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# **PREVALENCE OF POLIOMYELITIS**

During the week ended October 7, 390 cases of poliomyelitis were reported in the United States, as compared with 469 cases during the preceding week, and a median of 290 cases for the corresponding week of the 5 years 1934-38. The gradual decrease which has been noted since the week ended September 16, when 501 cases were reported, continued during the current week. The States reporting 10 or more cases are given in the following table:

	Cases		Cases
New York.	77	Minnesota	40
New York City.	8	Minneapolis	13
New Jersey.	10	Towa	14
Pennsylvania.	28	Texas	14
Philadelphia.	15	Colorado	12
Ohio.	12	Utah	10
Michigan.	38	California	42
Wisconsin.	10	Los Angeles	6

# CULTIVATION OF PHASE I H. PERTUSSIS IN A SEMI-SYNTHETIC LIQUID MEDIUM

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Most workers who have grown Phase I H. pertussis on other than Bordet-Gengou media have found it necessary to add blood or serum to obtain growth. Wollstein (1) could obtain growth only on B.-G. media, ascitic broth, rabbit serum agar, serum, or blood bouillon. Truschina, Pechletzkaja, and Murawjewa (2) used 10 percent human Teissier, Reilly, Rivalier, and Cambessedes (3) serum in broth. Mishulow, Mowery, and Scott (4) used chocolate used blood gelatin. Cruickshank and Freeman (5) used Wright's agar and horse serum. heart agar with proteose peptone and horse serum. Lwoff (6) states that H. pertussis will grow on peptone water. However, he does not state whether Phase I organisms were used and whether serial transfers were made to rule out the possibility of transfer of growth substances from the inoculum.

There is need for a liquid culture medium of simple composition which will sustain a heavy growth of Phase I organisms. This would

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be helpful in providing large quantities of organisms, free from extraneous matter, for chemical studies. It would be useful for investigating the nature of any soluble antigen which may be evolved by the organism and, finally, it might open the way to a better method of preparing a vaccine.

It was first found that growth could be obtained in a 1 percent proteose peptone or hydrolyzed casein solution in buffered saline at pH 7.4, provided a cellophane sausage casing containing whole blood was suspended in the solution during the growth period. This medium produced a good growth but contained traces of unknown compounds contributed by the blood dialysate.

After further experimentation a medium was developed, containing known ingredients, consisting of inorganic salts, hydrolyzed casein, soluble starch, and either glutathione or cysteine. With the exception of the starch all of the ingredients are dialyzable. If it is desired to remove the unused starch when the growth has been completed this may be accomplished by the addition of a small amount of ptyalin. (Berkefeld filtered saliva, 0.5 cc. per 100 cc. of culture is satisfactory.) The action is completed in a few minutes at room temperature. After this step dialysis should remove all the original constituents of the medium.

Preparation of the medium.—The medium contains the following ingredients and they are added in the order given:

	Cc.
Distilled water	1, 000
	Gm.
Hydrolyzed case in <sup>1</sup>	7.00
Sodium chloride	5.00
Potassium chloride	
Calcium chloride, anhydrous	. 20
Magnesium chloride (6 H <sub>2</sub> O)	. 10
Sodium carbonate, anhydrous	. 50
Potassium acid phosphate, monohydrated	. 25
Soluble starch <sup>2</sup> (reagent)	1.00
Yeast extract (optional, see below) (8)	

<sup>1</sup> Commercial case is acid leached and alcohol extracted according to the method of McCollum, Simmonds, Shipley, and Park (Bull. Johns Hopkins Hosp., **33**: 298 (1922)), and is hydrolyzed by the method of Berg and Rose (J. Biol. Chem., **82**: 479 (1929)).

<sup>9</sup> The use of starch is not new. The Lederle Laboratories have been using it for some time in the cultivation of *H. pertussis*.

After the reaction has been adjusted to 7.4 the medium is autoclaved for 20 minutes at 20 pounds. On cooling, the reaction is readjusted and the medium filtered through paper. One hundred cc. quantities are then placed in Blake bottles and reautoclaved. Before inoculation 0.5 cc. of a 0.2 percent solution of either glutathione or cysteine is added. This solution must not be heated but is sterilized by Berkefeld filtration. The bottles are inoculated from a B.-G. slant, placed on their sides so as to allow a large surface exposed to the air, and incubated at 37° C. Growth is complete in from 48 to 96 hours, depending upon the size of the inoculum. When growth is completed a preservative may be added if desired.

Effect of serial transfer on growth.—In order to determine if growth was due to the transfer of blood from the Bordet-Gengou slant with the inoculum and to determine if a change of phase took place in the new medium, the following experiment was carried out.

Four Blake bottles of medium were prepared as above (containing yeast extract). One loopful of organisms from a B.-G. slant was suspended in 5 cc. of saline. The first bottle was inoculated with 0.5 cc. of this suspension. When growth had taken place, 1 cc. was transferred to the second bottle, and so on. The results were as follows:

	growth (hours)
Blake bottle No. 1	- 48
Blake bottle No. 2	- 72
Blake bottle No. 3	- 72
Blake bottle No. 4	- 72

Material from bottle No. 4 was centrifuged, the organisms washed once and agglutinated with Phase I antiserum. The titer was the same as with Phase I organisms from the same original source but transferred on B.-G. medium. The bacilli from the fourth bottle had the same morphology as Phase I organisms and were hemolytic when transferred to B.-G. medium. They would not grow when transferred to plain nutrient agar slants.

It would appear that growth does not depend upon transfer of growth promoting substances with the inoculum and that H. pertussis remains in Phase I for at least 4 transfers on the new medium.

Action of the organism on starch.—Since starch is necessary it would be interesting to know whether it is acted upon by the organism. The following experiment indicates that the starch is broken down. A 10-cc. quantity of media containing starch was divided into two equal parts. One was inoculated and both were placed in the incubator for 3 days. At the end of that time an equal amount of Gram's iodine was added to each and the two compared in the colorimeter. It was found that the color of the inoculated tube was less intense than that of the uninoculated tube and that the latter was blue while the inoculated tube was violet.

Factors involved in the growth of H. pertussis.—As a result of some preliminary experiments it was found that organic nitrogen was essential for growth. Tests indicated that hydrolyzed casein was a satisfactory source of nitrogen and had the advantage over peptone of being dialyzable.

Certain polysaccharides are also necessary for growth. Soluble starch is one of these. Another polysaccharide which may be used in place of starch is Beta dextrin (7), obtained by the action of B. macerans on potato starch and purified by three recrystallizations. Alpha dextrin may also be used. (Our sample of Alpha dextrin was of doubtful purity.) Such substances as glycogen, saliva-hydrolyzed starch, commercial dextrin, glucose, lactose, maltose, celliobiose, glucosan, laevoglucosan, trihexosan, acacia, mucin, and agar cannot be used in place of starch.

Organic sulfur also proved to be essential for growth. This may be in the form of glutathione, cysteine, or cystine, but not methionine.

These three substances, namely, organic nitrogen as in amino acids, certain polysaccharides, and organic sulfur, are considered absolutely essential ingredients in this liquid medium in order to obtain a growth of H. pertussis.

In order to ascertain whether growth could be improved, tests were made by adding other substances to this basic medium and culturing under comparable conditions. It was found that blood serum, freshly hemolyzed red cells, whole blood dialysate, and an aqueous extract of dried brewers' yeast prepared according to the method of Lwoff and Lwoff (8) contain a growth-stimulating substance which. if added to the basic medium, will greatly increase growth. If the extraneous material which is thereby added is not considered objectionable, it is recommended that 0.5 cc. of the above yeast extract be added to each 100 cc. of the medium.

Other substances were also tested in a similar manner and were found to have no stimulating effect. The substances tested included vitamin B<sub>6</sub>, Beta indole acetic acid, cevitamic acid, cholesterol, diphospho-pyridinenucleotid, filtrate factor, vitamin concentrate, glycerophosphate, hemin, lactoflavine, liver catalase (9), nicotinic acid, pimilic acid, sodium citrate, thiamin, thyroxin, triphosphopyridinenucleotid, and tryptophane.

### SUMMARY

1. The formula of a simplified, serum-free liquid medium is presented which supports a heavy growth of Phase I H. pertussis.

2. It has been demonstrated that, aside from organic nitrogen, two groups of substances are necessary for growth of Phase I H. pertussis: (a) Certain polysaccharides, and (b) sulfur-containing compounds such as glutathione or cysteine. An unknown substance present in yeast extract stimulates growth but is not essential.

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# DEVELOPMENT AND GENETIC CHARACTERISTICS OF THE ADENOMATOUS STOMACH LESION IN STRAIN I MICE<sup>1</sup>

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The occurrence of a spontaneous stomach lesion in strain I mice has been reported previously (1), and in a more recent publication (5) the pathology of the lesion has been described. The gastric process is characterized by hyperplasia of the mucosa of the glandular portion of the stomach and is found in virtually all mice of the strain when they are 8 months of age. Progressive growth of the lesion is the chief cause of death in strain I animals, which are known to die at an early age. The reader is referred to an earlier paper (5) for a detailed description of the macroscopic and microscopic appearance of the lesion as well as its effect on the organism.

