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#### PREVALENCE OP POLIOMYELITIS

During the week ended September 23, 484 cases of poliomyelitis were reported in the United States, as compared with 501 cases during the preceding week and a median of 274 cases for the corresponding week of the years 1934–38. The incidence during the current week was approximately 75 percent in excess of the 5-year median.

The States reporting more than 10 cases of poliomyelitis during the current week were as follows: New York 128 (with 22 cases in New York City and 48 in Buffalo), Michigan 53, Pennsylvania 50 (24 cases in Philadelphia), Minnesota 52 (with 26 cases in Minneapolis), California 33, New Jersey 38, Illinois 13, New Mexico 14, and Ohio 12 cases.

In the following article and accompanying table, a summary of poliomyelitis incidence, by geographic regions, is given for the 4 weeks ended September 9.

# PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES

#### August 13-September 9, 1939

The accompanying table summarizes the prevalence of eight important communicable diseases, based on weekly telegraphic reports from State health departments. The reports from each State 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-week period ended September 9, 1939, the number reported for the corresponding period in 1938, and the median number for the years 1934–38.

#### DISEASES ABOVE MEDIAN PREVALENCE

Poliomyelitis.—The number of cases of poliomyelitis rose from 783 for the preceding 4-week period to 1,648 for the 4 weeks ended September 9. The current incidence was more than 5 times the number of cases reported for the corresponding period in 1938, and more than 1.3 times the 1934-38 average incidence for this period.

Every section of the country except the New England and East South Central has contributed largely to the recent increase of this

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However, with the exception of the Middle Atlantic region. the increases seem to be largely due to a high incidence in one or two States in the region rather than to an increase in the whole area. the Middle Atlantic region, New York reported 287 cases, Pennsylvania 89 cases, and New Jersey 85 cases. In the East North Central region. Michigan reported 377 cases and Illinois 49 cases; in the West North Central region, Minnesota alone reported an excess of cases (183); in the South Atlantic region, South Carolina reported 49 cases and North Carolina 33 cases; in the West South Central region, Texas reported 41 cases. States in the far Western regions reporting a relatively high incidence were California (Pacific region), 200 cases, and Arizona and Colorado (Mountain region), 17 and 12 cases, respectively. Approximately 85 percent of the total cases were reported from 12 States.

A total of 3,454 cases of poliomyelitis has been reported since January 1, 1939, as compared with 1,164 cases during the same period in 1938, and 5,512 cases in 1937. During 1938 the incidence of poliomyelitis was the lowest on record, but the disease was epidemic in the central and northeastern parts of the country in 1937. For the week ended September 16, 1939, there were approximately 500 cases

Number of reported cases of 8 communicable diseases in the United States during the 4-week period Aug. 13-Sept. 9, 1939, the number for the corresponding period in 1938, and the median number of cases reported for the corresponding period 1934-381

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Division	Cur- rent pe- riod	1938	year me- dian	Cur- rent pe- riod	1938	year me- dian	Cur- rent pe- riod	1938	year me- dian	Cur- rent pe- riod	1938	year me- dian
	D	Diphtheria		I	Influenza ²			Measle:	; 3	Meningococcus meningitis		
United States 1	1, 446	1, 909	1, 909	1, 492	1, 561	1, 257	1,857	2, 819	2, 909	99	136	216
New England Middle Atlantic East North Central West North Central South Atlantic East South Central West South Central Mountain Pacific	17 84 172 90 515 248 196 56	17 139 159 103 705 336 299 80 71	28 169 201 105 484 336 251 48 86	3 17 131 14 831 119 219 107 51	29 88 107 501 154 513 98 67	4 29 161 107 367 65 221 45 67	280 374 247 166 136 56 118 116 364	210 684 545 189 320 117 121 184 449	210 735 683 139 240 137 121 154 208	1 30 12 5 20 8 9 12 2	7 23 18 11 23 21 16 11 6	7 40 37 19 41 21 13 8 13
	Pol	iomye	litis	See	Scarlet fever			mallpo	x	Typhoid and para- typhoid fever		
United States 1	1,648	307	1, 251	3, 148	3, 264	3, 492	89	147	141	2, 141	2, 295	2, 467
New England Middle Atlantic East North Central West North Central South Atlantic East South Central West South Central Mountain Pacific	30 461 484 209 130 25 55 42 212	18 79 68 31 41 21 15 9 25	22 89 217 50 65 88 15 14 113	94 453 1,002 343 389 329 171 114 253	161 514 918 435 329 269 230 120 288	212 725 1,098 431 329 245 187 138 335	0 0 28 27 7 1 8 7	0 28 21 1 3 8 24 62	0 0 25 21 0 8 5 24 39	33 148 513 144 383 311 434 89 86	42 272 315 169 537 318 449 107 86	42 265 452 209 537 520 449 107 86

 <sup>148</sup> States. Nevada is excluded and the District of Columbia is counted as a State in these reports.
 144 States and New York City.
 17 States. Mississippi is not included.

reported, which is the highest weekly incidence reported since the beginning of the present rise. The highest incidence of this disease normally occurs during the month of September.

Influenza.—The influenza incidence (1,492 cases) was slightly below that for the corresponding period in 1938, but it was about 15 percent above the median level for this period. The South Atlantic, East South Central, and Mountain regions reported excesses over the seasonal expectancy, but in all other regions the incidence compared very favorably with that of recent years.

#### DISEASES BELOW MEDIAN PREVALENCE

Diphtheria.—For the 4 weeks ended September 9, there were 1,446 cases of diphtheria reported, as compared with 1,909, 1,468, and 1,393 for the corresponding period in 1938, 1937, and 1936, respectively. A few more cases than normally occur during this period were reported from the South Atlantic and Mountain regions, but in all other regions the incidence was relatively low.

Measles.—The incidence of measles was also comparatively low. For the current 4-week period there were 1,857 cases reported, about 65 percent of the 1934-38 average incidence for this period. The Pacific region reported a 75-percent increase in the number of cases over the preceding 5-year average incidence. Other groups either closely approximated last year's figures or showed significant decreases in the incidence of the disease.

Meningococcus meningitis.—For the country as a whole the incidence of meningococcus meningitis was the lowest reported during this period in the 11 years for which these data are available. The number of cases reported was 99, as compared with 136, 216, and 220 for the corresponding period in 1938, 1937, and 1936, espectively. The Mountain region alone reported an increase (50 percent) in the number of cases over the average incidence of recent years. For the years 1932–34, and 1936, other years of exceptionally low meningitis incidence, the average number of cases for this period was 138, which indicates further the low incidence of this disease that has prevailed during the current year.

Scarlet fever.—For scarlet fever, also, the comparison with recent years was favorable. The number of cases reported (3,148) was slightly lower than the number reported for the corresponding period in 1938 and approximately 90 percent of the 1934–38 average incidence for the period. In the South Atlantic and East South Central regions the number of cases was somewhat above the seasonal expectancy, but in all other regions the incidence was relatively low.

Smallpox.—The number of cases (89) of smallpox reported for the current period was the lowest recorded for this period since the years 1934 and 1933, when there were 70 and 83 cases, respectively, reported

for the corresponding period. From 1934 to 1938, inclusive, there was a steady increase in the incidence of smallpox in the United States, the high incidence, however, being confined largely to the Western and Central regions. During the latter part of 1938 a decline in the number of cases became apparent and in the last few months of the current year the incidence has dropped considerably below the average seasonal expectancy.

Typhoid fever.—Reports indicate that typhoid fever is maintaining a relatively low level. For the current period there were 2,141 cases reported, about 85 percent of the 1934-38 average number of cases for the corresponding period. Of the 513 cases reported from the East North Central region, 259 occurred in Illinios during the week ended September 2. In the Pacific region the number of cases was about normal, but all other regions reported decreases from last year's figures, as well as very significant decreases in some regions from the 1934-38 average figure for this period.

#### MORTALITY, ALL CAUSES

The average mortality rate from all causes in large cities for the 4 weeks ended September 9, based on data received from the Bureau of the Census, was 9.5 per 1,000 inhabitants (annual basis). The average rate for the corresponding period in the 5 preceding years was 9.8.

# THE TREATMENT OF LYMPHOPATHIA VENEREUM WITH SODIUM SULFANILYL SULFANILATE 1 AND SODIUM SULFANILATE \*

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The history of lymphopathia venereum with all its varied manifestations is being clarified rapidly since the discovery by Hellerström (1) that the etiologic agent is a filterable virus, and also, prior to this, the introduction by Frei (2) of a specific skin test antigen of great diagnostic significance. The disease has become recognized in recent years as a distinct entity, consisting of three progressive stages: Primary, or local infection; secondary, spreading of this infection to the inguinal glands, buboes; and tertiary, or chronic state, in which esthiomene, lympheroids, fistulae and rectal strictures are character-

<sup>&</sup>lt;sup>1</sup> Prior to June 15, 1938, the sodium sulfanilyl sulfanilate was generously contributed by Mr. S. D. Beard of the Lederle Laboratories, Pearl River, N. Y.

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1751 September 29, 1939

istic. In this preliminary report no attempt will be made to include an extensive review of the literature, but rather reference is made to the excellent one given by Frei in 1938 (3). Suffice it to say that the first two stages respond to different kinds of treatment, surgical or medical, or both. Such medical treatment is exemplified in the recent work of Hamilton (4), and of Trautman and Thomason (5), in which it is reported that sulfanilamide has proved of distinct value before stricture development, and that the results have been equal to those obtained with surgical methods, including excision of the gland and cauterization. Also, Trautman and Thomason, in making a comparison of fever therapy and this drug in the early stages of the disease, state that the latter is preferred because of low cost of administration. In their series of 15 consecutive cases treated by fever therapy or sulfanilamide, surgical incision was unnecessary.

In this report, however, our interest is limited to the tertiary stage. During the last 30 years, prior to establishment of the clinical entity of the disease, one of us (Hebb) had been treating this stage of the disease with many different therapeutic measures, including cauterization and other surgical procedures. As a last resort, palliative colostomy was performed, truly a temporary measure, but the only treatment which afforded relief to the patient. Dilatation or incision of the stricture did not result in permanent cure. In recent years, a study was made of the influence of various medical agents, including intravenous tartar emetic, Frei antigen (2) injected intravenously, However, none of these proved effectual in the and sulfanilamide. tertiary stage. The results with sulfanilamide were a confirmation of the work of Shropshear (6) who reported improvement, with administration of this drug over a prolonged period (as long as 52 days), in the patient's general health as well as in the inflammatory process about the rectum, but with persistence of the stricture. collaborators (7) reported that sulfanilamide as adjunct therapy has proved valuable but does not appear to affect the strictural lesions per se.

While we were investigating the possibility of a chemotherapeutic agent which might be active against this disease, Dochez and Slanetz (8) reported the antiviral activity of sodium sulfanilyl sulfanilate in dog distemper. Their results have not been fully confirmed (9, 10, 11), but this drug undoubtedly had antiviral activity against the strain of virus which they used. It was this original observation of Dochez that led us to try sodium sulfanilyl sulfanilate in the tertiary stage of lymphopathia venereum. Preliminary experiments carried on in white mice infected with this virus indicated prolongation of survival time of treated animals as compared with that of control animals. For this reason it was thought worth while to investigate its effect on the tertiary stage of this disease in man for which no

September 29, 1939 1752

effective treatment is known. This inadequacy of treatment has been emphasized in a recent article by Shaffer and Arnold (12) in which it is stated that "our experiences with the commonly accepted methods of treatment of this disease have been entirely unsatisfactory."

In addition to this compound, a simpler one was also studied, the sodium salt of the well-known sulfanilic acid. Both of these compounds have been found to have slight activity in white mice against pneumococcus, meningococcus, and hemolytic streptococcus, but appreciably less than that exhibited by sulfanilamide. The structural formulas are as follows: Sodium sulfanilyl sulfanilate, NH<sub>2</sub>SO<sub>3</sub>Na; sodium sulfanilate, NH<sub>2</sub>SO<sub>3</sub>Na.

Toxicity tests of single injections of these compounds, made in groups of 3 mice, showed that sodium sulfanilyl sulfanilate was significantly more toxic than sodium sulfanilate. This was found true regardless of the route of injections, whether intraperitoneal, subcutaneous, or intravenous. When freshly prepared 10 percent solutions were used, the mice injected with sodium sulfanilyl sulfanilate tolerated 25 mg. intravenously, 25 mg. intraperitoneally, and 75 mg. subcutaneously, and the mice receiving sodium sulfanilate tolerated 100 mg., 150 mg., and 250 mg., respectively. These results represent the highest single doses tolerated by 3 out of 3 mice injected. It has been noted that, after storage for a period of 9 months, sodium sulfanilyl sulfanilate exhibited a definite decrease in toxicity. In one sample, stored in the icebox from September 12, 1938, to June 7, 1939, the highest dose tolerated by all three routes of injection was practically double that of the freshly dissolved material. The toxicity of sodium sulfanilate apparently remains constant on storage.

Since it was observed in preliminary experiments that repeated injections caused a reduction of the hemoglobin content, it was thought that this activity might serve as indicator to establish a dose which would be safe in prolonged medication. Hence, repeated daily injections of 7.5 mg, were made in groups of 10 mice over a period of The blood of each mouse was tested every other day for 2% months. hemoglobin content. The mean content for the mice given sodium sulfanilyl sulfanilate was 105 percent before injection and 55 percent at the end of the series; for the mice given sodium sulfanilate it was 113 percent and 78 percent, respectively. Unquestionably both compounds in 7.5-mg. doses caused a significant decrease in percent of hemoglobin. The dose of 7.5 mg. is equivalent to 375 mg. per kg., and, consequently, for a 60-kg. individual this dose would be 22.5 grams. Hence, continued daily injections of this dose might produce a similar effect in human beings. On the other hand, 100 mg. of each compound were injected intravenously into 2-kg. rabbits over a

period of 21 days with no significant decrease in hemoglobin content. This dose is equivalent to 3 grams for a 60-kg. individual.

For human beings, intravenous injection was chosen both because of the high solubility of the compounds and because it was thought that. in treatment of the human disease, better tissue penetration would be obtained through this route. The solution for intravenous injection was made up in the following manner. On the basis of a liter lot. 150 grams of dry sodium sulfanilyl sulfanilate powder were placed in a graduated flask with 700 to 800 cc. of water, and sufficient normal NaOH added to bring the pH not higher than 5.5 (11.7 cc. per liter was the average amount required). The volume was then made up to one liter and any insoluble material removed by filtration through hard paper. For sterilization a final filtration was made through a Seitz pad. After ampouling and testing for sterility, the solution was ready for use. Evidently there was some oxidation, for the final material was not quite colorless. Solutions not kept in an icebox became brown, the color of very strong tea. It has been found inadvisable to use such preparations because of reactions obtained following their injection. In some instances the patient would experience a severe chill, pain in the epigastrium, abdominal cramps, and a feeling of suffocation. At no time, however, has any alarming reaction occurred even with 30 cc. doses (4.5 grams). The sodium sulfanilate 2 solution was prepared in the same manner, but in 10 percent concentration. When kept in the icebox these solutions were suitable for human use for a period of at least 3 months.

