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## A FILTER-PASSING INFECTIOUS AGENT ISOLATED FROM TICKS<sup>1</sup>

### I. ISOLATION FROM *DERMACENTOR ANDERSONI*, REACTIONS IN ANIMALS, AND FILTRATION EXPERIMENTS

By GORDON E. DAVIS, *Bacteriologist*, and HERALD R. COX, *Associate Bacteriologist*,  
*United States Public Health Service*

In the spring of 1935 a filter-passing infectious agent was recovered from a group of 200 *Dermacentor andersoni* collected near Nine Mile Creek about 32 miles west of Missoula, Mont.

It is quite possible that this agent is the same as the "filter-passing virus" reported by Noguchi (1) in 1926 as having been recovered from *D. andersoni* collected on the west side of the Bitterroot Valley about 50 miles south of Missoula. Further discussion of this point will be found in a subsequent paper of this series.

The 200 ticks here concerned, which had recently emerged from hibernation, were divided into four groups of 50, and each such group was placed under a feeding capsule on the clipped belly of a guinea pig. One of the host guinea pigs died on the second day of unknown cause, and two remained afebrile. The fourth guinea pig showed a temperature of 41° C. on the twelfth day and a continuous temperature ranging between 40° and 41° C. for the 6 succeeding days. On the second day of fever (41° C.) there was some slight reddening and swelling of the scrotum. Four cc of blood were removed on this day by cardiac puncture and 2 cc were injected intraperitoneally into each of 2 normal guinea pigs. The donor died 7 days later, that is, on the twentieth day after tick infestation. Its spleen was enlarged about 4 times, was smooth and deep red, and there was a slight injection of the testes and tunicae.

On the fourth day following inoculation, one first-transfer guinea pig showed a temperature of 40.4° C., and the other 40.6° C. In both, fever was continuous until death, which occurred on the fourteenth and seventeenth days, respectively. At autopsy the spleens were enlarged. There was no involvement of the testes and adnexa.

The infection has subsequently been maintained in guinea pigs by blood or spleen tissue injected intraperitoneally.

In the following studies of this disease the usual inoculum was spleen tissue removed on the fifth or sixth day of fever. When un-

<sup>1</sup> From the Rocky Mountain Laboratory, Division of Infectious Diseases, National Institute of Health, Hamilton, Mont.



TABLE 2.—A comparison of the susceptibility of guinea pigs inoculated with the intracerebral, intramuscular, intraperitoneal, subcutaneous, and intradermal routes. Infectious material used was the centrifuged supernatant fluid of a 10 percent spleen suspension diluted in Tyrode's solution. Dosage in every case was 0.2 cc

Dilution	Route of injection <sup>1</sup>					Dilution	Route of injection <sup>1</sup>				
	I. C.	I. M.	I. P.	S. C.	I. D.		I. C.	I. M.	I. P.	S. C.	I. D.
10 <sup>-1</sup> -----	2/2	2/2	2/2	2/2	2/2	10 <sup>-4</sup> -----	0/2	0/2	0/2	0/2	0/2
10 <sup>-2</sup> -----	2/2	2/2	2/2	2/2	2/2	10 <sup>-6</sup> -----	1/2	0/2	0/2	0/2	0/2
10 <sup>-3</sup> -----	2/2	2/2	2/2	2/2	2/2	10 <sup>-7</sup> -----	0/2	0/2	0/2	0/2	0/2
10 <sup>-4</sup> -----	2/2	2/2	2/2	2/2	1/2						

<sup>1</sup> I. C.=intracerebral; I. M.=intramuscular; I. P.=intraperitoneal; S. C.=subcutaneous; and I. D.=intradermal.

<sup>2</sup> The denominator indicates the number of guinea pigs injected; the numerator the number that developed infection and that were later shown to be immune.