The appearance of the gastric process in a mouse 2½ months of age and the normal development of the process in animals over 6 months of age were described in the earlier report (5), but it was thought necessary to study the normal development of the growth in younger mice before beginning experimental procedures which may influence its course. Since the gastric process is known to occur in practically all mice of strain I, it was considered of interest to determine what genetic factors are involved.

In the experiments reported here the macroscopic appearance of the stomachs of strain I mice was used to trace the normal development in younger mice and to ascertain whether the lesion has a genetic The process can be easily detected by macroscopic examinabasis. In advanced cases the glandular portion of the stomach is tion. enlarged and firm with nodular elevations beneath the serosa. When the stomach is opened, the lumen of the glandular portion is found to be reduced in caliber and the mucosa is thickened with coarse hypertrophied rugae. In the less advanced cases the lesion is not

<sup>&</sup>lt;sup>1</sup> From the Office of Cancer Investigations, U. S. Public Health Service, Gibbs Memorial Laboratory, Harvard University, Cambridge, Mass.

so pronounced but is easily detected by comparing the stomachs of strain I mice with those of mice of other strains.

All the mice used in the investigation were maintained on a diet of Purina dog chow exclusively.

# DEVELOPMENT OF LESION IN NORMAL STRAIN I MICE

To determine the development of the adenomatous lesion, litters of strain I mice were separated as to sex as soon as the nursing period was ended and each animal was numbered. When these mice were 2 months old, 10 animals (5 males and 5 females) were selected to be sacrificed at 1-month intervals. Each group of 10 was made up to include litter mates so far as possible and usually consisted of representatives of 2 or 3 litters. The procedure was followed over a period of 7 months, making a total of 8 groups of mice. In addition to these animals, other normal strain I mice of both sexes, ranging in age from 1 to 15 months, were used in the study.

Immediately after death of the animal the stomach was preserved by ligating the orifices, injecting 0.5 cc. of fixative into the lumen and placing the entire stomach in fixative. After hardening, the stomach was cut longitudinally, the esophageal and pyloric orifices bisected, one-half stained for histologic study and the other half kept for macroscopic observation. In this manner a complete series of gross and stained specimens was available.

Stomachs of strain I mice 1 or 2 months of age were normal in appearance, i. e., they were similar to those seen in mice of the same age belonging to other strains. Early lesions were seen in mice, especially males, 3 to 4 months of age and consisted of a few hyperplastic areas in the glandular mucosa of the greater curvature. The lesion developed progressively in all mice over 3 to 4 months of age and was pronounced in every 8-month-old animal.

A comparison of the stomachs obtained from male and female mice from 2 to 6 months old revealed that the lesion appeared earlier in the males. By the fourth month hyperplasia had occurred in practically every male animal while many females of the same age had normal stomachs. The lesion is obvious in virtually all 6-month-old animals of both sexes but is more pronounced in males, and this same order of susceptibility is maintained, on the average, throughout life. The difference in the degree of development in male and female mice is shown in figure 1. The reason why the lesion appears earlier and is more pronounced in males than in females is obscure.

# GENETIC STUDIES

Routine autopsies performed in this laboratory during the past few years (5) have revealed a somewhat similar stomach lesion in a few old mice belonging to other inbred strains as well as in "stock" or

PLATE I

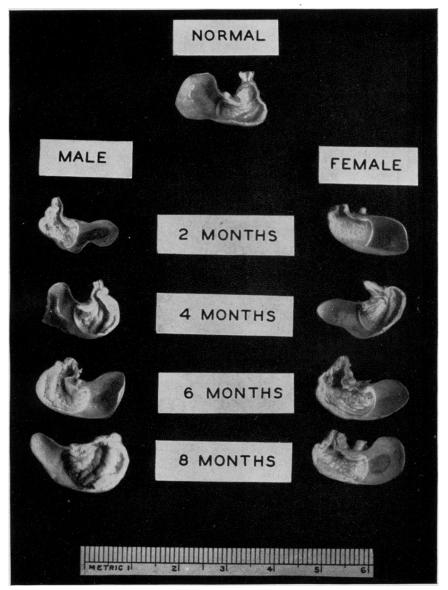


FIGURE 1.—Difference in degree of development of the spontaneous stomach lesion in male and female mice of strain I. Each specimen was prepared by injecting fixative into the lumen and placing the stomach in fixative. After hardening, the stomach was split longitudinally. The specimen at the top is from a male mouse of strain C, age 1 year, and is designated as a normal stomach. The other 8 specimens are stomachs from strain I mice. At the age of 2 months both sexes have normal stomachs. At the age of 4 months the stomach from the male shows hypertrophy of the glandular mucosa, while the stomach from the female is similar to the normal specimen. The lesion is seen in the stomachs of all strain I mice 6 or 8 months of age but is more pronounced in the specimens from the males. Actual size. "market" mice, but these lesions were far less extensive than those occurring in younger mice of strain I. The occurrence of gastric hyperplasia in mice of other strains is of some significance for it shows that the tendency, at least, is not limited to strain I mice, and suggests that consistent inbreeding has produced, in strain I, a stock in which the tendency has become pronounced. The inbreeding of mice has resulted in the production of strains which are highly susceptible to the development of spontaneous breast cancer (2) and strains which show a high incidence of spontaneous pulmonary tumors. Furthermore, the susceptibility to spontaneous pulmonary growths is known to be inherited (4) as a dominant characteristic.

The high incidence of gastric lesions in strain I mice presents an opportunity to determine whether the lesion is inherited in accordance with genetic principles. Strain I mice were mated to strain C57 black animals to procure outcross mice for genetic studies. Mice of strain C57 black were selected because the lesion has not been seen in any member of the strain under 1 year of age and because the females take excellent care of their young.

During September 1937, reciprocal crosses were made between strain I and strain C57 black mice by mating 11 of the C57 black females to I males and by mating 9 strain I females to C57 black males. These mice are referred to as the F generation. The young were all black and consisted of 41 females and 32 males (from C57 black females mated to I males), and 31 females and 36 males (from I females mated to C57 black males). The 140 mice thus procured are designated as the F<sub>1</sub> hybrid generation.

Two of the strain I females, after having been bred to C57 black males, were mated to their brothers and 14 strain I mice (7 males and 7 females) were obtained. These animals were kept with the  $F_1$ hybrid mice and are designated as normal strain I mice.

During January 1938, 14 females of the  $F_1$  hybrid generation were mated to C57 black males and 14 additional females of the  $F_1$  hybrid generation were mated to I males. The following numbers of mice were obtained from these matings: 34 females and 33 males from  $F_1$ hybrid females  $\times$  C57 black males; 49 females and 33 males from  $F_1$ hybrid females  $\times$  I males. The 77 mice obtained by mating  $F_1$ hybrid females to C57 black males were all black and are called black backcross mice. The 82 mice born to  $F_1$  hybrid mothers and strain I males had a variety of coat colors and are called I backcross mice.

Results in the F generation mice.—The 11 C57 black females died or were sacrificed at an average age of 14 months; none had any evidence of the stomach lesion. The 9 strain I females lived to an average age of 8.6 months and all had pronounced stomach lesions. Results in the  $F_1$  hybrid generation mice.—Of 132 mice of this group which were kept for one year and then killed, none had a stomach lesion.

During October 1938, all of the 14 normal strain I mice, which were then 8 to 8.5 months old, were sacrificed; all showed definite stomach lesions. At the same time 8 of the  $F_1$  hybrid mice, which were 10.5 months of age, were killed. These animals had been born to the same mothers as were the normal I mice but had had a C57 black father. None had the stomach lesion.

The absence of the lesion in the  $F_1$  hybrid generation reveals clearly that if the lesion has a genetic basis, it is inherited as a recessive characteristic. The result in the  $F_1$  hybrids of this experiment is similar to the finding reported in an earlier publication (3). When strain I mice were mated to strain  $C_3H$  animals, none of the resultant hybrids developed a stomach lesion.

It is generally accepted that susceptibility to tumor growth is inherited as a dominant characteristic. The recessive nature of the stomach lesion, as reported here, suggests that it may not be a malignant growth. This postulation is supported by the histologic appearance of the lesion as well as by the absence of metastases in strain I mice exhibiting pronounced gastric hyperplasia (5).

*Results in backcross mice.*—All of the 77 black backcross mice were kept until they were 1 year of age and were then necropsied; all were free from the stomach lesion. This is further evidence that susceptibility to the lesion is inherited as a recessive characteristic.

The I backcross mice were sacrificed and necropsied when they were 1 year old. Some had stomach lesions comparable to those found in year-old strain I mice, some had normal stomachs, and many had a few hyperplastic areas in the glandular mucosa of the stomachs which were similar to those seen in 3- to 4-month-old strain I mice. It is obvious that such findings in year-old mice cannot be interpreted with certainty. However, the occurrence of definite stomach lesions in some of the I backcross animals is evidence that the lesion is inherited as a recessive characteristic, while the small degree of hyperplasia in the stomachs of others suggests that a number of factors are involved which may control the time of appearance of the lesion or its degree of development.

# CONCLUSIONS

The adenomatous lesion of the stomach which occurs spontaneously in practically all adult mice of strain I appears earlier and is more pronounced in the male mice.