The dose for human beings was determined by gradually increasing the dose, by 5-cc. amounts, to the maximum that a patient would well tolerate. From preliminary trial it was found possible to inject intravenously a 15-percent solution of sodium sulfanilyl sulfanilate without producing any local reaction in case any of the solution escaped into the surrounding tissue. A concentration of 20 or 25 percent was definitely too high. Ten percent solutions of sodium sulfanilate, practically saturated, were used throughout. Blood concentration varied with each individual, and thus far no optimum blood level has been determined. The rate of excretion was rapid and seemed to vary with the individual. No demonstrable amount was present after 24 hours. In most cases a daily intravenous injection of 20 cc. was used for either drug, representing 3 grams of sodium sulfanilyl sulfanilate and 2 grams of sodium sulfanilate, respectively.

To determine the type of reaction and the effect on blood cells, two individuals were used for controls. One was a normal individual, the other a patient with cancer of the rectum. The former, Mrs. D., who was convalescing from fracture of the hip, received a

<sup>&</sup>lt;sup>3</sup> A c. p. grade of commercial sodium sulfanilate was used throughout.

September 20, 1939 1754

total of 75 grams of sodium sulfanilyl sulfanilate in daily intravenous injections of 10- and 20-cc. doses of a 15-percent solution. The blood picture before and after injections was as follows: Before, hemoglobin 83 percent, red cells 3,980,000, white cells 11,000, polymorphonuclears 68 percent, and lymphocytes 32 percent; after, hemoglobin 86 percent, red cells 4,870,000, white cells 11,100, polymorphonuclears 65 percent, lymphocytes 33 percent, and eosinophiles 2 percent. The other control, J. F., a white male, aged 47, received 186.75 grams of this drug and later 257 grams of sodium sulfanilate in 20-cc. doses daily. Prior to the injections, the blood picture showed hemoglobin 57 percent, red cells 2,600,000, white cells 6,100; and after the injections, hemoglobin 82 percent, red cells 4,370,000, and white cells 10,500. In both of these cases urine examination from time to time showed normal characteristics. From these observations it would appear that neither drug caused destruction of red or white cells with daily injections of 3 grams. On the contrary, in the cancer case, there was an increase in hemoglobin percent. At no time did either individual suffer any untoward reaction from the drug.

#### CASE REPORTS

In the present series there were 14 patients with lymphopathia venereum (13 in the tertiary stage), 8 of whom were treated with sodium sulfanilyl sulfanilate, 2 with this compound followed by sodium sulfanilate, and 4 with sodium sulfanilate alone. In addition, treatment was given to 4 cases of chronic ulcerative colitis. These patients were so treated because of the possibility of this disease being caused by a virus, and also because of the fact that all 4 failed to respond to usual medication. The following are abstracts of the case histories, including only salient facts which have bearing on this study.

#### CASES TREATED WITH SODIUM SULFANILYL SULFANILATE

Case 1.—L. S., colored female, aged 41, was in the hospital from May 2, 1938, to June 10, 1938. Onset of illness came in December 1937 with a large lump in the right inguinal region extending down the thigh. On examination Frei test was positive, Wassermann negative. Blood picture showed hemoglobin 48 percent, red cells 3,270,000, white cells 8,000, polymorphonuclears 79 percent, lymphocytes 18 percent, and basophiles 3 percent. On May 7, 1938, diagnosis was made of abscess of right thigh with acute inguinal adenitis due to lymphopathia venereum. This was aspirated subcutaneously, yielding 600 cc. thin, greenish-yellow pus; culture was negative; no tubercle bacilli were found. On May 11 treatment was begun with sodium sulfanilyl sulfanilate and continued to June 10, 32 days, a total

of 49.5 grams being given. The gland receded to a small nodule with no discharge. The patient was apparently cured.

Case 2.—C. K., colored male, aged 30, was admitted to the hospital on April 28, 1938, remaining until December 9, 1938. In 1934, he had had an operation for fistula in ano; in 1937 swelling developed about the anus with purulent bloody discharge. On March 20, 1938. colostomy was performed at another hospital. Examination showed continued discharge, and rectal stricture with orifice smaller than examining finger. Frei test was positive and Wassermann negative. Blood picture showed hemoglobin 55 percent, red cells 3,530,000, white cells 11,000, polymorphonuclears 70 percent, and lymphocytes 30 percent; blood protein was total 11.4 percent, albumin 2.17 percent, and globulin 9.24 percent. Diagnosis was lymphopathia venereum and rectal stricture. Treatment with sodium sulfanilyl sulfanilate was begun on April 29, 1938, and continued until December 8, 1938, a total of 386.55 grams being administered in the 224 days. On July 7, 1938, colostomy was closed, but broke down. On August 3 lympheroidectomy and excision of fistula were performed. On September 22 colostomy was closed, but again broke down; November 11 it was closed and healed. On September 12 stricture was absent, but on October 23 again faint, and treatment was resumed; by December 8 stricture had disappeared and colostomy remained closed. Treatment was discontinued. Blood picture then showed hemoglobin 70 percent, red cells 3,760,000, white cells 8,800, polymorphonuclears 80 percent, and lymphocytes 20 percent. The only reaction to the drug was soreness around anus and sore mouth (small ulcerations and slight bleeding). When the drug was discontinued the mouth healed readily. The patient was apparently cured; stricture was absent.

Case 3.—O. D., colored female, aged 22, was in the hospital from February 10, 1937, to March 25, 1937, and from October 29, 1937, to August 5, 1938. Four months prior to first admission hemorrhoidectomy was performed: stricture was found, with pain in rectum; blood and mucus were present in stool, and tenesmus became more acute. Patient had lost 15 pounds in a year. On admission, February 10, 1937, Frei test was positive and Wassermann positive. Blood picture showed hemoglobin 55 percent, red cells 2,950,000, white cells 7,200, polymorphonuclears 51 percent, lymphocytes 47 percent, eosinophiles 1 percent, basophiles 1 percent; total protein 16.1 percent, albumin 3.1 percent, and globulin 13.0 percent. Diagnosis was lymphopathia venereum, rectal stricture, syphilis. Sigmoidostomy was performed on February 12, 1937, and resection of rectum on November 16, 1937; the area did not heal and profuse purulent discharge continued. Treatment with Frei antigen, a total of 30.6 cc. in 10 weeks, showed no effect; after treatment with 1,145 grains of sulfanilamide discharge was still profuse every 4 or 5 days. Treatment with sodium sulfanilyl sulfanilate was begun on June 21, 1938, and in 42 days 123 grams had been injected. The discharge changed from yellow purulent to thin yellow clear material. When treatment was stopped, drainage ceased. When the patient was discharged from the hospital on August 5, 1938, there was a raw area 0.5 cm. in diameter. At this time blood picture showed hemoglobin 81 percent, red cells 4,270,000, white cells 4,900, polymorphonuclears 64 percent, lymphocytes 36 percent; protein 8.86 percent, with albumin 4.25 percent and globulin 4.61. Frei test was positive, with erythema 2 cm. and edema 0.5 cm. in diameter. On September 13, 1938, the patient returned for observation. She had gained 35 pounds in weight. A small raw area remained with slight discharge daily. On January 9, 1939, there was still a small moist area and slight discharge. Patient was apparently cured, with no stricture.

Case 4-R. C., colored female, aged 32, was in the hospital from November 8, 1937, to April 2, 1938, from June 7, 1938, to July 14, 1938, and from November 28, 1938, to December 22, 1938. Onset occurred 8 years before, with abscess of rectum with suppurative inguinal lymphadenitis. Perirectal abscesses were incised three times, the last 3 years ago. At this time there was hemorrhage from rectum. Fistula was discovered 6 months prior to examination. Physical examination showed fistula and rectal stricture with bloody discharge. Frei test was positive, Wassermann negative. Blood picture showed hemoglobin 62 percent, red cells 4,050,000, white cells 9,550, polymorphonuclears 64 percent, lymphocytes 32 percent; protein 13.4 percent. with albumin 3.3 percent and globulin 10.1 percent. Diagnosis was lymphopathia venereum with rectal stricture and fistula in ano. Patient was treated with Frei antigen for 3 weeks, a total of 35.5 cc. The discharge decreased somewhat, but stricture was unchanged. Sulfanilamide was administered for 6 days, a total of 360 grains. After this treatment, the fistula closed but reopened later. Discharge from rectum was not stopped and there was no change in stricture. On May 19, 1938, treatment was begun with sodium sulfanilyl sulfanilate and continued until December 2, 1938, 198 days, a total of 364.5 grams being administered. On December 3 the fistula recurred and was incised. When the stricture disappeared, treatment was discontinued. The blood picture at this time was hemoglobin 73 percent, red cells 3,910,000, white cells 7,250, polymorphonuclears 66 percent, lymphocytes 34 percent, total protein 10.16 percent, with 2.57 percent albumin and 7.59 percent globulin. actions to drug consisted of headaches at beginning of treatment, chill lasting 10 minutes on June 8, 1938, but treatment was continued the following day with no untoward reaction; one attack of abdominal pain on July 30, 1938, lasted about 5 minutes. The patient was apparently cured; no stricture was demonstrable.

Case 5.—M. C., colored female, aged 35, was in the hospital from September 10, 1937, to September 28, 1937, and from October 30, 1937 to October 17, 1938. On first admission diagnosis was hemorrhoids and rectal stricture. Hemorrhoidectomy was performed on September 11, 1937. On second admission, the condition was much worse, with purulent discharge from rectum. Rectal examination showed sloughing of perianal tissue; within the rectum there was a large amount of lymphoid tissue with firm stricture. Bloody purulent discharge was profuse. Frei test was positive, Wassermann negative. Diagnosis was lymphopathia venereum, rectal stricture. On November 1, 1937, blood picture showed hemoglobin 45 percent, red cells 3.340.000, white cells 14,700, polymorphonuclears 67 percent, lymphocytes 31 percent, basophiles 1 percent, eosinophiles 1 percent; and on June 23, 1938, protein 15.4 percent, with albumin 3.2 percent and globulin 12.2 percent. On January 6, 1938, ileostomy was performed and was followed by immediate improvement. From February 9 to March 27, 1938, the patient gained in weight from 62 to 73 pounds. Patient was treated with Frei antigen until May 6, 1938, but with no further improvement. On May 12, 1938, treatment with sodium sulfanilyl sulfanilate was begun and continued until July 27, 1938, for 77 days, a total of 174.25 grams being given. The discharge ceased after administration of 14.25 grams. During the first 2 weeks of this period, frequent headaches occurred; no other reactions were noted. After the twenty-fifth dose, the nodules and stricture dis-Treatment was continued for 40 more doses. was closed on July 6, 1938, and again on September 22, 1938. discharged from the hospital on October 17, 1938, the patient weighed 82 pounds. Blood picture showed hemoglobin 78 percent, red cells 4,320,000, white cells 7,200, polymorphonuclears 52 percent, and lymphocytes 48 percent; and protein 7.35 percent, with albumin 2.89 percent and globulin 4.04 percent. When examined on May 11, 1939, patient weighed 110 pounds; there was an external scar at site of old slough and no internal stricture. The patient was apparently cured.

Case 6.—G. J., colored female, aged 33, was in the hospital from February 23 to March 26, 1938, and from July 14 to August 1, 1938. Four months prior to admission, there was severe pain and tenderness in the lower abdomen, and profuse rectal discharge. Examination revealed rectal stricture 1½ inches inside anus, admitting only tip of finger, and external hemorrhoids. The Frei test was positive, and Wassermann negative. The blood picture showed hemoglobin 62 percent, red cells 4,020,000, white cells 4,400, polymorphonuclears 80 percent, lymphocytes 20 percent; total protein 8.89 percent, albumin 3.98 percent and globulin 4.91 percent. Diagnosis was lymphopathia venereum with rectal stricture and hemorrhoids. Although

September 29, 1939 1758

treated with Frei antigen for more than 9 weeks, and although stricture was manually dilated 10 times, the condition remained unchanged. On May 19, 1938, treatment with sodium sulfanilyl sulfanilate was begun and continued until December 19, 1938, for 246 days, a total of 278.75 grams being given. The only untoward reaction, on November 9, 1938, was a slight dizziness and feeling of faintness. After December 19, the patient did not return for treatment because she was unable to leave her position. Blood picture then showed hemoglobin 70 percent, red cells 3,790,000, white cells 9,950, polymorphonuclears 68 percent, lymphocytes 32 percent. In this patient the stricture was decreased, and there was 75 percent improvement.

Case 7.—M. P., colored female, aged 29, was in the hospital from August 1 to September 30, 1938. Duration of illness had been 6 years. with abdominal pain and purulent yellow-brown, sometimes bloody, rectal discharge. Three weeks before admission the patient had chills and fever lasting a week. Examination revealed stricture, which X-ray showed to be extended from 1 inch from the anus 16 inches from the rectum into the sigmoid colon. Frei test was positive. Wassermann negative. Blood picture showed hemoglobin 71 percent, red cells 3,610,000, white cells 9,950, polymorphonuclears 52 percent. lymphocytes 46 percent, eosinophiles 2 percent; protein 8.91 percent, albumin 2.65 percent, and globulin 6.26 percent. Diagnosis was lymphopathia venereum with rectal stricture. Treatment with sodium sulfanilyl sulfanilate was begun on August 3, 1938, and continued to January 19, 1939, for 170 days, a total of 372 grams being given. After administration of 207 grams a papulovesicular rash. resembling ivy poisoning, developed over the entire body and lasted for 2 weeks. Treatment was then resumed with small doses, increasing to 10 cc., without untoward reaction. On September 11, 1938, examination from barium enema showed that stricture was decreased but not cured. Patient vomited twice following 20 cc. doses. January 10, 1939, stricture was dilated. Blood picture on December 21, 1938, showed hemoglobin 89 percent, red cells 4,300,000, white cells 6,450, polymorphonuclears 68 percent, and lymphocytes 32 percent. There was 50 percent improvement in this case.

Case 8.—B. T., colored female, aged 32, was in hospital from March 25 to April 17, 1938, and from July 7 to August 5, 1938. Three years before admission to this hospital the case was diagnosed as hemorrhoids, with rectal stricture; stricture was dilated several times. Profuse discharge continued. On March 25, 1938, examination showed external lympheroids and rectal stricture which would not admit examining finger. From barium enema, definite irregularity was observed in stricture of lower 4 inches of rectum. Frei test was positive, Wassermann negative. Blood picture showed hemoglobin 65 percent, red cells 3,730,000, white cells 4,850, polymor-

1759 September 29, 1939

phonuclears 54 percent, lymphocytes 41 percent, eosinophiles 2 percent, monocytes 3 percent; protein 8.92 percent with albumin 3.92 percent and globulin 5.0 percent. Diagnosis was lymphopathia venereum with rectal stricture and lympheroids. For 3 weeks Frei antigen was used with no apparent benefit. On May 19, 1938, treatment was begun with sodium sulfanilyl sulfanilate, and continued to November 23, 1938, 189 days, a total of 385.5 grams being given. On September 16 stricture was dilated. On December 7 lympheroids were quite edematous. On December 23 stricture admitted finger; some discharge continued. On November 18 blood picture showed hemoglobin 71 percent, red cells 3,750,000, white cells 8,050, polymorphonuclears 70 percent, lymphocytes 30 percent. There was 50 percent improvement in this patient.