TABLE 3.—Susceptibility of guinea pigs to plantar pad injection or to dropping the infectious material in the conjunctival sac, nose, or mouth or on the unabrased skin of the abdomen. The centrifuged supernatant fluid of a 10 percent spleen suspension in Tyrode's solution was employed in every case. All animals received 0.2 cc of inoculum unless otherwise stated

Experiment number	Route of introduction					Control:
	Plantar pads	Conjunctival sac	Intra-nasally	Orally	On un-abrased skin	
1-----			1/4			2/2 S. C. <sup>1</sup> 2/2 I. C. 2/2 I. P. 2/2 I. M. 2/2 I. D.
2-----	1/4		4/4			4/4 S. C.
3-----			4/4			3/3 I. P.
4-----	0/3	0/3	0.15 cc	0/3	0/2	0.15 cc. 2/2 S. C.
5-----	3/3	0.05 cc	1/3			2/2 S. C.
6-----		0.1 cc		0/3	0/2	2/2 S. C.
		3/3	0.15 cc	0/3 cc		2/2 I. P.
		2/3		0.3 cc		
		0.1 cc				

<sup>1</sup> The denominator indicates the number of guinea pigs tested; the numerator, the number that definitely developed infection.

<sup>2</sup> S. C.=subcutaneous; I. C.=intracerebral; I. P.=intraperitoneal; I. M.=intramuscular; and I. D.=intradermal.

*Gross pathology.*—The typical findings in guinea pigs sacrificed at the height of fever or at death, when not delayed, are as follows: The inguinal lymph nodes are enlarged (up to 3 or 4 times normal) but usually not injected; the spleen is enlarged from 2 to 12 times by weight, and is smooth and engorged with blood. On a few occasions engorgement has been so marked that the spleen ruptured transversely on the ventral surface and large blood clots were present in the abdominal cavity. The mesenteric lymph nodes are enlarged but not injected. The polar fat of the testes appears slightly icteric. Frequently the adrenals and lungs appear injected.

Guinea pigs injected subcutaneously or intradermally show, also, a marked inflammatory thickening of the skin. The skin lesion gen-

erally becomes evident on the second or third day of fever as a small indurated area which rapidly enlarges to reach its maximum size on the seventh or eighth day of fever. The maximum size of the lesion may vary in individual guinea pigs from an area 2 or 3 centimeters in diameter to one that practically covers the entire abdomen, but is less extensive and less thickened when the inoculation is made intradermally. After the temperature of the animal returns to normal, the inflammatory exudate gradually lessens and the lesion is replaced by scar tissue which apparently persists indefinitely.

Guinea pigs frequently die, possibly as a result of this infection, 2 to 3 weeks after the temperature has become normal. The chief finding in such animals is marked emaciation. The spleen frequently is pale in color, but normal in size. All other tissues appear normal. In this connection it should be noted that, in some animals at least, the infectious agent persists after defervescence.

Testicular washings were infectious 6 days after defervescence, spleens 6, 22, and 23 days, and lymph nodes 23 days. The brain and liver were infectious on the twenty-third day.

*Infectivity of urine.*—Intraperitoneal inoculation of a guinea pig with 1 cc of urine, drawn by bladder puncture from an infected guinea pig at death, resulted in typical reaction. The virus was recovered from the spleen of this animal.

Further tests showed fatal infections or febrile reactions and immunity to reinoculation.

*Infectivity of washed blood cells.*—Ten cc of blood were drawn in sodium citrate from an infected guinea pig on the third day of fever. Each of 2 guinea pigs received an intraperitoneal injection of 0.5 cc of the citrated whole blood within 5 minutes after it was drawn. The cells in the remaining blood were then washed 3 times in physiologic saline and 0.5 cc of the supernatant fluid following each washing was injected intraperitoneally into each of 2 guinea pigs. Following the third washing sufficient physiologic saline was added to the cells to bring the volume to that of the citrated blood, and 0.5 cc of this suspension was injected intraperitoneally into each of 2 guinea pigs. All 10 test animals passed through the usual febrile period; 6 died in 2 weeks or less, and each showed the typical enlarged spleen. The remaining 4, 3 injected with supernatant fluid (1 of each pair) and 1 with the washed cells, died a week later showing a spleen approximately normal in size, but a marked degree of emaciation including wasted polar fat.

*Duration of immunity.*—It has been repeatedly shown that guinea pigs which have recovered following injection of the infectious material were completely immune to a second injection of the homologous strain.

