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COMPARISON OF THE SPIROCHETICIDAL ACTIVITY OF ARSPHENAMINES AND PHENARSINES (ARSENOXIDES) IN EXPERIMENTAL SYPHILIS [1]

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INTRODUCTION

Previous reports by the author (*1–5*) on the therapeutic activity of the arsphenamines were concerned entirely with neoarsphenamine. These studies demonstrated that two brands of neoarsphenamine varying in trypanocidal activity were remarkably uniform in spirocheticidal activity in experimental syphilis in rabbits (*1, 2, 4*) and were equally effective in the routine therapy of syphilis in man (*3*). Evidence was presented also which proved that the 7 American brands of neoarsphenamine (*5*), 17 different lots, were uniformly active in curing experimental syphilis in rabbits.

The results recorded were in agreement with the observation of Voegtlin and Dyer (*6*) that the sterilizing action of the arsphenamines was identical in terms of the absolute amount of arsenic used, irrespective of the type of the arsphenamine. The progressive increase in the percentage of rabbits cured of the experimental infection which followed the increased dosage also confirmed the Voegtlin-Dyer thesis that there is an essential relation between the dose and the sterilizing effect of the arsphenamines in experimental syphilis.

These observations indicate that all sulfarsphenamines, which have approximately the same arsenic content as neoarsphenamine, would be uniformly active and as effective as neoarsphenamine in curing experimental syphilis in rabbits. It was to test the theses of Voegtlin and Dyer, as they applied to the several different American brands of sulfarsphenamine, that the chemotherapeutic activity study was continued. The increased use of the arsenoxide type of arsenical in the therapy of syphilis suggested that the study be broadened to include

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the arsenoxide type of products. Thus, the spirocheticidal activity of the arsphenamines, neoarsphenamine, and sulfarsphenamine could be compared with that of the phenarsine type, dichlorophenarsine hydrochloride, and oxophenarsine hydrochloride.

REVIEW OF LITERATURE

Neoarsphenamine (*6*, *7*, *8*, *10*, *11*) has been reported by numerous investigators to be an effective spirocheticidal agent. The effective single curative dose in experimental syphilis in rabbits has been reported as varying from 20 to 40 mg. per kilogram. The single outstanding example of ineffectiveness that we have found was that given by Tatum and Cooper (*9*). They stated that the effective dose of neoarsphenamine was 180 mg. per kilogram of body weight.

Comparatively little experimental work has been done with sulfarsphenamine (*6*, *11*), but the reports in general indicate that sulfarsphenamine and neoarsphenamine are equally spirocheticidal. Voegtlin et al. (*6*) in their original investigation of the American product indicated that sulfarsphenamine was as effective as arsphenamine and neoarsphenamine in terms of the amount of arsenic injected, but that the "index of sterilization" was more favorable for sulfarsphenamine.

In the review of the pharmacology of arsphenamine, Voegtlin (*12*) suggested that if arsenoxide is really the parasiticidal substance formed from arsphenamine it might appear more desirable to use arsenoxide in therapeutics instead of arsphenamine. He reported, however, that the margin of safety as established by the chemotherapeutic index is somewhat lower in the case of arsenoxide than in the case of arsphenamine. The work of Dale was referred to as further evidence of the superiority of the arsphenamines to the arsenoxides.

Tatum and Cooper (*9*) in their restudy of arsenoxide reported that the chemotherapeutic index of arsenoxide, 1.66, was distinctly greater than that of neoarsphenamine, 1.11, in experimental syphilis in rabbits. They reported that the single sterilizing dose of arsenoxide was no more than 6 mg. per kilogram and that of neoarsphenamine was 180 mg. per kilogram, a ratio of 1:30.

Because the results reported by Tatum and Cooper contradicted those of other workers, especially the results of the spirocheticidal activity of neoarsphenamine, Raiziss and Severac (*8*) decided that reinvestigation was indicated. In their study, the chemotherapeutic index of arsenoxide, 0.92, was definitely unfavorable compared with that of neoarsphenamine, 5.0. The single sterilizing dose of arsenoxide was 12 mg. per kilogram and that of neoarsphenamine 40 mg. per kilogram or a ratio of 1:3.3.

Gruhzit (*10*), "because of the contradictory opinions," also undertook a study to ascertain the value of arsenoxide in the treatment of spirochetosis. He found that the sterilizing indices for mapharsen and neoarsphenamine in single doses in experimental syphilis were approximately equal, 4 and 3.75, respectively. In his study, the sterilizing dose of mapharsen was 3.5 mg. and that of neoarsphenamine 40 mg., a ratio of 1:12.

Kolmer, Kast, and Rule (*11*) demonstrated that neoarsphenamine (five different brands) and sulfarsphenamine (one brand) were equally spirocheticidal and cured experimental infection at 20 mg. per kilogram. Mapharsen, being effective at 5 mg. per kilogram, is four times as efficient as the two arsphenamines.

In a revaluation of their previous studies, Eagle, Hogan, and Kemp (*13*) reported that the curative dose of mapharsen was approximately 7 mg. per kilogram.

In a preliminary study, Alture-Werber et al. (*14*) reported that clorarsen (dichlorophenarsine hydrochloride) was at least as effective in its spirocheticidal action as mapharsen.

Although arsenoxide was generally accepted as being the active principle of the arsphenamines and the basis of the oxidation-reduction theory of Voegtlin (*15, 16, 17*), it was not until 1932 that definite evidence was offered to support this thesis. In that year Rosenthal (*18*) developed the color reaction with β-naphthoquinone as a test for arsenoxide. Using this reaction, he demonstrated arsenoxide in the liver after injection of arsphenamine, and in the kidneys after injection of neoarsphenamine. Negative tests obtained in some tissues, even after injection with maximum doses, do not mean that arsenoxide is absent but that it is present in concentrations too low to be detected by this reaction. Consequently, the test cannot be used, as was suggested by Gruhzit (*10*), as the method of estimating the percentage of arsenoxide formed in vivo following injection with arsphenamines.

It is apparent that there is still considerable disagreement with regard to the relative merits of the arsphenamines and the phenarsines in curing experimental syphilis in rabbits. Considered opinion is that arsenoxide is approximately five times as effective as neoarsphenamine or sulfarsphenamine. However, arsenoxide has been demonstrated by practically every investigation to be many times more toxic than the arsphenamines. On the basis of the toxicity requirements (*19*) for the control of the trivalent organic arsenicals, the arsenoxides, dichlorophenarsine and oxophenarsine, are at least 16 times more toxic than neoarsphenamine and sulfarsphenamine.

EXPERIMENTAL PROCEDURE

The experimental procedure followed, described in previous reports (*4*, *5*), is the tissue-transfer method and is the generally accepted procedure for the evaluation of the chemotherapeutic activity of antisyphilitic drugs in experimental syphilis in rabbits. The sterilizing or curative efficiency of the drugs was based upon the minimal single dose of the drug which cured rabbits with well-developed primary syphilitic lesions.

The observation periods of the several stages, pretreatment, posttreatment, and transfer periods, previously defined (*5*), are stated in the protocol. The validity of studies in experimental syphilis in rabbits is definitely modified by the extent of these observation periods (*5*). In the evolution of the procedure for the study of experimental syphilis in rabbits, workers have repeatedly emphasized the absolute necessity of adequate observation periods (*5*, *20*).

The spirocheticidal activities of 5 lots of neoarsphenamine, 6 lots of sulfarsphenamine, 6 lots of dichlorophenarsine hydrochloride, and 5 lots of oxophenarsine hydrochloride, as determined by the sterilizing or curative efficiency in experimental syphilis, is recorded in the protocol. This report consists of 6 independent tests, series 10 to 15, inclusive, to which is appended the spirocheticidal activity of the 17 lots of neoarsphenamine previously reported (*5*). In 5 of the 6 series of this report and in the 9 series of the previous report, neoarsphenamine, brand E, was used as the control product.

The therapeutic efficacy of the 6 lots of sulfarsphenamine, representing 4 American brands, is detailed in series 10, 11, and 13. The curative dose of sulfarsphenamine is reported at 20 mg. per kilogram in series 10 and at 30 mg. per kilogram in series 11 and 13. The curative dose of the several lots of neoarsphenamine used as control in this study, series 10 to 14, inclusive, is 40 mg. per kilogram. In the total compilation, sulfarsphenamine, 6 lots, cured 71 percent of 38 rabbits at 20 mg. per kilogram, 92.3 percent of 39 rabbits at 30 mg., and all of 37 rabbits receiving 40 mg. per kilogram. On the basis of this compilation, sulfarsphenamine at 20 mg. (71.0 percent) and 30 mg. per kilogram (92.3 percent) was as effective as neoarsphenamine at 30 mg. (75.2 percent) and 40 mg. (92.0 percent), respectively. The minimal effective dose, therefore, may be placed at 30 mg. for sulfarsphenamine and at 40 mg. per kilogram for neoarsphenamine, a ratio of 3:4.

The arsenic content of the 6 lots of sulfarsphenamine was uniform, varying from 20.61 percent (A103) to a maximum of 21.57 percent (H101), with an average of 20.99 percent. The 5 lots of neoarsphenamine used as control, series 10 to 14, inclusive, varied from 19.45 percent (E12) to 19.93 percent (E15), with an average

of 19.54 percent. Including the 17 lots of neoarsphenamine of the previous report, series 1 to 9, inclusive, the average arsenic content of all (22) lots studied was 19.21 percent. Based on the average arsenic content, the 6 lots of sulfarsphenamine contained approximately 7 percent more arsenic than did the 5 control lots of neoarsphenamine, series 10 to 14, inclusive, and 9 percent more than the 22 lots of neoarsphenamine of the entire series. It would appear, therefore, that the difference in arsenic content does not entirely account for the greater efficacy of sulfarsphenamine in experimental syphilis.

The spirocheticidal efficiency of six lots of dichlorophenarsine hydrochloride, representing three different brands, and five lots of oxophenarsine hydrochloride (mapharsen) all of which were made by the same manufacturer, are reported in series 11 to 15, inclusive.