# SUCCESSIVE TREATMENTS WITH SODIUM SULFANILYL SULFANILATE AND SODIUM SULFANILATE

Case 9.-W. B., colored male, aged 26, was in hospital from February 23 to March 26, 1938, and from June 16 to July 6, 1938. Onset of illness occurred a year previously with boil on right side of anus. Soon after, there was purulent discharge from anus. Rectal examination showed external lympheroids, fistulous openings on each side of anus, and profuse discharge; there was no stricture, but anal canal was filled with large firm nodules. Frei test was positive, Wassermann negative. Blood picture showed hemoglobin 84 percent, red cells 4,590,000, white cells 8,000, polymorphonuclears 54 percent, lymphocytes 44 percent, eosinophiles 2 percent; blood protein 13.5 percent, albumin 4.8 percent, and globulin 9.7 percent. Diagnosis was lymphopathia venereum with fistula in ano. On February 24, 1939, fistula was excised; treatment with Frei antigen from March 3 to May 17, 1938, produced no change in condition. On May 19. 1938, treatment with sodium sulfanilyl sulfanilate was begun and continued until September 19, 1938, 123 days, a total of 158 grams being administered. Reaction to drug was severe pain, with cramps, and headache on July 20 and 21 and September 19. For this reason treatment was changed to sodium sulfanilate from September 26 to December 13, 99 days, a total of 111 grams being given. No reaction followed injection of this latter drug. Discharge decreased and lesions disappeared. Treatment was discontinued. Blood picture showed hemoglobin 93 percent, red cells 4,660,000, white cells 6,300, polymorphonuclears 66 percent, lymphocytes 34 percent, protein 7.35 percent, albumin 3.91 percent, and globulin 3.44 percent. This patient was apparently cured.

Case 10.—I. R., colored female, aged 40, was in the hospital from June 23 to September 19, 1938. Rectal stricture was discovered in 1923. Bleeding and purulent rectal discharge had been checked

with two courses of fifty 5-grain tablets of sulfanilamide, but stricture remained. Patient was also treated with tartar emetic and mercurochrome. Hysterectomy was performed on February 3, 1938. examination, nodule in anal canal was found and stricture which would not admit finger. Frei test was positive, Wassermann negative. Blood picture showed hemoglobin 70 percent, red cells 3,930,000 white cells 5,550, polymorphonuclears 58 percent, lymphocytes 40 percent, eosinophiles 2 percent; protein 8.57 percent, with albumin 4.19 percent and globulin 4.38 percent. Diagnosis was lymphopathia venereum with rectal stricture. Treatment with sodium sulfanilyl sulfanilate was begun on June 24 and continued to August 8, 1938. 46 days, a total of 243 grams being given. A chill followed injection on July 29. On August 9 blood picture showed hemoglobin 80 percent, red cells 4,600,000, white cells, 3,650, polymorphonuclears 56 percent. Treatment was changed to sodium sulfanilate from August 8 to September 19, 43 days, a total of 84 grams being given. On February 24, 1939, stricture still remained, but orifice was larger. Another series of treatments was instituted.

#### CASES TREATED WITH SODIUM SULFANILATE

Case 11.-M. B., colored female, aged 39, was in the hospital from October 7, 1938, to March 5, 1939. Illness began 3 years ago with perianal swelling and difficulty in bowel movement and purulent discharge. Examination showed multiple (14) anal fistulae, purulent discharge, and stricture of rectum which admitted only tip of examining finger. Frei test was positive, Wassermann negative. Blood picture showed hemoglobin 38 percent, red cells 2,370,000, white cells 5,250, polymorphonuclears 55 percent, lymphocytes 28 percent, monocytes 3 percent, eosinophiles 13 percent, basophiles 1 percent: total protein 8.29 percent, albumin 3.15 percent, and globulin 5.14 percent. Diagnosis was lymphopathia venereum with rectal stricture and multiple fistulae. From October 11, 1938, to February 4, 1939, 86 days, a total of 270 grams of sodium sulfanilate was injected intravenously. On December 3 fistulae were opened radically with the electric knife. The patient began to improve from this time on: daily intermittent fever, with rise of temperature to 104° F., gradually dropped to normal. Examination on February 4 showed that stricture had disappeared, but slight drainage of unhealed fistula persisted. On March 5 patient was discharged, apparently cured, with great improvement in general health. On March 24 examination showed that stricture was absent, incisions of fistulae were practically healed, and there was no purulent discharge. On May 30, 1939, incisions were healed, and there was no stricture or discharge present.

Case 12.-L. J., colored female, aged 25, was in the hospital from

November 30 to December 17, 1938. For 3 years there had been bleeding of rectum, and for 2 years difficulty in bowel movement. For a year a purulent discharge from the anus was becoming more profuse. Examination revealed a rectal fistula to right of anus, with stricture which admitted the examining finger, and a moderate amount of discharge. Frei and Wassermann tests were positive. The blood picture showed hemoglobin 78 percent, red cells 4,240,000. white cells 5,650, polymorphonuclears 64 percent, lymphocytes 27 percent, monocytes 2 percent, eosinophiles 5 percent, and basophiles 2 percent; total protein 7.65 percent, with albumin 3.13 percent and globulin 4.52 percent. The diagnosis was lymphopathia venereum. fistula, and rectal stricture. On December 1, 1938, fistula was excised and healed readily. On December 12 treatment was begun with sodium sulfanilate and continued to March 23, 1939, 100 days, a total of 110 grams being given. At the end of this series, stricture and rectal discharge had disappeared. Blood picture on April 5, 1939, showed hemoglobin 76 percent, red cells 4,070,000, white cells 3,650, polymorphonuclears 58 percent; and lymphocytes 42 percent; protein 7.64 percent, with albumin 4.28 percent and globulin 3.36 percent. Drug was tolerated well without untoward manifestations. The patient was apparently cured.

Case 13.—B. S., colored female, aged 32 years, was in the hospital from January 13 to 28, 1939. Onset of illness a year previously was characterized by mucus and blood in stool. A stricture was discovered and dilatations begun. At this time, yellow purulent mucoid discharge developed. With sulfanilamide treatment, discharge ceased very promptly. Examination showed stricture inside anus, large enough to admit index finger, also slightly nodular piling up of inflammatory tissue. Frei test was positive, and Wassermann negative. Blood picture showed hemoglobin 55 percent, red cells 3,360,000, white cells 10,050, polymorphonuclears 64 percent, lymphocytes 32 percent, monocytes, 4 percent; total protein 11.4 percent, albumin 1.16 percent and globulin 10.24 percent. Diagnosis was lymphopathia venereum with rectal stricture. From January 19 to March 11, 1939, 52 days, sodium sulfanilate was injected, a total of 125.5 grams, with no untoward reactions. Patient is still being treated, but to date improvement is considered 50 percent both in regard to drainage of the stricture and general health of the patient.

Case 14.—L. S., colored female, aged 28, was in the hospital from September 9, 1938, to November 15, 1938. Patient had been in hospital in 1935 with hemorrhoids and rectal stricture. Colostomy was performed on February 6, 1935; typhoid vaccine was administered on July 10, 15, and 18, 1935. She was discharged from hospital on July 31, 1935, only slightly improved. On August 20, 1938, she developed pneumonia. Colostomy closed and discharge increased.

Examination on September 9 showed colostomy almost closed with small hernia, rectal stricture, and moderate amount of discharge. Frei test was positive, Wassermann negative. Blood picture showed hemoglobin 60 percent, red cells 3,720,000, white cells 8,700, polymorphonuclears 82 percent, lymphocytes 18 percent; total protein 8.6 percent, albumin 2.94 percent, and globulin 5.66 percent. Diagnosis was lymphopathia venereum with rectal stricture. Treatment with sodium sulfanilate was begun on September 12, 1938, and continued until March 11, 1939, 181 days, a total of 249 grams being given. Patient had intermittent fever until October 1, 1938. She had severe pains until manual dilatation was performed on September 8, 1938. On October 5 discharge was less; on November 15 stricture was open-On January 5 there was marked improvement; finger could be passed through stricture with ease and caused no pain. Blood picture on January 5 showed hemoglobin 70 percent, red cells 4,150,000, white cells 3,350, polymorphonuclears 58 percent, and lymphocytes 42 percent. Treatment was continued with doses as large as 30 cc.: by March 11 a total of 249 grams had been injected and Frei test was still positive. However, stricture was much smaller. Treatment is being continued, and there has been about 75 percent improvement.

Table 1.—Summary of treatment of 8 cases of lymphopathia venereum with sodium sulfanily sulfanilate

Patient	Serum albu- min	Serum glob- ulin	Dura- tion of treat-	Tota! amount of drug	Hemoglobin (percent) (Sahii stand.)		Results		
	(per- cent)	(per- cent)	ment (weeks)	injected (grams)	Before drug	After drug	Before drug	After drug	
L. S	2.17 3.1 3.3 3.2 3.98 2.65 3.92	9. 24 13. 0 10. 1 12. 2 4. 91 6. 26 5. 0	4. 5 32 6 28 11 35 24 27	49. 5 386. 55 123 364. 5 174. 25 278. 75 372 385. 5	48 55 55 62 45 62 71 65	70 81 73 78 70 89 71	8,000 11,000 7,200 9,550 14,700 4,400 9,950 4,850	8, 800 4, 900 7, 250 7, 200 9, 950 6, 450 8, 050	Adenitis cured. Stricture absorbed. Do. Do. Do. Stricture reduced 75 percent. Stricture reduced 50 percent. Do.

A summary of the results of the treatment of 8 cases of lymphopathia venereum with sodium sulfanilyl sulfanilate is given in table 1. All were in the tertiary stage except one, L. S. It is noted that the serum albumin-globulin ratio is the reverse of that of normal individuals, an observation which confirms the recent work of Rosen et al. (13), who have found this condition in 100 percent of stricture cases. In addition, all these patients gave positive Frei tests; consequently the diagnosis of lymphopathia venereum was assured. The average duration of treatment was long, varying from 6 to 35 weeks. Despite this prolonged medication, blood picture was, if anything, improved,

particularly in hemoglobin content. The white cell count varied somewhat, but there was no indication of bone marrow destruction even in the case, G. J., treated for 35 weeks.

Successive treatment of 2 cases, first with sodium sulfanilyl sulfanilate and then with sodium sulfanilate because of lack of tolerance of the former drug, is shown in table 2. The only difference between these cases and those previously described is, perhaps, the alteration in the blood picture of the one case, I. R. The white cells were reduced from 5,500 to a low count of 3,650, 56 percent of which were polymorphonuclears. Although there is no indication of abnormal cells at present, the patient will be followed very closely as treatment continues. Certainly the low leucocyte count suggests a possible destructive action on the white cell formation. The stricture in this patient was of 15 years' duration. To maintain bowel movement, she was in the habit of taking magnesium sulfate after each meal to assure a liquid stool. Many different treatments had been used during the 15-year period but without results. At the time of this report, after 2 weeks' additional treatment, the stricture is reduced so that the examining finger can be passed through readily without causing any discomfort to the patient.

Table 2.—Summary of treatment of 2 cases of lymphopathia venerum with sodium sulfanily sulfanilate (I) followed by sodium sulfanilate (II)

Patient	Com-	Serum al- bumin (per-	Serum globu- lin	01	Total amount of drug	(per	globin cent) hli nd.)			Results
	роши	(per- cent)	(per- cent)	treat- ment (weeks)	in- jected (grams)	Be- fore drug	After drug	Be- fore drug	After drug	
W. B	I II	4.8	9. 7	18 14	158 111	84	93	8, 000	6, 300	Apparently cured.
I. R	Ï	4. 19	4.38	6. 5	243	70	1 80	5, 550	1 3, 650	Stricture reduced 50 percent, treatment continues.
	п			6	84					continues.

<sup>&</sup>lt;sup>1</sup> On Apr. 5, 1939, hemoglobin was 97 percent, W. B. C. 6,800.

A summary of the results of the treatment of 4 cases with sodium sulfanilate is given in table 3. Two of the four cases were cured, treatment being continued 12 and 14 weeks, respectively, and in all cases the time in which there was a change in the stricture, noted first by a softening of the tissues, was shorter than in those treated with sodium sulfanilyl sulfanilate. This was true despite the fact that each dose was only two-thirds as much, in other words, the same volume of a 10 percent solution as compared with a 15 percent solution of sodium sulfanilyl sulfanilate. It would appear, however, that the sodium sulfanilate has some destructive action against blood cells, particularly the leucocytes.

Table 3.—Summary of treatment of 4 cases of lymphopathia venereum with sodium sulfanilate

Patient	Serum albu- min	Serum globu- lin	Dura- tion	Total amount of drug	Hemo (pero (Sa stan	ent) hli	Leucocyte		Resu!ts
	(per- cent)	(per- cent)	treat- ment (weeks)	in- jected (grams)	Be- fore drug	After drug			
M. B L. J B. S	3. 5 3. 13 1. 16	5. 14 4. 52 10. 24	12 14 7. 5	270 110 125. 5	38 78 55	62 76 55	5, 250 5, 650 10, 050	9, 100 3, 650 8, 000	Stricture absorbed. Do. Stricture reduced 50 percent: treatment
L. 8	2.94	5. 66	26	249	60	70	8, 700	3, 350	Stricture reduced 75 percent: treatment continues.

The treatment in all these cases was followed by general improvement in health, increased appetite, increase in weight, and the absorption of strictural tissue. The mechanism of cure and general improvement in health is purely speculative, and yet it may be assumed that both drugs cause destruction of the virus, and that absorption of strictural tissue with return to normal bowel function follows the destruction of the infective agent.

#### CASES OF ULCERATIVE COLITIS

Case 1.—A. C., white male, aged 20, was in the hospital from June 7 to July 19, 1938. Onset of illness was 16 months prior to admission. For the preceding 3 months stools had been watery, there was pain in epigastrium 1 hour after meals and occasionally during the night, and weight had decreased from 160 to 130 pounds. Patient became so weak that he was compelled to go to bed. Proctoscopic examination showed inflammation, as high as 20 cm., with bleeding ulceration. Wassermann test was negative. Diagnosis was chronic ulcerative colitis. Despite the usual methods of treatment of this disease, the patient became worse, losing weight and strength very rapidly. On June 30, 1938, weight was 109 pounds. A transfusion and intravenous injection of glucose were resorted to as sustaining measures. He continued to have six bloody watery stools daily. On July 7 treatment with sodium sulfanilyl sulfanilate was begun, and on the fourth day of treatment great improvement in general condition was noted. No blood was found in the stool after the fifth day. By the seventh day, stools were well formed. On the thirteenth day, no lesions were observed by proctoscopic examination. The patient was discharged on July 19, 1938, weighing 125 pounds, and having only two stools daily with no blood. Thus far, 30 grams of sodium sulfanilyl sulfanilate had been administered. On September 24 the patient returned with history of blood in stool, and on examination small hyperemic areas

were noted, but no ulceration as high as 20 cm. Appetite was good and weight was 140 pounds. On September 24 treatment was begun again with the same drug and continued until December 17, 85 days, a total of 121 grams being given. On October 25 proctoscopic examination showed red granular mucosa with no ulceration. Patient seemed well, and was having normal bowel movements, but still with some blood in stools. Hemorrhoidectomy was done because of the possibility that blood came from this source. The patient was apparently cured.