On December 10, 1935, 2 guinea pigs each received intraperitoneally 0.5 cc of serum-virus, 2 others received 0.25 cc and 1 received 0.1 cc.

Each guinea pig showed temperatures of 39.8° C. to 40.6° C. for 6 to 7 consecutive days following the usual incubation period.

On April 4, 1936, 115 days following the initial injection, the above guinea pigs each received 1.0 cc of a saline suspension of infected spleen tissue. There was no rise in temperature, while two controls showed typical fever curves, one dying on the tenth day. The spleen was enlarged approximately 5 times. The second control animal survived.

#### FILTRATION

The first filtration experiment was performed with blood drawn on the fifth day of fever from a ninth passage guinea pig. The citrated blood was sedimented by centrifugalization and a portion of the citrated plasma passed through a Mandler filter. Two guinea pigs each received 1 cc of unfiltered plasma intraperitoneally and 2 others each received 1 cc of filtrate. One cc of the latter placed in fresh infusion broth and incubated at 37° C. showed no growth in 10 days. Both test and control guinea pigs showed a typical rise in temperature, but the rise in those receiving the filtrate was slightly delayed.

Numerous subsequent filtration experiments have conclusively shown that the infectious agent readily passes Berkefeld N and W filters which are impermeable to ordinary bacteria and that it passes through Berkefeld W filters that retained typhus and spotted fever viruses before and after the test filtration. The filtrates have consistently remained free of bacterial growth when cultivated aerobically or anaerobically on suitable media.

Titration tests carried out with Berkefeld filtrates have shown that, while the infectious agent readily passes these filters, it does not do so in undiminished quantity.

In table 4 are summarized the results obtained from a number of titration tests in which unfiltered and filtered spleen suspensions were compared for activity. The results show that the infectivity end-points of unfiltered 2 or 5 percent spleen suspensions are reached in dilutions of  $10^{-4}$  and  $10^{-5}$ , while the end-points of the same suspensions after passage through a Berkefeld N or W candle are from 10 to 1,000-fold less. In repeated titration tests of unfiltered 10 percent spleen suspensions it has been shown that such suspensions are usually infectious in dilutions of  $10^{-3}$  or  $10^{-4}$  and occasionally  $10^{-5}$ , indicating that the spleen may contain from 10,000 to 1,000,000 infective units per gram of tissue.

TABLE 4.—Comparative titration tests of unfiltered and filtered spleen suspensions. In every case the spleen suspensions were prepared in Tyrode's solution and consisted of centrifuged supernatant fluids (1,500 to 2,000 r. p. m. in an angle centrifuge for 15 minutes). Guinea pigs were injected with 1 cc each

Experiment number	Concentration of stock suspension	Suspension titrated	Route of inoculation <sup>1</sup>	Dilutions						
				0	10 <sup>-1</sup>	10 <sup>-2</sup>	10 <sup>-3</sup>	10 <sup>-4</sup>	10 <sup>-5</sup>	10 <sup>-6</sup>
1.....	Percent 5	Unfiltered.....	I. P.	<sup>1</sup> 2/2	2/2	2/2	2/2	1/2	0/2	0/2
		Berkefeld W.....	I. P.	2/2	2/2	2/2	2/2	0/2	0/2	0/2
2.....	5	Unfiltered.....	I. P.	2/2	2/2	2/2	2/2	2/2	0/2	0/2
		Berkefeld W.....	I. P.	2/2	2/2	0/2	0/2	0/2	0/2	0/2
3.....	2	Unfiltered.....	S. C.	2/2	2/2	2/2	2/2	2/2	2/2	( <sup>2</sup> )
		Berkefeld N.....	S. C.	2/2	2/2	2/2	2/2	2/2	( <sup>2</sup> )	( <sup>2</sup> )
4.....	2	Unfiltered.....	I. P.	2/2	2/2	2/2	2/2	2/2	1/2	0/2
		Berkefeld W.....	I. P.	2/2	2/2	2/2	1/2	0/2	0/2	0/2

<sup>1</sup> I. P. = intraperitoneal injection; S. C. = subcutaneous injection.