The susceptibility to the development of the lesion is inherited as a recessive characteristic, and a number of factors are involved.

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# EFFECTS OF EXTRACTS OF HUMAN URINE ON TUMORS IN MICE<sup>1</sup>

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Rhodenburg and Nagy (1) in 1937 described a method of extraction whereby a growth stimulating substance and a growth inhibiting substance were derived from human urines.<sup>2</sup> The growth stimulation and growth inhibition of these substances were measured by their effects on the rate of proliferation of a protozoan, Colpidium campylum. in culture medium.

The eight tests described here were conducted for the purpose of determining the effects of these substances on (a) transplanted, (b)spontaneous, and (c) chemically induced tumors in mice.

# MATERIALS AND METHODS

The tests were divided into three types:

Type 1.-Mice were injected with a cancerigenic hydrocarbon, and then given daily injections of the urinary growth affecting substances. There were three tests in which 152 strain D (dilute brown) and 79 strain C<sub>a</sub>H mice were utilized. Male mice were used in order that spontaneous mammary tumors would not be a complicating factor.

Type 2.- The growth affecting substances derived from urine were tested in mice bearing transplanted dermal sarcoma No. 37. There were three tests in 189 male and female strain ABC mice. As these were short duration experiments in young mice, spontaneous tumors were not encountered.

Type 3.—The growth affecting substances were fed to mice. All mice were strain  $C_{a}H$ . Eleven females had spontaneous mammary tumors. In another experiment 37 males had been injected with one

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<sup>&</sup>lt;sup>1</sup> Inasmuch as Rhodenburg and Nagy called these a "growth stimulating substance" and a "growth inhibiting substance," these terms are so used in this paper. However, it is possible that the physiological response obtained with these urinary fractions may not be due to specific growth factors.

dose of 1:2:5:6-dibenzanthracene prior to the feeding of the growth affecting substances.

A total of 468 mice were used in eight experiments. The controls showed the susceptibilities of these strains of mice to chemically induced tumors.

In extracting the urinary growth affecting substances, the methods of Rhodenburg and Nagy were closely followed. Nevertheless, different batches of material varied somewhat in physical properties. For example, while most of the batches of growth inhibiting substance resulted in a white powder, an occasional batch would be a light tan color. The batches of growth stimulating substance were uniformly a dark brown liquid, but, on storage, a precipitate settled out in some but not in others. Normal human urine was used.

The injections of cancerigenic hydrocarbons were all made in the right axillas of the mice, subcutaneously. The dose of 1:2:5:6-dibenzanthracene was 10 mg. of the crystals moistened with glycerine for injection in one test and 1 mg. in 0.25 cc. of lard in another test. The dose, per mouse, of 20-methylcholanthrene was 1 mg. in 0.25 cc. of lard. The injections of the urinary growth affecting substances were, unless otherwise stated, subcutaneous and as far away as practicable from the hydrocarbon, that is, in the left inguinal region. Daily doses, as used here, means daily except Sundays and holidays.

#### TYPE 1 TESTS

EXPERIMENT 1. DAILY DOSES OF URINARY GROWTH STIMULATING AND GROWTH INHIBITING SUBSTANCES INJECTED INTO MICE WHICH HAD RECEIVED ONE SUB-CUTANEOUS INJECTION OF 1:2:5:6-DIBENZANTHRACENE

Seventy-two male strain D (dilute brown) mice 21/2 months old were each injected subcutaneously in the right axillas, with a dose of 10 mg. of 1:2:5:6-dibenzanthracene moistened with glycerine. The mice were then divided into 5 groups. Group 1 received no other Group 2 received, on the same day, 0.25 cc. of a solution treatment. containing 1 cc. of growth stimulating substance in 1 cc. of distilled water. Group 3 received, subcutaneously in the left inguinal region, daily doses of 0.025 cc. of the above solution of growth stimulating substance. Group 4 received, subcutaneously in the left inguinal region, 1 dose of 0.025 cc. of a suspension containing 1 gm. of the growth inhibiting substance in 1 cc. of distilled water. Group 5 received daily doses of 0.0025 cc. of the above solution. The daily injections continued for 9 months. All mice died in 18 months or less.

*Kesults.*—At the end of the test several mice in each group had developed tumors at the site of injection of the 1:2:5:6-dibenzanthracene, with the exception of group 5 which had received daily injections of the growth inhibiting substance. One mouse in group 5, however,

had a tumor in the right inguinal lymph node, while the crystalline 1:2:5:6-dibenzanthracene was found *in situ* in the right axilla without tumor.

Calcific deposits were noted in the heart muscle and at the site of the dibenzanthracene injection in some of the mice in group 5.

 
 TABLE 1.—Experiment 1. Effects of substances derived from human urine on tumor formation induced by 1:2:5:6-dibenzanthracene subcutaneously

Substance injected, in addition to 10 mg. 1:2:5:6- dibenzanthracene	Number of mice injected, Mar. 10, 1937	Number of mice living, July 10, 1937	Number of mice develop- ing tumors	Number of mice not de- veloping tumors	Percent of mice living on July 10, 1937, which do- veloped tumors
Group 1: Controls, 1:2:5:6-dibenzanthracene only Group 2: One dose of urinary growth stimulating	15	13	12	3	92
substance	12	12	10	2	83
Group 3: Daily doses of urinary growth stimulating substance for 9 months	15	13	10	5	77
Group 4: One dose of urinary growth inhibiting sub- stance.	15	14	11	4	78
Group 5: Daily doses of urinary growth inhibiting substance for 9 months	15	15	1	14	7

# EXPERIMENT 2. DAILY DOSES OF URINARY DERIVATIVES INJECTED INTO MICE WHICH HAD RECEIVED 1 DOSE OF CANCERIGENIC HYDROCARBON SUBCUTANEOUSLY

Fifty-nine male strain C<sub>3</sub>H mice, 2½ months old, were each injected in the right axillas with a dose of 1 mg. of 1:2:5:6-dibenzanthracene in 0.25 cc. of lard. They were divided into 2 groups of 20 and 1 group of 19 mice. Twenty other untreated C<sub>3</sub>H male mice were set aside as controls, making 79 mice in the experiment. Group 1 consisted of untreated controls. Group 2 mice had received 1 dose of 1:2:5: 6-dibenzanthracene subcutaneously and no other treatment. Group 3, consisting of 19 mice, had received 1:2:5:6-dibenzanthracene, 1 dose subcutaneously, and daily doses of urinary growth stimulating substance (0.25 cc. of 1 to 10 dilution). Group 4 had received 1 subcutaneous dose of 1:2:5:6-dibenzanthracene and daily doses (0.5 cc. of a 1 to 10 dilution) of urinary growth inhibiting substance. The daily injections were discontinued after 17 weeks because of extensive ulcerations at the site of injections in the group receiving the growth inhibiting substance. The ulcers healed and all test mice lived more than 5 months. Results are shown in table 2 and figure 1.

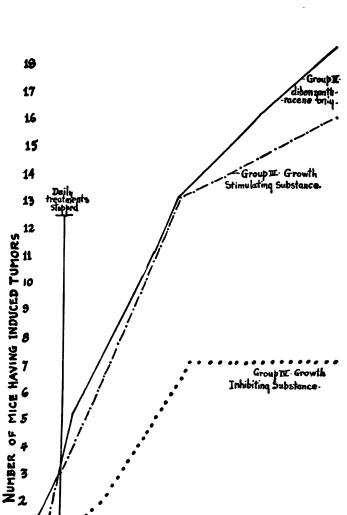


FIGURE 1.-Experiment 2. Time of onset of tumors induced by 1:2:5:6-dibenzanthracene in mice given daily doses of urinary growth affecting substances.

32

36

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16 TIME IN WEEKS -

Substance injected, in addition to 1 mg, 1:2:5:6-di- benzanthracene (controls untreated)	Number of mice injected, Mar. 28, 1938	July 28,	Number of mice develop- ing tumor at site of dibenzan- thracene	veloping	Percent of mice alive on July 28, 1938, which de- veloped tumors
Group 1: Untreated controls, 20 mice. Group 2: 1:2:5:6-dibenzanthracene only. Group 3: Daily doses of urinary growth stimulating substance for 17 weeks. Group 4: Daily doses of urinary growth inhibiting substance for 17 weeks.	0 20 19 20	19 20 19 20	0 18 17 7	20 2 2 13	0 90 89 35

**TABLE 2.**—Experiment 2. Effects of daily doses of substances derived from urine on tumor formation induced by subcutaneous injection of 1 mg. of 1:2:5:6-dibenzanthracene in lard

#### EXPERIMENT 3. DAILY DOSES OF URINARY GROWTH AFFECTING SUBSTANCES INJECTED INTO STRAIN D (DILUTE BROWN) MICE WHICH HAD RECEIVED 1 DOSE OF METHYL-CHOLANTHRENE

Twenty male strain D mice from 3 to 4 months old served as untreated controls (group 1). Sixty other similar mice each received 1 mg. of methylcholanthrene in 0.25 cc. of lard, subcutaneously in the right axillas on October 5, 1938. Twenty mice, group 2, received no other treatment. Group 3, 20 mice, received daily injections of 0.1 cc. of a 1 to 2 dilution of the urinary growth stimulating substance. Group 4, 20 mice, received daily injections of 0.2 cc. of a suspension of 1 gm. of urinary growth inhibiting substance in 4 cc. of distilled water. The daily injections were administered subcutaneously in the left inguinal region for  $6\frac{1}{2}$  months.

