
November 1937										
Arizona	1	37	232	2	22	----	0	30	1	5
Hawaii Territory	0	16	85	----	35	----	0	----	0	5
December 1937										
Delaware	0	1	----	----	7	----	0	54	0	1

November 1937

Arizona:	Cases
Chicken pox	92
Dysentery	64
Mumps	15
Trachoma	16
Whooping cough	38
Hawaii Territory:	
Chicken pox	49
Conjunctivitis, follicular	277
Dysentery (amoebic)	1
Hookworm disease	5

November 1937—Continued

Hawaii Territory—Con.	Cases
Impetigo contagiosa	27
Jaundice, infectious	24
Leprosy	5
Mumps	14
Ophthalmia neonatorum	4
Paratyphoid fever	1
Septic sore throat	20
Trachoma	6
Typhus fever	4
Whooping cough	23

December 1937

Delaware:	Cases
Anthrax	1
Chicken pox	136
German measles	9
Mumps	42
Tularaemia	1
Whooping cough	52

WEEKLY REPORTS FROM CITIES

City reports for week ended Dec. 25, 1937

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. Weekly reports are received from about 700 cities, from which the data are tabulated and filed for reference.

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	264	1,205	139	1,193	915	1,464	13	376	29	931	----
Current week [1]	139	254	63	2,035	750	1,099	24	327	21	635	----
Maine:											
Portland	0	----	0	1	2	1	0	0	0	6	26
New Hampshire:											
Concord	0	----	0	9	1	0	0	0	0	2	12
Manchester	0	----	0	0	1	6	0	0	0	0	7
Nashua	0	----	----	2	----	0	0	----	0	0	7
Vermont:											
Barre	----	----	----	----	----	----	----	----	----	----	----
Burlington	0	----	0	0	0	0	0	0	0	4	7
Rutland	0	----	0	2	0	0	0	0	0	2	11
Massachusetts:											
Boston	0	----	2	43	25	51	0	9	0	5	233
Fall River	2	----	0	0	2	0	0	1	0	16	28
Springfield	0	----	0	2	4	10	0	2	0	10	44
Worcester	0	----	0	1	2	7	0	3	0	6	36
Rhode Island:											
Pawtucket	0	----	0	0	0	0	0	0	0	0	9
Providence	0	----	0	2	3	21	0	5	0	13	81
Connecticut:											
Bridgeport	0	----	0	1	0	8	0	1	0	0	31
Hartford	0	----	0	0	2	20	0	1	0	3	26
New Haven	0	----	0	0	1	2	0	1	0	3	35
New York:											
Buffalo	0	----	1	2	17	19	0	6	0	21	146
New York	25	6	4	18	142	127	0	75	2	87	1,535
Rochester	0	----	0	0	7	5	0	1	1	0	85
Syracuse	0	----	0	0	4	7	0	0	0	6	52
New Jersey:											
Camden	0	1	1	0	2	4	0	0	0	1	42
Newark	0	4	0	1	9	10	0	2	0	15	80
Trenton	1	----	0	80	5	1	0	1	0	3	42
Pennsylvania:											
Philadelphia	4	2	1	52	35	88	0	26	5	20	540
Pittsburgh	0	6	2	228	27	28	0	5	0	13	170
Reading	0	----	0	1	0	4	0	2	0	2	34
Scranton	0	----	----	10	----	1	0	----	0	2	----
Ohio:											
Cincinnati	1	----	2	3	14	20	0	4	0	4	145
Cleveland	1	10	1	110	13	42	0	13	0	20	173
Columbus	2	----	0	4	6	2	0	4	0	1	80
Toledo	1	2	1	34	8	5	0	3	0	4	90
Indiana:											
Anderson	0	----	0	0	5	3	1	0	0	4	10
Fort Wayne	1	----	0	2	2	5	0	1	1	0	24
Indianapolis	5	----	3	7	20	16	0	3	0	0	119
South Bend	0	----	0	1	5	5	0	0	0	0	12
Terre Haute	1	----	0	2	0	0	0	0	0	0	23
Illinois:											
Alton	0	----	0	17	0	5	0	1	0	1	9
Chicago	11	11	3	381	52	173	0	41	0	26	690
Elgin	0	----	0	0	1	5	0	0	0	3	6
Moline	0	----	0	17	1	6	0	0	0	0	8
Springfield	0	----	0	14	0	4	0	0	0	0	15
Michigan:											
Detroit	9	3	1	173	32	77	1	7	2	54	257
Flint	0	----	0	2	4	28	0	0	0	5	21
Grand Rapids	0	----	0	1	3	14	0	0	0	4	38
Wisconsin:											
Kenosha	0	----	0	2	0	2	0	0	0	9	11
Madison	0	----	0	1	3	8	0	1	0	1	36
Milwaukee	0	----	0	73	12	15	0	2	0	20	123
Racine	----	----	----	----	----	----	----	----	----	----	----
Superior	0	----	0	0	0	0	0	0	0	1	9