The effective dose of dichlorophenarsine hydrochloride is placed at 8 mg. per kilogram. Lot E301 in series 14, included in the protocol and computations, might well be deleted from the study as it represents an early experimental batch. This lot failed to indicate a satisfactory end point at both 8 mg. and 10 mg. per kilogram, but another lot of the same brand (E302) in series 15, a regular commercial batch manufactured approximately 1 year later, cured all infected rabbits at both dose levels.

The composite protocol of the 6 lots of dichlorophenarsine shows that, with 4 mg. per kilogram, 46.9 percent of 32 infected rabbits were cured; with 6 mg., 74.3 percent of 35 rabbits were cured; with 8 mg., 88.2 percent of 34 animals were cured; and with 10 mg., 86.5 percent of 37 rabbits were cured. However, if lot E301 is excluded from the computation, the effective dose of the 5 lots of dichlorophenarsine is 8 mg. per kilogram, curing approximately 93 percent of the infected rabbits.

The sterilizing dose of oxophenarsine hydrochloride also is placed at 8 mg. per kilogram, only one of the five lots, K205 in series 15, failing to give a definite end point. The progressive increase in the sterilizing or curative efficiency with the increase in dosage, as reported for the other arsenicals, was apparent also for oxophenarsine. The percentage of efficiency increased from 14.3 percent with 2 mg. per kilogram to 41.4 percent with 4 mg., to 56.7 percent with 6 mg., to 96.8 percent with 8 mg. per kilogram.

On the basis of the composite protocol, dichlorophenarsine and oxophenarsine are approximately equally spirocheticidal, as the minimal effective dose for both products is 8 mg. per kilogram. Whatever advantage may be attributed to oxophenarsine because of the slightly higher percentage of animals cured or more definite end point at 8 mg. per kilogram would be compensated for by the fact that dichlorophenarsine contains less arsenic than oxophenarsine, 26.3 percent and

31.3 percent, respectively. Both products are equally effective in terms of their arsenoxide content.

Toxicity experiments in rabbits indicated that the maximum tolerated dose, with at least 60 percent of the animals surviving, is 200 mg. per kilogram for neoarsphenamine, 300 mg. for sulfarsphenamine, and 10 mg. for dichlorophenarsine and oxophenarsine. Inasmuch as these findings are in agreement with those of other reports, it is not necessary to give the protocol of our tests.

According to the results of this study, the chemotherapeutic ratio would be 5 for neoarsphenamine, 10 for sulfarsphenamine, and approximately 1.3 for both of the phenarsines. It is apparent, therefore, that the chemotherapeutic ratios for the phenarsines are inferior not only to those for the arsphenamines but also indicate that there is little, if any, margin of safety between the dose which sterilizes the infected rabbit and the maximum tolerated dose.

OBSERVATIONS

In general, the results reported in this study indicate that different brands of sulfarsphenamine are of uniform therapeutic activity. Additional evidence is presented confirming the previous report that different brands of neoarsphenamine also are uniformly spirocheticidal, but that sulfarsphenamine is more effective in "curing" experimental syphilis in rabbits than is neoarsphenamine, 30 mg. and 40 mg. per kilogram being the minimal effective doses, respectively. The two phenarsines, dichlorophenarsine and oxophenarsine, are equal in spirocheticidal efficacy, with a minimal effective dose of 8 mg. per kilogram.

The phenarsines are 4 to 5 times more effective than the arsphenamines on the basis of the compounds, but computed on the basis of their arsenic content the ratio is approximately 1: 3. It is apparent, therefore, that these results, which in general confirm those of other investigators, are in conflict with those reported by Tatum and Cooper (*9*) that mapharsen (oxophenarsine) at 6 mg. per kilogram, is 30 times more effective than neoarsphenamine, at 180 mg. per kilogram.

The sterilizing action of the arsphenamines, neoarsphenamine and sulfarsphenamine, as indicated herein, is not dependent solely on the arsenic content, as suggested by Voegtlin and Dyer (*6*), but rather on the arsenoxide (therapeutically active arsenic) availability of the arsenic contained in the product. This is true also for the phenarsines. The pharmacologic action of the trivalent organic arsenicals may vary according to the oxidation-reduction theory of Voegtlin (*15*, *16*, *17*), but the spirocheticidal activity, irrespective of the type of compound used, depends on the therapeutically active arsenic being available in

TABLE 1.—*Spirocheticidal activity of neoarsphenamine, sulfarsphenamine, dichlorophenarsine hydrochloride, and oxophenarsine hydrochloride in experimental syphilis*

Series No.	Brand and lot	Results of tissue transfer																												Minimal effective dose	Observation period		
		Neoarsphenamine, dose [1]								Sulfarsphenamine, dose [1]						Dichlorophenarsine HCl, dose [1]								Oxophenarsine HCl, dose [1]										
		20		25		30		40		20		30		40		4		6		8		10		2		4		6		8		10				
		Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative		Pretreatment	Posttreatment	Transfer
																																		Milligrams	*Days*	*Weeks*	
10	E11	2	4			3	3	0	6																									40	76	13	22
	A101									1	5	0	6	0	7																			20			
	H101									0	5	0	5	0	6																			20			
	F101									1	6	0	6	0	7																			20			
11	E12	4	1			4	3	0	7																									40	66	10	22
	A102									4	3	1	6	0	5																			30			
	E101									4	3	1	7	0	5																			30			
	K201																											1	4	0	5	0	4	8			
12	E13	4	2			3	5	1	6																									40	70	13	21
	K202																							6	1	4	4	3	5	0	6			8			
13	E14	4	2			1	6	2	5																									40	61	11	22
	A103									1	5	1	6	0	7																			30			
	K203																									6	2	1	4	0	7			8			
14	E15	6	1			2	5	1	6																									40	74	15	22
	E301															4	2	1	6	2	5	2	5											8			
	H302															2	4	0	7	1	3	1	6											8			
	A301															6	1	1	5	0	5	0	5											8			
	K204																									5	3	3	3	0	8			8			
15	H303															2	2	2	3	1	5	1	5											8	67	11	24
	E302															1	4	3	2	0	6	0	6											8			
	A302															2	2	2	3	0	6	1	5											8			
	K205																									2	3	5	1	1	4			8			
1 to 9 [2]		61	35	22	60	22	84	3	51																									40			
		81	45	22	60	35	106	7	81	11	27	3	36	0	37	17	15	9	26	4	30	5	32	6	1	17	12	13	17	1	30	0	4				
			35.7		73.2		75.2		92.0		71.0		92.3		100		46.9		74.3		88.2		86.5		14.3		41.4		56.7		96.8		100				

[1] In milligrams per kilogram.
[2] Reference 5.

sufficient concentration for a sufficient length of time to sterilize the infected animal.

SUMMARY

Different brands of sularsphenamine, dichlorophenarsine hydrochloride, oxophenarsine hydrochloride, and neoarsphenamine, as previously reported, each within their respective categories, are uniformly active in curing experimental syphilis in rabbits with one treatment late in the active stage of the disease.

Sulfarsphenamine has greater spirocheticidal activity than neoarsphenamine, and the two phenarsine products, of approximately equal efficiency, are more active therapeutically than the two arsphenamines.

The chemotherapeutic ratio, minimal lethal dose: minimal effective dose, for the phenarsines, indicating little, if any, margin of safety, is definitely inferior to that for the arsphenamines.

The spirocheticidal activity of the trivalent organic arsenicals depends on the arsenoxide, or therapeutically active arsenic, being available in sufficient concentration for a sufficient length of time to sterilize the infected animal, irrespective of the type of arsenical used.

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TOXIC EFFECTS OF TETRANITROMETHANE, A CONTAMINANT IN CRUDE TNT [1]

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INTRODUCTION

In the manufacture and use of TNT much attention has been devoted to the potential dangers of nitrous fumes and of TNT itself. Most of the complaints of occupational origin in plants where TNT is manufactured or used probably have been rightfully attributed to these two agents only. There is, however, one toxic and extremely irritating agent which may occasionally be overlooked as a cause of symptoms. This chemical is tetranitromethane, an impurity which is formed in varying amounts during the nitration of toluene.

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PHYSICAL AND CHEMICAL PROPERTIES OF TETRANITROMETHANE

Tetranitromethane, $C(NO_2)_4$, is a colorless, oily fluid at room temperature, boils at 125.7° C., and solidifies at 13° C. It has a molecular weight of 196.04, with a specific gravity of 1.64 at 16° C. It is freely soluble in ether or alcohol but is insoluble in water. It is moderately volatile and has a characteristic pungent odor similar to that of nitrous fumes but much more irritating. As an explosive, it is more powerful than nitroglycerin. For example, 10 students were killed and 20 others severely injured by a 10-gram tetranitromethane-toluene mixture which exploded in a classroom at the University of Münster in 1920. In fact, because of the high percentage of available oxygen (48.5 percent), it has also been used as an oxygen carrier in combination with petroleum or soot in preparing explosives It has a high surface tension which enhances its toxic potentialities in the handling of TNT (*1*). (For the determination of tetranitromethane in air samples, see experimental work of this report, page 1053.)

According to Moore, tetranitromethane may be present to the extent of 0.12 percent in crude TNT (*2*). Fischer states that the formation of tetranitromethane during TNT manufacture occurs when the stronger acids and higher temperatures are used (*3*). It owes its development to the destruction of the aromatic molecule by oxidation followed by nitration. During the purification of crude TNT by sulfitization, tetranitromethane is destroyed and the two asymmetrical trinitrotoluenes are removed. The removal of the latter is the main purpose in using sodium sulfite. The chemical reaction between tetranitromethane and sodium sulfite results in formation of sodium nitrate and the sodium salt of dinitromethane-sulfonic acid (*4*).

