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SULFARSPHENAMINE IN THE THERAPY OF SYPHILIS. A COMPARATIVE STUDY OF THE TOXIC MANIFESTATIONS OF NEOARSPHENAMINE AND SULFARSPHENAMINE*

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The 1936 Conference on Venereal Disease Control Work (*1*) recommended that the ideal antisyphilitic drug for distribution by health departments to clinics and practitioners should be effective, easily administered, free from reactions, and low in price.

In several respects sulfarsphenamine would qualify as such a drug, especially for its ease and flexibility of administration. It has, however, the reputation of being a dangerous drug when given to adults, which would exclude it from consideration. There is equally good evidence that sulfarsphenamine is a safe and reliable drug to use in the treatment of syphilis and is the drug of choice especially for the general practitioner. Because of this difference of opinion concerning the toxicity of sulfarsphenamine, the clinical and laboratory evidence is reviewed to determine the usability of this drug in the treatment of syphilis.

Although sulfarsphenamine had been manufactured and used extensively for several years in France under the trade name of Sulfarsenol, and the Laboratorie de Biochemie held United States license and exported some material to America, it was not until Voegtlin and Johnson (*2*) developed the process of manufacture that it was given extensive clinical trial in this country.

Laboratory investigations (*3*, *4*, *5*, *6*) indicated that sulfarsphenamine would be the equal of, if not superior to, other members of the

*This study was instituted at the suggestion of W. T. Harrison, Medical Director, and approved by the Cooperative Clinical Group of the Public Health Service. Medical Director R. A. Vonderlehr effected the arrangements for the clinical facilities at Hot Springs to conduct the clinical investigation. The active interest and cooperation of Doctors Vonderlehr and Harrison was of material assistance in organizing and conducting the study.

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arsphenamine group. The product was more stable both in the ampule and in solution; it was less toxic in laboratory animals, slightly less effective trypanocidally than neoarsphenamine (*3*), but as a spirocheticidal agent equally effective as arsphenamine and neoarsphenamine (*5, 6*); it was the most effective arsphenamine derivative and compared favorably with the highly effective pentavalent arsenicals in penetrating into the cerebrospinal fluid (*4*). In addition to these advantages, laboratory investigations also indicated that sulfarsphenamine injected intramuscularly was equally as effective as arsphenamine or neoarsphenamine injected intravenously (*6*). In this respect sulfarsphenamine indicated a definite advance in the therapy of syphilis as arsphenamine and neoarsphenamine had both proved to be definitely unsatisfactory when injected intramuscularly.

When first placed on the market, sulfarsphenamine was used extensively but owing to reactions it has been discarded to a great extent in general therapy of syphilis. Clinical experience indicated that the reaction incidence was high, the reactions being severe and showing a tendency to blood dyscrasias (*7*). The drug was introduced for the general therapy of syphilis on the basis of early laboratory investigations before the necessary clinical work had been done to determine dosage, treatment schedules, etc.

Salvarsan, neosalvarsan, and the other derivatives of salvarsan were similarly unsatisfactory when first introduced. The report of the Salvarsan Committee of Great Britain on the toxic effects following the employment of arsenobenzol preparations (*8*) reviewed the history of the German investigations of 1914 and 1917 relating to the salvarsan treatment of syphilis and the ill effects observed after its use. These investigations were instituted because of severe criticism which finally resulted in a petition being presented to the Chamber of Deputies demanding prohibition of the use of salvarsan. Because of the high fatality rate after neosalvarsan therapy, the Salvarsan Committee of the Allgemeiner Aerztlicher Verein of Munich in 1920 recommended restriction in the size of the dose to the maximum of 0.6 gm.

REACTIONS IN THE ARSPHENAMINE THERAPY OF SYPHILIS

Reactions following the administration of arsphenamines are due primarily to the arsenic content of the preparation and secondarily to the phenol or aminophenol radical. Possibly the combination plays a greater role as an etiologic agent than either one individually. Inorganic arsenical compounds (*9*) systemically relax the capillaries and increase their permeability, thus simulating inflammation. This change is most conspicuous in the splanchnic area. Acute arsenic poisoning results in extreme gastro-enteritis. The dilatation of capillaries—capillary paralysis—introduces changes in the circulation which cause secondary disturbances in the functioning of more remote

organs, particularly the nervous system. Fatty degeneration of the cells is evident, especially in glands and muscles, with other disturbances of nutrition and metabolism. This is true in chronic poisoning. There are also characteristic effects on the bones and bone marrow.

Kolmer (*10*) in his discussion of the clinical significance of the changes produced by arsphenamine and its derivatives—the toxic reactions due to arsenic—concludes that most of the tissue changes are due to some form of arsenic, and the outstanding changes are, first, an effect upon the capillaries characterized by relaxation and congestion with serous exudate and minute hemorrhages which are characteristic tissue changes consequent upon arsenic poisoning, and, second, parenchymatous degeneration and necrosis.

Post-mortem findings in fatal cases following arsphenamine therapy definitely indicate that arsenic is the agent causing death.

Cook (*11*), reviewing the autopsies of 44 cases of the 63 deaths reported during the 17-year period 1919–35, recorded that "the striking features are the frequency of edema, congestion, and hemorrhages in the different organs. This is not surprising when one recalls that one of the effects of arsenic is to cause dilation of the capillaries with increased permeability. An additional effect is attributed to the drug by many authorities, namely, damage to the endothelial lining of the capillaries. If this action extends to the reticulo-endothelial systems, one has a basis for nearly all the manifestations of arsenic poisoning. It is obvious that these factors will produce marked variations in symptomatology and pathology, depending on the location and amount of edema and hemorrhage." The pathologic findings presented, according to Cook, are suggestive of a common basis for the diverse clinical signs of arsphenamine poisoning.

Hahn (*12*) presents autopsy data on 35 of 47 deaths resulting from antisyphilitic treatment reported at the Johns Hopkins Hospital during the period from 1913 to 1940. It is his opinion that hemorrhage is not primarily a manifestation of arsenical toxicity but is a secondary complication. Hepatic necrosis, dermatitis, and hypoplasia of the bone marrow were the most frequent pathologic diagnoses. Multiple hemorrhages in the viscera, skin, and mucous and serous membranes were reported in 16 of the 35 autopsies.

The British Salvarsan Committee (*8*) concluded, from evidence presented for its study, that many of the ill effects of salvarsan could be attributed directly to its arsenical content, and that other complications such as liver and bone marrow damage probably were due to the whole chemical composition of the compound and not solely to arsenic.

Reactions following arsphenamine therapy are primarily quantitative, and to some extent qualitative. The quantitative aspect of arsphenamine reactions is illustrated in the classical reports of Meirowsky (Cologne, 1920) and the Salvarsan Committee of Munich, 1920.

These reports showed that the incidence of reaction definitely increased with increased dosage. While it is well established that toxic reactions, including death, occur at all dose levels, even following comparatively minute doses, in general (as stated by Kolmer (*10*)), the incidence of toxic reactions is greatly influenced by dosage. The qualitative phenomenon of arsphenamine reactions is manifested by the tendency of a specific type of reaction to occur at a higher incidence following a specific arsphenamine. It is, therefore, the quantitative index of that particular arsphenamine.

BLOOD DYSCRASIAS

Blood dyscrasias as a complication following arsphenamine therapy have been reviewed extensively by McCarthy and Wilson (*13*), Loveman (*14*), Falconer and Epstein (*15*), and Stokes, Beerman, and Ingraham (*16*). These reviews, citing a very extensive literature, definitely and conclusively agree that this phenomenon is not peculiar to any one of the arsphenamine products but every one has been shown to be capable of producing hematopoietic reactions (*16*).

Loveman, in the review of the general literature, traced the history of blood dyscrasias showing that inorganic arsenic, organic arsenic, and benzene products were capable of producing hemorrhagic and hematopoietic injury. Concerning the etiologic factor in cases of post-arsphenamine blood dyscrasias, Loveman suggests the probability that all play a part, the combination playing a greater role than any of the elements individually.

The blood dyscrasias following arsphenamine therapy, as classified by McCarthy and Wilson, are of two types, one a depression of the bone marrow function, and the other a toxic action on the platelets in the peripheral circulation. The thrombocytopenic type of reaction, they conclude, is of an "anaphylactoid" nature. It was noted that this reaction occurred in cases apparently rendered sensitive to the arsphenamines after treatment with a number of injections. Arsenic is believed to be the causative factor and not the benzene radical as there is no evidence of depression of the bone marrow function. Acute destruction of the platelets in the peripheral circulation with rapid regeneration is characteristic of this reaction.

Falconer and Epstein, studying purpura haemorrhagica following arsphenamine therapy, offer evidence to suggest that this reaction accompanied by varying degrees of shock is an allergic phenomenon rather than a toxic manifestation of the drug injected. The prompt loss of circulatory tone accompanying the reaction appears to be a vasomotor effect, with loss of capillary tone, dilatation of the capillary bed, and a rapid loss of platelets from the general circulation. A great number of these platelets can be returned promptly into the general circulation by injection of epinephrine.

The physiologic action of arsenic, reports Kolmer (*10*), is to produce paralysis of the capillaries with increased permeability, especially in vessels of the splanchnic area. This, he observes, has been known for years to be a well established fact in the pharmacology of arsenic and he cites the work of Ricker and Knape (1912) which showed by direct microscopic observations of the capillary bed in living animals that administration of the arsphenamines caused a slowing of the blood stream, dilatation of the capillaries, stasis, and hemorrhage.

A predisposed, weakened hematopoietic system (Loveman) or an abnormal change in the capillaries of the individual (Kolmer) are of great importance as a secondary factor in blood dyscrasias. Kahn (*17*) and Buxton (*18*) have observed that menstrual abnormality is present in practically all cases of blood dyscrasias in women. Menorrhagia is of outstanding diagnostic significance in cases of blood dyscrasias, especially purpura haemorrhagica. This suggests that females with menstrual disorders might possibly be poor risks for arsphenamine therapy.

BLOOD DYSCRASIAS AFTER SULFARSPHENAMINE

While blood dyscrasias have been reported following the use of all the arsphenamine products, and also arsenoxide, there is evidence to indicate that the incidence following sulfarsphenamine is higher than that following the other products.

In an evaluation of the three sulfarsphenamine products, bismuth arsphenamine sulfonate, sulfarsphenamine, and trisodium sulfarsphenamine, Stokes, Beerman, and Ingraham (*16*) noted the tendency toward hematopoietic accidents.