Case 2.—M. M., white female, aged 61, was in the hospital from June 6 to June 23, 1938, and from July 21 to August 10, 1938. May 1938 diarrhea began, with 6 to 12 stools in 24 hours. appeared in stools and cramping pains in abdomen. Barium enema showed narrowing and spasticity of the rectal-sigmoidal junction, suggesting ulcerative lesions. Proctoscopic examination showed ulcerative lesions in lower sigmoid and rectum. No amoebae were found in stool, but blood was present. Wassermann test was negative. Diagnosis was chronic ulcerative colitis. Patient improved for a short time with aluminum hydroxide and kaolin treatment, but the ulcer was still present at the rectal-sigmoid junction on July 22. Treatment was then begun with daily injections of sodium sulfanilyl sulfanilate, a total of 35 grams being given. Repeated proctoscopic examinations showed a gradual healing process, and on August 8, 1938, ulcers had healed. On March 29, 1939, patient reported no further symptoms, and was apparently completely cured.

Case 3.—W. W., white male, aged 48, was in the hospital from November 7 to December 8, 1938. Present illness began a year ago with four or five stools a day, and frequent movements during the night. No pain, tenesmus, or bladder disorders were felt. Some night sweats occurred. The patient lost 35 pounds. Proctoscopic examination revealed superficial ulcers, some exudate, and marked inflammation of mucosa. Wassermann test was negative. Diagnosis was early ulcerative colitis. On November 10, 1938, treatment was begun with sodium sulfanilyl sulfanilate and continued until March 22, 1939, 132 days, a total of 209 grams being administered. Proctoscopic examinations from time to time showed a gradual healing process, with accompanying improvement in bowel movements, which diminished to two daily, and sleep at night was uninterrupted. The patient was greatly improved.

Case 4.—R. E., white female, aged 31, was in the hospital off and on from 1935 to 1938, with diagnosis of chronic ulcerative colitis, as shown by proctoscopic examination. Onset of illness occurred in 1932, with frequent stools, mucus, and blood. Patient had lost 35 pounds in the 3 years prior to first admission. She suffered slight fever from time to time, also edema of ankles and severe abdominal cramps,

September 29, 1939 1766

and 8 to 40 stools a day. She had been given nearly every drug ever used in the treatment of colitis, but with no permanent improvement. Wassermann test was negative. On August 2, 1938, treatment with sodium sulfanilyl sulfanilate was begun and continued until December 22, 1938, 143 days, a total of 65.7 grams being given. The drug was somewhat toxic for the patient, as indicated by severe abdominal cramps and aggravation of condition. However, treatment was continued and the number of stools decreased to 3 or 4 a day, later followed by 1 or 2 well-formed stools. This condition has continued to time of this report. The patient's general health was greatly improved and the chronic ulcerative colitis was apparently cured.

These four cases of ulcerative colitis which apparently responded to sodium sulfanilyl sulfanilate suggest the possibility that this disease may be caused by a virus. Of course, before definite proof of the efficacy of this drug is established, a larger series of patients so treated must be studied. Hence, its general use is not advocated at present. It is realized that the disease is chronic, and, as shown by Mackie (14), exhibits an inherent tendency to progression and relapse. This author summarizes the general belief that there is no one etiological agent, as follows: "Chronic ulcerative colitis appears to be the complex expression of the interaction of several different factors." It is our intention to continue the use of one or the other of these drugs in the treatment of patients in whom the diagnosis is clearly chronic ulcerative colitis.

#### DISCUSSION

The number of cases reported is small, but the beneficial and curative action of these agents in the chronic tertiary stage of lymphopathia venereum would seem to make the results significant. Most of these patients have been under observation for over a year, and there can be no question that the majority have been cured by the treatment, as judged by the disappearance of the rectal stricture and the improvement in general health. In some instances, there is a slight residuum suggestive of stroma network which has not yet been entirely absorbed. Whether or not this absorption will ever be complete, at least normal bowel functions have been restored. It is pertinent to point out, however, that the Frei test is still positive in many cases and recurrence is possible. Accordingly, patients should be followed over a period of years and treatment repeated if necessary.

The intravenous route of injection has been used throughout in these reported cases. However, 3 other patients have been treated by mouth with sodium sulfanilate, 12 grams a day in divided doses being given, 3 grams every 4 hours, maintaining the level of 2.5 mg. percent in the blood. Results in these cases would indicate that oral administration would be at least as effective as intravenous injection,

and perhaps the method of choice. If individual variation in absorption does not prevent a constant blood concentration, perhaps the interval of medication may be significantly shortened by oral administration. This has been borne out by one patient in whom stricture. which failed to admit the examining finger, broke down completely in a period of 3 weeks when 12 grams daily of sodium sulfanilate were given orally. Yet, in the patients who received intravenous therapy with either drug, the average interval before any noticeable change occurred in the stricture was 6 weeks. This change was brought about by injections given once or twice daily, and the blood level, although very high for a short period, fluctuated greatly, may be added that patients do not object to taking sodium sulfanilate in a little water or milk, as the compound is almost tasteless. On the other hand, sodium sulfanilyl sulfanilate is somewhat disagreeable to the taste.

The reactions obtained from intravenous or oral administration were similar to those with sulfanilamide, but certainly not as severe. This might be expected, inasmuch as the toxicity for white mice is less than that of sulfanilamide. This is particularly true of sodium sulfanilate which has been found to be about one-fourth as toxic. Although the number of cases treated in this series is small, the actual number of treatments during the long periods of medication is sufficiently large to offer significant evidence as to the type of reaction following administration of either of these two drugs.

The symptoms observed in the various patients were occasional abdominal pains, chills, headaches, and dizziness with a feeling of lassitude. One patient suffered an extensive rash lasting for 2 weeks; the rash had the appearance of that seen in ivy poisoning. Two patients vomited following intravenous injection. All these symptoms were relatively light, and at no time were they considered alarming. the patients treated with sodium sulfanilate intravenously, the above symptoms were absent. It is to be remembered, however, that the dose of this drug was one-third less than that of sodium sulfanilyl sulfanilate. The milder reactions following treatment with sodium sulfanilate are indicated in the 2 patients in whom it was used after sodium sulfanilyl sulfanilate, which had caused some discomfort and irritation of the intestine. Again, this relatively milder toxicity of sodium sulfanilate was brought out in the reactions obtained in the treatment of the 4 cases of ulcerative colitis. With both drugs, the dose had to be reduced to about half that used in the cases of lymphopathia venereum because of intestinal irritation following each administration. Yet this irritative effect has been observed less often with sodium sulfanilate. It is noteworthy that with the doses used blood hemoglobin content not only was not decreased, but in reality increased. With sodium sulfanilyl sulfanilate the number of white cells

September 29, 1939 1768

was not reduced, nor were there any abnormal cells observed. With sodium sulfanilate, although the leucocyte count was somewhat reduced after prolonged treatment, there was no evidence of bone marrow degeneration.

From this preliminary paper no conclusions may be drawn as to the relative merits of the two drugs. Much must be learned as to the optimum blood concentration necessary to give the desired effect. as well as the route and mode of medication. Inasmuch as our purpose was to ascertain whether a virus disease of human beings could be influenced by a chemotherapeutic compound, for the most part one route of injection (intravenous) was used in these patients. Our experience would indicate that each individual case must be studied to ascertain the highest dose that will be tolerated without untoward effect. In the present series, this was done by injecting 5 cc. of a 15-percent solution (of sodium sulfanily sulfanilate) for the first dose. 10 cc. for the second, 20 cc. for the third, and if possible 30 cc. for the The last was too large a dose for most patients. fourth dose. determining the tolerated dose, reactions such as intestinal cramps. pain in the epigastrium, and a feeling of suffocation would indicate an overdose. With oral administration the same general procedure is advocated, beginning with 0.5 gram of the drug, dissolved in a little water or milk, after each meal and at bedtime, one gram in each dose on the second day, 2 grams on the third day, and on the fourth day 3 grams. An effective blood level concentration was found to be 2.5 mg. percent for oral administration of sodium sulfanilate. Whatever the method of medication, it must be emphasized that blood studies should be made repeatedly, at frequent intervals, and if signs of cell degeneration occur, the dose should be reduced, or the drug discontinued until the blood picture becomes normal.

If these observations are substantiated by successful treatment of a significantly large number of patients in the tertiary stage of lymphopathia venereum, then the use of a chemotherapeutic agent would be established as a cure for the chronic state of a virus disease. However, inasmuch as sulfanilamide, among other drugs, has already been used successfully in the earlier stages of this disease, it would seem a more logical procedure to attempt to cure the disease before it had advanced to the chronic tertiary stage. Such a program, making use of sulfanilamide, sodium sulfanilate, or sodium sulfanilyl sulfanilate, would readily determine whether these compounds kill the virus. If the drugs are effective, then the disease in individuals so treated would not progress to the teritary stage, for which no satisfactory treatment had been found up to the time of the present report.

#### SUMMARY AND CONCLUSIONS

Fourteen cases of lymphopathia venereum, diagnosed by positive Frei test, with demonstration of rectal stricture and high globulinemia, 1769September 29, 1939

were cured or greatly improved by prolonged treatment of 6 to 35 weeks with either sodium sulfanilyl sulfanilate or sodium sulfanilate, or both, as indicated by cessation of the bloody purulent discharge, disappearance of fistulae, or lympheroids, and absorption of the rectal stricture. Four of the cases, in which colostomy had previously been performed with no improvement, responded to treatment with closure and healing of colostomy and restoration of normal bowel function.

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# THE PROTECTION OF MICE AGAINST HEMOPHILUS INFLU-ENZAE (NON-TYPE-SPECIFIC) WITH SULFAPYRIDINE

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During the past few years many bacterial infections have been given trial treatment with one or more of the newly compounded. drugs (see review by Reimann (1)). The present report adds to the list one more experimental bacterial infection which responded favorably to treatment. This infection, induced in mice with Hemophilus

September 29, 1939 1770

influenzae, non-type-specific, was treated with sulfapyridine. There have been several reports of the use of drugs in the treatment of *Hemophilus influenzae* meningitis, which is usually caused by type-specific strains (2) but the results as a whole have been equivocal (see review by Bilger and Haralambie (3)).

Interest in this experimental study was aroused by the favorable response, following treatment with sulfapyridine, of a baby suffering from an apparent *Hemophilus influenzae* infection. The baby was a patient of Dr. J. H. McLeod, who has kindly given permission for the publishing of a brief history.

The baby, 8 months old, developed conjunctivitis which was followed by an upper respiratory infection, double otitis media, and pneumonia. Two days before the onset of pneumonia a pure culture of *Hemophilus influenzae* was isolated from the eyes. A throat culture made at that time showed the same microorganism to be present in large numbers. It was also the predominating organism in the sputum after the development of pneumonia. A few pneumococci, which were not of Type I-XXXII, were also present in the throat and sputum cultures. Treatment with sulfapyridine was begun after the onset of pneumonia. Within 24 hours the child showed marked improvement, followed by a rapid and uneventful recovery.

The culture of *Hemophilus influenzae* was in all respects typical of the strains that are generally isolated from respiratory infections. These strains are not encapsulated and consequently are devoid of type specificity as determined by capsular carbohydrate. They are, therefore, different from the strains usually isolated from meningitis, which are encapsulated and type-specific.

Although the common respiratory strains do not have a capsule, they are at least sometimes pathogenic ((4) and others). Not infrequently they are isolated in practically pure culture or as the predominating organism from upper respiratory infections, or even from pneumonia. Moreover, *Hemophilus influenzae* was certainly at times actively associated with influenzal pneumonia during the 1918-19 pandemic of influenza (5). It is not known, however, whether the strains associated with influenza were type-specific or not, but the present knowledge of this organism leads some to think that they were not type-specific. Furthermore, in rare instances the non-type-specific strain may cause meningitis (2).

In the present investigation only non-type-specific *Hemophilus influenzae* was used. Type-specific cultures were not included.

#### MATERIALS AND METHODS

Culture.—The Hemophilus influenzae culture (No. 544) was isolated on April 26, 1939. It was frequently passed through mice and

between passages it was kept on rabbit blood agar slants at 37° C. All of the experimental work was done within 6 weeks after the primary isolation. The virulence of the culture was such that 1 cc. of a 10<sup>-6</sup> dilution of a broth culture in 3.5 percent mucin solution was lethal for a mouse. Two percent proteose peptone solution containing 1 percent Fildes' peptic digest blood (6) was employed for broth medium.

One cc. of a 10<sup>-4</sup> dilution of an 18-hour broth culture, in 3.5 percent mucin, was used as the infective dose in determining the action of the drug. This amount was equivalent to at least 100 minimal fatal doses. The inoculations were made intraperitoneally 30 minutes after the administration of the drug. Virulence titrations of the culture were made in each experiment.

Drug.—Sulfapyridine was suspended in 5 percent gum arabic about 30 minutes before using. The suspensions were so prepared that the desired dose was contained in a volume of 0.4 cc. They were administered into the stomach by means of a silver eustachian catheter, child's size, attached to a tuberculin syringe. Except in a few instances, only one dose of drug was given.

Mice.—Inbred albino Swiss mice weighing 16 to 18 grams were used. In the majority of the tests only males were employed.

#### PROTECTION OF MICE WITH SULFAPYRIDINE

Several experiments were made to determine the influence of sulfapyridine on *Hemophilus influenzae* infections in mice. The results of three experiments are given in table 1. It is shown that the survival of mice was directly proportional to the amount of drug administered. None survived which received only 1 mg.; 20 to 40 percent of those receiving 2 mg. survived, as did 40 to 80 percent of those receiving 4 mg., and 70 to 100 percent receiving 8 mg. Furthermore, those mice which did succumb after receiving the larger amounts of drug lived longer than the control mice. The average survival time of the mice which received 4 mg. was 7 to 11 hours longer than for the controls, while for the mice which received 8 mg. it was two or more times longer than for the controls, that is, 38 and 42 hours, respectively, in contrast to 19 and 18 hours for the controls. In one experiment no mice died which received 8 mg. of the drug.

By means of the Reed and Muench method of estimating 50 percent end-points (7) it was calculated that approximately 2.9 mg. of sulfapyridine protected 50 percent of the mice.