TOXICOLOGIC EXPERIENCE WITH TETRANITROMETHANE IN MUNITIONS PLANTS DURING WORLD WAR I

The high incidence of TNT intoxication in England and the United States during World War I has been ascribed by some to the fact that during the early part of the war the asymmetrical isomers of TNT and tetranitromethane were not removed. The irritating property of tetranitromethane fumes constituted an industrial nuisance and at times limited the efficiency of workers. Persons exposed to the fumes from crude TNT complained of nasal irritation, burning of the eyes, dyspnea, expectoration, coughing, oppression in chest, and dizziness. These complaints increased in proportion to the strength of the odor of tetranitromethane in the air. Continued or moderately heavy exposure led to drowsiness, headache, anemia, marked cyanosis with respiratory distress, and bradycardia. In the

American plants, it was reported that the odor of crude TNT so handicapped the workers that it seriously interfered with production. It is interesting to note that in 1915, the plants in this country had introduced an alkaline sulfite wash, supposedly for the sole purpose of removing this unpleasant odor. In England, both the amount and severity of illnesses in the arsenals were reduced after the introduction of the sulfitization process (*5*). The French noted the odor of tetranitromethane during the grinding of impure TNT and during the washing of the product with hot water. However, there was remarkably little disability in their TNT plants, and they considered the danger from tetranitromethane to be minimal after the sulfite treatment was introduced. In Germany, on the other hand, this irritant byproduct seems to have been considered an important hazard, as a number of serious poisonings were ascribed to inhalation of its fumes.

Koelsch, whose publication is probably the most complete on this subject, reported observations made on tetranitromethane intoxication both in industry and in experimental animals (*6*). He described toxic effects in three cases occurring in one plant, two of which were fatal. The first case was that of a female worker who began coughing while leaning over a melting pot and consequently inhaled large amounts of heavily contaminated air. She ran out of the room, fell unconscious, and was not revived for several hours. She was deeply cyanotic; her pulse was weak, and respirations were not visible. Consciousness was regained only after treatment with oxygen and skin stimulation. Recovery was almost complete the following day. The second case was that of a man who had worked with impure TNT for 30 days, the last 14 of which were spent at the melting pot. This patient developed severe chest pains during the night. He attempted to continue work despite respiratory distress, oppression over the chest, and foamy sputum. Oxygen therapy gave temporary relief, but he became unconscious on the second day of illness, and died of pulmonary edema and methemoglobinemia. The third case was that of a worker who developed marked irritation of the respiratory tract after 14 days of exposure at the melting pot and subsequently, during work in a less contaminated atmosphere, developed fatal croupous pneumonia.

PREVIOUS TOXICOLOGIC STUDIES WITH TETRANITROMETHANE ON ANIMALS

Studies on the toxic effects of tetranitromethane on animals have not been conducted on an extensive scale. Koelsch has reported in detail on a limited number of experiments, and Flury (*7*) has commented briefly in "Schädliche Gase" on several short experiments.

The latter found that a cat exposed for 20 minutes to a concentration of tetranitromethane of about 10 p. p. m. became seriously ill and died 10 days later. Another cat exposed to 10 times this concentration for 20 minutes died an hour later.

Koelsch's experiments involved the administration of tetranitromethane by inhalation, stomach tube, cutaneous, and subcutaneous routes. Seventeen animals were used—8 cats, 8 rabbits, and 1 guinea pig. The inhalation experiments revealed that fumes given off from 10 to 15 cc. of tetranitromethane in a beaker or narrow-necked flask placed in a moderate-sized exposure chamber were fatal in 2 to 5 hours to two cats and one guinea pig, and within 24 hours to one rabbit. The immediate response was restlessness followed by lacrimation, salivation, blepharism, sneezing, coughing, increased respiratory rate, a gasping for breath, and, finally, death. Exposure of a cat under similar conditions to 1 to 2 drops of tetranitromethane placed on a strip of filter paper hung inside the chamber produced signs of marked irritation. The same cat exposed in the same manner 10 days later to 4 drops of tetranitromethane died within one-half hour after removal from the chamber. The autopsy revealed tracheitis, bronchopneumonia, severe pulmonary edema, and methemoglobinemia.

The fumes from 1 kg. of TNT contaminated with tetranitromethane had no apparent effect on a rabbit exposed for 3 hours in a chamber maintained at 18° C. The fumes from this TNT when heated to 100° C. and drawn through the chamber 4 to 5 hours daily caused marked irritation of mucosal surfaces, and the exposed rabbit died on the eighth day, having tracheitis, bronchopneumonia, and pulmonary edema. Exposure to fumes from 100 gm. of the same TNT heated to 150° C. produced similar symptoms and death in another rabbit.

The administration of tetranitromethane to one rabbit by stomach tube in small doses of one to five drops for several consecutive days was without effect. A cat given a total of 90 drops of tetranitromethane in cold water by stomach tube over a period of 4 weeks suffered a weight loss of approximately 30 percent; a final dose of 10 drops of tetranitromethane was given in warm water, and the animal died 5 hours later. The autopsy findings were pulmonary edema, fatty liver, and methemoglobinemia. The microscopic examination showed fatty degeneration of the liver and kidneys. Another cat given 15 drops of tetranitromethane in 90-percent alcohol died 5 days later. Pulmonary edema and a hemorrhagic gastric mucosa were noted at post mortem examination. It was thought that in these instances tetranitromethane was absorbed, volatilized, and removed from the body by exhalation, thus causing a secondary irritation of the lungs.

Repeated application of patch tests containing tetranitromethane

dissolved in olive oil on the shaved skin of a cat gave no sign of absorption or of skin irritation. The subcutaneous injection of 1 cc. of tetranitromethane resulted in increasing weakness and death in 4 to 5 hours, but caused no specific symptoms.

Koelsch concluded: Tetranitromethane is a powerful local irritant and a general poison; the irritant action is particularly marked on the mucous membranes of the eyes, nose, and respiratory tract; acute pulmonary edema from tetranitromethane differs from that of nitrous fume poisoning in that there is no latent period of 6 to 10 hours before onset of symptoms; methemoglobin is formed in the less acute cases of poisoning.

MEDICAL PROBLEMS ASSOCIATED WITH TETRANITROMETHANE IN MODERN TNT MANUFACTURE

In general, the final TNT product of the present-day TNT manufacturing plant is practically free of tetranitromethane. The crude TNT, however, is still a potential hazard with respect to this byproduct. This is especially true since the nitration cycles have been drastically shortened, resulting in more frequent emptying and charging of nitrators and washing units per workday. The presence of tetranitromethane in these units may become most troublesome when the ventilating system works improperly or when inadequate precautions are taken during breakdowns and repair of such units. Ordinarily little actual difficulty is involved because the nitration of toluene and sulfitization are enclosed processes with adequate exhaust systems for removal of all fumes.

There have been a number of instances, though, in which the cause of complaints was not immediately recognized. As illustrations of such instances, the following examples are cited. In some plants, the neutralization of the "tri-oil" is carried out by washing the crude product with large quantities of water. Before disposal of this water, it is passed through a "catch basin" in order to collect, by sedimentation, the moderate quantities of TNT carried in the waste water. The workmen in these plants who remove the sediment from these catch basins frequently visited the plant hospitals with complaints of eye irritation, sore throat, stubborn cough, and persistent substernal pain. A few had mild gastrointestinal complaints, but the respiratory complaints predominated. The disability and absentee rates were unusually high in this group because of respiratory troubles.

Difficulties also arose when several plants altered the sulfitization procedure slightly by lowering the temperature of the sulfite (sellite) wash. TNT purified by this technique resulted in numerous complaints among the workers in the wash houses, particularly among those employed in the flaking, boxing, and weighing procedures. The

complaints were confined to irritation of the eyes and respiratory tract; they were more of an annoyance than actual distress and tended to interfere with the efficiency of these workers. TNT purified in this manner gave off a rather irritating, pungent odor which was particularly noticeable when a partially filled container was opened.

EXPERIMENTAL WORK WITH TNT CONTAINING TETRANITROMETHANE

Because it has been generally overlooked that tetranitromethane is a contaminant of TNT and because of the paucity of reports on its toxicologic properties, a series of simple animal experiments were conducted with TNT obtained during the various steps of purification.

Five experiments were conducted, in order to determine the reaction of cats exposed to the fumes emanating from TNT obtained during three different steps of purification and to the fumes of two waste products accumulated in "catch basins" during purification. Eleven cats were used, two animals for each of four experiments, and three in a fifth experiment. The animals were placed in a cage within an exposure chamber measuring 30″ x 30″ x 30″. The temperature in the chamber ranged between 23° and 25° C. From 700 to 800 gm. of the material to be tested was spread out on a glass tray (12″ by 8″) and placed on top of the cage located within the chamber. An air flow of 5 to 6 liters per minute through rubber tubing was allowed to pass over the material in the tray. Several small openings in the chamber allowed excess air to escape. The duration of exposure is indicated separately for each experiment. Blood samples were taken before and after exposure. Determinations were made for hemoglobin and methemoglobin concentration, turbidity of hemolyzed blood, Heinz bodies, total cell volume, and icteric index. Air samples were taken during the exposure period to determine the concentration of tetranitromethane in the chamber.[4]

METHOD FOR THE DETERMINATION OF TETRANITROMETHANE IN AIR SAMPLES

Sampling.—The air sample (40 liters) was drawn through a midget impinger containing 10 ml. of ethyl alcohol. The alcohol sample in the impinger was transferred to a sample bottle and the impinger rinsed with a small amount of alcohol.

Colorimetric method for determination of tetranitromethane (tentative).—Preparation of standard solution: A few grams of tetranitromethane were prepared as described by Chattaway (*8*). A weighed amount of the tetranitromethane was dissolved in alcohol and diluted with alcohol to a known volume. By repeated dilution with alcohol,

[4] The authors are indebted to D. A. Holaday, Division of Industrial Hygiene, Bureau of State Services, U. S. Public Health Service, for the collection of air samples.

a solution was finally obtained which contained 0.01 mg. of tetranitromethane per milliliter.