Clinical reports on the use of trisodium sulfarsphenamine and bismuth arsphenamine sulfonate are favorable. The reaction incidence is low but a tendency toward the hematopoietic reaction is reported. The reactions, however, are rare.

A review of 14 years' experience with bismarsen for the treatment of syphilis was reported by Beerman, Shaffer, and Livingood (*19*). The study reports the results of treatment of 823 syphilitic patients receiving 18,286 injections. The literature concerning the hemorrhagic reactions to bismarsen is reviewed. Bismarsen, the authors observed, is a relatively nontoxic and easily administered drug for the treatment of syphilis. Although it was frequently used in treating patients sensitive to the other arsenicals, the reaction incidence was low, only 5 cases each of arsphenamine dermatitis and purpura haemorrhagica occurring, with no fatalities. It is interesting to note that in the discussion of the study Combes (*20*) reported that he abandoned bismarsen because he "developed an aversion to preparations containing the sulfonate radical," whereas Appel's (*21*) experience

with this product has led him to rely on it in cases in which intravenous therapy is contraindicated.

Sulfarsphenamine, states Stokes (*16*) in his review, "exhibits the curious paradox of warm allegiance on the part of some undoubtedly competent observers, side by side with damnation from others equally competent."

CLINICAL REVIEW

Pfeiffer (*22*, *23*) reported satisfactory results with the use of sulfarsphenamine in Massachusetts and later in New York.

The Massachusetts report covered a period of 2 years in which sulfarsphenamine was used in various types and stages of syphilis in 20 different clinics and in 7 hospitals for mental diseases, over 15,000 doses being administered. The one adverse report stated that the only excuse for giving sulfarsphenamine was "inability to find veins." The observations reported sulfarsphenamine to be a safe (reactions not as frequent as with arsphenamine and neoarsphenamine) and a reliable drug to use in the treatment of syphilis and the drug of choice especially for the general practitioner.

The report on the use and status of sulfarsphenamine in New York State is more extensive than the Massachusetts survey. During the period from 1925 to 1934, the State distributed 159,034 gm. of sulfarsphenamine to hospitals, State institutions, clinics, and practicing physicians. The experience was satisfactory and at variance with that of some observers as to its value and dangers. A detailed statistical study of the reactions following sulfarsphenamine therapy in three clinics and one penal institution is reported. In the three clinics, 29,510 injections, of which all but 693 were intravenous, were administered to 920 patients in doses varying from 0.3 to 0.6 gm. In one clinic, 0.6 gm. twice weekly was used for a short time. It was found, however, that doses of 0.45 gm. gave good therapeutic results and fewer reactions. The case histories compiled by the Division of Vital Statistics of the State Health Department of New York showed that with the exception of purpura, which occurred six times, the reaction rates were lower than those reported for all arsenicals by the Cooperative Clinical Group. There were no cases of aplastic anemia, cerebral hemorrhage, or acute yellow atrophy of the liver, and there were no fatalities. At the penal institution, 8,198 intravenous injections averaging 0.72 gm. were administered during the period from 1929 to 1932. In the beginning the dose was 0.9 gm., without heavy metals, but later, in 1930, it was reduced to the maximum of 0.6 gm. The severe reactions reported were five cases of dermatitis, one of jaundice, and three deaths. In each of the three fatalities the dosage ranged from 0.6 to 0.9 gm., with a very high proportion, 68 percent, as the top figure.

The medical service of the United States Navy (*24*) during the period from 1925 to 1941 administered 30,834 injections of sulfarsphenamine, reporting 17 mild, 8 severe, and no fatal reactions. The reported reaction ratio is 1 in every 1,233 injections as compared with 1 to 1,362 injections of neoarsphenamine. No fatal reactions were reported following sulfarsphenamine, while the ratio of deaths to doses following neoarsphenamine was 1 to 27,101 injections. During the 4 years 1938–41 (*25*), 4,290 injections of sulfarsphenamine were administered without a single reported reaction. Of the total injections, only 293, approximately 7 percent, were administered to "active service personnel," and in 3,978 cases, over 92 percent, the dosage was less than 0.6 gm. It is apparent, therefore, that the record of this 4-year period refutes the criticism that the Navy experience is not a particularly good criterion because of the "good risk" of the naval personnel. The good record in these reports is possibly due to the treatment schedule.

Reports of the Cooperative Clinical Group (*7*), which included Cole's study (*29*), recorded that the reaction ratio following sulfarsphenamine therapy, 7,912 doses, was slightly lower in minor reactions but the major reaction rate (3.54 per 1,000 injections) was higher than that experienced with arsphenamine (2.17 per 1,000) and neoarsphenamine (2.43 per 1,000), principally because of the high incidence of dermatitis and purpura haemorrhagica.

The incidence for purpura following sulfarsphenamine was high, 0.76 per 1,000 injections, as compared with arsphenamine, 0.04 per 1,000, and neoarsphenamine, 0.16 per 1,000. Aplastic anemia as a complication of the therapy with neoarsphenamine and sulfarsphenamine occurred at practically the same rate, 0.10 and 0.13 for 1,000 injections respectively.

Aplastic anemia and purpura are recorded as occurring most frequently in white females. Of the 16 cases of purpura, 12 are reported in females, 10 of whom were white; the 4 cases of anemia were in white females.

Sulfarsphenamine, in doses never larger than 0.6 gm., was used a great deal (1923 to 1926, inclusive) but because of the reactions it has been almost entirely discarded. The proportion of fatalities was higher after sulfarsphenamine than after the other arsenical preparations.

In summarizing the results of the 5-year period from 1927–31, Osborne, Rickloff, and Butler (*26*) reported that 10 reactions—5 cases of jaundice, 3 of dermatitis, and 2 of purpura—occurred following 896 injections of sulfarsphenamine to adults. During the same period, 22,336 injections of arsphenamine were administered with 54 reactions—no instance of purpura, 28 cases of jaundice, and 26 of dermatitis, 2 of which were fatal. In adults, the authors felt, sulfarsphenamine is an

effective therapeutic agent but its use should be limited strictly to those individuals who present physical obstacles to intravenous therapy.

ICTERUS FOLLOWING ARSPHENAMINE THERAPY

Icterus as a manifestation of toxic complication following arsphenamine therapy is recorded in practically every compilation of arsenical reactions. The very extensive literature on the disorders of the liver following arsenical therapy has been reviewed by the British Salvarsan Committee (*8*), Lane (*27*), Mohr, Padget, and Moore (*28*), and Stokes, Beerman, and Ingraham (*16*).

Jaundice following arsenical therapy, observed Stokes, may be due to a number of causes. Arsenic is, of course, one of the direct causes, if not the principal factor, in hepatic injury due to arsphenamine therapy. The British Salvarsan Committee (*8*) reported that the incidence of jaundice and yellow atrophy increased following the introduction of salvarsan therapy in syphilis. It was the opinion of this Committee that this complication of treatment apparently was not due to toxic batches of the drug, nor to faulty technique of administration, but was more probably caused by the unwise pushing of the dosage, both as regards size of dose and frequency. It is the Committee's belief that it is the nature of the whole arsenobenzol drug, as an aminobenzol derivative, which causes the liver damage. Jaundice, says Kolmer (*10*), is to be ascribed primarily to the necrosis of liver cells by arsenic or to an exacerbation of syphilis lesions in the liver. It is Lane's opinion (*27*) that arsenic exerts an influence in most cases but is not the only factor in hepatic injury.

Cole (*29*) reported that icterus was more frequently experienced after neoarsphenamine therapy than after arsphenamine. The Cooperative Clinical Group report, of which Cole's is a part, found the icterus incidence practically the same for arsphenamine (1.16 per 1,000 injections) and neoarsphenamine (1.20 per 1,000), but slightly lower for sulfarsphenamine (0.88 per 1,000). The incidence in the white race (males 1.04 and females 1.31) was higher than in the colored race (males 0.83 and females 0.57). Stokes' review (*16*) cites Soffer, and Gott and Doyle as noting this racial difference.

RECENT LABORATORY STUDY ON SULFARSPHENAMINE

Recent studies on the stability of neoarsphenamine at the National Institute of Health (*30*) and the Division of Preventive Medicine, United States Navy (*31*), indicate that age has a direct influence on the stability of the drug (*30*), that the reaction expectancy increases with the age of the product (*31*), and that the "heat test" at 70° C.

offers a reliable and sensitive procedure for the determination of the stability of neoarsphenamine (*32*).

Similar studies (unpublished) were made on arsphenamine and sulfarsphenamine, and it was found that both of these drugs were more stable than neoarsphenamine.

As a result of these investigations the Public Health Service arsphenamine regulations (*33*) were amended to require more rigid stability and solubility ("heat") tests and to provide expiration dates (the date beyond which the contents of the package cannot be expected beyond reasonable doubt to yield their specific results) for all licensed arsphenamines. The expiration date for neoarsphenamine is 3 years, and for the other arsphenamines, including sulfarsphenamine, 5 years from the date of official release by the National Institute of Health.

Investigation of the therapeutic activity of sulfarsphenamine at the National Institute of Health, begun in 1938 and only recently completed, indicates that sulfarsphenamine is more effective than neoarsphenamine in curing rabbits infected with experimental syphilis. The sterilizing dose of sulfarsphenamine appears to be 30 mg. per kg. of body weight as compared with 40 mg. for neoarsphenamine.

On the basis of these animal experiments, it would appear that comparable clinical results in the therapy of syphilis might be expected with sulfarsphenamine and neoarsphenamine, in dosage ratio of 3 to 4 respectively. It would appear also that on the basis of equal dosage the reaction expectancy of sulfarsphenamine might be higher.

SUMMARY

This review indicates that reactions to the arsphenamines, including sulfarsphenamine, are due primarily to the arsenic content of the drug and secondarily to the aminophenol radical, or possibly to the combination of these factors. All types of reactions have been observed after each of the arsphenamines but there appears to be a tendency for definite types of reactions to occur more frequently with certain products. Purpura haemorrhagica, for instance, has been reported after all the arsphenamines, but there is evidence to indicate that after sulfarsphenamine it occurs more frequently. And, too, icterus appears more frequently after neoarsphenamine. Reactions incident to arsphenamine therapy are therefore quantitative, dependent on the quantity administered, and qualitative, according to the type of arsphenamine used.