<sup>2</sup> Denominator indicates number of guinea pigs injected; the numerator, the number developing infection.

<sup>3</sup> Not tested.

An experiment was twice performed to compare the infective titers obtained when a lightly centrifuged spleen suspension (1,800 r. p. m. for 15 minutes in an angle centrifuge) is split into 4 parts and the portions treated as follows:

(a) Titrated without further treatment.

(b) Titrated after passage through a Berkefeld W.

(c) Titrated after centrifugalization in an angle centrifuge for 1 hour at 5,000 r. p. m.

(d) Titrated after passage through a Berkefeld W filter followed by centrifugalization in an angle centrifuge for 1 hour at 5,000 r. p. m.

All suspensions were held under the same conditions of time and temperature until tested. Guinea pigs received 1 cc subcutaneously.

The results obtained are shown in table 5.

TABLE 5.—Titration of spleen tissue suspensions before and after filtration and centrifugalization

Experiment number	Titrated	Dilutions					
		0	10 <sup>-1</sup>	10 <sup>-2</sup>	10 <sup>-3</sup>	10 <sup>-4</sup>	10 <sup>-5</sup>
1.....	Without further treatment.....	<sup>1</sup> 2/2	2/2	2/2	2/2	0/2	0/2
	After filtering.....	2/2	2/2	2/2	0/2	0/2	0/2
	After centrifuging.....	2/2	2/2	2/2	0/2	0/2	0/2
	After filtering and centrifuging.....	2/2	2/2	2/2	0/2	0/2	0/2
2.....	Without further treatment.....	2/2	2/2	2/2	2/2	2/2	0/2
	After filtering.....	2/2	2/2	1/2	0/2	0/2	0/2
	After centrifuging.....	2/2	2/2	0/2	0/2	0/2	0/2
	After filtering and centrifuging.....	2/2	2/2	0/2	0/2	0/2	0/2

<sup>1</sup> Denominator indicates number of guinea pigs injected; the numerator, the number developing infection.

It will be noted in table 5 that an appreciable loss in infectivity (from 10 to 1,000-fold) takes place when lightly centrifuged suspensions of the infectious agent are subjected to filtration through a Berkefeld filter or spun in an angle centrifuge at 5,000 r. p. m. for

1 hour. No further loss in infectivity is shown when filtrates are subsequently subjected to centrifugalization.

Repeated attempts to pass the infectious agent through a single Seitz disc have thus far failed.

#### RESISTANCE OF VIRUS TO GLYCERINE

The spleen of an infected guinea pig was placed in glycerine at 8° C. Sixteen days later a portion of the spleen was ground in saline and 1.5 cc of the suspension was injected intraperitoneally into each of 2 guinea pigs. Following febrile periods of 5 and 6 days, respectively, both guinea pigs died, one on the fifteenth and one on the thirteenth day. The spleens of both were enlarged and typical.

In a second experiment the spleen was placed in 50 percent glycerine in distilled water. Tests for the viability of the disease agent were made at 30, 63, 74, 84, 98, 106, and 116-day intervals by injecting each of 2 guinea pigs intraperitoneally with 1 cc of a saline suspension of the glycerinated spleen. Of the 2 guinea pigs receiving the 30-day spleen, one showed no elevation in temperature and the other only 1 day of 39.9° C. However, both were subsequently immune to a dose of virus. One guinea pig receiving 74-day spleen and one receiving 98-day spleen reacted in a similar manner. One receiving the 106-day spleen showed no elevation in temperature and was not immune when subsequently injected with the control virus. The other one of this pair died of pneumonia on the tenth day after injection. All other test animals, including the 2 receiving the 116-day spleen, reacted with a typical febrile period and were subsequently immune to a dose of virus. All immunity tests were controlled by the inoculation of previously infected guinea pigs with the same dose of the same virus.