Procedure: A suitable aliquot of the sample (8 ml. or less) was neutralized with pyridine (drop by drop) until the slightly acid solution was brought to a pH of about 6. "Alkacid" paper was used as an outside indicator. One drop of pyridine usually sufficed to neutralize the acid. If necessary, alcohol was added to make the total volume 8 ml. Then 2 drops of pyridine and 5 ml. of alcoholic benzidine solution (20 mg. per 100 ml.) were added. After mixing, the sample was compared with the standards.

To the comparison tubes were added 0, 1, 2, 3, 4, 5, 6.5, and 8 ml. of the dilute standard tetranitromethane solution. Alcohol was added to each tube to make the total volume 8 ml. Then 2 drops of pyridine and 5 ml. alcoholic benzidine were added. After mixing, the solutions were ready for comparison. The color comparison can be made visually or with a spectrophotometer at 400 millimicrons. Small Nessler tubes, or better, matched test tubes (about 20 ml.) are suitable for visual comparison.

Notes: The color is relatively stable, but not sufficiently stable to permit the use of the same set of standards for comparison with samples made up at other times. Tests indicate that HNO_2, HNO_3, and reaction products of HNO_3 with alcohol do not seriously interfere. The color produced by these materials is of the order of one one-hundredth of that produced by an equivalent amount of tetranitromethane. TNT offers no interference whatever. The possible interference of other substances has not been investigated, nor have the optimum amounts of pyridine and benzidine been determined. For these reasons, the procedure as described is considered tentative. A suggested improvement is the use of propylene glycol as the collecting medium.

RESULTS OF EXPERIMENTS

Experiment 1.—TNT obtained immediately after crystallization of the "tri-oil" was used. The two cats showed immediate signs of irritation, such as ptyalism, blepharism, marked lacrimation, and sternutation during the first hour. During the second hour, restlessness and increased respiratory rates were noted. These were followed by severe dyspnea and frequent attempts at swallowing the tenacious strings of saliva hanging from the mouth. Marked weakness was followed by unconsciousness and death. One cat died 4 hours and the other 5½ hours from onset of exposure.

Blood samples were secured from cat No. 5 about 10 minutes before death and from cat No. 6 just as it expired. Autopsies were performed immediately. The lungs were slate-colored, heavy, and crepitant, and the surfaces showed numerous patchy hemorrhagic

areas. Upon section, serous fluid flowed freely from the cut surfaces. The slate color of the lungs was thought to be due to methemoglobin. The kidneys appeared to have congested medullas and light brown discoloration of the cortices.

According to the laboratory tests, the erythrocytes showed marked anisocytosis (see table), and approximately 11 percent of the total hemoglobin of both animals was converted to methemoglobin. The increase in total cell volume and hemoglobin concentration of cat No. 6 was attributed to fluid loss into the lungs.

Two air samples were taken, one at the end of the first hour and the second at the end of 3½ hours. The tetranitromethane concentration of the first sample was 25.2 p. p. m. and of the second sample, 7.2 p. p. m.

Experiment 2.—The TNT used was the crude product after it had been washed with a large volume of water to remove excess acids, the next step in purification after crystallization. The three cats exposed to this material exhibited signs of irritation within 5 minutes. The manifestations were identical to those described in the first experiment except that the cats passed more rapidly through the various stages. The first animal died at the end of 1 hour of exposure, the second after 1½ hours, and the third after 2¼ hours of exposure.

The lungs at post mortem examination appeared the same as those described in experiment 1, with the exception that the lungs of only one animal were slate-colored. The remaining viscera appeared normal.

The total hemoglobin values are inaccurate because the blood samples were taken a few minutes after death. These data are presented only for the purpose of calculating the methemoglobin percentage, which was nearly 20 percent for one animal and about 5 and 7 percent for the second and third, respectively.

Two air samples taken immediately after the last animal died (2¼ hours from the start of the experiment) contained seven parts of tetranitromethane per million parts of air.

Experiment 3.—The TNT for this experiment was obtained from another ordnance works. The crude product from this plant was treated with a soda ash wash for neutralization rather than being washed with a large volume of water for the same purpose.

Two cats were exposed to this TNT 6 hours a day for 3 days. The sample in the tray was stirred up each day before placing the animals in the chamber. The cats showed signs of moderate irritation, lacrimation, and salivation within 5 minutes. Upon removal from the chamber after 6 hours of exposure, the animals still showed the same signs of irritation, which did not disappear until an hour later. The animals appeared normal before the second exposure was begun

on the following day. However, the same manifestations noted the first day reappeared after the animals were in the chamber for 5 minutes. Unfortunately, toward the end of the second day of exposure, the air compressor, and consequently the air flow into the chamber, stopped. Both cats were breathing rapidly, about 55 to 60 respirations per minute, when they were removed from the chamber. The increased respiratory rate was attributed in part to accumulation of CO_2. Moist rales could be heard in the chest of cat No. 9. At the onset of the third day of exposure, both cats had respiratory rates of 32 to 36 respirations per minute, and cat No. 9 had a muco-purulent nasal discharge. At the end of the third day, cat No. 9 was dyspneic, whereas cat No. 4 showed only hypernea.

Because cat No. 9 appeared near death, the animal was killed and an autopsy performed. The lungs appeared the same as described in experiment 1. The kidneys were very pale and light yellow in color.

The blood findings on these two animals over the 3-day period showed only slight methemoglobin formation. Turbidity ratios remained unchanged and only a few small atypical Heinz bodies were noted in the erythrocytes.

The concentration of tetranitromethane in the chamber at the end of the first hour on the first day was 9.2 p. p. m.; after 5 hours it was 3.3 p. p. m. On the second day, 1 hour after the onset of exposure, the concentration of tetranitromethane was 9.5 p. p. m. On the third day, 1 hour after exposure, the chamber contained 5.7 p. p. m.

Experiment 4.—Two cats were exposed to the material collected by sedimentation in the catch basins from the waste water which had been used to neutralize the crude TNT.

During the first day of exposure (6 hours), the cats evidenced mild irritation, i. e., slight lacrimation. The animals behaved normally throughout the second day's exposure. They were kept under observation for 1 week thereafter without further exposure and showed no signs of ill effects. No significant changes were noted in the blood determinations.

Atmospheric samples taken during the first and fifth hour of exposure of the first day contained 0.4 and 0.1 p. p. m. of tetranitromethane, respectively. Air samples taken during the second day of the experiment had only a trace of tetranitromethane.

Experiment 5.—Two cats were exposed to the sludge collected from "red water waste." This sludge, resulting from reaction of sellite on the two asymmetric trinitrotoluenes and tetranitromethane, is composed mostly of dinitrotoluene-sulfonic acid derivatives and a small amount of the sodium salt of dinitromethane-sulfonic acid.

Animals exposed to this material for 6 hours did not reveal the slightest evidence of irritation.

Blood findings in cats exposed to tetranitromethane fumes

Item	Experiment 1				Experiment 2					
	Cat No. 5		Cat No. 6		Cat No. 1		Cat No. 2		Cat No. 3	
	Hours of exposure				Hours of exposure					
	Pre-experimental	4½	Pre-experimental	5½	Pre-experimental	1	Pre-experimental	1½	Pre-experimental	2¼
Total cell volume (in percent)	26.3	28.0	30.0	43.0	.....	.....	.....	.....	.....	.....
Methemoglobin (in gm. per 100 cc.)	0.45	1.36	0.18	1.61	0.201	1.25	0.402	3.82	0.268	1.60
Methemoglobin (in percent)	3.88	11.0	1.41	10.7	1.18	4.8	2.78	18.9	1.86	7.0
Total hemoglobin (in gm. per 100 cc.)	11.6	12.4	12.8	15.0	16.9	26.0	14.4	19.7	14.4	23.0
Turbidity ratio [1]	1.16	1.15	1.12	1.08	1.02	0.94	1.07	1.08	1.02	1.02

Item	Experiment 3								Experiment 4			
	Cat No. 9				Cat No. 4				Cat No. 7		Cat No. 8	
	Hours of exposure								Hours of exposure			
	Preexperimental	6	12	18	Preexperimental	6	12	18	Preexperimental	6	Preexperimental	6
Total cell volume (in percent)	36.0	.....	.....	35.1	30.0	.....	.....	33.2	36.0	.....	26.0	.....
Methemoglobin (in gm. per 100 cc.)	0.04	0.09	0.51	0.42	0.09	0.71	0.11	0.31	0.40	0.18	0.40	0.45
Methemoglobin (in percent)	0.25	0.67	4.1	2.88	0.66	6.3	1.1	2.31	2.56	1.3	3.92	4.1
Total hemoglobin (in gm. per 100 cc.)	16.2	13.4	12.4	14.6	13.7	11.3	10.0	13.4	15.6	13.8	10.2	11.0
Turbidity ratio [1]	1.11	1.08	1.19	1.15	1.01	1.14	1.02	1.04	1.07	1.12	1.24	1.14

[1] Horecker, B. L.: Public Health Bulletin No. 285, U. S. Public Health Service, Washington, Government Printing Office (1944), p. 46.

HISTOPATHOLOGIC FINDINGS

Sections were prepared from the adrenals, bone marrow, heart, kidney, liver, lungs, lymph node, pancreas, sciatic nerve, skeletal muscle, spleen, thymus, thyroid, and urinary bladder. These were stained routinely with eosin azure, modified Van Giesen's stain for hemoglobin, and acidified ferrocyanide. Frozen sections of heart, kidney, and liver were stained for fat by the isopropanol technique. The sciatic nerves were stained for myelin by a modified Weigert technique.

Lungs.—In all the animals there was a small to moderate amount of serocellular alveolar exudate in the peribronchial areas.

The animals which died within 1 to 2¼ hours (experiment 2) showed marked patchy to diffuse congestion. Many, but not all, alveoli in the peribronchial areas contained a variable amount of serocellular exudate. Very few cells, chiefly large mononuclears, were present.