Reactions following sulfarsphenamine therapy are in no way different from those following the other arsenicals, except in the tendency to be of specific type, and their excessive occurrence indicates that the dosage, size and frequency, is approaching the limit of tolerance.

It is suggested that the reputation of sulfarsphenamine as a dan-

gerous drug for use in adults is at least debatable. However a considerable part of the unfavorable clinical experience was obtained while the use of the drug in the therapy of syphilis was in the introductory or experimental stage. The continued satisfactory clinical reports of the United States Navy Medical Services and the recent laboratory studies appear to indicate that sulfarsphenamine products of more recent manufacture are superior, both with respect to efficacy and toxicity, to those of the earlier period.

It would appear from this survey that the whole question of the toxicity of sulfarsphenamine should be reinvestigated, and should it be determined that this drug is no more toxic than neoarsphenamine, its greater stability and ease of administration should increase its utilization in antisyphilitic therapy.

Hot Springs Neoarsphenamine-Sulfarsphenamine Study

The clinical facilities of the United States Public Health Service at Hot Springs, Ark., were made available for the reinvestigation of sulfarsphenamine, to determine whether, under comparable clinical

TABLE 1.—*Type and severity of reactions to neoarsphenamine and sulfarsphenamine*

Type of reaction	Neoarsphenamine (9,148 injections)							
	Severity of reaction							
	Mild		Moderate		Severe		Total	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Minor:								
Gastrointestinal	171	18.69	64	7.00	10	1.09	245	26.78
Nitritoid	2	.22	2	.22	1	.11	5	.55
Pruritus	20	2.19	10	1.09	2	.22	32	3.50
Slight skin eruption	23	2.51	11	1.20	1	.11	35	3.83
Shock					2	.22	2	.22
Febrile	37	4.04	11	1.20	7	.77	55	6.01
Other	17	1.86	6	.66	5	.55	28	3.06
Edema of eyelids, face, or hands								
Fainted or faint feeling following injection	1	.11					1	.11
Cardiac distress and shortness of breath								
Pain in shoulders and wrist joints								
Nosebleed	1	.11					1	.11
Headache	10	1.09	5	.55	5	.55	20	2.19
Blind for few minutes after injection								
General malaise	2	.22	1	.11			3	.33
Dizziness	3	.33					3	.33
Total minor reactions	270	29.51	104	11.37	28	3.06	402	43.94
Major:								
Aplastic anemia					1	.11	1	.11
Arsenical stomatitis			1	.11			1	.11
Icterus	10	1.09	11	1.20	9	.98	30	3.28
Purpura haemorrhagica			3	.33	1	.11	4	.44
Agranulocytosis			1	.11	1	.11	2	.22
Hemorrhagic encephalitis			1	.11	1	.11	2	.22
Arsenical dermatitis	13	1.42	7	.77	4	.44	24	2.62
Unspecified	5	.55	2	.22			7	.77
Macular	1	.11					1	.11
Papular	5	.55	4	.44			9	.98
Maculopapular								
Papulovesicular	1	.11	1	.11	1	.11	3	.33
Vesicular								
Exfoliative					3	.33	3	.33
"Fixed" exanthems	1	.11					1	.11
Death					2	.22	2	.22
Total major reactions	23	2.51	24	2.62	19	2.08	66	7.21
Total reactions	293	32.03	128	13.99	47	5.14	468	51.16

TABLE 1.—*Type and severity of reactions to neoarsphinamine and sulfarsphenamine*—Continued

Type of reaction	Sulfarsphenamine (7,730 injections)							
	Severity of reaction							
	Mild		Moderate		Severe		Total	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Minor:								
Gastrointestinal	116	15.01	81	10.48	9	1.16	206	26.65
Nitritoid	2	.26	4	.52	1	.13	7	.91
Pruritus	29	3.75	13	1.68	2	.26	44	5.69
Slight skin eruption	51	6.60	8	1.03			59	7.63
Shock	4	.52			1	.13	5	.65
Febrile	22	2.85	5	.65	4	.52	31	4.01
Other	22	2.85	7	.91	1	.13	30	3.88
Edema of eyelids, face, or hands	3	.39					3	.39
Fainted or faint feeling following injection	4	.52					4	.52
Cardiac distress and shortness of breath	2	.26					2	.26
Pain in shoulders and wrist joints					1	.13	1	.13
Nosebleed			1	.13			1	.13
Headache	10	1.29	6	.78			16	2.07
Blind for few minutes after injection	1	.13					1	.13
General malaise	2	.26					2	.26
Dizziness								
Total minor reactions	246	31.82	118	15.27	18	2.33	382	49.42
Major:								
Aplastic anemia					1	.13	1	.13
Arsenical stomatitis								
Icterus	3	.39	2	.26	3	.39	8	1.03
Purpura haemorrhagica	10	1.29	4	.52	8	1.03	22	2.85
Agranulocytosis	1	.13			2	.26	3	.39
Hemorrhagic encephalitis								
Arsenical dermatitis	11	1.42	11	1.42	2	.26	24	3.10
Unspecified	3	.39	1	.13			4	.52
Macular			2	.26			2	.26
Papular	3	.39	6	.78			9	1.16
Maculopapular	1	.13					1	.13
Papulovesicular	2	.26			1	.13	3	.39
Vesicular	1	.13					1	.13
Exfoliative	1	.13	2	.26	1	.13	4	.52
"Fixed" exanthems								
Death					2	.26	2	.2
Total major reactions	25	3.23	17	2.20	18	2.33	60	7.76
Total reactions	271	35.06	135	17.46	36	4.66	442	57.18

conditions, the incidence of reactions, severity, etc., are greater than with neoarsphenamine therapy.

The several brands of neoarsphenamine and sulfarsphenamine were used. The two arsenicals of the same brand were administered concurrently, and after approximately 1,000 doses of each, the brand was changed. The treatment procedure—size and frequency of dosage, method of administration, concentration of solution, etc.—was the same for both products. The patients, irrespective of the stage of syphilis, race, age, or sex, were entered for the type of arsphenamine on the basis of alternate case selection and maintained on the particular arsenical during the study.

The investigation was instituted in January 1940, and was continued for approximately 18 months. During this period 16,878 intravenous injections of the arsphenamines were administered, of which 9,148 were neoarsphenamine and 7,730 were sulfarsphenamine.

The type and frequency of reactions observed following injections of neoarsphenamine and sulfarsphenamine are shown in table 1. These

reactions have been divided into two main groups: (1) minor reactions, under which are included gastrointestinal, nitritoid, pruritus, slight skin eruptions, shock, febrile, and other (headache, nosebleed, dizziness, etc.), and (2) major reactions, under which are included aplastic anemia, arsenical stomatitis, icterus, purpura haemorrhagica, agranulocytosis, hemorrhagic encephalitis, arsenical dermatitis, and death. In addition to these two main groupings, each type of reaction has been classified as mild, moderate, or severe.

The difference in minor reactions, 43.9 per 1,000 injections of neoarsphenamine and 49.4 per 1,000 injections of sulfarsphenamine, was not statistically significant. This was also true in the group of major reactions, the rate per 1,000 injections being 7.2 for neoarsphenamine and 7.8 for sulfarsphenamine.

Although the differences in total minor and total major reactions were not statistically significant, pruritus and slight skin eruptions in the minor group were observed more frequently following sulfarsphenamine; in the major group icterus was observed more frequently following neoarsphenamine (3.28 to 1.03 per 1,000 injections) and purpura haemorrhagica was more frequent after sulfarsphenamine (2.85 to .44 per 1,000 injections).

Four deaths occurred after treatment, two following treatment with neoarsphenamine and two following treatment with sulfarsphenamine. The cause of death in one of the two patients receiving neoarsphenamine, both females, was hemorrhagic encephalitis, no autopsy; in the other, the clinical diagnosis was agranulocytosis and aplastic anemia, confirmed by histopathologic examination. Both the fatalities reported as being caused by sulfarsphenamine offer points of interest incident to the therapy.

J. Mc.—Male. A patient with long-standing neurosyphilis had received 16 doses of 0.4 gm. each of sulfarsphenamine during this course of treatment. At the time of his last treatment he had developed what he thought were chigger bites on his legs and failed to report the condition, contrary to clinic instructions. He died 9 days after the appearance of hemorrhages, 3 days after the last treatment. The clinical diagnosis was acute purpura haemorrhagica, and the histopathologic report was meningeal and cerebral hemorrhage, petechial hemorrhage in kidney and stomach, syphilitic aortitis with focal arteriosclerosis, acute splenitis.

R. D. H.—Female. This patient, who had a mixed infection of gonorrhea and syphilis, was receiving concurrent therapy of sulfarsphenamine and sulfanilamide. During the period from February 16, 1940, to August 21, 1940, she received 2,660 gr. of sulfanilamide. The last sulfarsphenamine was administered on August 20 at which time she developed purpura haemorrhagica and aplastic anemia. The patient died September 20. Permission for autopsy was not granted.

Although this case is recorded as a death due to sulfarsphenamine, there is serious question whether the combined therapy, or one of the drugs individually, was the primary cause of death, since either drug is capable of producing blood dyscrasia.

An additional fatal case, M. B. B., white female, not recorded as part of the study, occurred 3 months after the third injection of 0.2 gm. of sulfarsphenamine. Her history disclosed a previous reaction, "bruised areas" on legs, following neoarsphenamine and on admission she had anemia and also menorrhagia of at least 1 year's duration. The histopathologic examination confirmed the clinical diagnosis of purpura haemorrhagica and reported also chronic endometritis but questioned the role that sulfarsphenamine played in the condition. This case is reported, even though it is not a part of the study, because it illustrates the dangers of arsenic therapy in patients with weakened hematopoietic systems, particularly females with menstrual disorders.

The patients were treated under two procedures with arsenical therapy, (1) two injections a week with dosage varying from 0.2 to 0.35 gm., and (2) one injection a week with dosage from 0.35 to 0.6 gm. The average total weekly dose per patient was approximately the same under both procedures.

Some very high doses (in a study of the Herxheimer reaction) and some very small doses (to reactors) were administered. As would be expected, the reaction rate was high.