[1] Figures for Barre, Vt., Racine, Wis., and Boise, Idaho, estimated; reports not received.

City reports for week ended Dec. 25, 1937—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Minnesota:											
Duluth	0	-------	0	0	3	2	0	0	1	6	19
Minneapolis	0	-------	0	0	9	19	0	2	0	0	101
St. Paul	0	-------	0	2	8	3	9	0	0	3	62
Iowa:											
Davenport	1	-------	-------	3	-------	0	1	-------	0	0	-------
Des Moines	2	-------	-------	0	-------	49	1	-------	0	0	39
Sioux City	0	-------	-------	0	-------	2	0	-------	0	0	-------
Waterloo	0	-------	-------	0	-------	6	0	-------	0	0	-------
Missouri:											
Kansas City	1	2	1	9	8	20	0	4	0	1	120
St. Joseph	0	-------	0	1	5	4	0	0	0	0	21
St. Louis	12	1	0	485	4	53	3	4	0	3	208
North Dakota:											
Fargo	0	-------	0	0	1	0	1	0	0	1	10
Grand Forks	0	-------	-------	0	-------	8	0	-------	0	0	-------
Minot	0	-------	0	0	0	0	0	0	0	9	6
South Dakota:											
Aberdeen	0	-------	-------	0	-------	0	0	-------	0	0	-------
Sioux Falls	0	-------	0	0	0	0	0	0	0	0	15
Nebraska:											
Lincoln	1	-------	-------	0	-------	6	0	-------	0	0	-------
Omaha	0	-------	0	0	3	2	0	1	0	0	59
Kansas:											
Lawrence	0	-------	0	0	1	2	0	0	0	4	8
Topeka	0	-------	0	0	1	2	0	0	0	14	8
Wichita	0	-------	0	2	2	1	0	0	0	0	21
Delaware:											
Wilmington	0	-------	0	0	3	5	0	0	0	3	43
Maryland:											
Baltimore	8	-------	9	0	38	21	0	20	0	45	302
Cumberland	0	-------	1	0	1	0	0	0	0	0	16
Frederick	0	-------	0	0	0	0	0	0	0	0	6
District of Columbia:											
Washington	5	5	0	8	7	8	0	8	1	3	135
Virginia:											
Lynchburg	5	-------	0	0	4	0	0	1	0	2	15
Richmond	0	-------	2	0	7	5	0	1	0	0	45
Roanoke	1	-------	0	2	0	0	0	0	0	0	15
West Virginia:											
Charleston	0	-------	0	2	1	1	0	0	0	0	7
Huntington	0	-------	-------	18	-------	2	0	-------	0	0	-------
Wheeling	0	-------	0	0	4	5	0	2	0	3	22
North Carolina:											
Gastonia	0	1	-------	0	-------	0	0	-------	0	1	-------
Raleigh	0	-------	0	0	1	0	0	0	0	11	9
Wilmington	0	-------	0	0	3	0	0	0	0	2	20
Winston-Salem	0	-------	0	0	0	1	0	2	0	11	13
South Carolina:											
Charleston	0	23	2	5	10	2	0	0	4	0	34
Florence	0	-------	0	0	3	0	0	0	0	0	10
Greenville	0	-------	0	0	4	1	0	0	0	7	17
Georgia:											
Atlanta	4	43	3	39	12	9	0	4	0	3	81
Brunswick	0	-------	0	0	0	0	0	1	0	0	4
Savannah	1	60	2	0	2	3	0	2	0	0	37
Florida:											
Miami	2	1	0	20	2	2	0	1	0	0	28
Tampa	1	1	1	0	1	0	0	0	0	3	28
Kentucky:											
Covington	0	1	0	0	2	1	0	0	0	1	22
Lexington	0	-------	0	2	4	1	0	1	0	0	18
Tennessee:											
Knoxville	0	1	1	1	3	1	0	3	0	0	22
Memphis	2	2	0	105	9	4	0	6	0	3	81
Nashville	0	-------	0	2	9	5	0	0	0	2	52
Alabama:											
Birmingham	2	4	3	15	9	2	0	2	0	0	57
Mobile	1	-------	2	1	5	1	0	1	0	0	33
Montgomery	1	1	-------	0	-------	1	0	-------	0	0	-------