The lumina of the bronchi and atria contained a similar serocellular exudate which in the larger ones was mixed with mucin plus degenerating epithelial cells. The epithelium was focally oxyphilic, with or without pyknosis, and stratified; in the larger bronchi and atria it was frayed or absent. The congested mucosa was infiltrated by a few cells, chiefly large mononuclears and lymphocytes.

About the arteries there was often a wide zone of serous exudate containing a few cells.

The two animals which died after 4 and 5½ hours, respectively, (experiment 1) showed a progression of the lesion. The changes noted included an increase in the number of cells, chiefly large mononuclears, in the interalveolar septa and the exudate, and occasionally a desquamation of the epithelium of the smaller bronchi and atria. In the alveoli of one animal, frequently near respiratory bronchioles, there were nodular areas of large, loosely arranged epithelial cells with vesicular nuclei and a few erythrocytes, polymorphonuclears, and a little foreign vegetable material.

The animal which was killed after three exposures (experiment 3) showed different stages of this process. The interalveolar septa were thickened in patchy areas, caused by congestion or the presence of large septal cells, some of which were foamy. The alveolar exudate differed from field to field, consisting of variable proportions of serum, fibrin, and large, often foamy mononuclears, polymorphonuclears, and erythrocytes. Focally, the serum was quite dense. The fibrin occurred diffusely in the exudate or condensed into a film on the surface of an alveolus.

A similar exudate, occasionally undergoing organization, appeared in the bronchi. In the smaller bronchi and atria, the epithelium was occasionally oxyphilic and occasionally pyknotic, but more often it consisted of large basophilic epithelial cells with prominent round nuclei. These epithelial cells seemed closely packed, occasionally stratified, and a few were in mitosis. The larger bronchi showed a few epithelial cells containing mucin and an occasional mitotic figure. The mucosa was infiltrated by a small to moderate number of cells consisting of a variable mixture of large mononuclears, lymphocytes, and polymorphonuclears, and an occasional lymphoid nodule.

Liver.—In the three animals which died within 2¼ hours, there were fine fat droplets in a few scattered liver cells and sinus phagocytes. In the remainder, a few fine fat droplets were seen in most of the liver cells. Slight congestion was noted in most of the animals. Hemosiderin in Kupffer cells was variable; usually only a small amount was noted. Erythrophagia was rarely noted.

In the cat exposed for 2¼ hours there was an occasional oxyphilic, karyolytic liver cell, and in the animal exposed for 4 hours, a rare

nodular area composed of loosely arranged large mononuclears, with a polymorphonuclear cell and a little basophilic reticular or oxyphilic material.

Kidneys.—The three animals which died within 2¼ hours showed changes in a small to moderate number of glomeruli. These glomeruli appeared as oxyphilic, vacuolated material, occasionally with a visible nucleus; some nuclei, judging from their position and shape, seemed to be a portion of the capillary loop. Occasionally a glomerulus was congested. The two animals which died at 4 and 5½ hours, respectively, showed several small cortical areas of atrophy and scarring. All the animals had the usual large amount of fat in the epithelium of the convoluted tubules.

Occasionally in the lumina of the tubules there was a little eosinophilic coagulum or a degenerating epithelial cell. Congestion was variable, being marked in several of the medullas.

Spleen.—The follicles were small to medium in size, usually with large secondary nodules and some phagocytosed nuclear fragments. There was a small to moderate amount of blood in the pulp; only one spleen had more than a trace of hemosiderin in pulp phagocytes.

Heart.—Only one animal, which also had diffuse fat in the liver cells, showed more than a trace of fat in the myocardium. This occurred as moderate numbers of very fine drops in a subendocardial band about half the thickness of the ventricle. Sections of the ventricle showed slight to moderate congestion in most of the animals.

A variable but usually small amount of phagocytosed hemosiderin was noted in mesenteric lymph nodes and bone marrow of the animals which survived over 4 hours.

Sections of the pancreas, sciatic nerve, skeletal muscle, thymus, thyroid, and urinary bladder showed no noteworthy changes.

The significant pathologic findings are those of a chemical serous pneumonia and degenerative changes in the epithelium of the bronchi and atria. These changes were not seen in animals exposed to TNT treated with sellite.

DISCUSSION OF FINDINGS

These limited experiments have demonstrated that the small quantities of tetranitromethane present in crude TNT give off at room temperatures sufficient amounts of tetranitromethane vapor to produce fatal concentrations within a confined space. In one respect, this finding is contrary to the observation of Koelsch (*6*). He found that an experimental animal exposed to the fumes of TNT containing tetranitromethane was unaffected at room temperature. Only upon heating the TNT was Koelsch able to produce sufficient fumes to cause marked irritation and death in experimental animals.

The concentrations of tetranitromethane found in the exposure chamber indicate that the lethal concentration is relatively low. It is apparent, even from the meager data presented here, that the safe limit for the workmen concentration of tetranitromethane is probably less than 5 p. p. m.

These experiments indicate that tetranitromethane is not removed in appreciable quantity during neutralization of the "tri-oil" by washing with a large quantity of water or soda ash solution. Thus, prior to sellite treatment, the presence of tetranitromethane in crude TNT is a potential health hazard, usually well controlled because the processes are enclosed and exhaust ventilated. It is obvious that under certain circumstances, such as repair of a breakdown or excessive spillage of "tri-oil," tetranitromethane poisoning may occur in the absence of adequate protection.

The suggestion that tetranitromethane was responsible for the irritating fumes emanating from the final product at several TNT plants following alteration in the sellite treatment appears reasonable.

The results of this investigation confirm those of Koelsch; namely, that tetranitromethane produces marked irritation of the mucous membrane, acute pulmonary edema, mild methemoglobinemia, and probably fatty degeneration of the liver. There is no evidence of a delayed onset of pulmonary edema such as is observed in nitrous fume poisoning.

CONCLUSIONS

Tetranitromethane fumes are given off from crude TNT in sufficient quantity at room temperature to be fatal to cats confined in an exposure chamber.

Tetranitromethane in concentrations ranging from 3.3 to 25.2 p. p. m. produced marked irritation of mucuous membrances of eyes, mouth, and upper respiratory tract, acute pulmonary edema, mild methemoglobinemia, and probably fatty degeneration of liver and kidneys.

Tetranitromethane in concentrations of 0.1 to 0.4 p. p. m. caused mild irritation in cats but no other untoward effects with exposure for 6 hours on two consecutive days.

A chemical procedure (tentative) is presented for the determination of tetranitromethane in atmospheric samples.

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DEATHS DURING WEEK ENDED JUNE 21, 1947

[From the Weekly Mortality Index, issued by the National Office of Vital Statistics]

	Week ended June 21, 1947	Corresponding week, 1946
Data for 93 large cities of the United States:		
Total deaths	8,489	8,628
Median for 3 prior years	8,628	
Total deaths, first 25 weeks of year	242,006	239,968
Deaths under 1 year of age	637	645
Median for 3 prior years	621	
Deaths under 1 year of age, first 25 weeks of year	19,339	15,446
Data from industrial insurance companies:		
Policies in force	67,278,470	67,219,810
Number of death claims	12,393	11,325
Death claims per 1,000 policies in force, annual rate	9.6	8.8
Death claims per 1,000 policies, first 25 weeks of year, annual rate	9.8	10.3

INCIDENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED JUNE 28, 1947

Summary

A total of 76 cases of poliomyelitis was reported for the current week (the same number as reported last week), as compared with 273 for the corresponding week last year and a 5-year (1942–46) median of 190. For the current week, only 4 States reported more than 3 cases each—California 33 (last week 23), New York 6 (last week 4), Ohio and Illinois 4 each (last week 2 and 3, respectively). Of the total of 589 cases reported since March 15, the approximate average date of lowest seasonal incidence (as compared with 1,385 for the corresponding period last year and a 5-year median of 782), 368 occurred in the 7 States reporting more than 13 cases each during the period, as follows (last year's corresponding figures in parentheses): California 197 (132), New York 45 (70), Texas 44 (264), Illinois 24 (58), Florida 23 (233), Nebraska 20 (3), Washington 15 (23).

A fatal case of plague was reported on June 30 in a 12-year old boy in Modoc County, Calif. (See p. 1068).

Of the current total of 108 cases of typhoid fever, as compared with 88 last week and 138 for the 5-year median, 22 occurred in Texas (last week 19), 9 in California, 10 in Arkansas, and 7 each in Oklahoma and Oregon.

A total of 21 cases of Rocky Mountain spotted fever was reported for the week, as compared with 29 last week, 16 for the corresponding week last year, and a 5-year median of 25. Only 1 State (Virginia, 7 cases), reported more than 2 cases for the current week. The total to date is 175, as compared with 170 for the same period last year and a 5-year median of 172.

One case of smallpox was reported during the week, in Idaho, and 2 cases of anthrax were reported in New York.

Deaths registered during the week in 93 large cities of the United States totaled 8,637, as compared with 8,489 last week, 8,557 and 8,747 for the corresponding weeks of 1946 and 1945, respectively, and a 3-year (1944–46) median of 8,557. The total for the year to date is 250,640, as compared with 248,525 for the corresponding period last year.