#### THE INFECTION IN OTHER ANIMALS

*White rats and mice.*—The infectious agent was successfully carried through 6 serial transfers in white rats and through a similar number of passages in white mice. In every case a 10 percent spleen suspension was used as inoculum, the white rats receiving 1 cc and the white mice 0.5 cc intraperitoneally. Transfers were made every 7 or 8 days. None of the rats or mice showed any signs of illness, although when sacrificed to continue the series by spleen transfer the spleens were found to be enlarged 2 to 3 times by weight. All other tissues appeared normal to gross inspection.

*Rabbits.*—Four attempts have been made to establish the infection in rabbits and to carry it in series in these animals by means of blood transfer.

Transfers were made every 7 or 8 days using heart blood as inoculum. The rabbits were injected either intraperitoneally or subcutaneously.

The results obtained may be summarized by stating that the rabbit does not react with a definite febrile response so that control guinea pigs must be relied upon as an index of whether the infectious agent is still present. In three experiments the infectious agent could be carried through only 2 passages in the rabbit, while in the fourth test the agent was carried through three passages, but failed in the fourth.

*Monkeys.*—Three attempts were made to induce infection in monkeys (*Macacus rhesus*).

Two monkeys and 2 guinea pigs each received subcutaneously 1 cc of a 10 percent guinea pig spleen suspension. The guinea pigs developed typical infection. The monkeys remained afebrile for 30 days, and no lesion was apparent at the site of inoculation.

One monkey received subcutaneously 1 cc of a 10 percent suspension of guinea pig spleen. Two others each received 1 cc subcutaneously and 1 cc intraperitoneally. Two control guinea pigs each received 1 cc subcutaneously.

The guinea pigs developed signs of typical infection. Again the monkeys remained afebrile for 30 days and no lesions developed.

Similar results were obtained with two additional monkeys tested at a later date.

*Chipmunks and ground squirrels.*—One chipmunk and 2 ground squirrels were injected with infected spleen tissue. These animals were sacrificed on the seventh day and blood and spleen suspension transfers were made to guinea pigs, all of which showed typical infections. One guinea pig that recovered was immune to passage virus.

#### CROSS IMMUNITY TESTS

Cross immunity tests with Rocky Mountain spotted fever and endemic typhus have failed to indicate any relationship between this infection and the rickettsial diseases at present known to be endemic in North America.

#### SUMMARY

An infectious agent which passes Berkefeld N and W filters has been recovered from the Rocky Mountain wood tick, *Dermacentor andersoni*.

The infection in guinea pigs is characterized particularly by high and continuous fever and an enlarged, smooth spleen, with animals injected subcutaneously or intradermally showing also a pronounced skin lesion at the site of inoculation. The infectious agent cannot be separated from the blood cells by repeated washings. It is resistant to glycerine.

White rats and white mice have been found susceptible, but the infection could not be carried beyond the third transfer in rabbits. Inoculated monkeys have remained afebrile.

#### REFERENCE

- (1) Noguchi, Hideyo: A filter-passing virus obtained from *Dermacentor andersoni*. J. Exp. Med., 44:1-10 (July 1, 1926).

#### II. TRANSMISSION BY *DERMACENTOR ANDERSONI*<sup>1</sup>

By R. R. PARKER, *Director, Rocky Mountain Laboratory*, and GORDON E. DAVIS, *Bacteriologist, United States Public Health Service*

The isolation of a filter-passing agent, infectious for guinea pigs, from *Dermacentor andersoni* collected in nature has been reported by Davis and Cox (1). The possible identity of this agent with that reported by Noguchi in 1926 (2) will be discussed in a subsequent paper of this series. In this paper data will be presented showing transmission of the agent to guinea pigs (a) by nymphal and adult *D. andersoni* that ingested infectious blood as larvae, and (b) by the progeny of infected females.

The identity of the infectious agent originally ingested by the ticks with that which caused infection in the host guinea pigs used for the subsequent transmission tests was checked (a) by testing recovered host animals for immunity, (b) by testing the ticks fed on infected guinea pigs, whenever numbers permitted, for the presence of the infectious agent (the triturated tissue of several ticks was injected into duplicate guinea pigs and survivors tested for immunity), (c) by blood or spleen transfer from tick hosts (i. e., guinea pigs) or from tick-injected guinea pigs to obtain multiple recovered animals for further immunity tests, (d) by testing the infectiousness of Berkefeld W filtrates of the blood serum of host or other test guinea pigs, all survivors receiving immunity tests, and (e) by the character of the gross lesions in animals which died or were sacrificed.