In experiments 3 and 5, a series of mice was given two repeated doses of the drug. The results shown in table 1 indicate that this method of treatment would give more protection than one single dose, but the number of mice so treated is too small to permit the drawing of conclusions. The fact, however, that one single dose

seems to afford protection is probably more significant than if repeated doses were required.

TABLE 1.—The protection of mice against Hemophilus influenzae with sulfapyridins

	Amount	_	Result		A verage time of	
Experiment No.	of drug (mg.)	Survived	Died	Survival (percent)	death (hours)	
May 17, 1939 3	1 2 12.6 4 8	0 1 2 4 5	5 4 3 1 0 5	0 20 40 80 100	15 20 22 28	
May 23, 1939	2 4 8	4 7 7 1	6 3 3 9	40 70 70 10	22 30 38 19	
June 7, 1939	2 26 8	4 7 7 0	6 3 3 10	40 70 70 0	18 33 42 18	

<sup>13</sup> doses: 1 mg. before culture, 0.8 mg. 6 and 24 hours after culture.
23 doses: 2 mg. before culture, and 6 and 24 hours after culture.

# THE INFLUENCE OF SULFAPYRIDINE ON THE INVASION OF THE BLOOD BY HEMOPHILUS INFLUENZAE

In two of the experiments the course of the infection in the mice was followed by repeated blood cultures made from the tip of the The tail was disinfected with alcohol, dried with ether, and snipped: then one loopful of blood was collected and streaked on a chocolate blood agar plate. The course of the blood infections in each experiment was similar. In table 2 the recordings of one experiment are given. It is shown that the drug did not prevent the organisms from invading the blood stream. Within an hour bacteria were present in the blood of the majority of the mice and by the end of 3 hours they were demonstrable in the blood of all except one mouse. At this time the number of bacteria in the blood was not significantly different in the treated or untreated mice. ever, at the end of 5 hours there was a noticeable difference. controls and in those which received the smaller amounts of drug, 1 or 2 mg., there had been a marked increase in bacteria, while in those that received 4 or 8 mg. there had been only a slight or no increase. Within 24 hours all except two of the mice in the former group were dead, and all in the latter group were living. Nevertheless, each of the mice in the latter group had a bacteriemia, in some a large number of bacteria being present. Only one mouse of this group succumbed, dying 28 hours after inoculation, although five of

the remaining nine still had bacteria in the blood at the end of 48 hours.

Table 2.—The influence of sulfapyridine on the invasion of the blood by Hemophilus influenzae

Marin No.	Amount of drug	Blood cul	tures: Hou	ırs after in	oculation of	culture—	Develo
Mouse No.	(mg.)	1	3	5	24	48	Result
1	] 1	{ '(2) (2) -(2) (2)	+ + + +	++ ++ ++ ++			D. 14 hours. D. 23 hours. D. 17 hours. D. 14 hours. D. 16 hours.
6 7 8 9	2	C (1) (3) (1)	+ + + + +	++ + ++ ++ ++	+		D. 17 hours. D. 23 hours. D. 22 hours. D. 19 hours. S.
11	} 4	(3) (1) -	+ + (3) -	+ + + + +	†+++ ++++ (1) (2)	++ ++ 	S. S. D. 28 hours. S. S.
16	8	(2) (3) - -	.#####	+ ± + +	# ++ ++ +++	- + (3) - -	8. 8. 8. 8. 8.
21222324	} •	(3) (1) (1) (4) -	++±±±	+ +++ ++ + +			D. 22 hours. D. 12 hours. D. 22 hours. D. 32 hours. D. 19 hours.

<sup>1</sup> Figures in parentheses indicate the actual number of colonies which grew from 1 loopful of blood.

-, ±, +, +++, ++++=None, very few, few, moderate number, many, very many colonies which grew from 1 loopful of blood.

#### DISCUSSION

The work presented in this paper clearly indicates that sulfapyridine influenced the course of infection experimentally induced in mice by a non-type-specific strain of *Hemophilus influenzae*. The majority of the mice receiving as much as 4 mg. of drug survived, and if death did occur it was much later than for the controls. The drug, however, did not prevent the bacteria from entering the blood stream. From 1 to 3 hours after inoculation of the culture, treated and untreated mice gave positive blood cultures alike, but after 3 hours more bacteria were present in the cultures from the untreated mice. The latter mice usually died within 24 hours while those treated (4 and 8 mg. of drug) lived longer, the majority of them surviving in spite of heavy infections at the end of 24 hours.

The influence of sulfapyridine on the survival of mice parallels the rapid recovery of the baby following treatment with sulfapyridine. Although this may have been a coincidence, it is obvious that the drug enabled mice to survive. It, therefore, seems justifiable to

C=Contaminated.

D=Died. S=Survived.

September 29, 1939 1774

suggest that the drug be given further trial in the treatment of non-type-specific *Hemophilus influenzae* infections.

It was not the purpose of this study to determine the mode of action of sulfapyridine on Hemophilus influenzae. It is obvious that it was not bactericidal. The fact that the increase of the bacteria in the blood was slower in the treated mice suggests that there was some bacteriostatic action. Nevertheless, some of the treated mice which survived developed a heavy bacteriemia. Repeated doses of the drug might have shown more bacteriostasis. On the other hand, the fact that the majority of the treated mice survived in spite of a bacteriemia suggests that the drug may have had some action on the primary toxicity of the culture. It has been generally observed that when experimental animals are inoculated with Hemophilus influenzae, if death results it occurs within a few hours, rarely after 24 hours. is, if they are able to overcome the primary toxicity of the culture, they usually survive. In certain other infectious diseases, both American and British investigators have largely held the view that sulfanilamide exerts its beneficial effects by limiting or preventing the growth of the bacteria (1). Carpenter, Hawley, and Barbour (8), however, observed that sulfanilamide protected mice against gonococcal "toxin."

Comment should be made on the high virulence of this culture. which is in contrast to the findings of Chandler, Fothergill, and Dingle (9). They studied, with the aid of mucin, the virulence of a number of type-specific and non-type-specific strains, the latter group including converted rough and respiratory strains. found that the type-specific strains were significantly more virulent than the non-type-specific. The latter were relatively avirulent. It required 1,300,000 organisms of their most virulent respiratory strain to kill 50 percent or more of the injected mice while our strain killed 50 percent or more in a dilution of 1×10-8 which contained approximately 500 organisms. This comparison must not be taken too literally, as the methods of growing the culture were different and different preparations of mucin may vary tremendously in their influence on the virulence of bacteria. These authors state, however, that it is possible that an occasional virulent respiratory strain might have been found if a much larger series of strains had been examined. Nevertheless, they seem to be of the opinion that non-type-specific strains are of little significance pathologically.

#### CONCLUSIONS

- 1. Sulfapyridine was effective in protecting mice against experimental infections of non-type-specific *Hemophilus influenzae*.
- 2. The drug did not prevent the bacteria from entering the blood stream but it apparently retarded their increase in the blood.

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## POSSIBLE RELATION OF CALCIUM DEFICIENCY TO THE UTILIZATION OF VITAMIN B<sub>1</sub>

#### PRELIMINARY REPORT

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In the studies of the relation of malnutrition to rat leprosy, observations were made which were of interest aside from the subject under investigation. The results obtained to date would indicate that calcium deficient rats are incapable of utilizing the vitamin B1 available in the diet.

Vitamin B1 deficient rats have been found to be much more susceptible 1 to rat leprosy than were normal control rats, and rats on the vitamin B1 deficient diet which received vitamin B1 in the purified form by mouth were no more susceptible than were the normal control rats.

Calcium deficient rats showed approximately the same susceptibility as did the vitamin B1 deficient rats.

As a result of these observations the following questions arose:

- 1. Are vitamin B<sub>1</sub> deficient and calcium deficient rats equally susceptible to the infection?
  - 2. Are vitamin B, deficient rats also deficient in calcium?
- 3. Are the vitamin B<sub>1</sub> deficient rats unable to utilize the calcium in the diet?

<sup>&</sup>lt;sup>1</sup> The appearance of gross evidence of a generalized infection was employed as a measure of susceptibility.

- 4. Do the calcium deficient rats receive an adequate intake of vitamin B<sub>1</sub>?
- 5. Are the calcium deficient rats unable to utilize the vitamin B<sub>1</sub> available in the diet?
- 6. Is the increased susceptibility due to a vitamin B<sub>1</sub> deficiency or to a calcium deficiency, or to a deficiency in both calcium and vitamin B<sub>1</sub>?

Several experiments have been conducted in an attempt to answer these questions.

Question 1.—Are vitamin B<sub>1</sub> deficient and calcium deficient rats equally susceptible to rat leprosy? The results obtained in four experiments indicate that they are equally susceptible, as shown by the percentages of rats in each group with gross evidence of a generalized infection.

•	Experi- ment 40 (percent)	Experi- ment 50 (percent)	Experi- ment 60 (percent)	Experi ment 62 (percent)
Vitamin B <sub>1</sub> deficient	_ 90. 9	100. <b>0</b>	90. 0	96. 2
Calcium deficient	_ 90. 9	100. 0	80. 9	95. 8
Controls	_ 0	<b>72. 2</b>	20. 8	16. 6

Question 2.—Are vitamin B<sub>1</sub> deficient rats also deficient in calcium? Analysis <sup>2</sup> of the calcium content of the tails of vitamin B<sub>1</sub> deficient rats showed the percentage of calcium to be approximately the same as in those of the control rats, as shown by the following figures.

	Experi-	Experi-	Experi-
	ment 50	ment 60	ment 69
	(percent)	(percent)	(percent)
Vitamin B <sub>1</sub> deficient	10. 08	11. 43	11. 02
Controls	9. 08	11. 33	11. 13

There is no apparent calcium deficiency in the vitamin B<sub>1</sub> deficient rats.

Question 3.—Are the vitamin B<sub>1</sub> deficient rats unable to utilize the calcium in the diet? This question may be answered in the negative, since determinations of the calcium in the tails of the vitamin B<sub>1</sub> deficient rats gave the same results as in those of the controls.

Question 4.—Do the calcium deficient rats receive an adequate intake of vitamin  $B_1$ ? The vitamin  $B_1$  intake of the rats on the calcium deficient diet is apparently adequate. The source of the vitamin  $B_1$  in the calcium deficient diet is in the liver. To check on the vitamin  $B_1$  content of the calcium deficient diet part of the casein in the vitamin  $B_1$  deficient diet was replaced by the liver used in the calcium deficient diet. The gain in weight of the rats fed this test diet was practically identical with that of rats fed the normal control diet.

Question 5.—Are the calcium deficient rats unable to utilize the vitamin B<sub>1</sub> available in the diet? Evidence has been obtained which

<sup>&</sup>lt;sup>2</sup> The percentage of calcium in a section of the tails with the skin removed.

strongly suggests that calcium deficient rats are incapable of utilizing the vitamin B<sub>1</sub> available in the diet.

Rats maintained on the calcium deficient diet and receiving additional vitamin  $B_1$  in the purified form showed a greater increase in size and weight than did rats maintained on the calcium deficient diet without the additional vitamin  $B_1$ . Rats maintained on the calcium deficient diet and receiving both vitamin  $B_1$  and calcium by mouth showed a greater increase in size and weight than did rats maintained on the calcium deficient diet and receiving vitamin  $B_1$  by mouth. Neither the group receiving the vitamin  $B_1$  alone nor the group receiving both vitamin  $B_1$  and calcium showed gains equal to that of the normal control group.

Question 6.—Is the increased susceptibility due to a vitamin  $B_1$  deficiency or to a calcium deficiency, or to a deficiency in both calcium and vitamin  $B_1$ ? Evidence has been obtained which strongly suggests that the increased susceptibility is due to vitamin  $B_1$  deficiency and not to calcium deficiency.

Vitamin  $B_1$  deficient rats were found to be much more susceptible to rat leprosy than normal rats. Rats maintained on the vitamin  $B_1$  deficient diet which received vitamin  $B_1$  in the purified form by mouth were found no more susceptible than normal rats.

Calcium deficient rats were found much more susceptible to rat leprosy than normal rats and about as susceptible as vitamin  $B_1$  deficient rats. Rats maintained on the calcium deficient diet which received vitamin  $B_1$  in the purified form by mouth were found to be no more susceptible than normal rats.

These observations are illustrated in the following table in which the percentages of rats of the different groups with gross evidence of a generalized infection are given.

	Experiment 60, 16 weeks after inoculation	Experiment 62, 15 weeks after inoculation
Vitamin B <sub>1</sub> deficient	90.0% of 20 rats	96. 2% of 27 rats
Vitamin B <sub>1</sub> deficient receiving vitamin B <sub>1-</sub>	. 0.0% of 23 rats	11.5% of 26 rats
Calcium deficient	. 80. 9% of 21 rats	95.8% of 24 rats
Calcium deficient receiving vitamin B <sub>1</sub>		
Controls		

Although vitamin  $B_1$  deficient rats were much more susceptible than normal rats, the percentage of calcium in the tails was the same as in normal rats. Although calcium deficient rats which received vitamin  $B_1$  in the purified form by mouth were no more susceptible than normal rats, the percentage of calcium in the tails was much less than in normal rats.

In one experiment, analysis, after 11 weeks on the diets, showed the average percentage of calcium in the tails of 23 vitamin B<sub>1</sub> deficient rats to be 11.43, while it was 11.30 in the tails of 24 control rats.

In another experiment, after 10 weeks on the diets, the average per-

centage of calcium in the tails of 30 vitamin B<sub>1</sub> deficient rats was 11.02; of 27 calcium deficient rats, 7.02; of 29 calcium deficient rats receiving vitamin B<sub>1</sub>, 4.67; and of 30 control rats, 11.13.

In the same experiment, after 19 weeks on the diets, the average percentages of calcium in the tails of 10 rats of each group were as follows: Vitamin  $B_1$  deficient, 13.2; calcium deficient, 5.1; calcium deficient receiving vitamin  $B_1$ , 4.67; controls, 13.3.

The amount of vitamin  $B_1$  in the circulating blood of calcium deficient rats was found to be approximately the same as in the blood of vitamin  $B_1$  deficient rats. Determinations 3 showed that the blood of the vitamin  $B_1$  deficient rats contained an average of 2.5 micrograms of vitamin  $B_1$ , while that of the calcium deficient rats contained an average of 2.3 micrograms per cubic centimeter of blood.

The blood of calcium deficient rats receiving an additional amount of vitamin  $B_1$  in the purified form contained an average of 17.5 micrograms of vitamin  $B_1$  per cubic centimeter, while that of the vitamin  $B_1$  deficient rats receiving an additional amount of vitamin  $B_1$  contained but 11.5 micrograms per cubic centimeter. This difference in the determinations in these two groups may possibly be explained by the fact that, in addition to the vitamin  $B_1$  administered, there was also vitamin  $B_1$  present in the calcium deficient diet.