Telegraphic morbidity reports from State health officers for the week ended June 28, 1947, and comparison with corresponding week of 1946 and 5-year median

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

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median 1942-46	Week ended—		Median 1942-46	Week ended—		Median 1942-46	Week ended—		Median 1942-46
	June 28, 1947	June 29, 1946		June 28, 1947	June 29, 1946		June 28, 1947	June 29, 1946		June 28, 1947	June 29, 1946	
NEW ENGLAND												
Maine	2	1	0				42	101	101	0	0	
New Hampshire	0	0	0				2	22	15	0	0	0
Vermont	0	1	0				100	139	55	0	0	0
Massachusetts	12	3	1				252	1,351	457	0	2	4
Rhode Island	0	0	0				58	84	53	0	0	0
Connecticut	1	0	0				365	268	141	1	2	2
MIDDLE ATLANTIC												
New York	21	10	10	[1] 2	[1] 4	[1] 3	538	1,563	611	9	6	17
New Jersey	1	4	2		4	4	537	811	344	1	1	3
Pennsylvania	7	7	7	(2)	(2)	(2)	87	785	390	2	10	8
EAST NORTH CENTRAL												
Ohio	2	10	9	2		1	360	613	90	1	6	6
Indiana	1	4	4			4	25	95	37	1	0	1
Illinois	2	9	9	21		3	216	254	254	1	5	6
Michigan [3]	2	4	6	1			83	279	259	2	2	11
Wisconsin	2	0	1		10	9	575	1,066	789	1	1	1
WEST NORTH CENTRAL												
Minnesota	7	0	2				310	22	66	1	3	3
Iowa	2	5	1				123	120	51	0	3	2
Missouri	1	8	1	1		1	69	46	36	3	1	3
North Dakota	0	0	0		3	1	39	13	9	0	0	0
South Dakota	0	0	0				35	7	7	0	0	0
Nebraska	0	0	1	1			12	58	22	0	1	1
Kansas	6	3	3		1	1	11	34	35	1	2	2
SOUTH ATLANTIC												
Delaware	0	0	0				1	7	4	1	0	0
Maryland [3]	5	6	4				8	326	65	1	0	5
District of Columbia	0	0	0				8	64	30	0	0	0
Virginia	5	6	4	125	70	70	231	336	61	2	7	5
West Virginia	5	5	2	5	2	2	44	282	31	1	0	0
North Carolina	1	10	4				30	115	115	3	0	3
South Carolina	0	44	6	128	104	90	65	163	34	1	0	2
Georgia	3	2	3	6	1	3	21	64	25	1	0	1
Florida	3	3	2	2	1	1	26	8	11	2	1	2
EAST SOUTH CENTRAL												
Kentucky	2	3	3			1	1	17	20	1	1	1
Tennessee	3	4	2	8	7	4	16	54	35	4	3	3
Alabama	2	6	3	1	17	6	90	62	16	1	6	3
Mississippi [3]	3	7	3	7			3			0	0	0
WEST SOUTH CENTRAL												
Arkansas	1	0	[1]		2	2	24	49	28	0	0	0
Louisiana	6	1	4	6		1	11	53	29	0	0	1
Oklahoma	3	0	0	3	2	9	11	67	39	1	1	1
Texas	16	24	24	196	214	249	97	441	208	2	4	6
MOUNTAIN												
Montana	0	0	0	7			37	60	35	0	0	1
Idaho	1	0	0	4			4	14	7	0	1	0
Wyoming	0	0	0	1			2	2	16	0	1	0
Colorado	3	6	5	19		9	28	130	61	0	0	1
New Mexico	0	1	2	5	2	1	16	33	11	0	0	0
Arizona	0	2	0	19	9	28	36	56	18	0	0	0
Utah [3]	0	1	1		3	1	8	74	74	0	0	1
Nevada	0	0	0						2	0	0	0
PACIFIC												
Washington	6	0	4			1	9	55	137	0	3	2
Oregon	1	3	2	3		1	19	123	48	0	1	0
California	11	15	16	10	5	13	95	654	667	3	7	9
Total	149	218	159	583	461	592	4,780	11,040	6,333	48	81	144
26 weeks	6,165	8,421	6,314	299,394	188,206	78,126	169,282	612,399	509,829	2,108	3,964	5,419
Seasonal low week [4]	(27th) July 5–11			(30th) July 26–Aug. 1			(35th) Aug. 30–Sept. 5			(37th) Sept. 13–19		
Total since low	13,731	20,065	15,198	332,369	550,454	113,988	192,169	638,523	547,842	3,080	5,468	7,871

[1] New York City only.
[2] Philadelphia only.
[3] Period ended earlier than Saturday.
[4] Dates between which the approximate low week ends. The specific date will vary from year to year.

Telegraphic morbidity reports from State health officers for the week ended June 28, 1947, and comparison with corresponding week of 1946 and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever		
	Week ended—		Median 1942–46	Week ended—		Median 1942–46	Week ended—		Median 1942–46	Week ended—		Median 1942–46
	June 28, 1947	June 29, 1946		Apr. [2]28, 1947	June 29, 1946		June 28, 1947	June 29, 1946		June 28, 1947 [5]	June 29, 1946	
NEW ENGLAND												
Maine	0	0	0	8	10	10	0	0	0	0	0	1
New Hampshire	0	0	0	6	3	2	0	0	0	0	1	0
Vermont	0	0	0	0	4	3	0	0	0	0	0	0
Massachusetts	0	0	0	71	91	124	0	0	0	4	24	4
Rhode Island	0	0	0	4	1	2	0	0	0	0	1	1
Connecticut	1	1	0	21	14	20	0	0	0	0	0	1
MIDDLE ATLANTIC												
New York	6	14	14	148	204	176	0	0	0	3	6	3
New Jersey	0	3	2	42	70	37	0	1	0	1	0	1
Pennsylvania	0	2	1	57	96	96	0	0	0	2	3	4
EAST NORTH CENTRAL												
Ohio	4	7	5	110	119	95	0	0	0	4	6	4
Indiana	0	2	1	11	21	20	0	1	0	2	1	1
Illinois	4	18	2	36	77	62	0	1	1	1	5	2
Michigan [3]	0	3	1	86	74	74	0	0	0	4	3	3
Wisconsin	0	1	0	47	48	68	0	0	0	0	1	0
WEST NORTH CENTRAL												
Minnesota	0	10	1	27	16	22	0	0	0	1	0	0
Iowa	2	3	0	12	15	15	0	0	0	2	0	0
Missouri	2	8	1	13	8	12	0	0	0	2	2	2
North Dakota	0	0	0	6	2	3	0	0	0	0	5	0
South Dakota	0	3	0	2	2	3	0	0	0	0	0	0
Nebraska	3	1	0	13	3	4	0	0	0	0	13	0
Kansas	1	5	1	5	22	18	0	0	0	0	3	3
SOUTH ATLANTIC												
Delaware	0	0	0	2	1	1	0	0	0	0	1	1
Maryland [3]	1	0	0	9	21	24	0	0	0	0	0	1
District of Columbia	0	0	0	1	4	7	0	0	0	0	0	0
Virginia	1	0	1	9	39	16	0	0	0	1	6	6
West Virginia	1	1	1	7	11	11	0	0	0	1	2	2
North Carolina	1	3	3	3	9	9	0	0	0	4	2	4
South Carolina	0	1	2	1	3	2	0	0	0	1	5	5
Georgia	3	8	1	6	3	3	0	0	0	5	5	6
Florida	3	21	1	5	3	4	0	0	0	2	5	5
EAST SOUTH CENTRAL												
Kentucky	0	4	4	3	6	10	0	1	0	0	0	5
Tennessee	1	6	6	2	3	9	0	0	0	5	5	6
Alabama	1	6	1	4	4	5	0	0	0	0	5	4
Mississippi [3]	0	3	2	4	4	4	0	0	0	2	3	3
WEST SOUTH CENTRAL												
Arkansas	2	8	4	3	1	2	0	1	0	10	3	7
Louisiana	0	13	2	3	3	4	0	0	0	2	3	3
Oklahoma	0	10	3	11	5	4	0	1	0	[6]7	0	1
Texas	3	52	52	19	23	28	0	0	0	22	12	15
MOUNTAIN												
Montana	0	0	0	2	3	6	0	0	0	0	0	0
Idaho	0	1	0	1	2	1	1	0	0	0	4	1
Wyoming	0	0	0	0	0	5	0	0	0	0	0	0
Colorado	2	25	1	13	39	23	0	0	0	0	0	0
New Mexico	0	1	0	3	3	3	0	0	0	2	0	1
Arizona	0	1	1	10	8	8	0	0	0	2	0	0
Utah [3]	0	3	0	12	8	10	0	0	0	0	0	0
Nevada	0	0	0	0	0	0	0	0	0	0	0	0
PACIFIC												
Washington	1	3	0	0	18	21	0	0	0	0	1	1
Oregon	0	0	0	7	20	17	0	0	0	7	0	0
California	33	22	13	72	79	110	0	0	0	9	2	3
Total	76	273	190	937	1,223	1,223	1	6	6	108	138	138
26 weeks	1,200	1,854	1,084	58,958	82,114	92,168	140	256	267	[6]1,147	1,586	1,807
Seasonal low week [4]	(11th) Mar. 15–21			(32d) Aug. 9–15			(35th) Aug. 30–Sept. 5			(11th) Mar. 15–21		
Total since low	589	1,385	782	85,644	120,685	130,489	194	332	384	[6]967	1,111	1,222

[3] Period ended earlier than Saturday.
[4] Dates between which the approximate low week ends. The specific date will vary from year to year.
[5] Including paratyphoid fever reported separately, as follows: Massachusetts 4 (salmonella infection); New Jersey 1; Georgia 1; Arkansas 1; Oklahoma 2; Texas 1; New Mexico 1; Arizona 1; California 2.
[6] Delayed report: Typhoid fever, Oklahoma, 5 cases, included in cumulative totals only.

Telegraphic morbidity reports from State health officers for the week ended June 28, 1947, and comparison with corresponding week of 1946 and 5-year median—Con.