All transfer and immunity test inocula were injected intraperitoneally in 1 cc amounts. Citrated heart blood was employed for blood transfers and triturated spleen tissue suspended in physiological saline for spleen transfers. The inoculum for immunity tests was invariably a saline suspension of infected spleen tissue from strain guinea pigs and each lot of virus thus used was checked in control animals. Each

<sup>1</sup> From the Rocky Mountain Laboratory, Division of Infectious Diseases, National Institute of Health, Hamilton, Montana.

lot of citrated blood and of filtered blood serum used for transfers and each lot of spleen virus employed for immunity tests was cultured for bacterial contaminants.

SURVIVAL OF THE VIRUS FROM LARVAL TO ADULT *D. ANDERSONI* AND TRANSMISSION BY NYMPHS AND ADULTS

*Infective feeding of larvae.*—On March 5, 1937, a guinea pig was injected with spleen virus. It was febrile from the fourth to twelfth day and died the sixteenth day. On the first day of fever it was infested with noninfected *D. andersoni* larvae and 30 engorged larvae were recovered 6 days later.

*Nymphal feeding.*—On May 5, the above ticks, as nymphs, were placed on 2 guinea pigs for feeding. One of the guinea pigs became typically febrile beginning with the seventh day and was immune to virus injected the twenty-sixth day. Eight engorged nymphs were removed on the seventh day. The other guinea pig became febrile on the sixth day, and 6 engorged nymphs were recovered on the eighth day. On the thirteenth day, while still febrile, this animal was exsanguinated. Spleen transfer was made to 2 guinea pigs and 2 others received filtered blood serum.

*Spleen-injected guinea pigs.*—Both animals injected with spleen were febrile for 6 days, beginning on the sixth and eighth days, respectively, and both were immune to virus injected the fortieth day.

*Filtered serum-injected guinea pigs.*—Both animals injected with filtered serum were typically febrile and one was later immune to the same virus used to test the spleen-injected animals. The other was sacrificed on the fifth day of fever, and spleen transfer was made to 8 guinea pigs. All had characteristic febrile reactions; 4 died, 3 survived and were later shown to be immune to homologous virus, and 1 was sacrificed on the fifth day after defervescence and transfer to 7 more guinea pigs was made by heart blood. All 7 survived and were immune to virus subsequently injected.

*Test of engorged nymphs.*—On the same day that the engorged nymphs were recovered from the host guinea pigs, 3 from each host were triturated in physiological saline and each of the resultant tick tissue suspensions was used to inject 2 test animals. All 4 test animals were febrile the next day and died between the sixth and tenth days.

*Adult feeding.*—On July 28, 1937, 8 adult ticks from the above engorged nymphs were used to infest a guinea pig. The latter was febrile from the fifth to ninth days and the ticks, which fed poorly, were removed on the thirteenth day. The host animal was immune to virus injected on the thirty-fourth day.

*Test of fed adults.*—On August 10, 3 of the partially fed adult ticks were triturated in the same manner as the engorged nymphs

and the resultant saline suspension was injected into 2 guinea pigs. The latter became febrile on the second day. One died on the tenth day, the other was sacrificed on the sixth day, and filtered blood serum was transferred to 2 guinea pigs and spleen tissue to 8.

*Filtered serum-injected guinea pigs.*—These 2 animals had 5-day febrile periods beginning on the fifth and seventh days, respectively, and both were immune to virus injected the twenty-first day. Heart blood taken from one of these animals during the febrile period was injected into 6 guinea pigs. All 6 exhibited the usual course of fever; one died on the eleventh day and the remaining 5 were later immune to homologous virus.

*Spleen-injected guinea pigs.*—The 8 spleen-injected guinea pigs all died and the gross findings were typical.

*Retest of partially fed adults.*—On August 18, 1937, the 5 remaining partially fed adults were placed on a normal guinea pig. Three fully engorged females were recovered, but 2 males died on the host. The latter was febrile from the fifth to ninth day and on the twelfth day, and remained afebrile following an immunity test given the eighteenth day.