*Results.*—Group 1 developed 1 tumor, a spontaneous lymphoma; group 2 developed 13 tumors; group 3, 16 tumors, and group 4, which had received the inhibiting substance, developed 9 tumors (table 3). It is believed that different batches of the urinary extracts varied somewhat in potencies.

 
 TABLE 3.—Experiment 3. Effects of substances derived from urine upon tumor formation induced by methylcholanthrene

Substance injected, in addition to 1 mg. 20-methyl- cholanthrene (controls untreated)	Number of mice injected, Oct. 5, 1938	Number of mice alive, Feb. 5, 1939	Number of mice develop- ing tumors	Number of mice not de- veloping tumors	Percent of mice alive on Feb. 5, 1939, which de- veloped tumors
Group 1: Untreated controls. 20 mice Group 2: Methylcholanthrene only Group 3: Dally doses of urinary growth stimulating substance Group 4: Daily doses of urinary growth inhibiting substance	0 20 20 20	17 19 20 19	<sup>1</sup> 1 13 16 9	19 7 4 11	6 68 80 47

1 Lymphoma.

		, canceri- hydrocar- ly	lowed injec growth	enic hy- toon fol- by daily tions of stimulat- ostance	Cancerigenic hy- drocarbon fol- lowed by daily injections of growth inhibit- ing substance		
	Number of mice alive 4 months after in- jection of hydro- carbon	Number of mice which devel- oped tumors	Number of mice alive 4 months after in- jection of hydro- carbon	Number of mice which devel- oped tumors	Number of mice alive 4 months after in- jection of hydro- carbon	Number of mice which devel- oped tumors	
Experiment 1, strain D mice Experiment 2, strain C <sub>1</sub> H mice Experiment 3, strain D mice	13 20 19	12 (92%) 16 (80%) 13 (68%)	13 19 20	10 (80%) 17 (90%) 16 (80%)	15 20 19	1 (7%) 7 (35%) 9 (47%)	
Total	52	41 (av. 80%)	52	43 (av. 83%)	54	17 (av. 30%)	

**TABLE 4.**—Experiments 1, 2, and 3. Summary of three experiments in which 158 mice were injected with cancerigenic hydrocarbons (one dose), then given daily doses of growth affecting substances derived from human urine

Fewer tumors developed in the mice which were given the urinary growth inhibiting substance.

### TYPE 2 TESTS

### EXPERIMENT 4. URINARY GROWTH AFFECTING SUBSTANCES ADMINISTERED TO MICE BEFORE AND AFTER TRANSPLANTATION OF SARCOMA 37

Sixty strain ABC mice of both sexes, 4 to 5 weeks old, were used in the test. They were divided into 3 groups of 20 mice each. On March 24, 1938, 20 mice were injected subcutaneously in the left inguinal region with 0.25 cc. of a 1 to 10 dilution of urinary growth stimulating substance. This same dose was repeated daily for 6 days. Then a mash of sarcoma 37 tumor tissue was injected dermally into the shaved abdomens of the mice, following which the same daily dose of urinary growth stimulating substance was administered for another 5 days. The same procedure was followed in a second group of 20 mice, except that a daily dose of 0.5 cc. of a 1 to 10 dilution of urinary growth inhibiting substance was administered. A third control group of 20 mice received only the transplanted tumor tissue on the sixth day of the test. Each of the 60 resulting tumors was measured daily for 11 days, then every second day until the mice died or the tumors regressed, a period of 1 month.

Results.—All of the tumors grew. On the twenty-second day after transplantation, the average maximum diameter of the tumors in the group receiving growth stimulating substance was 17 mm., that of the tumors in the group given growth inhibiting substance was 15.8 mm., and that of the tumors in the untreated control group, 18.8 mm. The final regression rate of 10 percent was roughly the same in all three groups.

#### EXPERIMENT 5. URINARY GROWTH INHIBITING SUBSTANCE ADMINISTERED TO MICE WITH TRANSPLANTED S-37 TUMORS

Thirty-six strain ABC mice of both sexes, 7 to 8 weeks old, were given dermal injections of S-37 tumor mash on September 30, 1938. They were then divided into 3 groups of 12 each. Group 1 was given daily intraperitoneal injections of 10 mg. of growth inhibiting substance in 0.1 cc. of distilled water. The second group received the same daily dose of growth inhibiting substance subcutaneously, at a distance from the tumor implantations. The injections were continued until 22 daily doses had been given to the mice of each group. The third group of 12 mice received the implantation of tumor tissue but no other treatment. The results of this experiment are shown in table 5. No striking effects were observed.

 
 TABLE 5.—Experiment 5.
 Daily doses of urinary growth inhibiting substance injected into mice with S-37 dermal tumors

Group	Num-			Num- ber of				
	ber of mice	Material injected	Route of injection	daily doses	Grow- ing	Smaller	Re- gressed (Gone)	
1 2 8 (untreated controls)	12 12 12	Inhibiting substance_ do	Intraperitoneal. Subcutaneous	22 22 None	Percent 59 59 77	Percent 8 25 8	Percent 33 16 15	

#### EXPERIMENT 6

Urinary growth affecting substances were mixed with sarcoma 37 tumor mash and injected dermally into strain ABC mice. Physiological saline and broth were mixed with tumor mash and used for injecting controls. Ninety-three mice were tested. The test substances, the growth stimulating and growth inhibiting substances derived from urine, were poisonous to the cells of the tumor mash in proportion to the concentrations used. The regression rates were as great in the control groups as in the test groups.

Results of type 2 tests.—The slight inhibition of tumor growth observed in these experiments may have been a result of interference with normal systemic physiology.

#### TYPE 3 TESTS

# EXPERIMENT 7. URINARY GROWTH INHIBITING SUBSTANCE FED TO C<sub>3</sub>H MICE BEARING SPONTANEOUS MAMMARY TUMORS

This feeding test was started on October 24, 1938; 11 female strain  $C_3H$  mice, about 9 months old, each bearing one or more spontaneous mammary tumors, were fed in drinking water a 1 to 100 dilution of the growth inhibiting substance derived from human urine. The test

terminated on January 6, 1939. During the 10½ weeks of the test, the mice consumed about 3,900 cc. of the 1 to 100 dilution. All the tumors increased in size, being apparently unaffected by the treatment.

### EXPERIMENT 8. URINARY GROWTH AFFECTING SUBSTANCES FED TO MICE INJECTED WITH 1.2:5:6-DIBENZANTHRACENE

The mice used in this experiment were strain C<sub>3</sub>H males about 2% months old. Each mouse received 1 mg. of 1:2:5:6-dibenzanthracene in 0.25 cc. of lard, subcutaneously in the right axillas, on April 14. 1938. The mice were then divided into 2 groups. Eighteen were fed a 1 to 100 dilution of urinary growth stimulating substance; 19 were fed a 1 to 100 dilution of urinary growth inhibiting substance. The feedings were given ad libitum in the drinking water for 8½ months. During the first month accurate amounts of the ingested materials were recorded. The first group consumed 32.2 gm. of the urinary growth stimulating substance in that period of time and the second group consumed 35.1 gm. of the urinary growth inhibiting substance. Sixteen (88 percent) of the 18 mice fed urinary growth stimulating substance developed tumors at the site of the injected hydrocarbon. while but 12 (63 percent) of the 19 mice fed the urinary growth inhibiting substance developed tumors. Ninety-three percent of the 20 controls which had received only the hydrocarbon developed tumors at the site of injection.

# DISCUSSION

That there are growth controlling factors in the normal bodies of all living things is evident. Whether it be a mouse or an elephant, a bacterium or an oak tree, each has its predestined limitation of growth. In the healing of a wound, new tissue rapidly forms and yet, when the wound is healed, the growth of the tissue is stopped; there has been stimulation of growth and growth inhibition. Doubtless the process is an intricate biological process involving several factors. The tests described here were performed in an attempt to ascertain whether, by these crude methods, such substances could be found grossly present in a human waste product. Whether the meager results attained in the experiments on the growth of tumors were due to such a metabolic growth inhibiting factor, to an extraneous chemical compound attributable to the process of extraction of the urine which affected the tumor cells directly or through rendering the food less utilizable to the tumor cells, has not been determined.

Development of tumors induced by 10 mg. of 1:2:5:6-dibenzanthracene as crystals moistened with glycerine was inhibited to a greater extent than development of tumors induced by 1 mg. of methylcholanthrene in lard, in the same strain of mice.

If cancers are formed by the mutation of normal cells, the inhibitory action may be due to a specific interference with a chain of biological transformation processes necessary in the metamorphosis of normal cells to malignant cells. Whether in the chemical induction of tumors such a change has been prevented by maintenance of the chemical structures of the cell, the tissue fluids, or the intracellular enzymes. or by prevention of alteration of the chromosomes is not known. Methylcholanthrene (2) has been suspected of producing a deficiency in the sulfur-containing amino acids.