In the group receiving neoarsphenamine, twice as many reactions occurred in patients receiving one treatment a week as in those receiving two injections weekly. Among those receiving one treatment a week, reactions occurred as follows: Minor reactions, 47.4 per 1,000 injections, major reactions 7.5 per 1,000; among those receiving two injections a week, the observed reactions were: minor reactions 20.8 and major reactions 4.7 per 1,000 injections. In general this same quantitative relation in the reaction rate was found to exist between the two methods of treatment at the several comparable dose levels. In the sulfarsphenamine group, patients receiving one weekly injection reported one-third more minor and twice as many major reactions as did patients receiving two injections per week (minor 44.3, major 9.6, total 53.8 to minor 33.9, major 4.5, total 38.4 per 1,000, respectively). At several dose levels inconsistent results were noted which were due to unequal distribution of the highly reactive white females.

Icterus (2.5 per 1,000 injections) after neoarsphenamine occurred more frequently than purpura (0.5) following sulfarsphenamine in the cases receiving two treatments a week. In the patients receiving one injection a week both types of reactions occurred at higher and approximately equal rates (3.7 and 4.1, respectively).

In addition to the arsenicals, practically all patients received concurrent bismuth injections; consequently it is impossible to determine

the influence of bismuth on the frequency of reactions. Some patients received two arsenical and one bismuth injection a week; others received two bismuth and one arsenical. A few were treated intensively, receiving two arsenical and two bismuth injections a week during the first course. It was interesting to note that the administration of bismuth and arsenical on the same day resulted in an extremely high rate of minor reactions, particularly with neoarsphenamine, but the major reaction rate was not influenced.

Sulfonamide was administered concurrently (either simultaneously or within 1 month preceding arsenical injections) with the arsenical and bismuth therapy in a number of cases with syphilis and gonorrhea.

TABLE 2.—*Effect of sulfonamide drugs on frequency and severity of reactions*

Reactions per 1,000 injections	Sulfonamides administered within month preceding injection					
	Yes		No		Total [1]	
	Number	Rate	Number	Rate	Number	Rate
Neoarsphenamine:						
Minor reactions	52	44.4	344	44.1	402	43.9
Major reactions	7	6.0	55	7.1	66	7.2
Total reactions	59	50.4	399	51.2	468	51.2
Icterus	3	2.6	25	3.2	30	3.3
Purpura haemorrhagica			4	.5	4	.4
Total injections	1,170		7,798		9,148	
Sulfarsphenamine:						
Minor reactions	41	41.9	333	50.3	382	49.4
Major reactions	12	12.3	47	7.1	60	7.8
Total reactions	53	54.2	380	57.4	442	57.2
Icterus	1	1.0	7	1.1	8	1.0
Purpura haemorrhagica	6	6.1	16	2.4	22	2.8
Total injections	978		6,621		7,730	

[1] Includes unknown data on sulfonamide treatment.

Concurrent treatment with neoarsphenamine showed no significant influence, as the reaction rates for the combined therapy (minor 44.4, major 6.0 per 1,000) and with neoarsphenamine alone (minor 44.1, major 7.1 per 1,000) were not statistically different. With sulfarsphenamine the minor rate was slightly lower for the combined therapy (41.9) than with sulfarsphenamine alone (50.3), but major reactions were materially higher following concurrent therapy (12.3 to 7.1). In the combined therapy group, blood dyscrasias (9.2)—aplastic anemia (1.0), agranulocytosis (2.0), and purpura (6.1)—occurred at significantly higher rates than in the group receiving sulfarsphenamine without sulfonamide (2.6)—agranulocytosis (0.2), purpura (2.4).

Icterus after neoarsphenamine occurred at a slightly lower rate (2.6 per 1,000) after combined therapy than with the arsenical alone (3.2). As noted above, purpura in the sulfarsphenamine-sulfona-

mide group (6.1) was two and one-half times more frequent than when sulfarsphenamine (2.4) was administered alone.

Both the type and frequency of reactions seemed to vary according to race and sex of the patients. Females in each race experienced more minor reactions than males both in the neoarsphenamine and sulfarsphenamine groups. In the neoarsphenamine group, minor reactions occurred more frequently in white males than in colored males. In comparing minor reactions following the two drugs, the only significant difference was observed in colored males who had more reactions following sulfarsphonamine than following neoarsphenamine.

TABLE 3.—*Reactions in patients treated with neoarsphenamine and sulfarsphenamine, shown by race and sex*

Reactions per 1,000 injections	Males						Females					
	White		Colored		Total		White		Colored		Total	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Neoarsphenamine:												
Minor reactions	117	41.1	72	28.6	189	35.2	107	56.3	106	56.2	213	56.3
Major reactions	30	10.5	11	4.4	41	7.6	10	5.3	15	8.0	25	6.6
Total reactions	147	51.7	83	33.0	230	42.9	117	61.6	121	64.2	238	62.9
Icterus	18	6.3	6	2.4	24	4.5	3	1.6	3	1.6	6	1.6
Purpura haemorrhagica	2	.7	1	.4	3	.6			1	.5	1	.3
Total injections	2,845		2,518		5,363		1,900		1,885		3,785	
Sulfarsphenamine:												
Minor reactions	81	34.1	96	45.3	177	39.3	86	54.9	119	71.5	205	63.4
Major reactions	18	7.6	7	3.3	25	5.6	27	17.2	8	4.8	35	10.8
Total reactions	99	41.6	103	48.6	202	44.9	113	72.2	127	76.3	240	74.3
Icterus	2	.8	1	.5	3	.7	5	3.2			5	1.5
Purpura haemorrhagica	4	1.7	2	.9	6	1.3	14	8.9	2	1.2	16	5.0
Total injections	2,378		2,121		4,499		1,566		1,665		3,231	

White females suffered more severe reactions following the use of sulfarsphenamine than colored females or males of either race. In fact, the rate per 1,000 injections was more than twice as high in this group as in the white males who had the next highest rate (17.2 to 7.6 per 1,000 injections). This rate of 17.2 was also more than three times as great as the rate for white females following neoarsphenamine. The rate of 7.6 for white males following sulfarsphenamine was more than twice the rate for colored males (3.3). In the neoarsphenamine group the differences between race and sex were not as marked. Although more severe reactions were observed in white males, the only significant difference statistically was between the white and colored males. Here the rates were, respectively, 10.5 and 4.4 per 1,000 injections.

Icterus as a major complication of therapy was reported in 38

instances and purpura haemorrhagica was observed in 26 patients, 2.25 and 1.54 per 1,000 injections, respectively.

Of the 38 cases of icterus, 30 (3.28 per 1,000 injections) occurred following neoarsphenamine therapy and 8 (1.03) after sulfarsphenamine. Twenty-seven of the 38 reactions occurred in males; of these 24 (4.5) followed neoarsphenamine and 3 (0.7) sulfarsphenamine. Eleven cases were in females, and of these 6 (1.6) followed neoarsphenamine and 5 (1.5) sulfarsphenamine.

Purpura haemorrhagica was reported in 26 patients; of these 4 (0.44) followed neoarsphenamine therapy and 22 (2.85) sulfarsphenamine. In males 9 (0.91) reactions were recorded, 3 (0.6) following neoarsphenamine and 6 (1.3) sulfarsphenamine. Of the 17 (2.42) reactions occurring in females, 1 (0.3) was due to neoarsphenamine and 16 (5.0) to sulfarsphenamine. The incidence in white females (8.9) was materially higher than in colored females (1.2).

TABLE 4.—*Reactions in patients treated with neoarsphenamine and sulfarsphenamine by age of patient*

Reactions per 1,000 injections	Age of patient									
	15–24		25–34		35–44		45 and over		Total	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Neoarsphenamine:										
Minor reactions	170	43.5	118	39.5	67	59.1	35	43.9	402	43.9
Major reactions	31	7.9	21	7.0	11	9.7	1	1.3	66	7.2
Total reactions	201	51.5	139	46.5	78	68.8	36	45.1	468	51.2
Icterus	16	4.1	7	2.3	7	6.2	------	------	30	3.3
Purpura haemorrhagica	1	.3	2	.7	------	------	1	1.3	4	.4
Total injections	3,904		2,990		1,133		798		9,148	
Sulfarsphenamine:										
Minor reactions	182	55.6	121	45.4	49	45.1	25	47.6	382	49.4
Major reactions	24	7.3	16	6.0	12	11.0	7	13.3	60	7.8
Total reactions	206	62.9	137	51.3	61	56.1	32	61.0	442	57.2
Icterus	4	1.2	3	1.1	------	------	1	1.9	8	1.0
Purpura haemorrhagica	7	2.1	7	2.6	5	4.6	3	5.7	22	2.8
Total injections	3,274		2,668		1,087		525		7,730	

It is evident, therefore, that icterus following neoarsphenamine in males (4.5)—especially white males (6.3)—and purpura haemorrhagica following sulfarsphenamine therapy in females (5.0)—white females (8.9)—are serious complications in the therapy of syphilis. However, conclusions relative to the incidence of purpura following sulfarsphenamine should be evaluated in the light of its high incidence in concurrent therapy with sulfonamide, as previously noted.

The data were analyzed to determine the influence of the age of the patients and the stage of syphilis upon the frequency and severity of reactions. Among the various age groups, the only significant difference was noted in the group 45 years or over. Here the rate of severe reactions per 1,000 injections was 1.3 for neoarsphenamine and 13.3 for

sulfarsphenamine. Icterus as a major complication of neoarsphenamine is recorded in the first three age groups (15–24, 25–34, 35–44) as 4.1, 2.3, and 6.2 per thousand, but is not reported in the group 45 and over; the incidence of purpura following sulfarsphenamine, increasing with the age of the patient, 2.1, 2.6, 4.6, and 5.7 per 1,000 injections, respectively, was highest in the oldest age group, 45 and over.

Previous treatment is a factor influencing reactions following arsenical therapy. The minor reactions were materially higher after both drugs in patients classed as reactors to previous treatment. The major reactions to sulfarsphenamine were higher in patients who had been previously treated; with neoarsphenamine the incidence was slightly greater in the "no previous treatment" group.

Icterus following neoarsphenamine occurred at approximately the same rate in the three groups, slightly lower in nonreactors. The incidence of purpura after sulfarsphenamine was lowest in "no previous treatment" cases and highest among the reactors.

The influence of the dose sequence on the reaction rate was determined for those patients who were either untreated or had no treatment for at least 6 months prior to inclusion in the study.

The minor reaction rate in both drug groups decreased with each successive dose following a peak after the first injection, with a slight rise at the beginning of each course. The major reaction rate with neoarsphenamine during the first two courses, 8.1 and 7.9, respectively, was approximately the same, with a decrease (5.9) in the third course; with sulfarsphenamine there was a progressive increase with each succeeding course—3.6, 10.7, and 21.2, respectively.