City reports for week ended Dec. 25, 1937—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	18	0	0	0	1	0	0	
Louisiana:											
Lake Charles	0		0	0	0	0	0	0	0	0	4
New Orleans	2	42	6	1	20	2	0	5	3	7	177
Shreveport	0		1	0	5	0	0	3	0	0	63
Oklahoma:											
Oklahoma City	1		0	0	7	3	0	1	0	0	48
Tulsa	1			0		9	2		0	1	
Texas:											
Dallas	1	2	2	0	7	7	0	0	0	3	68
Fort Worth	3		0	0	4	15	0	0	0	0	29
Galveston	0		0	0	5	1	0	2	0	0	21
Houston	6		0	1	14	4	0	1	0	0	97
San Antonio	3		1	0	9	1	0	2	0	0	57
Montana:											
Billings	0		0	2	1	0	0	0	0	0	9
Great Falls	0		0	0	1	0	5	0	0	8	8
Helena	0		0	0	0	3	0	0	0	4	1
Missoula	0		0	0	1	0	0	0	0	0	4
Idaho:											
Boise											
Colorado:											
Colorado Springs	0		0	0	1	2	0	0	0	5	11
Denver	8		3	65	8	18	0	5	0	4	81
Pueblo	0		0	2	1	1	0	0	0	1	10
New Mexico:											
Albuquerque	0		0	48	1	3	0	2	0	0	27
Utah:											
Salt Lake City	0		0	0	3	13	0	0	0	0	44
Washington:											
Seattle	1		0	0	4	4	0	7	0	31	91
Spokane	0		0	0	4	1	0	1	0	6	30
Tacoma	0		0	0	1	3	1	0	0	0	14
Oregon:											
Portland	0	2	0	2	0	7	1	3	0	0	79
Salem	0	1		0		1	0		0	0	
California:											
Los Angeles	8	17	3	4	30	34	0	17	1	27	336
Sacramento	4		0	0	2	0	0	0	0	14	18
San Francisco	0		0	0	10	8	0	5	0	31	172

State and city	Meningococcus meningitis		Poliomyelitis cases	State and city	Meningococcus meningitis		Poliomyelitis cases
	Cases	Deaths			Cases	Deaths	
Maine:				Maryland:			
Portland	0	1	0	Baltimore	1	0	0
Vermont:				Kentucky:			
Rutland	0	1	0	Covington	1	1	0
New York:				Tennessee:			
Buffalo	3	0	0	Memphis	1	0	1
New York	2	0	0	Alabama:			
Pennsylvania:				Birmingham	3	0	0
Philadelphia	1	0	0	Arkansas:			
Pittsburgh	2	0	0	Little Rock	0	1	0
Ohio:				Louisiana:			
Cincinnati	3	2	0	New Orleans	2	0	0
Cleveland	2	1	0	Shreveport	0	1	0
Columbus	0	1	0	Texas:			
Illinois:				Houston	0	1	0
Chicago	2	0	1	Colorado:			
Michigan:				Pueblo	0	1	0
Detroit	0	0	3	Oregon:			
Minnesota:				Portland	1	0	0
St. Paul	0	0	1	California:			
Missouri:				Los Angeles	1	0	0
Kansas City	0	1	1				

Encephalitis, epidemic or lethargic.—Cases: New York, 2; Trenton, 1; Chicago, 1.
Pellagra.—Cases: Atlanta, 5; Savannah, 8; Tampa, 1; San Francisco, 1.
Typhus fever.—Cases: Atlanta, 1; Miami, 1.