That the inhibition of the formation of tumors following injection of a cancerigenic chemical was not a result of the development of a systemic resistance to tumor formation in general was evidenced by the finding that transplanted sarcoma 37 grew in several strain D mice in which tumors had been prevented by long-continued daily injections of urinary growth inhibiting substance following the injection of methylcholanthrene, a cancer inducing agent.

### SUMMARY

A growth inhibiting substance derived from human urine prevented, to a limited degree, the formation of tumors in mice following injection of cancerigenic chemicals, but the urinary derivative had little, if any, specific inhibiting effect on transplanted or spontaneous tumors in mice.

# ACKNOWLEDGMENT

I am indebted to Mrs. Theresa Shovelton for technical assistance.

#### REFERENCES

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   (2) White, J., and White, A.: Inhibition of growth of rat by oral administration of mathylabolatherape. See First and Ministration (1999).
- of methylcholanthrene. Proc. Soc. Exp. Biol. and Med., 39: 529 (1938).

# DEATHS DURING WEEK ENDED SEPTEMBER 23, 1939

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

	Week ended Sept. 23, 1939	Correspond- ing week, 1938
Data from 88 large cities of the United States: Total deaths Average for 3 prior years Total deaths, first 38 weeks of year Deaths under 1 year of age. Average for 3 prior years Deaths under 1 year of age, first 38 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 38 weeks of year, annual rate	7, 620 27, 457 316, 317 471 2514 19, 080 66, 671, 692 10, 591 8, 3 10, 2	1 7, 321 309, 287 1 497 20, 084 68, 268, 220 10, 891 8, 3 9, 3

Data for 86 cities.

# PREVALENCE OF DISEASE

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

# UNITED STATES

# CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers. In these and the following tables, a zero (0) indicates a positive report and has the same significance as any other figure, while leaders (---) represent no report, with the implication that cases or deaths may have occurred but were not reported to the State health officer.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 30, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median

		Diph	theria			Influenza				Measles			
Division and State	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934– 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934– 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934– 38, me- dian	
NEW ENG.													
Maine New Hampshire Vermont Massachusetts Rhode Island Connecticut	18 0 7 8 6	3 0 6 1 2	1 0 3 0 1	1 0 6 0 1	6  	1	1   3	  2	24 0 67 29 115 30	4 0 5 25 15 10	1 0 52 0 4	1 6 12 2 5	
MID. ATL.													
New York New Jersey Pennsylvania *	4 5 8	10 4 16	13 6 14	26 7 28	14 6 	16 5 		<sup>1</sup> 11 9 	11 12 12	28 10 23	60 5 46	60 18 46	
E. NO. CEN.													
Ohio Indiana <sup>\$</sup> Illinois <sup>\$</sup> Michigan <sup>\$</sup> Wisconsin	21 13 9 5 0	27 9 13 5 0	32 29 26 11 0	33 29 35 13 2	11 1 4 8 84	14 1 6 8 48	21 12 	15 15 9 	8 5 15 32	11 4 7 14 18	23 2 22 52 55	23 3 22 20 38	
W. NO. CEN.													
Minnesota Iowa Missouri North Dakota South Dakota Nebraska Kansas	8 22 5 22 8 15 11	4 11 4 3 1 4	11 31 25 3 1 7 6	8 9 38 2 1 6 7	6 102 11	3  14 	5 5 11 5 2 	28	12 10 5 7 23 0 20	6 5 4 1 3 0 7	37 6 3 63 10 2 6	10 3 15 4 2 2 5	

See footnotes at end of table.

(1864)

	Diphtheria					Influ	enza		Measles			
Division and State	Sept. 30, 1939, rate	Sept. 30, 1939, Cases	Oct. 1, 1938, cases	1934- 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934- 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934– 38, me- dian
80. ATL.												
Delaware. Maryland <sup>a</sup> Dist. of Col Virginia <sup>a</sup> West Virginia North Carolina <sup>a</sup> Georgia <sup>4</sup> Florida <sup>4</sup>	0	0 6 1 62 9 115 41 38 12	3 2 4 50 21 105 43 37 10	0 9 10 39 34 104 23 47 10	60 22 3 437 8	2 32 8 2 160 5	2 75 12 2	11 2 142	8 7 5 16	1 4 2 11 1 1	3 10	Ō
E. SO. CEN.												
Kentucky Tennessee Alabama <sup>4</sup> Mississippi <sup>3</sup>	46		43 34 78 33	43 43 48 30	53 12	30		13	7	4	2	12 3 7
W. SO. CEN.												
Arkansas Louisiana <sup>4</sup> Oklahoma Texas <sup>4</sup>	31	13 6		14 12	5 24	2	5 37	31	0	0	1 22 4 13	1 3 1 10
MOUNTAIN												
Montana Idaho Wyoming Colorado New Mexico Arizona <sup>3</sup> Utah <sup>3</sup>	0 87 24 37	0 4 5 3 2	0 2 25 3	0 0 10	63 12 564	1 46	16	2	65 39 0	3 3 8 0	1 6 7 3 3	3
PACIFIC							ł					
Washington Oregon California	15	3	1 4 40	2 0 29					438 70 59	14	9 8 130	
Total	24	609	853	853					24		799	748
39 weeks	15	14, 901	18, 252	18, 252	186	154, 152	49, 189	106, 475	364	351, 182	764, 564	672, 284
	Me	ningitis	s, meni	ngo-		Polion	nyelitis			Scarle	t fever	

	Mer	ningitis coc		ngo-		Polion	nyelitis		Scarlet fever			
Division and State	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934- 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934- 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934- 38, me- dian
NEW ENG.												
Maine New Hampshi <b>re</b>	0	0	0	0	Ó	0	0	6 0 0	Ó	0	4 3 7	3
Vermont Massachusetts	0	0	0	0	94 5 8	4	02005		39 8	33 1	40 3	59 8
Rhode Island Connecticut	0 0	0	1	1	6	2	5	5	65	22	10	10
MID. ATL.										54	125	128
New York New Jersey Pennsylvania <sup>3</sup>	0.4 0 0.5	1 0 1	2 1 2	6 1 4	44 20 18	109 17 36	1	16 4 4	54	45	25	35 149

See footnotes at end of table.

#### October 13, 1939

# 1866

### Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 30, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

••••••••••••••••••••••••••••••••••••••	Me	ningiti coo	s, meni œus	ingo-		Polior	nyeliti	8		Scarlet fever			
Division and State	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934– 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934- 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934- 38, me- dian	
E. NO. CEN.													
Ohio Indiana <sup>3</sup> Illinois <sup>3</sup> Michigan <sup>3</sup> Wisconsin	0.8 0 0.7 1.1 0	0	000000000000000000000000000000000000000	1 3 1	6 9 61	5 4 13 58 8	1 6 2	7	81 101 56 91 120	68 85 86	89 138 183	85 161	
W. NO. CEN.													
Minnesota Iowa Missouri North Dakota Bouth Dakota Nebraska Kansas	0 0 0 0 2.8	0 0 0 0 0 1	001100	1 1 0 0 0	32 2.6 7 0	34 16 2 1 0 1 <b>4</b>	1 0 0 1	3 2 0 1	$72 \\ 75 \\ 32 \\ 146 \\ 60 \\ 46 \\ 156 \\$	37 25 20 8 12	13 3 13	54 33 59 11 9 13 40	
SO. ATL.													
Delaware	0 0 7 8 0 2.7 0 3	0 0 4 3 0 1 0	0 3 0 1 0 0 0 0	0 3 0 1 0 0 1 0	0 6 16 6 14 1.7 0	0 2 2 3 0 4 5 1 0	1 0 1 1 0	5 1 1 2 1 0	59 77 49 67 94 94 25 30 12	25 6 36 35 64 9	2 8 8 37 48 83 13 23 8	2 28 8 34 57 83 8 23 4	
E. SO. CEN.													
Kentucky Tennessec Alabama 4 Mississippi 3	3 1.8 0 0	2 1 0 0	0 0 3 0	4 1 2 1	12 0 0 2.5	7 0 0 1	0 0 4 0	2 3 1 0	90 78 56 25	52 44 32 10	71 49 30 11	57 49 23 15	
W. 80. CEN.													
Arkansas Louisiana <sup>4</sup> Oklahoma Texas <sup>4</sup>	0 5 0 1.7	0 2 0 2	0 1 1 0	0 1 1 0	5 0 6 13	2 0 3 16	0 0 2 2	1 1 1 <b>2</b>	35 12 26 20	14 5 13 24	9 5 20 51	9 5 14 31	
MOUNTAIN													
Montana Idaho Colorado New Mexico Arizona <sup>3</sup> Utah <sup>3</sup>	0 0 0 25 0 0	0 0 0 2 0 0	00000000000000000000000000000000000000	0 0 0 0 0 0	0 20 22 63 124 25 129	0 2 1 13 10 2 13	000000000000000000000000000000000000000	1 0 1 0 0 0	84 10 87 91 12 25 79	9 1 4 19 1 2 8	21 7 3 19 4 3 5	21 9 4 19 6 5 7	
PACIFIC													
Washington Oregon California	0 0 0	0 0 0	0 0 1	0 1 1	0 15 47	0 3 57	0 0 7	5 3 26	96 45 70	31 9 85	10 23 111	19 23 111	
Total	1	24	20	52	19	469	52	277	59	1, 487	1, 871	2, 125	
89 weeks	1. 6	1, 526	2, 337	4, 499	5	4, 908	1, 354	5, 807	125	122,665	144, 157	172, 584	