As will be noted, the significant observation is the transposition from the low incidence of major reactions with sulfarsphenamine and high rate with neoarsphenamine in the first course to high rate with sulfarsphenamine and low incidence following neoarsphenamine in the third course of treatments.

The data were processed to determine what influence, if any, the discontinuance of therapy of either drug might have on the final computations. The tabulation determined the percentage of cases in which neoarsphenamine and sulfarsphenamine, in order named, were discontinued following the first, second, or third reaction (minor or major). When the reaction was minor, the drugs were withdrawn following the first reaction in 8 and 14 percent of the cases, after the second reaction in 15 and 20 percent, and after the third reaction in 27 and 29 percent, respectively. Therapy was terminated in 12 percent of the mild reactions to neoarsphenamine and 17 percent of those to sulfarsphenamine. In the case of major reactions the drugs were discontinued in 72 and 67 percent of the cases after the first reaction, in 75 and 83 percent reacting the second time, and following the third reaction in 80 and 100 percent, respectively. In approximately 75

percent of the major reactions to both drugs further treatment was abandoned. Although the differences in percentages are not great, treatment was discontinued more frequently when sulfarsphenamine caused the reaction. This precaution on the part of the physicians administering the drugs may have lowered the rate of severe reactions to sulfarsphenamine.

OBSERVATIONS AND CONCLUSIONS

This study presents a clinical comparison of the reactivity of neoarsphenamine and sulfarsphenamine in the treatment of syphilis. In general the clinical material was representative of the class in which venereal disease is probably highest; approximately one-eighth had mixed infections of gonorrhea and syphilis and might be considered "bad risks" for arsenical therapy because of their impoverished condition upon admission to the clinic. The reaction rate was consequently high and therefore comparison of these results with other reports on the reactivity of the arsphenamines must be evaluated on the basis of the clinical material available in each study.

The reaction rate for neoarsphenamine (minor 43.9, major 7.2 per 1,000 injections) is only slightly less than that for sulfarsphenamine (minor 49.2, major 7.8 per 1,000), and the difference is not statistically significant. These results are materially higher than the reaction incidence reported by the Cooperative Clinical Group for neoarsphenamine (minor 13.7, major 2.43 per 1,000) and sulfarsphenamine (minor 11.4, major 3.54 per 1,000). In this study the minor reaction rate was slightly higher for sulfarsphenamine than for neoarsphenamine, but in the Cooperative Clinical Group report the reverse was true. In the major reactions, however, the rate was approximately 50 percent higher for sulfarsphenamine in the Cooperative Clinical Group study, whereas in this report the rate for neoarsphenamine and sulfarsphenamine is the same.

Although the total rates are approximately the same, sulfarsphenamine appears to be a particularly toxic drug in white females. The rate of major reactions in this group (17.2) was more than twice the next highest rate (7.6) which was observed in white males following sulfarsphenamine; and more than 60 percent greater than the highest rate of major reactions following neoarsphenamine (10.5 per 1,000 injections in white males).

In the minor reactions gastrointestinal (26.8 per 1,000) and febrile (6.0) occurred most often following neoarsphenamine therapy; in the sulfarsphenamine group gastrointestinal (26.6), slight skin eruption (7.6) and pruritus (5.7) were most frequently encountered. With neoarsphenamine therapy, icterus (3.3) and dermatitis (2.6) were the major reactions of importance; with sulfarsphenamine, dermatitis (3.1) and purpura haemorrhagica (2.9). The significant observation of the comparative study of reactivity of neoarsphenamine and

sulfarsphenamine is that icterus occurred most frequently after neoarsphenamine, and purpura most frequently after sulfarsphenamine.

The incidence of icterus was highest in males (4.5 per 1,000 injections), especially in whites (6.3) receiving neoarsphenamine, and, in general, in the younger age groups.

Purpura haemorrhagica was reported at the highest incidence in females (5.0), especially whites (8.9), after sulfarsphenamine; the incidence increased with the age of the patient.

Concurrent treatment with sulfonamide and neoarsphenamine had no influence on the reaction rates, but combined with sulfarsphenamine the incidence of purpura haemorrhagica (6.1) was two and one-half times more frequent than when sulfarsphenamine (2.4) was administered alone.

Sulfarsphenamine is less toxic in patients receiving the first course of therapy than is neoarsphenamine; but, conversely, neoarsphenamine is less toxic than sulfarsphenamine in patients receiving the second and especially the third courses of therapy.

Laboratory investigations indicate that sulfarsphenamine is definitely more stable than neoarsphenamine, and apparently treponemicidally more active than neoarsphenamine, ratio of 3 to 4, respectively. On the basis of animal experiments, it is suggested that sulfarsphenamine may be clinically more effective than neoarsphenamine.

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PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES

April 23–May 20, 1944

The accompanying table summarizes the prevalence of nine important communicable diseases, based on weekly telegraphic reports from State health departments. The reports from each State for each week are published in the Public Health Reports under the section "Prevalence of disease." The table gives the number of cases of these diseases for the 4 weeks ended May 20, 1944, the number reported for the corresponding period in 1943, and the median number for the years 1939–43.

DISEASES ABOVE MEDIAN PREVALENCE

Measles.—The number of cases of measles dropped from 126,484 during the preceding 4 weeks to 104,755 during the 4 weeks ended May 20. The number of cases was about 11,000 more than might normally be expected, the 1939–43 median being approximately 93,000 cases. Each geographic region except the New England and Mountain reported a comparatively high incidence. The largest excesses over the median occurred in the West South Central and Pacific regions; in each of those regions the number of cases was about 2.6 times the 5-year median.

Meningococcus meningitis.—For the 4 weeks ended May 20 there were 1,636 cases of meningococcus meningitis reported, a decline of about 300 cases from the preceding 4-week incidence. Compared with preceding years the current incidence was about 25 percent below the 1943 figure for this period, but it was more than 9 times the 1939–43 median. The incidence was higher than in 1943 in the East North Central, West North Central, and West South Central regions, but other regions reported very significant declines. Compared with the preceding 5-year median, however, every section of the country reported an excess, the largest excess occurring in the East North Central region and the smallest in the South Atlantic region. This disease has maintained an unusually high level since the beginning of 1941, with approximately 18,000 cases reported for the year 1943, which was the highest on record. For the first 20 weeks of 1944 there have been 10,270 cases reported, as compared with 9,849 cases for the same weeks in 1943.

Poliomyelitis.—There were 105 cases of poliomyelitis reported for the current 4-week period, as compared with 118 for the corresponding period in 1943 and a 5-year median of 73 cases. The increase seemed to be mostly due to an excess of cases in the West South Central and Pacific regions; Louisiana in the former region reported 15 cases, as compared with a 5-year median of 2 cases, and California in the latter region reported 24 cases as against a 5-year median of 13 cases.

Scarlet fever.—For the 4 weeks ended May 20 there were 25,698 cases of scarlet fever reported. In 1943 there were 13,612 cases reported for the corresponding 4 weeks; the preceding 5-year median was represented by the 1943 figure. Every section of the country contributed to the comparatively high incidence of this disease. In the South Atlantic and Pacific regions the numbers of cases were about

Number of reported cases of 9 communicable diseases in the United States during the 4-week period April 23–May 20, 1944, the number for the corresponding period in 1943, and the median number of cases reported for the corresponding period, 1939–43

Division	Current period	1943	5-year median	Current period	1943	5-year median	Current period	1943	5-year median
	Diphtheria			Influenza [1]			Measles [2]		
United States	770	786	856	5,210	6,337	6,337	104,755	108,057	93,056
New England	27	18	26	78	4	14	8,086	10,317	9,550
Middle Atlantic	96	120	140	28	96	82	14,927	30,675	12,447
East North Central	117	194	157	323	352	352	19,422	33,719	11,276
West North Central	53	36	75	102	116	116	7,512	7,756	7,336
South Atlantic	143	107	147	1,399	1,572	2,012	14,683	6,866	7,852
East South Central	57	52	64	388	709	517	2,269	3,062	1,635
West South Central	120	124	158	2,245	2,156	2,156	15,429	3,310	5,873
Mountain	58	42	50	403	461	476	3,724	5,039	4,324
Pacific	99	87	67	244	471	376	18,700	7,313	7,313
	Meningococcus meningitis			Poliomyelitis			Scarlet fever		
United States	1,636	2,228	181	105	118	73	25,698	15,612	15,612
New England	83	228	11	6	1	1	2,252	2,773	1,206
Middle Atlantic	401	630	48	5	9	8	6,049	4,104	4,590
East North Central	412	313	20	6	14	8	7,115	4,013	4,189
West North Central	154	133	11	6	4	4	2,684	1,153	1,141
South Atlantic	189	376	45	18	3	16	2,425	1,104	718
East South Central	133	205	32	7	12	11	642	336	411
West South Central	106	90	23	26	19	11	658	319	299
Mountain	29	53	5	3	12	5	1,087	1,001	437
Pacific	129	200	8	28	44	14	2,786	806	771
	Smallpox			Typhoid and paratyphoid fever			Whooping cough [2]		
United States	48	93	218	343	286	384	7,061	16,934	15,291
New England	0	0	0	18	36	27	577	1,110	1,605
Middle Atlantic	0	0	0	29	44	56	1,008	2,640	3,100
East North Central	16	51	51	39	25	49	913	3,367	3,367
West North Central	8	14	84	10	15	19	343	1,143	573
South Atlantic	4	3	7	71	51	89	1,467	2,657	2,357
East South Central	6	9	15	40	25	48	468	641	673
West South Central	4	9	27	70	46	57	1,172	2,658	1,623
Mountain	1	5	8	9	25	21	536	560	758
Pacific	9	2	20	57	19	25	577	2,158	2,103

[1] Mississippi and New York excluded; New York City included.
[2] Mississippi excluded.

3½ times the 1939–43 median. The smallest excess (about 30 percent) was reported from the Middle Atlantic region.

DISEASES BELOW MEDIAN PREVALENCE

Diphtheria.—The incidence of diphtheria continued relatively low during the 4 weeks ended May 20. While the number of cases (770) was only slightly lower than the number reported during the corresponding week in 1943, it was about 10 percent below the 1939–43 median. The situation was comparatively favorable in all sections of the country except the Pacific, where the number of cases (99) represented an increase over the normal expectancy of almost 50 percent.