Division and State	Whooping cough			Week ended June 28, 1947							
	Week ended—		Median 1942–46	Dysentery			Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever, endemic	Undulant fever
	June 28, 1947	June 29, 1946		Amebic	Bacillary	Unspecified					
NEW ENGLAND											
Maine	48	10	19								1
New Hampshire	7	11									
Vermont	5	21	20								5
Massachusetts	83	146	107		4						4
Rhode Island	4	25	28								
Connecticut	58	39	39	1							11
MIDDLE ATLANTIC											
New York	205	111	258	13	1		1				3
New Jersey	189	130	174								
Pennsylvania	233	80	214								2
EAST NORTH CENTRAL											
Ohio	193	72	177						1	1	1
Indiana	29	23	33		2				1		
Illinois	103	92	92	2					2		20
Michigan [3]	206	126	122		1				1		4
Wisconsin	98	135	135								6
WEST NORTH CENTRAL											
Minnesota	58	5	9	1	1						9
Iowa	26	35	27								27
Missouri	40	15	23						5		4
North Dakota	3	2	2	2							
South Dakota	5							1			3
Nebraska	21	6	7								
Kansas	66	33	52								3
SOUTH ATLANTIC											
Delaware	2	1	1					2			
Maryland [3]	97	21	70			1		[7] 2			1
District of Columbia	21	13	22					1			
Virginia	126	80	67	2		125		7	1		1
West Virginia	48	53	24								
North Carolina	45	159	190							1	3
South Carolina	131	74	74		7					1	1
Georgia	58	47	19		2			1	1	19	9
Florida	55	36	33							2	1
EAST SOUTH CENTRAL											
Kentucky	27	17	46					1			
Tennessee	59	28	30	1		1		1	2		3
Alabama	56	32	31	1				1		6	3
Mississippi [3]	16			8	7				1	2	3
WEST SOUTH CENTRAL											
Arkansas	73	14	19	10	4			1	5		8
Louisiana	7			12					3	2	1
Oklahoma	60	8	14					2	2		3
Texas	568	249	254	49	349	14			1	34	6
MOUNTAIN											
Montana	6	3	8				1				
Idaho	14	3	4		1			1			1
Wyoming	3	32	4								
Colorado	34		24								1
New Mexico	25	17	8		1						
Arizona	8	7	12			9					
Utah [3]	6	13	31								4
Nevada											
PACIFIC											
Washington	23	23	23	18							
Oregon	34	55	20								
California	198	50	126	10	4		2				5
Total	3,480	2,152	2,673	130	384	150	4	21	27	67	157
Same week, 1946	2,152			75	463	272	11	16	28	70	155
Median, 1942–46	2,673			48	626	272	10	25	15	82	[8] 136
26 weeks: 1947	77,648			1,426	7,958	5,325	168	[7] 175	778	970	2,847
1946	49,215			1,092	9,099	3,269	236	170	471	1,325	2,396
Median, 1942–46	65,092			841	8,856	2,900	236	172	471	1,325	[8] 2,411

[3] Period ended earlier than Saturday.

[7] Delayed report: Rocky Mountain spotted fever, Maryland, 1 case, onset in May, included in cumulative total. [8] 2-year average, 1945–46.

Anthrax: New York 2 cases.

Alaska, week ended June 28: Typhoid fever 1; diphtheria 1; German measles 1.

WEEKLY REPORTS FROM CITIES [1]

City reports for week ended June 21 1947

This table lists the reports from 84 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

Division, State, and City	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland	0	0	1	0	16	0	1	0	3	0	0	3
New Hampshire:												
Concord	0	0	------	0	------	0	0	0	0	0	0	------
Vermont:												
Barre	0	0	------	0	15	0	0	0	0	0	0	------
Massachusetts:												
Boston	3	0	------	0	36	0	9	0	6	0	1	27
Fall River	0	0	------	0	27	0	2	0	0	0	0	7
Springfield	0	0	------	0	2	0	2	0	1	0	0	1
Worcester	0	0	------	0	8	0	5	0	2	0	0	2
Rhode Island:												
Providence	0	0	1	0	126	0	1	0	2	0	0	14
Connecticut:												
Bridgeport	0	0	------	0	23	0	0	0	8	0	0	------
Hartford	0	0	------	0	108	0	2	0	1	0	0	1
New Haven	0	0	1	0	47	0	1	0	7	0	1	16
MIDDLE ATLANTIC												
New York:												
Buffalo	0	0	------	0	2	0	2	0	4	0	1	2
New York	16	0	4	0	375	10	35	3	60	0	1	96
Rochester	0	0	------	0	1	0	2	0	5	0	0	7
Syracuse	0	0	------	0	1	0	0	0	8	0	0	26
New Jersey:												
Newark	0	0	2	0	22	0	0	0	4	0	0	34
Trenton	0	0	------	0	4	0	1	0	1	0	0	3
Pennsylvania:												
Philadelphia	2	0	1	0	19	0	12	0	20	0	0	58
Pittsburgh	1	0	1	1	13	0	2	0	9	0	0	16
Reading	0	0	------	0	2	0	1	0	0	0	0	------
EAST NORTH CENTRAL												
Ohio:												
Cincinnati	3	0	1	0	1	1	0	0	6	0	0	8
Cleveland	0	0	------	0	83	1	2	0	14	0	0	99
Columbus	0	0	------	0	113	0	2	1	1	0	0	------
Indiana:												
Fort Wayne	0	0	------	0	7	0	2	0	1	0	0	2
Indianapolis	1	0	------	1	5	0	1	1	8	0	0	15
South Bend	0	0	------	0	2	0	0	0	0	0	0	1
Terre Haute	0	0	------	0	1	0	2	0	0	0	0	8
Illinois:												
Chicago	0	0	------	2	46	9	22	3	29	0	0	21
Michigan:												
Detroit	1	0	------	0	8	0	8	0	63	0	0	86
Flint	0	0	------	0	------	0	4	0	1	0	0	------
Grand Rapids	0	0	------	0	5	0	0	0	3	0	0	6
Wisconsin:												
Kenosha	0	0	------	0	1	1	0	0	0	0	0	2
Milwaukee	0	0	------	0	31	1	2	0	13	0	0	29
Racine	0	0	------	0	1	0	0	0	13	0	0	5
Superior	0	0	------	0	------	0	0	0	1	0	0	2
WEST NORTH CENTRAL												
Minnesota:												
Duluth	0	0	------	0	1	0	0	0	0	0	0	7
Minneapolis	0	0	------	0	33	0	2	0	11	0	1	4
St. Paul	0	0	------	* 0	293	1	2	0	4	0	0	16
Missouri:												
Kansas City	0	0	------	0	2	0	4	0	3	0	0	5
St. Joseph	0	0	------	0	2	0	0	0	0	0	0	------
St. Louis	5	0	------	0	43	0	7	0	3	0	0	34

[1] In some instances the figures include nonresident cases

City reports for week ended June 21, 1947—Continued

Division, State, and City	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL—continued												
Nebraska:												
Omaha	0	0	------	0	3	0	0	1	1	0	0	------
Kansas:												
Topeka	0	0	------	0	------	0	0	0	0	0	0	7
Wichita	0	0	------	0	------	0	3	0	1	0	0	13
SOUTH ATLANTIC												
Delaware:												
Wilmington	0	0	------	0	------	0	0	0	0	0	0	------
Maryland:												
Baltimore	1	0	1	1	9	0	1	0	2	0	0	68
Cumberland	0	0	------	0	------	0	0	0	0	0	0	------
Frederick	0	0	------	0	------	0	0	0	0	0	0	2
District of Columbia:												
Washington	0	0	------	0	8	0	5	0	1	0	0	19
Virginia:												
Lynchburg	0	0	------	0	------	0	1	0	0	0	0	------
Richmond	0	0	1	1	14	1	2	0	2	0	0	10
Roanoke	0	0	------	0	2	0	0	0	0	0	0	------
West Virginia:												
Wheeling	0	0	------	0	1	0	2	0	0	0	0	1
North Carolina:												
Raleigh	0	0	------	0	1	0	0	0	0	0	0	3
Winston-Salem	0	0	------	0	4	0	3	0	0	0	0	------
South Carolina:												
Charleston	0	0	11	0	10	0	2	0	0	0	0	6
Georgia:												
Atlanta	0	0	1	1	3	0	0	0	3	0	3	6
Brunswick	0	0	------	0	------	0	0	0	0	0	0	------
Savannah	0	0	------	0	------	0	0	0	0	0	0	12
Florida:												
Tampa	1	0	------	0	1	2	0	0	0	0	0	6
EAST SOUTH CENTRAL												
Tennessee:												
Memphis	0	0	------	1	3	1	8	0	0	0	0	9
Nashville	0	0	------	0	------	0	3	0	0	0	0	6
Alabama:												
Birmingham	0	0	------	0	5	0	0	1	0	0	0	4
Mobile	0	0	------	0	------	0	0	0	1	0	0	------
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock	0	0	------	0	3	0	0	0	0	0	0	10
Louisiana:												
New Orleans	0	0	1	0	8	0	4	1	1	0	1	4
Shreveport	0	0	------	0	------	0	4	0	0	0	0	------
Oklahoma:												
Oklahoma City	0		2	0	1	1	1	0	2	0	0	------
Texas:												
Dallas	0	0	------	0	52	0	0	0	1	0	0	13
Galveston	0	0	------	0	------	0	0	0	0	0	0	------
Houston	0	0	------	0	------	0	3	0	0	0	0	4
San Antonio	0	0	------	0	------	0	3	0	0	0	0	12
MOUNTAIN												
Montana:												
Billings	0	0	------	0	------	0	1	0	0	0	0	------
Great Falls	0	0	------	0	4	0	0	0	0	0	0	3
Missoula	0		------	0	------	0	0	0	0	0	0	------
Colorado:												
Denver	0	0	------	0	5	0	3	0	11	0	1	12
Pueblo	0	0	------	0	4	0	0	0	1	0	0	1
Utah:												
Salt Lake City	0	0	------	0	4	0	2	0	6	0	0	10

City reports for week ended June 21, 1947—Continued

Division, State, and City	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle	0	0	------	0	5	1	0	0	2	0	1	3
Spokane	0	0	------	0	------	0	1	0	0	0	0	3
Tacoma	0	0	------	0	------	0	0	0	0	0	0	2
California:												
Los Angeles	4	0	3	1	6	1	6	7	32	0	1	51
Sacramento	0	1	------	0	------	0	0	0	1	0	0	------
San Francisco	2	0	------	0	19	0	5	1	6	0	2	------
Total	40	1	32	9	1,700	31	201	19	389	0	14	963
Corresponding week, 1946*	63	------	15	11	3,308	------	216	------	497	1	23	491
Average 1942–46*	53	------	27	[2] 9	[3] 2,910	------	[2] 240	------	600	0	17	797

*Exclusive of Oklahoma City.
[2] 3-year average, 1944–46.
[3] 5-year median, 1942–46.