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 30, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

	Smallpox Typhoid and paratyphoid fever							phoid	Wh	ooping c	ough
Division and State	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934– 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934- 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases
NEW ENG. Maine New Hampshire Vermont Massachusetts Rhode Island Connecticut	0 0 0 0 0	0000000	000000000000000000000000000000000000000	0 0 0 0 0	000000000000000000000000000000000000000	0	2 0 2 3 2	3	362 75 183	27 0 27 64 24 55	18 0 15 78 9 37
MID. ATL. New York New Jersey Pennsylvania <sup>2</sup>	0	0 0 0	0 0	000000000000000000000000000000000000000	12	10	5	20 11 34	98	274 82 311	481 187 186
E. NO. CEN. Ohio Indiana <sup>3</sup> Illinois <sup>9</sup> Michigan <sup>3</sup> Wisconsin		0	1 2 0 1 0	0 0 1 0 1	16 38 2	11 58	17 17 29 4 2	35 9 29 11 2	101 103 89	184 68 157 84 124	228 18 334 271 287
W. NO. CEN. Minnesota Iowa Missouri North Dakota South Dakota Nebraska Kansas	2 0 7 8	1 0 1 1	2 7 0 0 0 2	2 2 0 3 0 0 1	140 6 17 22 15 4 11	3 13 3 2 1	4 1 9 1 3 0 5	4 7 17 1 2 0 5	134 24 30 73 23 4 45	69 12 23 10 3 1 16	45 16 19 23 1 15 -49
80. ATL. Delaware. Maryland <sup>3</sup> Dist. of Col Virginia <sup>3</sup> West Virginia North Carolina <sup>3</sup> South Carolina <sup>4</sup> Georgia <sup>4</sup> Florida <sup>4</sup>		0 0 7 0 0	0	0 0 0 0 0 0 0 0 0 0 0 0 0 0	19 8 43 40 15 38 23	6 1 23 15 10 14 14	5 19 15 5 15 10	16 2 20 24 24 15 19	163 137 30 19 120 36 33	16 7 82 13 20	29 154 70 7
E. SO. CEN. Kentucky Tennessee Alabama 4 Missisippi 3	002	001	1		42 18 5	24 10 8	8	28 20	30	52 17 55	25 38 20
W. SO. CEN. Arkansas Louisiana <sup>4</sup> Oklahoma Texas <sup>4</sup>	000001	Ō	0 0 2 1	0 0 0 1	39	16 11	22	22 12	56 10	23 5	7
MOUNTAIN Montana Idaho Wyoming Colorado New Mexico Arizona <sup>8</sup> Utah <sup>8</sup>	0 0 10 0	0 0 2 0	0 0 0 6 1 2 0	0 0 4 0 0	10 0 19 12 61	1 0 4 1 5	1 0 14 10	10 10 20	0 44 111 494 282	0 23 40 23	19 6 3 29 24 8 31

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept 30, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

	Smallpox				Typh		l parat; ver	yphoid	Whooping cough			
Division and State	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	1934- 38, me- dian	Sept. 30, 1939, rate	Sept. 30, 1939, cases	Oct. 1, 1938, cases	
PACIFIC												
Washington Oregon California	0 5 2	0 1 2	2 4 2	8 0 0	46 30 2	15 6 3		4 4 13	74 159 89	32	33 9 105	
Total	1	19	38	33	20	498	387	574	94	2, 328	3, 140	
89 weeks	9	<b>*8,813</b>	12,932	6, 253	10	10, 160	11, 273	11, 766	147	141, 753	1 <b>64, 5</b> 95	

1 New York City only.

<sup>1</sup> New York City only.
<sup>2</sup> Rocky Mountain spotted fever, week ended Sept. 30, 1939, 8 cases as follows: Pennsylvania, 1; Indiana, 1; Illinois, 1; Virginia, 2; North Carolina, 3.
<sup>3</sup> Period ended earlier than Saturday.
<sup>4</sup> Typhus fever, week ended Sept. 30, 1939, 76 cases as follows: Kansas, 1; North Carolina, 1; South Carolina, 7; Georgia, 33; Florida, 5; Alabama, 10; Louisiana, 5; Texas, 14.
<sup>4</sup> The total numbers of cases of smallpox reported for the first 37 and 38 weeks of 1939 were 8,763 and 8,794, respectively, with an average case rate of 9 in each instance.
<sup>6</sup> During the week ended Sept. 23, 1939, the number of cases of scallet fever in Wyoming should have been 1, with a case rate of 22. The total for the week was 12,178.

# 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	Menin- gitis, menin- gococ- cus	Pella- gra	Polio- mye- litis	Scarlet fever	Small- pox	Ty- phoid and paraty- phoid fever
May 1959										
Wisconsin	4	229		8, 938	3		1	633	10	4
June 19 <b>39</b>										
Puerto Rico	81	41	1, 259	29	0		0	0	0	41
July 1939	•-	-	-,				, ,		Ŭ	
Wisconsin	3	51	2	471	2		2		2	4
August 1939										
Alaska Arizona California Hawaii Territory Indiana Nevada Oregon Utah Virginia Wisconsin	0 22 28 23 23 24 25 25 85 85 85	4 46 49 3 14 8 	2 41 139 9 3 3 1	264 13 493 4 60 14 9 63 35 79 148	1 4 3 4 0 0 1 1 	7 8 3  9	0 10 272 15 40 4 2 6 3 6 21	0 9 232 1 222 91 1 21 31 49 230	0 1 21 0 21 3 0 0 0 0 0 6	$     \begin{array}{r}       1 \\       16 \\       55 \\       2 \\       190 \\       34 \\       1 \\       20 \\       9 \\       89 \\       14 \\       \end{array} $

Cases 

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9 5

22 10

Arizona 114 California 530 Hawaii Territory 244 Illinois 1, 199

Indiana..... Nevada Oregon Utah Virginia Wisconsin

Summary	ı of	monthly reports from S	tates-	-Continued
May 1939	I	August 1939—Continued	1	August 1989—Continued
Wisconsin: Ca	IS <b>6</b> S		_	-
Chickenpox	671	Dy sentery-Continued.	Cases	Scabies: Ca
Encephalitis, epidemic		Oregon (bacillary)	1	Oregon
or lethargic	2	Virginia (bacillary)	730	Septic sore throat:
German measles	63	Encephalitis, epidemic or		California
Mumps 1,		lethargic:		Hawaii Territory
Septic sore throat	27	Arizona	1	Illinois
	8	California	23	Oregon
Undulant fever	698	Illinois	7	Utah
W HOODING CONRT	000	Nevada.	2	Virginia
		Virginia	ĩ	Wisconsin
June 19 <b>39</b>		Food poisoning:	-	Tetanus:
		California	132	California
Puerto Rico:			132	Hawaii Territory
Chickenpox	46	Illinois German measles:	2	
Dysentery	14		4	Illinois
Mumps	2	Alaska		Virginia
Ophthalmia neonato-		Arizona		Trachoma:
rum	- 4	California		Arizona
Puerperal septicemia	2	Hawaii Territory		California
Tetanus	8	Illinois		Hawaii Territory
Tetanus, infantile	3	Utah		Illinois
Whooping cough	93	Wisconsin	. 29	Indiana
11 200p 8 8 8 8 8 8 8 8 8 8 8 8 8 8		Granuloma, coccidioidal:	-	Oregon
July 19 <b>39</b>		California	. 5	Utah
		Hookworm disease:		Wisconsin
Wisconsin:	366	Hawaii Territory	. 7	Trichinosis:
Chickenpox		Impetigo contagiosa:		California
Encephalitis, epidemic	2	Alaska	. 3	Utah
or lethargic	26	Hawaii Territory		Tularaemia:
German measles	272	Oregon	. 20	California
Mumps	- 5	Jaundice (epidemic):		Illinois
Septic sore throat	1	California	. 7	Nevada
Tularaemia		Leprosy:		Oregon
Undulant fever	6	California	. 1	Utah
Whooping cough	893	Hawaii Territory		Virginia
		Illinois		Wisconsin
August 1939		Mumps:		Typhus fever:
			. 41	California
Actinomycosis:		Arizona		Hawaii Territory
Illinois.	1	California Hawaii Territory		Virginia
Chickenpox:				Undulant fever:
Alaska	1	Illinois	-	Arizona
Arizona	- 11	Indiana		California
California	272	Oregon		Illinois
Hawaii Territory	30	Utah	-	Indiana
	132	Viiginia		Nevada
Illinois	11	wisconsin	213	Oregon
Indiana	12	Ophthalmia neonatorum:		Utah
Nevada	26	California		Virginia
Oregon	32	1111nois	. 1	Wisconsin
Utah	19			Vincent's infection:
Virginia	193	C. Hermin	. 49	Illinois
Wisconsin	193	Illinois		Oregon
Conjunctivitis, infectious:		Tadiana		Whooping cough:
Hawaii Territory	29	Rabies in man:		Arizona
Dysentery:		Rabics III IIIau.	9	Arizona Galifornia

Illinois.....