According to the determination of the amount of vitamin  $B_1$  in the blood, the rats fed the calcium deficient diet were also deficient in vitamin  $B_1$  and were incapable of utilizing the vitamin  $B_1$  available in the diet.

These findings strongly suggest that the increased susceptibility is due to vitamin  $B_1$  deficiency and not to a calcium deficiency. The vitamin  $B_1$  deficient rats are not deficient in calcium, as shown by chemical analysis of the tails, and the calcium deficient rats are deficient in vitamin  $B_1$ , as shown by the determinations of the amount of vitamin  $B_1$  in the blood. The administration of vitamin  $B_1$  to either group, the vitamin  $B_1$  deficient or the calcium deficient, causes them to be no more susceptible to the infection than are normal rats, yet the amount of calcium in the tails of the calcium deficient rats receiving the vitamin  $B_1$  is below that of the calcium deficient rats. The vitamin  $B_1$  deficiency in the calcium deficient rats is apparently brought about by the inability of these rats to utilize the vitamin  $B_1$  available in the diet.

#### DIETS EMPLOYED

The diets employed in these experiments were as follows:

Calcium deficient.—Beef liver 20, casein (purified) 10, sodium chloride 1, potassium chloride 1, corn starch 65, butter fat 3 (McCollum,

<sup>&</sup>lt;sup>2</sup> The method employed to determine the amount of vitamin B<sub>1</sub> in the blood was that of Meiklejohn as used by Rowlands and Wilkinson, with slight modification. (Rowlands, E. N., and Wilkinson, J. F.: Brit. Med. J.. 2: 878 (Oct. 29, 1938).)

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Vitamin B<sub>2</sub> deficient.—Casein (purified) 18, Wesson oil 3, cod liver oil 2, salt mixture 4, autoclaved yeast 15, corn starch 58.

### COURT DECISION ON PUBLIC HEALTH

Fixing of term of city health officer.—(New Jersey Supreme Court; Larkey v. City of Bayonne et al., 8 A.2d 68; decided August 8, 1939.) An ordinance of the city of Bayonne, adopted in April 1938, fixed the term of the city health officer at 5 years and imposed upon such officer the duty of enforcing the sanitary code and all other ordinances relating to the public health. An ordinance, adopted in January 1939, repealed such earlier ordinance. A proceeding to test the validity of these two ordinances was instituted by the prosecutor, who had been duly appointed as health officer in November 1938. The statute involved provided as follows:

The local board [of health] may employ such personnel as it may deem necessary, including health officers, sanitary inspectors, and plumbing inspectors, to carry into effect the powers vested in it. It shall fix the duties, term, and compensation of every appointee. The appointee, agents, and officers of a local board shall hold their offices during the term for which they are severally appointed, and shall not be removed except for cause and after an opportunity has been given them for a hearing. Any duly appointed health officer shall, during the term of his appointment and subject to the superior authority of the local board appointing him, be its general agent for the enforcement of its ordinances and the sanitary laws of the State within the territorial jurisdiction of the board.

The supreme court in its opinion stated that the provisions of the said statute applied "to municipalities like Bayonne operating under the commission government" and that "The legislature having conferred on the municipality authority to fix the term without limitation, the cases, to the effect that the board of commissioners being a noncontinuous body cannot fix a term extending beyond its life, are inapplicable." The court also quoted from a prior case in which it was said that "an office or position which is created by municipal ordinance or resolution adopted pursuant to power conferred by the legislature upon the governing body for that purpose is just as much created by law, and its term, when fixed by such ordinance or resolution, is just as much fixed by law, as if the legislature itself had acted in the premises."

Concluding, the court held that, the record disclosing that the 1938 ordinance was properly and lawfully adopted pursuant to legislative power, the repealing ordinance of 1939 was, therefore, invalid insofar as it affected the prosecutor's term.

## DEATHS DURING WEEK ENDED SEPTEMBER 9, 1939

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

	Week ended Sept. 9, 1939	Correspond- ing week, 1938
Data from 88 large cities of the United States: Total deaths. Average for 3 prior years. Total deaths, first 36 weeks of year Deaths under 1 year of age. Average for 3 prior years. Deaths under 1 year of age, first 36 weeks of year Data from industrial insurance companies: Policies in force Number of death claims. Death claims per 1,000 policies in force, annual rate Death claims per 1,000 policies, first 36 weeks of year, annual rate	7, 117 1 6, 854 301, 250 456 1 488 18, 141 66, 735, 832 7, 914 6. 2 10. 3	6, 737 294, 413 477 19, 054 68, 305, 733 8, 320 6. 4 9. 2

<sup>1</sup> Data for 86 cities.

# PREVALENCE OF DISEASE

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

## UNITED STATES

#### CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health offices.

the State neutro outcors.

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

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 16, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median

		Diph	theria			Influ	ienza			Mea	sles	
Division and State	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934– 38, me- dian	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934– 38, me- dian	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934- 38, me- dian
NEW ENG.												
Maine	6 0 0 2 0 6	1 0 0 2 0 2	0 0 4 2 0	0 0 2 6 0 1	12	2	i	1	42 20 27 26 84 9	7 2 2 22 11 3	1 2 0 21 2 5	0 0 1 17 2 4
MID. ATL.												
New York New Jersey Pennsylvania	4 1 9	11 1 17	20 8 19	15 8 22	1 3 4	1 <b>4</b> 3	1 <u>4</u> 7	1 <u>4</u> 7	24 7 8	60 6 16	46 27 33	46 20 33
E. NO. CEN.												
Ohio Indiana Illinois Michigan <sup>3</sup> Wisconsin	12 21 11 2 0	16 14 17 2 0	14 9 18 7 2	14 13 23 11 2	5 25 3 2 46	7 17 5 2 26	6 7 1 10	15 9 7	13 1 13 0 77	17 1 20 0 44	7 1 9 52 30	8 2 18 13 40
W. NO. CEN.												
Minnesota. Iowa. Missouri. North Dakota. South Dakota. Nebraska. Kansas	0 6 17 0 38 4 31	0 3 13 0 5 1	4 1 25 1 8 2 5	4 2 25 1 1 3 9	29 38	4 5	3 7 1 2 2 2	14 2 1	12 14 6 15 45 8 25	6 7 5 2 6 2 9	18 4 3 8 0 7 8	6 3 5 3 0 1 4
SO. ATL.												
Delaware. Maryland initial Dist of Col. Virginia. West Virginia. North Carolina initial Ceorgin initial Ceorgi	0 6 16 81 27 105 33 63 21	0 2 2 43 10 72 12 38 7	0 6 0 52 11 107 31 39 8	0 6 2 33 16 72 18 30 10	3 79 24 325 22	1 42 9 119 13	13 13 137	14 104	20 6 0 17 19 6 19 7	1 2 0 9 7 4 7 4	0 9 1 2 0 29 10 0 3	0 5 0 6 3 18 1 0

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 16, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

		Dipb	theria			Infl	uenza			Me	asles	
Division and State	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934– 38, me- dian	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	38, me-	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934- 38, me- dian
E. SO. CEN.										į		
Kentucky Tennessee Alabama * Mississippi * *	14 39 72 66	22 41	20 33	34 33	16			9	7	' 4	2	3
W. SO. CEN.		l										
Arkansas Louisiana 3 Oklahoma Texas 3	62 34 16 33	14	8	10 8	2	1 16	37	3 10	2	1 2	17	8
MOUNTAIN				l			l				ļ	
Montana Idaho Wyoming Colorado New Mexico Arizona Utah <sup>3</sup>	0 10 0 5 0 0	0 1 0 1 0 0	0 1 0 17 2 2 0	0 7	24	5	1 1 1 23 3	1  15	47 51 0 0 12 25 70	5 0 0 1	1 5 1	0
PACIFIC												
Washington Oregon California	0 5 12	0 1 15	2 0 28	0 0 22	3 45 8	9 10	11 13	10 13	148 15 31		5 10 145	11 7 38
Total	20	504	642	642	18	385	420	371	19	463	591	577
37 weeks	15	13, 739	16, 640	16, 675	195	153, 176	47, 715	105, 458	382	350, 169	763, 061	670, 967

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 16, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

	Ме	ningiti coc	s, meni cus	ngo-		Polion	yelitis	1		Scarle	et fever	
Division and State	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934- 38, medi an	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934– 38, medi- an	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934- 38, medi- an
NEW ENG.												
Maine	0 0 0 1.2 0	0 0 0 1 0 0	0 0 0 2 0 1	0 0 0 1 0	0 0 0 5 8 3	0 0 0 4 1 1	0 0 1 0 0	4 0 1 4 0 2	30 0 40 21 8 21	18 18	0 9 28 0	3 45 4
MID. ATL.						l						
New York New Jersey Pennsylvania	1. 6 0 1. 5	4 0 3	7 0 3	7 2 5	46 33 21	116 28 41	8 3 5	14 3 8	25 14 31	62 12 61	70 13 78	100 17 82
E. NO. CEN.  Ohio	0. 8 0 0. 7 1. 1	1 0 1 1 0	0 2 1 1 0	2 1 2 3 1	10 9 10 64 4	13 6 16 61 2	0 0 3 5 2	17 2 18 16 8	61 45 34 62 98	80 30 52 59 56	58 34 94 127 39	94 37 101 81 55
W. NO. CEN.												
Minnesota	0 0 0 8 0 6	0 0 0 1 0 2	0 2 1 0 0 0	0 2 0 0 0	116 24 2.6 7 15 19 11	60 12 2 1 2 5 4	6 3 0 2 0	8 4 0 2 1 3	47 38 32 44 98 42 50	24 19 25 6 13 11 18	27 20 29 5 8 11 58	23 24 30 5 10 10 32
SO. ATL.												
Delaware.  Maryland  Dist. of Col.  Virginia  West Virginia  North Carolina  South Carolina  Georgia  Florida  Florida  Florida	0 3 0 1.9 5 2.9 0 0	0 1 0 1 2 2 0 0	1 1 0 0 0 0 0 1 2	0 1 0 1 3 0 0 0	0 3 8 6 0 4 14 0 12	0 1 3 0 3 5 0 4	1 5 2 0 0 0 2 1	0 3 2 4 4 2 0 2	59 40 16 37 91 25 35	3 13 2 20 34 62 9 21 4	6 9 8 23 31 46 13 10 4	3 15 8 23 31 44 8 10 4
Kentucky Tennessee Alabama 3 Mississippi 2 3	0 0 1.8 2.5	0 0 1 1	0 1 2 2	2 3 2 0	16 0 1.8 5	9 0 1 2	1 0 5 6	4 3 3 4	59 49 33 15	34 28 19 6	53 23 15 6	48 25 17 8
W. SO. CEM.	0	0	0	0	2. 5	1	اه	1	22	9	3	3
Arkansas Louisiana 3 Oklahoma Texas 3	0 2 0.8	0 1 1	1 2 1	1 1 1	0 2 10	0 1 12	0 2 2	1 2 2	17 18 21	7 9 25	4 15 <b>3</b> 5	4 9 19
MOUNTAIN										••	,,	1,5
Montana Idaho Wyoming Colorado New Mexico Arizona Utah <sup>2</sup>	9 0 22 0 0 12 0	1 0 1 0 0 1 0	1 0 0 0 0 0	0 0 0 0 0	0 0 87 99 98 40	0 0 18 8 8 4	0 1 0 1 1 0 0	1 1 0 1 1 3 0	94 20 65 96 74 0 149	10 2 3 20 6 0 15	15 3 3 4 10 2 7	15 1 4 9 6 2 13
PACIFIC			ا	ا		,	,		52	17	20	14
Washington Oregon California	0	0 0 0	0 0 0	0 0 1	3 10 34	1 2 42	1 0 2	2 2 19	50 59	10 72	22 65	16 75
Total	1.1	27	35	53	20	501	73	310	41	1,022	1, 182	1, 298
37 weeks	1.6	1, 479	2, 285	4, 389	4	3, 955	1, 236	5, 292	129	119, 962	140, 899	168, 788

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 16, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

		Sma	allpox		Typ	hoid an	d parat	yphoid	Wh	ooping	cough
Division and State	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934- 38, me- dian	Sept. 16, 1939, rate	Sept. 16, 1939, cases	Sept. 17, 1938, cases	1934- 38, me- dian	Sept. 16, 1939, rate	Sept. 16, 1939, cases	17, 1938,
NEW ENG.											
Maine	000			0	0 0 6			0 1 1 1 0 0 3 4 2 1	48 15 23	3 3 8 13 7	0 0 6 27 4 105 1 7
• MID. ATL.  New York  New Jersey  Pennsylvania	000		0	l o	13	1	1 4	31 5 12 7 45	16.	13	5 306
E. NO. CEN. Ohio	0 4 5 0 2	7	0 0	0 1 0 0	15 13 54 7 0	19 9 82 7	2 16	13 20 13	180 180	27: 27: 17:	12 428 330
W. NO. CEN.  Minnesota	0 18 1 0 8 4	0 9 1 0 1 1	1 0 1 1 0	0 1 0 0 1 0	2 4 32 15 15 0 8	1 2 25 2 2 0 3	14 14 0	5 31 1 1 0	140 14 24 231 30 23 98	32	22 9 46 4 10
80. ATL. Delaware. Maryland <sup>3</sup> . Dist. of Col. Virginia West Virginia. North Carolina <sup>3</sup> . South Carolina <sup>3</sup> . Florida <sup>3</sup> .	00000000	0 0 0 0 0 0	0 0 0 0 0 1 0 0	0 0 0 0 1 0	39 9 40 28 43 6 30 13 15	2 3 5 15 16 4 11 8	13 33 14 19	15 1 25 23 14	157 120 210 52 5 115 38 23	39 26 28 2 79 14	39 5 22 39 174 76 17
E. SO. CEN.  Kentucky Tennessee Alabama 3 Mississippi 2 3	0 0 0	0	2 2 1 0	0 0 0	52 21 16 10	30 12 9 4	36 16 20 9	38 37 18 9	68 58 26	39 33 15	16
W. SO. CEN. Arkansas Louisiana s Oklahoma Texas s MOUNTAIN	2 0 16 0	1 0 8 0	0 0 3 0	000	35 36 46 41	14 15 23 49	25 10 27 55	13 17 20 46	12 89 22 39	5 37 11 47	4 10 7 88
Montana	19 0 0 34 0 0	2 0 0 7 0 0	0 2 0 3 1 0	0 0 2 0 0	9 31 153 19 12 37	1 3 7 4 1 3 0	6 4 0 7 17 6 0	3 6 0 5 16 3	66 0 87 53 568 184 437	7 0 4 11 46 15 44	40 3 7 27 15 4 30
PACIFIC Washington Oregon California	0 0 1	0 0 1	16 2 1	5 0 1	6 35 7	2 7 8	7 2 19	6 5 13	49 80 71	16 16 87	20 47 162
Total	2	42	42	35	19	468	559	633	113	2, 799	3, 287
37 weeks	5	4, 763	12, 852	6, 189	10	9, 211	10, 442	10, 614		137, 038	

New York City only.
 Period ended earlier than Saturday.
 Typhus fever, week ended Sept. 16, 1939, 82 cases as follows: North Carolina, 2; South Carolina, 13; Georgia, 23; Florida, 8; Alabama, 6; Mississippi, 3; Louisiana, 10; Texas, 17.