Influenza.—The number of cases of influenza reported for the current period was 5,210, as compared with 6,337 in 1943. The 1939–43 median was represented by the 1943 figure. In the New England

region, while the number of cases (78) was not large, it was about 5 times the preceding 5-year median, and in the West South Central region the incidence was slightly above the normal seasonal level; in all other regions the number of cases was relatively low.

Smallpox.—The number of cases (48) of smallpox reported was about one-half of the number reported for the corresponding weeks in 1943 and less than 25 percent of the 1939–43 median (218 cases). The situation was favorable in all sections of the country.

Typhoid and paratyphoid fever.—The incidence (343 cases) of this disease was about 20 percent above the incidence for the corresponding period in 1943, but it was about 10 percent below the preceding 5-year median. A comparison of geographic regions shows that the incidence was below the normal seasonal level in all regions except the West South Central and Pacific; Louisiana and Texas in the West South Central region and California in the Pacific seemed mostly responsible for the excess incidence in those regions. California reported 55 cases, as compared with a median of 19 cases for the preceding 5 years.

Whooping cough.—The incidence of this disease was also relatively low, 7,061 cases being reported for the current 4-week period, as compared with the 1939–43 median of 15,291 cases. Each section of the country shared in this favorable situation. In the East South Central, West South Central, and Mountain regions the numbers of cases were about 70 percent of the median, in the West North Central and South Atlantic regions the numbers were about 60 percent of the median, and in each of the other regions the incidence was less than 35 percent of the normal seasonal expectancy. For the country as a whole the number of cases was the lowest recorded in the 7 years for which data are available.

MORTALITY, ALL CAUSES

An average of approximately 9,000 deaths from all causes per week was reported to the Bureau of the Census by 93 cities in the United States during the 4 weeks ended May 20. The number of deaths reported for the 4 weeks was 3.2 percent more than the average for the same weeks in 1941–43. For each week of the 4-week period the number of deaths was higher than the preceding 3-year average. A comparison of geographic regions shows that the number of deaths was above the average in all regions except the New England and South Atlantic. The largest excess occurred in the West North Central region where there was an increase in the number of deaths during the current 4-week period over the preceding 3-year average of almost 20 percent.

PREVALENCE OF DISEASE

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

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED JUNE 3, 1944

Summary

The decline in the incidence of meningococcus meningitis continued. For the current week a total of 274 cases was reported, as compared with 332 for the preceding week, an average of 379 for the past 4 weeks, 437 for the corresponding week last year, and a 5-year (1939–43) median of 49. Five States, with reports of 19 to 37 cases each, reported an aggregate of 131 cases. The next largest numbers reported were 13 in Texas and 12 in Missouri. The total to date is still slightly larger than that for the same period last year, but the total since March 4 is 5,810, as compared with 6,962 for the corresponding period last year.

A total of 83 cases of typhoid fever was reported for the week, as compared with 114 for the preceding week and 123 for the 5-year median. The largest numbers reported were 9 cases in California, 8 in Texas, 7 in Louisiana, and 6 each in Massachusetts and South Carolina. The total for the year to date is 1,688, as compared with 1,316 for the same period last year and a 5-year median of 1,823.

For the country as a whole, a slight increase in the incidence of poliomyelitis was noted. A total of 46 cases was reported, as compared with 39 last week, 47 for the 5-year median, and 52 for the corresponding week last year. Only 3 States reported more than 3 cases—New York 9 and Louisiana and California 5 each. The cumulative figure is 547, as compared with 599 for the same period last year and a 5-year median of 503. The initial sharp rise last year occurred during the week ended June 5.

Further declines were recorded in the incidence of measles and scarlet fever. Totals of 16,130 for measles and 3,870 for scarlet fever were reported, as compared with 5-year medians of 16,646 and 2,559 respectively.

Only 7 cases of smallpox were reported, distributed in 6 States, as compared with a 5-year median of 42. The cumulative total to date is 248, as compared with 544 for the same period last year.

Deaths during the week in 93 large cities of the United States aggregated 8,436, as compared with 8,638 last week and a 3-year (1941–43) average of 8,496. The total to date is 213,762, as compared with 217,680 for the same period last year.

Telegraphic morbidity reports from State health officers for the week ended June 3, 1944, and comparison with corresponding week of 1943 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, 1939–43	Week ended—		Median, 1939–43	Week ended—		Median, 1939–43	Week ended—		Median, 1939–43
	June 3, 1944	June 5, 1943		June 3, 1944	June 5, 1943		June 3, 1944	June 5, 1943		June 3, 1944	June 5, 1943	
NEW ENGLAND												
Maine	0	2	0	1	1	------	331	95	95	2	5	0
New Hampshire	0	0	0	------	0	------	61	50	23	2	5	0
Vermont	0	0	0	------	0	------	88	178	130	------	0	0
Massachusetts	7	0	3	------	0	------	810	1,168	1,037	7	17	2
Rhode Island	0	0	0	13	0	------	39	96	136	------	3	0
Connecticut	1	1	0	------	2	1	345	271	397	3	7	0
MIDDLE ATLANTIC												
New York	9	14	14	[1] 2	[1] 4	[1] 6	922	3,205	2,150	37	76	7
New Jersey	1	3	4	------	5	2	724	2,041	990	6	27	2
Pennsylvania	10	7	14	------	1	------	440	949	949	24	32	17
EAST NORTH CENTRAL												
Ohio	3	7	7	6	16	13	285	644	320	[2] 25	11	1
Indiana	6	7	5	1	3	4	162	420	111	9	9	0
Illinois	5	30	23	2	12	9	396	1,707	241	19	26	1
Michigan [3]	6	6	3	1	1	1	503	2,279	610	9	9	1
Wisconsin	2	1	1	2	24	22	1,582	2,457	1,284	2	2	0
WEST NORTH CENTRAL												
Minnesota	1	2	2	------	0	1	275	466	216	4	0	0
Iowa	3	4	3	------	0	------	115	109	145	------	2	1
Missouri	3	2	2	------	0	------	124	234	172	12	23	0
North Dakota	0	1	1	------	3	1	34	11	14	------	0	0
South Dakota	1	0	0	------	0	------	13	602	27	------	3	0
Nebraska	5	2	2	2	2	2	149	190	160	3	1	0
Kansas	0	4	1	5	0	2	219	402	358	4	3	0
SOUTH ATLANTIC												
Delaware	0	1	0	------	0	------	4	47	36	2	1	0
Maryland [3]	6	2	2	------	2	2	193	186	186	5	14	1
Dist. of Columbia	0	0	1	------	0	------	88	104	104	------	5	1
Virginia	1	5	7	45	94	87	364	538	538	9	15	1
West Virginia	1	4	3	------	2	4	248	32	32	5	4	1
North Carolina	9	7	8	3	0	------	569	235	439	2	15	0
South Carolina	4	0	3	157	145	154	205	103	103	1	3	1
Georgia	2	2	2	7	2	12	96	58	103	------	8	1
Florida	3	2	3	------	36	14	124	127	116	2	20	0
EAST SOUTH CENTRAL												
Kentucky	0	2	2	------	11	2	88	111	79	5	6	1
Tennessee	2	2	3	15	4	10	102	120	151	9	7	1
Alabama	1	3	3	33	33	31	148	116	116	8	1	3
Mississippi [3]	3	5	3	------	0	------	0	------	------	1	1	1
WEST SOUTH CENTRAL												
Arkansas	2	2	2	64	2	7	92	43	77	1	2	1
Louisiana	3	2	2	1	6	4	31	35	35	3	7	1
Oklahoma	1	2	2	26	28	22	156	25	57	1	2	0
Texas	25	13	15	242	403	239	1,820	345	423	13	3	1
MOUNTAIN												
Montana	0	0	0	12	4	4	74	70	70	------	0	0
Idaho	0	0	0	------	0	------	21	29	37	------	2	0
Wyoming	0	0	1	------	15	------	77	94	26	1	0	0
Colorado	6	8	6	46	65	17	148	503	336	2	1	0
New Mexico	1	1	1	3	0	------	44	17	45	------	0	0
Arizona	0	3	1	25	44	40	48	34	35	------	3	0
Utah [3]	0	1	0	4	2	1	67	94	94	3	14	0
Nevada	4	0	0	------	0	------	27	20	0	------	1	0
PACIFIC												
Washington	4	1	1	3	1	------	250	115	320	4	2	0
Oregon	0	2	1	7	15	7	104	155	102	2	8	0
California	17	11	13	22	38	34	3,325	741	741	27	31	2
Total	158	174	175	750	1,026	804	16,130	21,671	16,646	274	437	49
22 weeks	4,921	5,471	5,824	333,291	74,749	147,113	537,629	444,654	408,494	10,883	10,720	1,062

See footnotes at end of table.