Dysentery, amebic.—Cases: New York 11; Chicago 1; Minneapolis 3; New Orleans 7.
Dysentery, bacillary.—Cases: Charleston, S. C., 2; Oklahoma City 1.
Dysentery, unspecified.—Cases: Cincinnati 14; Baltimore 3; San Antonio 16.
Leprosy.—Cases: Los Angeles 1.
Rocky Mountain spotted fever.—Cases: Philadelphia 1.
Tularemia.—Cases: Boston 1; St. Paul 1 (onset in May); Atlanta 2.
Typhus fever, endemic.—Cases: Los Angeles 1.

Rates (annual basis) per 100,000 population, by geographic groups, for the 84 cities in the preceding table (latest available estimated population, 34,248,300)

	Diphtheria case rates	Encephalitis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Poliomyelitis case rates	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
			Case rates	Death rates								
New England	7.8	0.0	7.8	0.0	1,066	0.0	60.1	0.0	78	0.0	5.2	186
Middle Atlantic	8.9	0.0	3.7	0.5	205	4.7	25.7	1.4	52	0.0	0.9	113
East North Central	3.1	0.0	0.6	1.8	186	8.0	27.6	3.1	94	0.0	0.0	174
West North Central	10.1	0.0	0.0	0.0	758	2.0	36.2	2.0	46	0.0	2.0	173
South Atlantic	3.4	0.0	23.8	5.1	90	5.1	27.2	0.0	14	0.0	5.1	226
East South Central	0.0	0.0	0.0	5.9	47	5.9	64.9	5.9	6	0.0	0.0	112
West South Central	0.0	0.0	7.6	0.0	163	2.5	38.1	2.5	10	0.0	2.5	109
Mountain	0.0	0.0	0.0	0.0	143	0.0	50.5	0.0	152	0.0	8.4	219
Pacific	9.5	1.6	4.7	1.6	47	3.2	19.0	12.7	65	0.0	6.3	93
Total	6.1	0.2	4.9	1.4	260	4.7	30.7	2.9	59	0.0	2.1	147

FATAL CASE OF PLAGUE IN CALIFORNIA

Under date of June 30, Dr. Wilton L. Halverson reported a fatal case of plague (sylvatic) in a 12-year old boy, living in Alturas, Modoc County, Calif. The diagnosis was confirmed by animal inoculation at the State laboratory. Field investigations had not been completed, but it was believed that the source of the infection was in the vicinity of the Fitzhugh Ranger Station, 13 miles southeast of Alturas.

This is the first case of plague acquired in nature in the United States since 1943, in which year one case was reported, and a death occurred in a case which was reported late in 1942, both in Siskiyou County, which borders Modoc County on the west of the latter county.[1] A case of primary pneumonic plague, in which the infection was acquired in the laboratory, occurred in San Francisco in 1944.[2]

PLAGUE INFECTION IN CALIFORNIA, OREGON, AND WASHINGTON

Under dates of June 24 and 25, plague infection was reported proved in fleas from rodents taken in California, Oregon, and Washington, as follows:

CALIFORNIA

Lassen County.—A pool of 158 fleas from 2 marmots, *Marmota* sp., taken 17 miles east and 10 miles south of Adin, Modoc County, Calif., proved positive on June 23.

Monterey County.—A pool of 200 fleas from 28 ground squirrels, *Citellus beecheyi*, taken 25 miles south of Monterey, proved positive on June 20.

OREGON

Lake County.—A pool of 8 fleas from 24 ground squirrels, *C. oregonus*, taken June 11 from Drake Flats, 22 miles northeast of Lakeview on road to Plush, proved positive on June 23.

WASHINGTON

Kittitas County.—A pool of 197 fleas from 106 meadow mice, *Microtus* sp., 200 fleas from 74 white-footed deer mice, *Peromyscus* sp., proved positive on June 23, and 200 fleas from 90 chipmunks, *Eutamias* sp., proved positive on June 25, all taken on June 12 from a location 6 miles southeast of Kittitas.

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[1] Public Health Report, September 3, 1943, p. 1361.
[2] Public Health Report, July 21, 1944, p. 962.

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended June 7, 1947.—During the week ended June 7, 1947, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox		63		209	374	34	26	92	118	916
Diphtheria			1	15	5	1		1		23
Dysentery:										
Amebic		1			1					2
Baciliary				1						1
German measles				27	42	2	9	7	7	94
Influenza					55	11			4	70
Measles		12	3	126	243	142	72	52	49	699
Meningitis, meningococcus					4				1	5
Mumps		28		69	374	21	39	15	94	640
Poliomyelitis					1		1	1	1	4
Scarlet fever		2	2	41	50	5	1	9	5	115
Tuberculosis (all forms)			24	144	17	15	1	7	59	267
Typhoid and paratyphoid fever			3	6	1			1	10	21
Undulant fever				8	1		1			10
Venereal diseases:										
Gonorrhea		6	8	104	86	40	18	38	81	381
Syphilis		10	5	73	65	17	8	6	51	235
Whooping cough		4		49	73	48	1	8	64	247

CUBA

Habana—Communicable diseases—5 weeks ended May 31, 1947.—During the 5 weeks ended May 31, 1947, certain communicable diseases were reported in Habana, Cuba, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Chickenpox	14		Measles	19	
Diphtheria	29	1	Tuberculosis	7	5
Malaria	4		Typhoid fever	17	2

Provinces—Notifiable diseases—Five weeks ended May 31, 1947.—During the five weeks ended May 31, 1947, cases of certain notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Rio	Habana [1]	Matanzas	Santa Clara	Camaguey	Oriente	Total
Cancer	5	9	17	19	3	27	80
Chickenpox		17	1		1	5	24
Diphtheria		28		5	2	1	36
Hookworm disease		18					18
Leprosy		8		1		1	10
Malaria	1	5		3	2	170	181
Measles		19	3	2	8	7	39
Poliomyelitis	1	3	1		2	1	8
Rabies (human)						1	1
Tuberculosis	18	31	22	42	22	48	183
Typhoid fever	13	41	13	44	30	41	182
Whooping cough		24			1		25

[1] Includes the city of Habana.

FINLAND

Notifiable diseases—April 1947.—During the month of April 1947, cases of certain notifiable diseases were reported in Finland as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis	13	Paratyphoid fever	193
Diphtheria	466	Poliomyelitis	10
Dysentery, unspecified	13	Scarlet fever	199
Gonorrhea	1,140	Syphilis	388
Lymphogranuloma inguinale	1	Typhoid fever	104
Malaria	1		

JAPAN

Notifiable diseases—5 weeks ended May 31, 1947, and accumulated totals for the year to date.—For the 5 weeks ended May 31, 1947, and for the year to date, certain notifiable diseases have been reported in Japan as follows:

Disease	5 weeks ended May 31, 1947		Total reported for the year to date	
	Cases	Deaths	Cases	Deaths
Diphtheria	3,201	234	15,124	1,410
Dysentery, unspecified	1,091	183	2,258	435
Encephalitis, Japanese "B"	----------	----------	1	2
Gonorrhea	22,447	----------	82,495	----------
Influenza	1,336	----------	----------	----------
Malaria	1,074	3	3,999	13
Measles	42,952	----------	[1] 71,513	----------
Meningitis, epidemic	511	196	2,201	662
Paratyphoid fever	332	23	1,215	76
Pneumonia	28,234	----------	[1] 55,109	----------
Scarlet fever	416	5	1,210	26
Smallpox	88	2	332	31
Syphilis	15,632	----------	56,370	----------
Tuberculosis	41,039	----------	[1] 68,606	----------
Typhoid fever	1,372	148	4,850	611
Typhus fever	105	12	743	63
Whooping cough	24,496	----------	43,274	----------

[1] For the period Mar. 30, 1947, to May 31, 1947.

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-named diseases, except yellow fever during recent months. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday of each month.

Cholera

India—Calcutta.—For the week ended June 14, 1947, 263 cases of cholera with 63 deaths were reported in Calcutta, India.

Plague

Indochina (French)—Cochinchina—Cholon.—For the period May 21–31, 1947, one case of plague was reported in Cholon, Cochinchina, French Indochina.

Peru.—For the month of May 1947, 6 cases of plague with 3 deaths were reported in Peru by Departments as follows: Lima, 5 cases, 3 deaths; Piura, 1 case.

Smallpox

Angola.—For the month of January 1947, 13 cases of smallpox were reported in Angola.

Colombia.—For the month of May 1947, 813 cases of smallpox with 13 deaths were reported in Colombia, including 290 cases of smallpox with 9 deaths reported in Santander Department.

Great Britain—England.—For the week ended June 21, 1947, 2 cases of smallpox were reported in Bilston, Staffordshire, England. In addition, 8 suspected cases of smallpox were reported as follows: Bilston, 6; Dudley, 1; Willenhall, 1.

Iraq—Basra.—For the week ended June 7, 1947, 4 cases of smallpox were reported in Basra, Iraq, occurring in Afghanistan pilgrims from Baghdad.

Typhus Fever

Colombia.—For the month of May 1947, 238 cases of typhus fever with 4 deaths were reported in Columbia, including 143 cases with 2 deaths reported in Antioquia Department, Colombia.

Tunisia.—For the month of May 1947, 129 cases of typhus fever were reported in Tunisia.

Yellow Fever

Colombia.—Yellow fever has been reported in Colombia as follows: Acacias, Intendencia of Meta, June 19, 1947, 2 deaths; Bolivar, Santander Department, May 10–13, 1947, 1 death.