## ROCKY MOUNTAIN SPOTTED FEVER

Cases reported by States, Feb. 26 to Sept. 23, 1939

State	Feb. 26 to Mar. 25	Mar. 26 to Apr. 22	Apr. 23 to May 20	May 21 to June 17	June 18 to July 15	July 16 to Aug. 12	Aug. 13 to Sept. 9	ended	Week ended Sept. 23
Eastern: New York New Jersey Pennsylvania Delaware Maryland District of Columbia Virginia West Virginia North Carolina Georgia Central: Ohio Indiana Illinois			7 2 1	3 4 6 3 13 2 13 3 3 2 1 1 3 2 1 1 1 1 1 1 1 1	3 8 3 3 11 2 10 13 1 1 2 1 5 5	12 1 7 4 23 3 11 1 13 1 1 4 4 3 7	1 8 1 1 12 2 11 6	1 1	1
Kentucky Tennessee Iowa Missouri Western:  Montana Idaho Wyoming Colorado Utah  Washington Oregon	1 2	2 4 3 2 2		10 1 5 4 16 9 5 2 7	5 9 1 5 4 6	5 6 4 2 5 2 1	1		

## SUMMARY OF MONTHLY REPORTS FROM STATES

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

State	Diph- theria	Influ- enza	Ma- laria	Mea- sles	Meningitis, meningococcus	Pella- gra	Polio- mye- litis	Scarlet fever	Small- pox	Ty- phoid and paraty- phoid fever
August 1939  Arkansas Colorado Maine Michigan New York North Dakota Pennsylvania South Dakota Tennessee Vermont	57 44 0 34 37 6 71 18 28	50 18 3 12  5 43	1, 127 3 1 8 20 1 2 256	11 26 22 120 479 7 159 9 23	1 1 0 3 9 1 18 0 3 0	97	8 12 0 389 199 3 76 0 8 2	38 60 36 275 253 19 238 39 61	4 2 0 3 1 2 0 4 1 0	124 13 4 52 56 6 83 5 88 3

<sup>1</sup> other case was reported in Montana as occurring in February, exact date not given.
2 Publication of 1 case each in Arizona and Utah, week ended Aug. 26, 1939, Public Health Reports,
Sept. 15 and 22, pp. 1699 and 1739, was an error, no cases being reported in those States during that week.

## Summary of monthly reports from States—Continued

August 1939		August 1939—Continue	d	August 1939—Continue	d
Anthrax:	Cases	Impetigo contagiosa:	Cases	Tetanus-Continued.	Cases
North Dakota	. 2	Tennessee.	18	North Dakota	. 1
Pennsylvania		Jaundice, infectious:		Tennessee	. 3
Chickenpox:	•	Michigan	4	Trachoma:	
Arkansas	8	Leprosy:	•	Arkansas	. 10
Colorado	ğ	Pennsylvania	1	North Dakota	ĭ
Maine	ğ	Mumps:	_	Tennessee	ī
Michigan	138	Arkansas	16	Trichinosis:	•
New York	364	Colorado	ğ	Arkansas	. 1
North Dakota	17	Maine	19	Maine	ī
Pennsylvania	238	North Dakota	7	Michigan	î
South Dakota	13	Pennsylvania	219	New York	10
Tennessee	4	South Dakota	14	Tularaemia:	
Vermont	28	Tennessee	- 5	Arkansas	. 11
Dysentery:		Vermont	43	North Dakota	i
Arkansas (amoebic)	7	Ophthalmia neonatorum:		Tennessee	
Arkansas (bacillary)	39	Arkansas	1	Typhus fever:	•
Colorado (amoebic)		New York	10	Arkansas	1
Colorado (bacillary)	18	Pennsylvania	3	New York	5
Michigan (amoebic)	-4	Psittacosis:	•	Tennessee.	ž
Michigan (bacillary)	13	Colorado	1	Undulant fever:	~
Michigan (unspecified).	3	Puerperal septicemia:	-	Arkansas	6
New York (amoebic)	ě	Arkansas	1	Colorado	
New York (bacillary)	143	Tennessee.	2	Maine	ī
Pennsylvania (bacil-		Rabies in animals:	-	Michigan	
lary)	7	Arkansas	15	New York	19
Tennessee (amoebic)	i	Michigan	ĭ	Pennsylvania	14
Tennessee (bacillary)	34	New York 1	6	South Dakota	- îi
Encephalitis (epidemic or	٠.	Vermont	ĭ	Tennessee	2
lethargic):		Rabies in man:	•	Vermont	4
Arkansas	1	Michigan	2	Vincent's infection:	-
Colorado	17	Pennsylvania	ī	Maine	3
Maine	i	Rocky Mountain spotted	•	Michigan	18
Michigan	3	fever:		Michigan New York <sup>1</sup>	55
New York	18	New York	2	North Dakota	8
North Dakota	4	Pennsylvania	4	Tennessee	4
Pennsylvania	2	Tennessee.	6	Whooping cough:	•
Tennessee	1	Septic sore throat:	١	Arkansas	48
German measles:	-	Arkansas	35	Colorado	74
Arkansas	2	Colorado	2	Maine	97
Maine	ī	Maine	7	Michigan	900
Michigan	13	Michigan	36	New York	1 681
New York	63	New York	94	North Dakota	67
North Dakota	ĩ	Tennessee	9	Pennsylvania	1 850
Pennsylvania	29	Tetanus:	٠ı	South Dakota	31
Tennessee.	-6	Arkansas	3	Tennessee.	171
Hookworm disease:	٠,	Michigan_	4	Vermont	199
Arkansas	6	New York	5		100

<sup>&</sup>lt;sup>1</sup> Exclusive of New York City.

## WEEKLY REPORTS FROM CITIES

City reports for week ended Sept. 9, 1939

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

	Diph-	Infl	uenza	Mea-	Pneu-	Scar- let	Small-	Tuber-	Ty- phoid	Whoop-	Deaths,
State and city	theria cases	Cases	Deaths	sles cases	monia deaths	fever cases	cases	culosis deaths	fever cases	ing cough cases	all causes
Data for 90 cities:	106	45	12	138	291	305		334	85	1 101	
5-year average Current week 1_	66	34	8	89	214	228	8	329	46	1, 131 858	
Maine:					·						
Portland New Hampshire: Concord	0		0	1	0	1 0	0	0	0	4 0	17
Vermont:	0		0	0	0	0	0	0	0	0	1
Burlington	ŏ		lŏ	ŏ	ŏ	ŏ	l ŏ	lŏ	۱ŏ	l ŏ	Î
Rutland	Ŏ		Ŏ	Ŏ	Ö	Ō	Ò	Ó	Ò	Ó	10
Massachusetts: Boston	0		0	2	0	5	0	9	0	19	166
Fall River	Ó		0	0	0	. 0	0	0	0	2	21 25
Springfield	0		0	0	0	0	0	1	0	5	25
Worcester	0		0	0	6	2	0	1	1	17	49
Rhode Island: Pawtucket	0		0	0	1	0	0	0	0	0	1 1
Providence	ĭ	i	ŏ	4	3	2	Ĭŏ	2	l ŏ	30	56
Connecticut:	•	1 -	·	•	"	_	ľ	_	4	"	1
Bridgeport	1		0	3	0	0	0	1	0	0	23
Hartford	0		0	0	0	0	0	0	0	24	38
New Haven	0		0	1	0	0	0	0	0	5	32
New York: Buffalo	0		0	1	0	0	0	3	0	6	87
New York	13	1	ĭ	11	32	13	ŏ	64	ğ	75	1, 128
Rochester	Õ		ô	-ô	l "il	ő	ŏ	i	ŏ	6	62
Syracuse	Ŏ		Ŏ	Ō	l õi	3	Ŏ	1	0.	21	29
New Jersey:					1 1				_		
Camden	0		0	0	0	3	0	8	0	1	24
Newark	0	2	0	2 1	4	1 0	0	4 2	0	34	67 26
Trenton Pennsylvania:	0		U		1	U	U	2	١	1	20
Philadelphia	2	1	0	5	8	11	0	19	1	80	391
Pittsburgh	ō	2	ĭ	ŏ	6	8	ŏ	10	1	21	146
Reading	0		0	0	0	0	0	3	Q	0	40
Scranton	0			0		0	0		0	1	
Ohio:										1	
Cincinnati	4	1	0 1	0	4	5	0	7	1	1	90
Cleveland	Õ		0	2	4 7	5 7	Ó	13	3	50	176
Columbus	0	1	1	1 2	3	2	0	4	0	5	78
Toledo	0		0	2	4	5	0	1	3	14	66
Indiana:	o		0	0	0	0	0	1	0	8	11
Anderson Fort Wayne	ŏ		ŏl	ŏ	ĭ	ĭ	ŏl	i l	ŏ	ŏ	36
Indianapolis	2		ŏ	ŏ	3	7	ŏ	4	Ŏ	23	106
Muncie	0		0	0	1	0	0	0	0	0	8
South Bend	0		0	1	3	0	0	0	0	0	21
Terre Haute	0		0	0	i	0	0	0	0	0	20
Illinois:	o		0	0	0	0	0	1	0	2	13
Alton Chicago	ĭ	i	ĭ	6	17	25	ŏl	35	4	86	630
Elgin	õ		ōl	ŏ	i	3	ŏl	Ō	Ō	2	6
Moline	0		0	0	0	1	0	0	0	2	9
Springfield	0		0	0	3	0	0	0	1	13	26
Michigan:	2		o	4	11	21	0	16	1	53	220
Detroit Flint	1		ŏ	õ	4	21	ŏ	10	ō	10	29
Grand Rapids	ó		ŏ	ŏ	ŏl	ĩ	ŏl	ĭl	ĭ	4	24
Wisconsin:	۲		١	۲	٠	- 1	٦	^ I	_		i
Kenosha	0		0	1	0	0	0	0	0	4	12
Madison	0		0	1	2	0	0	0	0	6	18
Milwaukee	0		0	2	1	9	0	1	0	20	87
Racine	0		0	1	0	0	0	0	0	2 0	13 10
Superior	0		0	0	1	١٧	0	0	٧	ا ا	10
Minnesota:			İ		- 1		ı	i			
Duluth	0		0	2	1	0	0	0	0	2	11
Minneapolis	0		0	1	5	8	0	1	0	9	89
St. Paul.	1 (	l	0	0	2	4 [	0	2	0 (	45	49

<sup>&</sup>lt;sup>1</sup> Figures for Fargo, Cumberland, Savannah, Shreveport, and Galveston, estimated, reports not received.

## City reports for week ended Sept. 9, 1939—Continued

	Diph	-1	fluenza	Mea		Scar-	Small		Ty- phoid	Whoop	Deams,
State and city	theris		Deaths	cases	monia deaths	former	pox cases	culosis deaths	favor	cough cases	causes
Tome											
Iowa: Cedar Rapids	1 0	. 1	l	1 0		1	0	ł	0	2	1
Davenport	Ιŏ			Ì		l î	ľ		ŏ	l ī	
Des Moines	Ò		. 0	Ì		Ō	l ō	0	Ō	Ō	25
Sioux City	0			1		2	0		0	1	
Waterloo	2			0		0	0		0	0	
Missouri:	١.	1	ا م	Ι.	l .	١.	١ .	ا ـ ا		١ .	
Kansas City	0		8	1		6	0	5	4	0	98
St. Joseph St. Louis	2		ŏ	0		1 7	l ŏ	0	0	16	28 184
North Dakota:	-		"	•	"	•	, ,	ا ا	_	10	101
Fargo		.	l		.		l				
Grand Forks	0			0		0	0		0	0	
Minot	0		0	0	0	0	0	0	0	0	8
South Dakota:	_	i .		0		_	١.				
Nebraska:	0			U		0	1		0	0	
Lincoln	0	I	l i	1	1 1	0	0		0	1	1
Omaha	ŏ		0	ō	i	ĭ	l ŏ.	0	ŏ	2	36
Kansas:	_		1 1		1 1			· 1			
Lawrence	0		0	Ō	1	1	0	0	0	0	3
Topeka	0		0	0	0	1	0	0	1	1	18
Wichita	1		0	2	1	0	0	0	0	3	24
Delaware:			1		1 1			1			
Wilmington	0		o	1	3	0	lol	ol	0	2	20
Maryland:	•		١ ١	-	"	•	ľ		١	~	
Baltimore	0	ll	0	0	9	7	0	6	2	33	148
Cumberland											
Frederick	0		0	0	0	0	0	0	0	0	4
Dist. of Col.:			اما								104
Washington Virginia:	1		0	1	5	4	0	8	1	11	164
Lynchburg	2		0	0	1 1	ol	o	0	1	17	9
Norfolk	ĩ		ŏl	ĭ	اةا	ŏl	ŏ	ĭ	δĺ	-i l	19
Richmond	î		ŏ	ō	l ĭ l	š	ŏi	5	ŏ	ĭ	55
Roanoke	ī		Ŏ	Ū	Ō	1	Ō	Ŏ	i	Ō	10
West Virginia:		ĺ				1		- 1	1		
Charleston	0		0	0	1	0	0	0	0	0	<b>2</b> 6
Huntington	0			0	i	0	0		1 0	0	
Wheeling North Carolina:	0		١	v	1 1	1	0	١	١	0	15
Gastonia	1			0		1	0		0	0	
Raleigh	4		0	Ō	0	i	Ŏ	0	ŏ	ŏ	3
Wilmington	0		0	0	1	1	0	0	0	0	9
Winston-Salem	0		0	0	1	0	0	1	0	0	16
South Carolina:	اہ	7	o		0		اه	.		اما	
Charleston Florence	0	'	öl	0	1	0	öl	0	. 1	0	17 10
Greenville	ŏ		ŏ	ŏ	2	ŏ	ŏ	ő	ŏ	ŏ	10
Georgia:	١		٠,	٠	- 1	١	١	١	١	١	10
Atlanta	3	1	0	0	6	0	0	6	0	0	82
Brunswick	0		0	0	0	1	0	1	0	0	3
Savannah			-				.	-	-		
Florida:		ا م		!		!	ا ا		ا ا	!	••
Miami	1	3	8	1	2	1 2	0	1	9	1	28
Tampa	0		١	2	0		0	1	1	0	25
Kentucky:		- 1	1	1	- 1	- 1	- 1	1	1	- 1	
Ashland	0		o l	0	0	0	0	0	2	0	5
Covington	0		0	1	1	0	0	1	0	1	8
Lexington	0		0	0	0	1	0	1	2	1	16
Louisville	2		0	0	1	1	0	1	0	11	39
Tennessee: Knoxville	1	1	o	o	o	3	اه	2	0	o	23
37 17	i 1.	- 1		1	۱ ۵	2	ا م	2	_ ^ i	انما	
Nashville	ō l		8	1	2	2	öl	3 3	ö	4	50
Alabama:	٠,١		١	- 1	- 1	-	٠,	١	١	- 1	•
Birmingham	1	1	0	0	3	1	0	4	0	3	81
Mobile	1 .		1	0	2	1	0	1	0	0	29
Montgomery	0	1		0		2	0  -		0	0  -	
A-1	- 1		- 1	ı	1	- 1		J		1	
Arkansas:	ام	- 1	l	اہ		اہ	اہ	1	.	اہ	
Fort Smith Little Rock	0	2	0	0	3	0	0 -	i	1 0	0 -	4
Louisiana:	١	-	١	١٣	۱	١	١	*	١	١	*
Lake Charles	0 .	1	0	ol	0	0	ol	0	0	0	12
New Orleans	2	2	ĭ	ŏΙ	ž	4	ŏ	16	ĭ	ŏ	138
Shreveport	-	-		.		-	-				