Telegraphic morbidity reports from State health officers for the week ended June 3 1944, and comparison with corresponding week of 1943 and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever [1]		
	Week ended—		Median 1939–43	Week ended—		Median 1939–43	Week ended—		Median 1939–43	Week ended—		Median 1939–43
	June 3, 1944	June 5, 1943		June 3, 1944	June 5, 1943		June 3, 1944	June 5, 1943		June 3, 1944	June 5, 1943	
NEW ENGLAND												
Maine	0	0	0	49	24	4	0	0	0	0	0	0
New Hampshire	0	0	0	4	8	5	0	0	0	0	1	0
Vermont	1	1	0	7	14	12	0	0	0	0	0	0
Massachusetts	2	0	0	221	381	138	0	0	0	6	0	2
Rhode Island	0	0	0	8	17	8	0	0	0	0	2	0
Connecticut	1	0	0	56	78	39	0	0	0	1	0	0
MIDDLE ATLANTIC												
New York	9	0	0	389	477	389	0	0	0	3	9	6
New Jersey	1	0	0	145	68	119	0	0	0	0	1	1
Pennsylvania	1	0	0	285	189	234	0	0	0	0	3	7
EAST NORTH CENTRAL												
Ohio	2	0	0	426	191	232	0	1	1	0	0	2
Indiana	0	0	0	85	53	78	0	2	1	2	0	1
Illinois	2	0	0	221	116	179	1	1	8	2	0	2
Michigan [3]	1	0	0	222	99	182	0	0	0	2	0	0
Wisconsin	0	0	0	253	292	109	0	0	2	0	0	1
WEST NORTH CENTRAL												
Minnesota	1	0	0	118	51	51	0	0	0	2	0	0
Iowa	0	0	0	51	34	26	0	0	3	2	1	1
Missouri	0	0	0	47	81	43	1	0	1	3	6	6
North Dakota	0	0	0	5	1	2	0	0	0	0	0	2
South Dakota	0	0	0	18	12	12	0	0	1	0	0	0
Nebraska	0	1	0	54	22	13	1	1	1	1	0	0
Kansas	0	1	0	43	29	38	1	0	0	0	0	0
SOUTH ATLANTIC												
Delaware	0	0	0	4	2	5	0	0	0	0	0	0
Maryland [3]	1	0	0	94	73	46	0	0	0	2	0	2
District of Columbia	0	0	0	35	8	8	0	0	0	0	4	1
Virginia	0	0	0	36	20	19	0	0	0	1	5	5
West Virginia	0	1	0	50	17	20	0	0	0	0	1	3
North Carolina	0	2	0	25	16	16	0	0	0	2	4	4
South Carolina	1	0	0	7	6	4	[4] 0	0	0	6	1	3
Georgia	1	0	0	33	10	10	0	0	0	5	9	11
Florida	3	3	1	5	4	4	0	0	0	3	5	3
EAST SOUTH CENTRAL												
Kentucky	2	0	0	27	29	29	2	0	1	0	1	5
Tennessee	0	0	0	59	10	38	0	0	3	1	2	4
Alabama	2	0	0	5	7	10	0	0	0	0	2	2
Mississippi [3]	1	0	0	3	1	1	0	0	0	3	1	1
WEST SOUTH CENTRAL												
Arkansas	0	2	0	4	8	4	0	0	5	2	4	4
Louisiana	5	0	0	0	7	5	0	0	0	7	3	10
Oklahoma	0	0	0	6	16	10	0	0	1	2	0	1
Texas	3	6	3	146	20	20	0	0	0	8	10	11
MOUNTAIN												
Montana	0	0	0	14	9	9	0	0	0	1	1	0
Idaho	0	0	0	33	74	4	0	1	0	0	0	0
Wyoming	0	0	0	16	15	4	0	0	0	0	0	0
Colorado	0	0	0	56	69	29	0	0	1	1	2	2
New Mexico	0	0	0	6	0	2	0	0	0	0	0	0
Arizona	0	1	0	9	5	4	0	0	0	0	0	0
Utah [3]	0	1	0	34	13	9	0	0	0	0	0	0
Nevada	0	0	0	13	0	0	0	0	0	4	0	0
PACIFIC												
Washington	0	0	0	120	16	22	1	1	0	1	0	2
Oregon	1	0	1	71	14	8	0	1	1	1	0	0
California	5	33	9	252	138	105	0	0	1	9	2	5
Total	46	52	47	3,870	2,844	2,559	7	8	42	83	80	123
22 weeks	547	599	503	132,109	85,342	85,342	248	544	995	1,688	1,316	1,823

See footnotes at end of table.

Telegraphic morbidity reports from State health officers for the week ended June 3, 1944, and comparison with corresponding week of 1943 and 5-year median—Con.

Division and State	Whooping cough			Week ended June 3, 1944								
	Week ended—		Median 1939–43	Anthrax	Dysentery			Encephalitis, infectious	Leprosy	Rocky Mt. spotted fever	Tularemia	Typhus fever
	June 3, 1944	June 5, 1943			Amebic	Bacillary	Unspecified					
NEW ENGLAND												
Maine	17	19	25	0	0	0	0	0	0	0	0	0
New Hampshire	1	4	4	0	0	0	0	1	0	0	0	0
Vermont	19	15	15	0	0	0	0	0	0	0	0	0
Massachusetts	39	97	130	0	1	3	0	1	0	0	0	0
Rhode Island	6	19	19	0	0	0	0	0	0	0	0	0
Connecticut	21	31	45	0	0	1	0	0	0	0	0	0
MIDDLE ATLANTIC												
New York	93	227	334	0	0	7	0	3	0	1	0	0
New Jersey	30	126	126	0	0	0	0	0	0	2	0	0
Pennsylvania	56	246	238	0	1	0	0	0	0	3	0	0
EAST NORTH CENTRAL												
Ohio	110	146	169	0	3	0	0	1	0	0	0	0
Indiana	30	60	54	0	0	0	0	0	0	0	0	0
Illinois	34	145	145	0	1	2	0	1	0	0	0	0
Michigan [2]	77	164	164	0	1	2	0	0	0	0	0	0
Wisconsin	81	199	140	0	0	0	0	1	0	0	0	0
WEST NORTH CENTRAL												
Minnesota	13	86	43	0	2	0	0	0	0	0	0	0
Iowa	10	38	26	0	0	0	0	0	0	0	0	0
Missouri	26	41	28	0	0	0	2	1	0	0	0	0
North Dakota	5	2	5	0	0	0	0	0	0	0	0	0
South Dakota	8	4	3	0	0	0	0	0	0	1	0	0
Nebraska	17	14	13	0	0	0	0	0	0	0	0	0
Kansas	46	76	63	0	1	0	0	0	0	0	0	0
SOUTH ATLANTIC												
Delaware	0	10	6	0	0	0	0	0	0	1	0	0
Maryland [3]	32	94	81	0	0	0	1	2	0	4	0	0
District of Columbia	1	30	21	0	0	0	0	0	0	0	0	0
Virginia	64	204	68	0	0	0	44	0	0	4	0	0
West Virginia	29	41	57	0	0	0	0	0	0	2	0	0
North Carolina	116	207	197	0	0	0	0	0	0	2	0	0
South Carolina	76	66	69	0	3	40	0	0	0	0	0	0
Georgia	20	47	47	0	1	7	0	0	0	0	2	12
Florida	21	26	26	0	0	51	0	2	0	0	0	3
EAST SOUTH CENTRAL												
Kentucky	56	29	65	0	1	0	0	1	0	0	0	0
Tennessee	61	42	48	0	1	0	4	0	0	1	2	0
Alabama	37	44	53	0	1	0	0	0	0	0	0	4
Mississippi [3]	0	----	----	0	0	0	0	0	0	0	4	8
WEST SOUTH CENTRAL												
Arkansas	13	52	20	0	0	21	0	0	0	0	7	0
Louisiana	2	2		0	1	2	0	0	0	1	0	6
Oklahoma	15	43	10	0	0	0	0	0	0	0	0	0
Texas	297	592	294	0	4	414	0	0	0	0	0	23
MOUNTAIN												
Montana	2	12	12	0	0	0	0	0	0	0	0	0
Idaho	11	8	8	0	0	0	0	0	0	0	0	0
Wyoming	10	3	3	0	0	0	0	0	0	1	1	0
Colorado	256	24	28	0	2	1	0	0	0	2	0	0
New Mexico	----	5	13	0	0	1	1	0	0	0	0	0
Arizona	22	23	18	0	2	0	41	0	0	0	0	0
Utah [3]	51	47	47	0	0	0	0	0	0	0	1	0
Nevada	20	0	0	0	0	0	1	0	0	0	0	0
PACIFIC												
Washington	16	23	41	0	0		0	0	0	0	0	0
Oregon	4	23	22	0	0	0	0	0	0	0	0	0
California	99	365	365	0	2	4	0	2	0	0	0	1
Total	2,070	3,821	3,765	0	28	556	94	16	0	25	17	57
22 weeks	39,767	89,019	87,076	17	562	6,002	1,643	241	13	72	238	998
22 weeks, 1943	----	----	----	30	677	4,612	1,139	244	11	86	387	1,017

[1] New York City only.
[2] A later report from Ohio for the week ended Apr. 1, 1944, showed 30 cases of meningococcus meningitis nstead of 56 as originally published.
[3] Period ended earlier than Saturday.
[4] Later information from South Carolina states that 3 cases reported as smallpox for the week ended May 20, 1944, were not smallpox.
[5] Including paratyphoid fever cases reported separately, as follows: Massachusetts 3, Connecticut 1, Florida 1, Louisiana 2, Texas 2.

WEEKLY REPORTS FROM CITIES

City reports for week ended May 20, 1944

This table lists the reports from 85 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland	0	0	-----	0	50	0	3	0	18	0	0	0
New Hampshire:												
Concord	0	0	-----	0	0	0	0	0	0	0	0	0
Massachusetts:												
Boston	0	0	-----	0	148	11	13	0	86	0	0	7
Fall River	0	0	-----	0	20	0	0	0	1	0	0	1
Springfield	0	0	-----	0	38	0	0	0	25	0	1	8
Worcester	0	0	-----	0	5	0	9	0	21	0	0	5
Rhode Island:												
Providence	1	0	-----	0	25	0	4	0	6	0	0	15
Connecticut:												
Bridgeport	0	0	-----	0	6	0	0	0	2	0	0	0
Hartford	0	0	-----	0	9	1	0	0	24	0	0	0
New Haven	0	0	2	0	40	1	1	0	0	0	0	0
MIDDLE ATLANTIC												
New York:												
Buffalo	0	0	-----	0	11	0	4	0	11	0	1	1
New York	13	0	3	1	624	30	43	1	252	0	0	31
Rochester	0	0	-----	0	40	0	5	0	9	0	1	3
Syracuse	0	0	-----	0	8	0	1	0	3	0	0	2
New Jersey:												
Camden	0	0	-----	0	1	1	0	0	19	0	0	0
Newark	0	0	-----	0	200	1	4	0	40	0	0	3
Trenton	0	0	-----	0	2	0	0	0	3	0	1	7
Pennsylvania:												
Philadelphia	3	0	3	2	52	10	24	0	89	0	1	6
Pittsburgh	1	0	3	3	16	10	16	0	17	0	0	2
Reading	0	0	0	1	1	0	3	0	2	0	0	0
EAST NORTH CENTRAL												
Ohio:												
Cincinnati	4	0	-----	0	24	6	3	1	32	0	0	5
Cleveland	0	0	-----	0	26	6	17	0	120	0	2	8
Columbus	0	0	-----	0	24	0	2	0	0	0	0	0
Indiana:												
Fort Wayne	0	0	-----	0	0	0	3	0	1	0	0	0
Indianapolis	2	0	-----	2	54	0	4	0	26	0	0	11
South Bend	0	0	-----	0	1	0	0	0	3	0	0	1
Terre Haute	0	0	-----	0	1	0	1	0	2	0	0	0
Illinois:												
Chicago	4	0	3	2	143	21	24	0	165	0	0	17
Springfield	0	0	-----	0	32	0	0	0	5	0	1	0
Michigan:												
Detroit	8	1	-----	0	126	14	13	0	126	0	0	28
Flint	0	0	-----	0	4	1	1	0	3	0	0	2
Grand Rapids	0	0	-----	0	16	1	1	0	6	0	0	0
Wisconsin:												
Kenosha	0	0	-----	0	258	0	0	0	0	0	0	1
Milwaukee	0	0	-----	0	265	3	2	0	52	0	0	14
Racine	0	0	-----	0	140	0	0	0	3	0	0	5
Superior	1	0	-----	0	5	0	0	0	21	0	0	0
WEST NORTH CENTRAL												
Minnesota:												
Minneapolis	0	0	-----	0	134	1	5	0	30	0	0	0
St. Paul	0	0	-----	1	71	4	6	0	22	0	0	2
Missouri:												
Kansas City	0	0	-----	1	86	1	5	0	28	0	0	1
St. Joseph	0	0	-----	0	2	1	0	0	4	0	0	0
St. Louis	0	1	1	0	33	13	7	0	38	0	0	1
Nebraska:												
Omaha	0	0	-----	0	101	2	7	0	20	0	0	0
Kansas:												
Topeka	1	0	-----	1	38	0	1	0	3	0	0	7
Wichita	0	0	-----	0	17	0	5	0	4	0	0	2