FOREIGN AND INSULAR

CZECHOSLOVAKIA

Communicable diseases—September 1937.—During the month of September 1937, certain communicable diseases were reported in Czechoslovakia, as follows:

Disease	Cases	Deaths
Anthrax	6	
Cerebrospinal meningitis	3	3
Chicken pox	39	2
Diphtheria	2,888	110
Dysentery	575	51
Influenza	49	2
Lethargic encephalitis	17	2
Malaria	345	
Paratyphoid fever	26	
Poliomyelitis	34	5
Puerperal fever	20	5
Scarlet fever	2,184	20
Trachoma	64	
Tularaemia		1
Typhoid fever	1,124	69

JAMAICA

Communicable diseases—4 weeks ended December 25, 1937.—During the 4 weeks ended December 25, 1937, cases of certain communicable diseases were reported in Kingston, Jamaica, and in the island outside of Kingston, as follows:

Disease	Kingston	Other localities
Chicken pox	6	21
Dysentery	[1] 9	[2] 4
Erysipelas	2	2
Meningitis		1
Puerperal fever	1	1
Scarlet fever		2
Tuberculosis	37	68
Typhoid fever	3	53

[1] Includes 7 cases of amoebic dysentery.
[2] Includes 3 cases of amoebic dysentery.

TASMANIA

Vital statistics—Year 1936.—The following are vital statistics for Tasmania for the year 1936:

	Number	Rate per 10,000 inhabitants
Number of births	4,581	[1] 19.84
Deaths	2,387	103.4
Deaths under 1 year of age	227	[2] 49.6
Deaths from:		
Accident or negligence	120	5.2
Cancer	283	12.3
Diphtheria and croup	20	.9
Homicide	6	.3
Influenza	7	.3
Measles	7	.3
Scarlet fever	6	.3
Suicide	22	.9
Syphilis	10	.4
Tubercular diseases	135	5.8
Typhoid fever	1	
Whooping cough	11	.5

[1] Per 1,000 inhabitants.
[2] Per 1,000 births.

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 December 31, 1937, pages 1952-1965. Similar cumulative tables will appear in future issues of the PUBLIC HEALTH REPORTS for the last Friday of each month.

Cholera

China—Shanghai.—Cholera has been reported in Shanghai, China, as follows: Week ended December 18, 1937, 3 cases; week ended December 25, 1937, 3 cases.

French Indochina.—Cholera has been reported in French Indochina, for the week ended December 25, 1937, as follows: Annam, 5 cases; Hanoi, 2 cases; Tonkin Province, 84 cases.

Plague

Belgian Congo—Dera.—During the week ended December 25, 1937, 2 cases of plague were reported in Dera, Lake Albert region, Belgian Congo.

Dutch East Indies—Java—Pasoeroean.—During the week ended November 6, 1937, 3 cases of plague with 3 deaths were reported in the mountain region near Pasoeroean, Java, Dutch East Indies.

Hawaii Territory—Island of Hawaii—Hamakua District.—Plague-infected rats have been found in Hamakua District, Island of Hawaii, Hawaii Territory, as follows: Hamakua Mill Sector—December 22, 1937, 1 rat: Paauhau Sector—December 20, 1 rat; December 22, 1 rat.

Peru.—During the month of November 1937, plague has been reported in Peru, as follows: Ancash Department, 3 cases, 3 deaths; Lima Department, 8 cases, 5 deaths; Libertad Department, 1 case.

Smallpox

Brazil—Santos.—During the week ended November 27, 1937, 1 case of smallpox was reported in Santos, Brazil.

Typhus Fever

Chile.—During the period October 3–23, 1937, 198 cases of typhus fever with 40 deaths were reported in Chile, among which were the following: Santiago Province, 84 cases, 28 deaths; Valparaiso Province—Baron, 10 cases; Ninhue, 17 cases, 2 deaths; Puerto, 1 case; Quinta Normal, 9 cases, 4 deaths; Renca, 8 cases; San Miguel, 13 cases, 2 deaths.

Yellow Fever

Nigeria—Enugu.—On December 21, 1937, 1 suspected case of yellow fever was reported in Enugu, Nigeria.

Sudan (French)—San.—On December 22, 1937, 1 case of yellow fever was reported in San, French Sudan.

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