## City reports for week ended Sept. 9, 1939-Continued

	Diph-	Infl	uenza	Mea-	Pneu-	Scar- let	Small-	Tuber-	Ty- phoid	Whoop- ing	Deaths,
State and city	theria cases	Cases	Deaths	sles cases	monia deaths	fever cases	pox cases	culosis deaths	fever cases	cough cases	all causes
Oklahoma: Oklahoma City_ Tulsa	0		0	0 1	4	0	0	2	2 1	0	47
Texas: Dallas Fort Worth Galveston	5 0	1	1 0	6 0	1 5	2 0	0	2 3	0 2	1 0	69
Houston San Antonio	3		0	0	3 4	2 0	0	5 7	1	5 3	73 79
Montana: Billings Great Falls Helena Missoula	0 0		0	0 0	0 3 0 1	0 0 1 1	0 0	0	0 0	2 0 0	7 17 2
Missoura Idaho: Boise Colorado:	0		0	0	1	0	0	1	0	0	4
Colorada Springs. Denver Pueblo	0 1 0		0	0 3 0	0 0 1	1 2 0	0 0	0 7 0	0 0 0	0 12 0	11 84 10
New Mexico: Albuquerque Utah: Salt Lake City.	ľ		0	0 2	1 0	3	0	1	0	30	18 24
Washington: Seattle Spokane Tacoma Oregon:	. 0		0 0	4 1 2	3 1 0	2 3 0	0 0	4 1 0	0 0	10 0	80 24 31
Portland Salem.	0		0	. 0	0	1 0	8	0	. 0	5 0	53
California:  Los Angeles Sacramento San Francisco	6 0 1	2	0 0 1	5 1 2	6 1 1	18 0 2	0 1 0	15 1 5	0 0	9 1 0	283 23 159

State and city		ngitis,	Polio- mye-	State and city		ngitis, ococcus	Polio- mye- litis
State and city	Cases	Deaths	litis cases		Cases	Deaths	cases
Massachusetts: Boston New York: Buffalo New York Rochester Syracuse. New Jersey: Camden Pennsvlvania: Philadelphia Pittsburgh Scranton Ohio: Cleveland Toledo Illinois: Chicago Michigan: Detroit Grand Rapids	0 0 1 1 0 0 0 2 0 1	0 0 2 2 0 1 0 0 0 0 0	2 40 16 4 0 11 25 3 0 4 1 1	Wisconsin: Milwaukee Minnesota: Minneapolis St. Paul Iowa: Davenport Baltimore Baltimore District of Columbia: Washincton. South Carolina: Charleston Texas: San Antonio Colorado: Pueblo California: Los Angeles Sacramento	0 0 0 0 0 1 0 0	0 0 0 0 0 1 0 0	5 16 4 1 1 1 3 3 3 2 4 4 6 1 1

Encephalitis, epidemic or lethargic.—Cases: Pittsburgh, 1; Toledo, 1; Alton, Ill., 1.

Pellagra.—Cases: Montgomery, 2.

Typhus fever.—Cases: New York, 1; Charleston, S. C., 4; Miami, 2; Birmingham, 1; Montgomery, 4;

Lake Charles, 1; New Orleans, 5; Dallas, 5; Los Angeles, 1.

## FOREIGN REPORTS

## CANADA

Provinces—Communicable diseases—Weeks ended August 19 and 26, 1939.—During the weeks ended August 19 and 26, 1939, cases of certain communicable diseases were reported by the Department of Pensions and National Health of Canada as follows:

Week ended Aug. 19, 1939

Disease	Prince Edward Island	Nova Scotia	New Bruns- wick	Que- bec	Onta-	Mani- toba	Sas- katch- ewan	Al- berta	British Colum- bia	
Cerebrospinal meningitis Chickenpox		4	2	2 8 32	6 52 2 4 13	7		5	9	8 87 34 4 21
Measles		2 1 1 3		44 3	82 7 18	6 3 3	6	4	4 2 1	148 16 20
Scarlet fever	3	7 4 1	28	26 66 11	47 1 60	7 4 2	3	5 5 1	3	97 1 170 24
Whooping cough		2	3	52	61	7	15	11	30	18

## Week ended Aug. 26, 1939

Disease	Prince Edward Island	Nova Scotia	New Bruns- wick	Que- bec	Onta-	Mani- toba	Sas- katch- ewan	Alber-	British Colum- bia	
Cerebrospinal meningitis. Chickenpox Diphtheria. Dysentery Influenza. Measles. Mumps. Pneumonia. Poliomyelitis. Bcarlet fever Trachoma. Tuberculosis Typhold and paraty- phold fever.		2 2 2 2 2 3	2 3 3 	1 22 39 1 45 2 5 18	30 1 1 5 62 6 9 7 45 1 48	1 5 7 8 1 7 7 5 5	1 11 3 	7	7 11 2 2 2 2 1 6 1	2 85 53 9 6 121 13 15 88 2 145
Tuberculosis. Typhoid and paraty-	2	_		68 29 48	48 8 65	5 16	10	2 8 9	<u>1</u>	

## **CUBA**

Provinces—Notifiable diseases—4 weeks ended August 19, 1939.— During the 4 weeks ended August 19, 1939, cases of certain notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Rio	Habana	Matan- zas	Santa Clara	Cama- guey	Oriente	Total
CancerChickenpox		2	1	12		5	20
DiphtheriaLeprosyMalaria	2 17	15 1 1	1 	2 25	2 1	1 17	22 6 61
Measles Poliomyelitis Scarlet fever	1	14	2	1 		<u>6</u>	15 8
Tuberculosis Typhoid fever Undulant fever	24 37	21 76	25 21 1	67 58	6 19	37 40	180 251 1

## **JAMAICA**

Communicable diseases—4 weeks ended September 2, 1939.—During the 4 weeks ended September 2, 1939, cases of certain communicable diseases were reported in Kingston, Jamaica, and in the island outside of Kingston, as follows:

Disease	Kings- ton	Other lo- calities	Disease	Kings- ton	Other lo- calities
Chickenpox	5 4 2 1	13 5 4 2	Leprosy	25 7	2 3 87 94

# WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

From medical officers of the Public Health Service, American consuls, International Office of Public Health, Pan American Sanitary Bureau, health section of the League of Nations, and other sources. The reports contained in the following table must not be considered as complete or final as regards either the list of countries included or the figures for which reports are given.

## CHOLERA

[C indicates cases; D, deaths; P, present]

	٤	i de								Week	Week ended—						
Place	Feb.	Mar.	Mar. 26-Apr. 29, 1939	May		June 1939	939			Jul	July 1939			7	August 1939	1939	
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Allahabad C C Assam	113	31 238 98	220 105	405 156	115	105	883	1.64	25	-13		1.01	746	0.83	12	15	
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Bombay Presidency  Burma  Caloutia  Caloutia  Cantral Provinces and Berar Chittagong  Delhi  Madras Presidency  Madras Presidency  Madras Presidency  Trumbal	1 For 2 weeks.

WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER-Continued

PLAGUE 1

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Place	29- Feb.	Mar.	Mar. 26-Apr. 29, 1939	May		June 1939	1939			J.	July 1939				August 1939	1939	
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Infunding placted in the United States and its possessions.
Infunding placted May 5, 1930, stated that 34 cases of placine with 8 deaths had occurred in Hsinking, Manchuria, China, since the beginning of the year.
Infunding a Ar report dated May 10, 1938, states that up to July 6, 84 deaths from pneumonic plague had occurred in Batavia Residency, Java, Dutch East Indies.
Includes 1 cases of pneumonic plague.
Information plague.
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Information plague.
Includes 4 cases of pneumonic plague.

# WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

## PLAGUE-Continued

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Place				29- Feb.	Mar.	Mar. 26-Apr. 29, 1939	May May		June 1939	939			July 1939	636		Ì	August 1939	839	
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Argentins (see also table above):  Mendoza Provinco  Bolivia  Algatosa State  C. Barall:  Algatos State  C. Pernambnoo State  Sao Paulo State  C. C	ω ω	61 11 11 6	1 9 1					Indochina: Cambodia	china: Cambodia [agascar (central ref. [agascar departural ambayeque Departural Departural Departural Department.] [Lima Department.] [ima Department.]	china: Cambodia.  lagascar (central region) Cajamarca Department. Lambayque Department. Libertad Department. Lima Department.	on)	00000000	07.70 44L	22. 12. 13. 13. 14. 15. 17. 18. 18. 18. 19. 19. 19. 19. 19. 19. 19. 19. 19. 19	222	841 18 7			13 7 7

Pneumonic plague.
 Last reported human case, Aug. 30, 1937, Fresno County, Calif. Intensive plague work is being conducted in the Western States and detailed reports of plague infection found in animals and ensect hosts are published currently in the Public Health Reports. The following summarizes recent reports for 1939: California—Ground squirrels, March and April; insects, March and June; Idaho—Insects, June 14; Montan—Ground squirrels, July 15; insects, July 15 and 17; Newige—Insects, April; New Marcho—Kangaroo rat, Apr. 15, Oregon—Ground squirrels, June; insects, May and June; Washington—Rabbit, May; insects, April and May; Wyoming—Insects, July 3.

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		Top.							We	Week ended-	- <del>p</del>					
Place	29- Feb.	Mar.	Mar. 28-Apr. 29, 1939	Kay S		June 1939	339		7	July 1939	6		4	August 1939	1939	
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Grecce. (See table below.)					_	_	_	_	_	_	_	-	-	-	_	!

WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER-Continued

# SMALLPOX-Continued

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Place	29- Feb.	Mar.	Mar. 26-Apr. 29, 1939	May 1930		June 1939	6861			Jul	July 1939				August 1939	1939	
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Imported.

Information dated Apr. 6, 1939, states that up to Mar. 31, 61 cases of smallpox were reported in Talwan, Japan.

Suspected.

WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

# SMALLPOX-Continued

		, ,								Week	Week ended-	1					
Place	Feb.	789- Mar.	Mar. 26-Apr.	Apr. 30- May		June 1939	6861			Ju	July 1939			~	August 1939	1939	
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July 1939	8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8
June 1939	199 199 118 178 178 178 178 178 178 178 183 183 183 183 183 183 183 183 183 18
May 1939	169 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
April 1939	140 70 4 174 900 E
March 1939	88 2422 2422 2422 2422 2422 2422 2422 24
Febru- ary 1939	26 26 1 1 16 20 20 20 20 20 20 20 20 20 20 20 20 20
Place	Argentina  Belgian Congo  Chylai  Chylai  Ta Faz Department  Courre Department  Courre Department  China: Harbin  China: Harbin  Chonnbia (see also table above)  Franco  Graden: Guayaquil and vicinity  Franco  Graden: Guayaquil see also  Graden: Guayaquil see also  Franco  Graden: Guayaquil see  Colombia (See also table above)  Franco  Gradenia  Troy Coast  Aguascalientes State  Chinanhan State  Chinanhan State  Chinanhan State  Colamajuanc State  D Guaranjuan State  Chinanhan

1 For February and March.
For May and June.
For January and February.

WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER-Continued

TYPHUS FEVER

C indicates cases: D. deaths: P. presen

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WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER-Continued

TYPHUS FEVER-Continued

	Jan	Feb.	Mar.				!				W 86	Week ended-	1							
Place	45.53	Kar Sir	\$ <u>1</u> 8		May 1939	1939			June 1939	330			July	July 1939			Ψ	August 1939	626	
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Union of South Africa. (See table below.) Venezucia. (See table below.) Vigoslavia. On vessels:	8	67	115	13	8	91	ю	10	69	11	i_	•	160	11	81	89			<del>-                                    </del>	
S. S. Mandrook at Mers el Kebir C S. S. Normandie at Plymouth C				<u>                                     </u>					Ħ			-				$\frac{\cdots}{11}$	$\frac{++}{11}$			

Place	Febru- ary 1939	March 1939	April 1939	May 1939	June 1939	July 1939	Place	Febru- ary 1939	March 1939	April 1939	May 1939	June 1939	July 1939
Bollyla: Cochabamba Department Cochabamba Department Far Pax Department Corner Department Corner Department Cotosi Department Cochina: Manchuria—Harbin Cochinasia Aguascalientes State Department Cochinabia Aguascalientes State Department Cochinabia Aguascalientes Cochinabia	\$ 5 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 7 1 23 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	5-1 74 7-8	11122 10 4 9	7 4 4 60 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	G	Mexico (see also table above) — Con.  Michoacan State — D.  Queretaro State — D.  Puebla State — D.  Queretaro State — D.  San Luis Potosi State — D.  San Luis Potosi State — D.  Tabasco State — D.  Tamanipas State — D.  Vera Crux State — D.  Vera Crux State — D.  Vera Crux State — D.  Vera Crux State — D.  Vera Crux State — D.  Vera Crux State — D.  Vera Crux State — D.  Vera Crux State — D.  Vera Crux State — D.  Vera Crux State — D.  Ramania — C.  Spain — C.  Spain — C.  Turkey — C.  Cupe Province — C.  Orange Free State — C.	4-1 8 1 1 2 4 2 × 1	2005 2005 4 4 4 17 17 17 17 17 17 17 17 17 17 17 17 17	8484 8845-	1 244 21 21 445 6	222. 42. 21. 11. 28. 21. 11. 28. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2.	23

For May and June.
For January and February.

# WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued YELLOW FEVER

	Jan	Feb.	Mar.								A	Week ended—	led –							
Place	작 주 주 주	Msr. 25,	* <u>F</u> 8		Ma	May 1939			June 1939	1939			-	July 1939				August 1939	t 1939	
	1939	1939	1939	9	13	8	27	8	10	17	22	1	00	15	8	82	2	12	61	8
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<sup>1</sup> See also reports of yellow fever in Brazil in preceding issues of the Public Health Reports.

3 Jungle type.

4 Exact date anded September 16, 1939, 1 fatal case of suspected yellow fever was reported in Bangui, French Equatorial Africa.

4 Exact date not given.

<sup>6</sup> Includes 1 suspected case.
6 Includes 4 suspected cases.
7 Suspected.