City reports for week ended May 20, 1944—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
SOUTH ATLANTIC												
Maryland:												
Baltimore	13	0	------	0	258	4	9	0	78	0	0	37
Cumberland	0	0	------	0	1	0	1	0	1	0	0	0
Frederick	0	0	------	0	0	0	0	0	1	0	0	0
District of Columbia:												
Washington	0	0	4	1	178	3	6	0	96	0	1	8
Virginia:												
Lynchburg	0	0	------	0	2	0	0	0	3	0	0	0
Richmond	0	0	------	0	21	0	2	0	5	0	1	2
Roanoke	0	0	------	0	4	0	0	0	2	0	0	4
West Virginia:												
Charleston	0	0	------	0	0	0	0	0	8	0	0	0
Wheeling	0	0	------	0	38	1	1	0	12	0	0	1
North Carolina:												
Raleigh	0	0	------	0	37	0	0	0	1	0	0	2
Wilmington	0	0	------	0	13	0	2	0	0	0	0	5
Winston-Salem	0	0	------	0	15	0	0	0	2	0	0	2
South Carolina:												
Charleston	0	0	3	0	0	2	4	0	2	0	0	0
Georgia:												
Atlanta	0	0	3	0	14	0	2	0	12	0	0	1
Brunswick	0	0	------	0	0	0	0	0	0	0	0	0
Savannah	0	0	------	0	0	2	0	0	1	0	0	1
Florida:												
Tampa	1	0	------	0	4	0	2	0	0	0	1	0
EAST SOUTH CENTRAL												
Tennessee:												
Memphis	0	0	1	0	29	1	4	0	25	0	0	14
Nashville	0	0	------	0	14	0	2	0	3	0	0	0
Alabama:												
Birmingham	0	0	4	1	3	2	3	0	2	0	0	0
Mobile	0	0	1	0	0	0	0	1	1	0	1	0
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock	0	0	1	0	13	0	1	0	0	0	0	1
Louisiana:												
New Orleans	3	0	1	2	10	7	10	6	1	0	0	3
Shreveport	0	0	------	0	5	0	0	0	0	0	1	1
Texas:												
Dallas	1	0	------	0	99	0	4	0	2	0	0	7
Galveston	0	0	------	0	3	0	0	0	2	0	0	0
Houston	2	0	------	0	12	4	2	0	3	0	1	0
San Antonio	0	0	2	0	5	2	5	2	0	0	0	1
MOUNTAIN												
Montana:												
Great Falls	0	0	------	0	7	0	0	0	2	0	0	0
Helena	0	0	------	0	1	0	0	0	0	0	0	0
Missoula	0	0	------	0	13	0	0	0	5	0	0	0
Idaho:												
Boise	0	0	------	0	0	0	0	0	2	0	0	0
Colorado:												
Denver	4	0	4	0	79	0	3	0	15	0	0	5
Pueblo	0	0	------	0	8	0	0	0	2	0	0	1
Utah:												
Salt Lake City	0	0	------	0	22	0	3	0	28	0	0	5
PACIFIC												
Washington:												
Seattle	0	0	------	1	51	1	1	0	41	0	1	2
Spokane	0	0	------	0	21	1	3	0	11	0	0	1
Tacoma	1	0	------	0	31	0	0	0	17	0	0	0
California:												
Los Angeles	5	0	14	0	487	6	6	2	25	0	0	4
Sacramento	0	0	1	0	76	1	0	0	9	0	0	8
San Francisco	1	0	------	0	291	0	8	0	40	0	0	6
Total	69	2	54	19	4,762	176	321	13	1,802	0	15	318
Corresponding week, 1943	76	------	58	16	9,026	------	363	------	1,397	0	19	1,177
Average, 1939–43	68	------	68	19	5,551	------	326	------	1,388	5	19	1,196

Dysentery, amebic.—Cases: New York, 1; Chicago, 1; St. Louis, 1; San Antonio, 1.
Dysentery, bacillary.—Cases: Providence, 3; Detroit, 3; Charleston, 6; Denver, 1; Los Angeles, 10.
Dysentery, unspecified.—Cases: Baltimore, 1; San Antonio, 7.
Rocky Mountain spotted fever.—Cases: Richmond, Va., 1.
Typhus fever.—Cases: New York, 3; Tampa, 1; New Orleans, 2; Houston, 4; San Antonio, 2.

Rates (annual basis) per 100,000 population, by geographic groups, for the 85 cities in the preceding table (estimated population, 1943, 34,254,800)

	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	2.6	0.0	5.2	0.0	891	34.0	78.4	0.0	478	0.0	2.6	94
Middle Atlantic	7.7	0.0	4.1	3.2	434	23.6	45.4	0.5	202	0.0	1.8	25
East North Central	11.6	0.6	1.8	2.4	683	31.7	43.3	0.6	345	0.0	1.8	56
West North Central	2.1	2.1	2.1	6.2	996	45.4	74.4	0.0	308	0.0	0.0	27
South Atlantic	23.7	0.0	16.9	1.7	990	20.3	49.1	0.0	379	0.0	5.1	107
East South Central	0.0	0.0	34.9	5.8	268	17.5	52.4	5.8	181	0.0	5.8	82
West South Central	17.0	0.0	11.4	5.7	417	36.9	62.5	22.7	227	0.0	5.7	37
Mountain	32.7	0.0	32.7	0.0	1,064	0.0	49.1	0.0	442	0.0	0.0	90
Pacific	11.5	0.0	24.7	1.6	1,578	14.8	29.7	3.3	236	0.0	1.6	35
Total	10.5	0.3	8.2	2.9	727	26.9	49.0	2.0	275	0.0	2.3	49

PLAGUE INFECTION IN QUAY COUNTY, N. MEX.

Plague infection has been reported proved in a pool of 13 fleas from 2 cotton rats, *Sigmodon hispidus*, collected on May 10, 1944, on U. S. Highway No. 66, 20 miles east of Tucumcari, in Quay County, N. Mex.

TERRITORIES AND POSSESSIONS

Hawaii Territory

Honolulu—Dengue fever.—For the period May 1–15, 1944, 12 cases of dengue fever were reported in Honolulu, T. H., bringing the total number of cases reported since the beginning of the outbreak during the summer of 1943 to 1,490. The current figure represents an increase of 7 cases over the previous semimonthly period.

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended May 6, 1944.—During the week ended May 6, 1944, 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		14	3	154	309	23	41	58	170	772
Diphtheria		8	2	13		2	1	1		27
Dysentery (bacillary)				3						3
German measles		11		163	73	4	24	12	64	351
Influenza					33	1	3		10	47
Measles		19	17	924	734	330	113	139	35	2,311
Meningitis, meningococcus		2		1	6	1			2	12
Mumps		15	12	184	168	45	9	61	86	580
Scarlet fever		27	4	78	187	68	24	79	87	554
Tuberculosis (all forms)		5	8	132	98	14	12	23	60	352
Typhoid and paratyphoid fever				5	1			8		14
Undulant fever					1			1		2
Whooping cough		44		62	28	2	14	12	46	208

IRAN

Typhus fever—March 22, 1943—April 2, 1944.—According to a report of the Iranian Ministry of Health, 15,435 new cases of typhus fever were reported in Iran from March 22, 1943, to April 2, 1944. The cases were distributed as follows: *1943*—Week ended March 28, 300 cases; April–June, 10,322; July–September, 1,191; October–December, 437; *1944*—January, 586 cases; February, 937; March, 1,662.

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-mentioned diseases, except yellow fever, during the current year. 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 in each month.

(Few reports are available from the invaded countries of Europe and other nations in war zones.)

Cholera

India—Calcutta.—Deaths from cholera have been reported in Calcutta, India, as follows: Weeks ended—April 8, 1944, 34; April 22, 1944, 58; April 29, 1944, 95; May 6, 1944, 98.

Plague

Madagascar.—During the period January 20–March 10, 1944, 50 cases of plague, with 41 deaths, were reported in Madagascar.

Smallpox

Bolivia.—For the month of April 1944, a total of 77 cases of smallpox, with 12 deaths, was reported for the Republic of Bolivia.

Typhus Fever

Bolivia.—A total of 18 cases of typhus fever, with 10 deaths, was reported in Bolivia for the month of April 1944.

Chile.—For the period February 27–March 25, 1944, 29 cases of typhus fever, with 5 deaths, were reported in Chile.

* * *

DEATHS DURING WEEK ENDED MAY 27, 1944

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

	Week ended May 27, 1944	Corresponding week 1943
Data for 92 large cities of the United States:		
Total deaths	8,016	8,384
Average for 3 prior years	7,653	
Total deaths, first 21 weeks of year	189,557	192,589
Deaths under 1 year of age	581	597
Average for 3 prior years	514	
Deaths under 1 year of age, first 21 weeks of year	12,422	13,648
Data from industrial insurance companies:		
Policies in force	66,565,613	65,536,014
Number of death claims	13,600	12,470
Death claims per 1,000 policies in force, annual rate	10.7	9.9
Death claims per 1,000 policies, first 21 weeks of year, annual rate	10.9	10.5

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