Relapsing fever: California

Rocky Mountain spotted fever: Illinois

Indiana\_\_\_\_\_

Oregon\_\_\_\_\_ Virginia\_\_\_\_\_

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Dysentery:

Arizona California (amoebic) California (bacillary) Hawaii Territory (amoe-

bic) Illinois (amoebic) Illinois (amoebic carri-

ers) Illinois (bacillary)

# WEEKLY REPORTS FROM CITIES

### City reports for week ended September 23, 1939

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

State and city	Diph- theria	Infl	uenza	Mea- sles	Pneu- monia	Scar- let	Small- pox	Tuber- culosis	Ty- phoid	Whoop- ing	Death
	Cases	Cases	Deaths	cases	deaths	fever cases	cases	deaths	foror	cough cases	all cause:
Data for 90 cities: 5-year average Current week <sup>1</sup> _	135 85	60 48	15 13	141 133	324 238	<b>429</b> 314	2 0	333 288	80 61	1, 031 951	
Maine: Portland	0		0	0	o	0	0	0	0	1	
New Hampshire: Concord	0		0	0	2	0	0	0	0	0	
Manchester	Ő		Ő	Ó	1	Ó	0	0	0	0	
Nashua Vermont: Barre	0		0	0	0	0	0	0	0	3	
Burlington	0		0	0	0	0	0	0	Ō	0	
Rutland Massachúsetts:	0		0	0	0	0	0	0	0	0	
Boston	0		0	2	8	12	0	3	0	31	19
Fall River	2 0		0	0	2	0	0	1	0	2	1
Springfield Worcester	2		0	ŏ	0 5	05	0	1	1	6 7	3
Rhode Island:						-		- 1			
Providence Connecticut:	0	2	0	13	0	0	0	0	0	6	ŧ
Bridgeport	1		0	0	0	0	0	0	1	0	2
Hartford New Haven	0		0	8	1 2	0	0	$1 \\ 1$	02	18 6	3
New York:										-	
Buffalo	0		0	0	2	3	0	2	0	8	12
New York	10	3	0	6	43	723	0	79	7	118	1, 35
Rochester	0		0	0	22	03	0	1	0	3 44	5
New Jersey:										71	a
Camden Newark	0	i-	0	8	1	12 4	0	07	07	2	2
Trenton	ŏ		ŏ	ŏ	2	ō	ŏ	4	i	31 1	6
Pennsylvania:		8	2	6			0	18		107	
Philadelphia Pittsburgh	1	2	1	4	14	18 16	ŏ	18	0	125 16	41 15
Reading	0		Ō	0	Ó	0	0	2	0	2	2
Scranton	0	·		0		2	0		0	0	
Ohio: Cincinnati			0	0	.	2	0	2			10
Cleveland	9	6	1	5	1 5	11	ŏ		8	9 42	13 16
Columbus	1		0	1	2	2	0	72	0	7	8
Toledo ndiana:	Ō	1	0	0	8	2	0	5	0	9	7
Anderson	0		0	0	0	0	0	0	0	5	
Fort Wayne Indianapolis	05		0	0	17	11	0	13	0	0 19	2 9
Muncie	0		0	0	2	4	0	0	0	2	1
South Bend	03		0	2	0	02	0	0	0	11	1
llinois:	3		v I		1	2	U I	٩V	U U	0	2
Alton	<u>0</u> .		0	0	0	0	0	0	o	3	
Chicago Elgin	0 7 0	3	0	4	20 0	33 2	0	20 0	5	96 1	62
Moline	0 .		0	0	Ó	Ō	0	0	0	0	1
Springfield fichigan:	0		0	0	0	0	0	1	0	1	2
Detroit	2		0	4	6	22	0	12	1	41	199
Flint Grand Rapids	0.		1	04	4	32	0 0	0	02	3	2
Visconsin:				-	-		-				-
Kenosha	ol.		0	0	0	0	0	0	0	2	
Madison Milwaukee	0		0	0	17	0 15	0	02	8	0 22	. 2
Racine	Ő.		0	0	0	1	0	0	0	11	90 1
Superior	01.		0	0	01	41	0	0	0	01	1

<sup>1</sup> Figures for Barre estimated; report not received.

City	1000		week e	nueu x		007 20	, 1950		nnue	a	
	Diph-	Infl	uenza	Mea-	Pneu-	Scar-	Small-	Tuber-	Ty-	Whoop-	Deaths,
State and city	theria cases	Cases	Deaths	sles cases	monia deaths	let fever cases	pox	culosis deaths	phoid fever cases	ing cough cases	all causes
Minnesota: Duluth	o		Q	1	0	1	0	2	0	3	24
Minneapolis	2		0	42	5	9 3		1	4	<b>26</b>	119
St. Paul	U		0	z	1	3	U U	0	0	<b>3</b> 6	48
Iowa: Cedar Rapids	0			0		0	0		0	0	
Davenport	0		0	0	0	2 6		0	0 0	1	
Des Moines Sioux City	1			ŏ		Ĭ	ŏ		ŏ	5	
Waterloo	3			Ó		1	0		0	1	
Missouri:	0		0	2	4	5	0	8	4	2	90
Kansas City St. Joseph	ŏ		ŏ	0	0	0	0	0	0	0	25
St. Louis	1		0	2	0	6	0	4	4	13	204
North Dakota:	0		0	0	2	0	0	0	0	5	11
Fargo Grand Forks	ŏ			0		1	0		0	0	
Minot	0		0	0	0	0	0	0	0	0	6
South Dakota: Aberdeen	1			lo		0	1		0	0	
Sioux Falls	i i		0	Ŏ	0	1	0	0	0	0	9
Nebraska:	2		0	0	4	1	0	0	0	3	.49
Omaha Kansas:	-		ľ	ľ	1						1
Lawrence	0		0	0	0	0	0	0	0	0	4
Topeka Wichita	0			0	0	32	0		0		16 25
wichita	ľ		ľ	ľ	-	-					
Delaware:				.	3	2	0	0	0	3	32
Wilmington	1		0	1	<b>°</b>	<b>1</b>	1		l .	ľ	
Maryland: Baltimore	1	1	0	4	7	7	0	10	0	43	162
Cumberland	0		0	0		20	0	0	0		93
Frederick District of Columbia:	Ó		0	0	l v	U U					
Washington	7		0	1	4	5	0	8	0	30	131
Virginia:	1	1	0	1	1	1	0	0	0	3	8
Lynchburg Norfolk	3		ŏ	l ô	3	0	0	0	0	1	
Richmond	1		0	0	2	3	0	3			
Roanoke	. 0		. 0	0	0	l v					1
West Virginia: Charleston	0		0	0	1	0		0	2	0	
Huntington	. 1			. 0	2	0					
Wheeling North Carolina:	. 0		. 1	U U	-						
Gastonia	. · •			. 0		. 0		0	. 0		
Raleigh			0		0	l ŏ		ŏ	ŏ	0	10
Wilmington Winston-Salem.			Ŏ	ŏ	Ō	4		1	0	0	11
South Carolina:					0	0	0	0	1	0	9
Charleston Florence	0		. 0	0	20	0	0	Ó	0	3	11
Greenville			Ŏ	Ō	0	0	0	0	0	0	4
Georgia:	4	4	0	0	1	6	0	4	0	0	80
Atlanta Brunswick		-	ŏ	0	0	0		1		0	21
Savannah	. 0	15	0	0	0	1	0	1			
Florida: Miami	1	1	0	0	0	1		0	1	4	
Tampa			Ó	0	2	0	0	0	1	0	1 11
							1				
Kentucky: Ashland	. 0		0	0	1	0		0			
Covington	. 0		- 0	0				l o	Ĭŏ	2	3
Lexington Louisville				0		ž	Ŏ	3	1	21	83
Tennessee:						1	0	1	4	1	16
Knoxville			- 8	02	02			5	1	12	86
Memphis Nashville			Ö	ő		5		3	2	0	50
Alabama:					0	2	0	5	2		63
Birmingham						1	0	Ĭ	Ō	0	29
Mobile Montgomery			·	ŏ	-	. 0	0		. 0	2	
2 .						1	1		1		
Arkansas: Fort Smith	1			0		. 0			2		
Little Rock			0			1 0	0 0	3	1 0		
	-										

# City reports for week ended September 23, 1939-Continued

Fort Wayne.... Illinois:

Chicago.....

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	1000			cnucu .	Septen	1061 20	0, 190	-00	nunu	eu	
State and city	Diph- theria		nfluenza	Mea- sles	Pneu- monia	Scar- let fever	pox	Tuber- culosis	former	Whoop ing cough	all all
	cases	Case	es Deaths	cases	deaths	cases	Cases	deaths	cases	cases	causes
Louisiana:											
New Orleans	1		. 0	0	8	1	0	01	5	10	122
Shreveport	0		0	Ó	2	Õ	Ŏ	Ö	ľ	Ő	33
Oklahoma: Oklahoma City	2		. 0	0	2	0	0	1	1	0	37
Tulsa	Ō			. ŏ		ľ	ŏ		Ô	ŏ	
Texas: Dallas	8		. 0	0	1	2	0	0	o	5	42
Dallas Forth Worth	0		. 0	Ó	1	1	Ó	0	2	3	25
Galveston Houston	0		- 0		13	0 1	0	1	12	01	15
San Antonio	ŏ		ŏ	Ĭ	4	i	ŏ	3 6	ő	6	65 61
Montana:											
Billings	0		. 1	0	0	0	0	0	1	2	8
Great Falls Helena	0		- 0	02	0	2 0	0	0	0	2	6
Missoula	ŏ		. ŏ	ő	ŏ	ŏ	ŏ	ŏ	ŏ	0	3
Idaho: Boise	0			0	0	0	0	0			
Colorado: [	-		-		Ů		-		0	0	8
Denver Pueblo	2		2 0	2	4	2	0	2	0	4	71
New Mexico:	•		1			-		1	0	1	7
Albuquerque Utah:	0		- 0	0	0	0	0	1	0	0	8
Salt Lake City.	0		_ 0	0	0	0	0	1	0	18	22
Washington:											
Seattle Spokane	0 1			8	3	1	0	2	0	2	78
Tacoma	ō		ŏ	3 33	02	2 1	0	1	0	0	28 27
Oregon: Portland	0		0	1	4						
Salem.	ŏ			0 I	4	5	8	0	0	6	73
California: Los Angeles	4	6	0				-				
Sacramento	ō	0	ŏ	9 2	8	13 5	00	14 2	0	23 1	329 35
San Francisco	0	1	Ó	ī	4	3	ŏ	12	ō	3	225
			·		11			<u> </u>			
	m	Mening	ococcus	Polio-				,	Menir neningo	gitis,	Polio-
State and city				mye- litis		State a	nd city				mye- litis
	c	ases	Deaths	C8.563	11				Cases	Deaths	Cases
					-						
Vermont:		o			Mich	igan:					
Burlington Assachusetts:		v	0	2		lint			8	8	39 1
Boston		0	0	2	Wisco	onsin:					•
Fall River		0	0	1	Minn	liiwauk esota:			0	0	4
Bridgeport	[	0	0	1	M	linneap	olis		0	0	26
lew York: Buffalo		0	o	48	Misso	t. Paul.			0	0	1
New York		0	Ó	22	SI SI	t. Louis			0	0	1
Rochester		0	0	6	Mary B		•		0	0	1
Camden		0	0	14	Distri	ct of C	e olumbia		-	° I	1
Newark Trenton		8	0	2	W Virgin	ashing	ton		0	0	2
ennsylvania:		-			N	orfolk			0	0	2
Philadelphia Pittsburgh		8	. 0	24 9	Georg	18: Wannel	h		0	0	
hio:		- 1			Oklah	oma:		1			
Cleveland Toledo		8	8	2 1	Utah:	klahom	a City		0	0	1
ndiana:		-	-	•		lt Lake	City		· • •	•	1

# City reports for week ended September 23, 1939-Continued

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Encephalitis, epidemic or lethargic.—Cases: New York, 5; St. Louis, 3; Topeka, 1. Pellagra.—Cases: St. Paul, 2 (imported); Atlanta, 1; Savannah, 2; New Orleans, 1; Los Angeles, 1. Typhus ferer.—Cases: New York, 2; Charleston, S. O., 2; Atlanta, 2; Savannah, 5; Miami, 1; Tampa, 1; Birmingham, 1; Dallas, 3; Fort Worth, 1; Galveston, 1; Houston, 1.

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. Salt Lake City\_

Los Angeles..... Sacramento.....

California:

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# FOREIGN REPORTS

# CANADA

Provinces—Communicable diseases—Week ended September 16, 1939.—During the week ended September 16, 1939, cases of certain communicable diseases were reported by the Department of Pensions and National Health of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Bruns- wick	Que- bec	Onta- rio	Mani- toba	Sas- katch- ewan	Al- berta	British Colum- bia	Total
Cerebrospinal meningitis. Chickenpox. Diphtheria. Dysentery. Influenza. Lethargic encephalitis. Mensles. Mumps. Pneumonia. Poliomyelitis. Scarlet fever. Trachoma. Tuberculosis. Typhoid and paraty- phoid fever Whooping cough.	    1	1 18 1 1 8 1 1 10	2 2 2 2 15 1 6	1 4 36 6 1 31 9  4 19  31 19 70	1 82 1 2 8 43 12 15 15 15 13 70 	4 4 4 7 7 14 5 3 35	6 	8 1  1  9 1 4 6	11 3 1 4 10 4 2 5 1 12	2 60 45 111 16 2 83 39 20 17 118 5 112 33 240

### DENMARK

Notifiable diseases—April-June 1939.—During the months of April, May, and June 1939, cases of certain notifiable diseases were reported in Denmark as follows:

Disease	April	May	June
Cerebrospinal meningitis Chickenpox Diphtheria Dysentery Epidemic encephalitis Erysipelas Gastroenteritis, infectious German measles Gonorrhea Influenza Lymphogranuloma Malaria Malaria Malaria Paratyphold fever Poliomyelitis Puerperal fever	7 1, 162 69 13 4 136 2, 315 182 543 15, 056 	May 7 958 66 9 9 1 184 2,354 573 7,054 2 1,570 2 1,570 210 8 4 114 703	6 759 60 32 171 2,576 15 3,800 1 1,237 145 15 15 1 1 9 444
Scarlet fever	32 1 45	35 5 1 46 3, 934	35 3 4 67 2 3, 863

### FINLAND

Communicable diseases—August 1939.—During the month of August 1939, cases of certain communicable diseases were reported in Finland as follows:

Disease	Cases	Disease	Cases
Diphtheria. Dysentery Influenza. Lethargic encephalitis. Paratyphoid fever	144 6 409 1 68	Poliomyelitis Scarlet fever Typhoid fever Undulant fever	5 229 10 1

### GREAT BRITAIN

England and Wales—Infectious diseases—13 weeks ended July 1, 1939.—During the 13 weeks ended July 1, 1939, cases of certain infectious diseases were reported in England and Wales as follows:

Disease	Cases	Disease	Cases
Diphtheria. Dysentery. Ophthalmia neonatorum. Pneumonia.	10, 007 430 1, 320 11, 014	Puerperal pyrexia Scarlet fever Typhoid fever	2, 552 21, 126 299

England and Wales—Vital statistics—Second quarter 1939.—During the second quarter ended June 30, 1939, 164,401 live births and 120,433 deaths were registered in England and Wales. The following statistics were taken from the Quarterly Return of Births, Deaths, and Marriages, issued by the Registrar General, and are provisional:

Birth and death rates in England and Wales, quarter ended June 30, 1939

Annual rates per 1,000 population:
Live births16.0 Stillbirths61
Deaths, all causes 11.7
Deaths under 1 year of age
Deaths from:
Diarrhea and enteritis (under 2 years of age) 1 4.3
Diphtheria
Influenza
Measles01
Scarlet fever
Whooping cough04
<sup>1</sup> Per 1,000 live births.

#### SWEDEN

Notifiable diseases—July 1939.—During the month of July 1939, cases of certain notifiable diseases were reported in Sweden as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis Diphtheria. Dysentery Epidemic encephalitis. Gonorrhea. Paratyphoid fever	21 107 1	Poliomyelitis Scarlet fever	16 2, 669 30 9 8 2

# SWITZERLAND

Communicable diseases—July 1939.—During the month of July 1939, cases of certain communicable diseases were reported in Switzerland as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis.	2	Paratyphoid fever	15
Chickenpox.	160	Poliomyelitis	33
Diphtheria.	61	Scarlet fever	250
German weasles.	10	Tuberculosis	269
Influenza.	1	Typhoid fever	9
Measles.	46	Undulant fever	11
Mumps.	81	Whooping cough	187

# YUGOSLAVIA

Communicable diseases—4 weeks ended August 13, 1939.—During the 4 weeks ended August 13, 1939, certain communicable diseases were reported in Yugoslavia as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Anthrax. Cerebrospinal menineitis Diphtheria and croup Dysentery Erysipelas Favus Paratyphoid fever	119 30 467 213 132 8 49	9 9 38 18 8 	Poliomyclitis Scarlet fever Sepsis	25 151 8 68 305 9	5 18 24

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

NOTE.—A cumulative table giving current information regarding the world prevalence of quarantinable diseases for a six-month period appeared in the PUBLIC HEALTH REPORTS of September 29, 1939, pages 1792-1806. A similar cumulative table will appear in future issues of the PUBLIC HEALTH REPORTS for the last Friday of each month.

#### Cholera

Afghanistan—Kandahar Province.—For the period August 2 to 11, 1939, 101 cases of cholera with 45 deaths were reported in Kandahar Province, Afghanistan.

China.—During the week ended September 23, 1939, cholera was reported in China as follows: Hong Kong, 18 cases; Macao, 21 cases; Shanghai, 71 cases. During the week ended September 30, 1939, 3 cases of cholera were reported in Tsinan, China.

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