#### TRANSMISSION OF THE VIRUS BY THE PROGENY OF INFECTED FEMALES

The engorged females recovered in the previous experiment failed to deposit fertile eggs and generation to generation survival of the virus was shown in another test. On March 5, 1937, the same day the first experiment was initiated, 2 guinea pigs were injected with virus and at once infested with noninfected male and female *D. andersoni*. Both host animals died following typical periods of fever. Six engorged females were recovered.

*Larval feeding.*—Groups of larvae from eggs of 3 of the engorged females were placed on separate host guinea pigs on June 2. All 3 host animals began a 4-day period of fever on the twelfth day after infestation and all remained afebrile following an immunity test given on the twenty-sixth day. Only a small number of engorged larvae were recovered.

*Nymphal feeding.*—All the nymphs that molted from the above larvae died except one. This was placed on a guinea pig on July 28 and was removed, fully engorged, on August 2. The host animal became febrile on the twelfth day after infestation and was sacrificed on the fifth day of fever. Spleen tissue was transferred to 6 guinea pigs and filtered blood serum to 2 others.

*Filtered serum-injected guinea pigs.*—The 2 guinea pigs receiving the serum had 4 and 5-day febrile periods, respectively, and both were later afebrile following an immunity test. Heart blood of one, drawn the fourth day of fever was transferred to 6 guinea pigs. All 6 were

typically febrile; one died and the remaining 5 were immune to virus injected on the fifteenth day.

*Spleen-injected guinea pigs.*—The 6 spleen-injected animals had earlier and longer febrile periods but all recovered. Five were subsequently fully immune to injected virus while one had 4 days of low fever.

The single adult tick, a male, that molted from the above engorged nymph, was not tested for infection.

In the above experiments all animals that were sacrificed while febrile or that died showed the typical picture described by Davis and Cox (1). All cultures of heart blood, of filtered blood serum, and of spleen suspensions used for immunity tests were bacteriologically sterile. All controls for the several lots of spleen virus used for immunity tests exhibited typical infections.

These data appear to justify the conclusion that the infectious agent present in the guinea pigs on which the experimental ticks were fed was the same agent which these ticks originally ingested.

#### SUMMARY

The filter-passing infectious agent recently reported as isolated from *Dermacentor andersoni* by Davis and Cox has been shown (1) to survive in, and be transmitted by, nymphal and adult *D. andersoni* that ingested the virus in the larval stage, and (2) to survive through the eggs deposited by infected females and to be transmitted by the progeny.

#### REFERENCES

- (1) Davis, Gordon E., and Cox, Herald R.: A filter-passing infectious agent isolated from ticks. I. Isolation from *Dermacentor andersoni*, reactions in animals, and filtration experiments. Pub. Health Rep., 53: 2259-2267 (Dec. 30, 1938).
- (2) Noguchi, Hideyo: A filter-passing virus obtained from *Dermacentor andersoni*. J. Exp. Med., 44: 1-10 (1926).

### III. DESCRIPTION OF ORGANISM AND CULTIVATION EXPERIMENTS<sup>1</sup>

By HERALD R. COX, Associate Bacteriologist, United States Public Health Service

Initial studies of a filter-passing infectious agent isolated from *Dermacentor andersoni* ticks, collected near Nine Mile Creek, western Montana, have been reported by Davis and Cox (1) and studies of experimental tick transmission have been reported by Parker and

<sup>1</sup> From the Rocky Mountain Laboratory, Division of Infectious Diseases, National Institute of Health, Hamilton, Montana.

Davis (2). Further observations, presented herein, suggest that this agent is rickettsia-like in nature.

The original strain and three others subsequently isolated from ticks were used in these studies.

#### ISOLATION OF A MINUTE, PLEOMORPHIC ORGANISM

In August 1937, a series of experiments were performed to try to determine if inclusion bodies (virus type) were present in the cells of the inflammatory exudate produced in guinea pigs injected subcutaneously with this infectious agent. Animals were sacrificed on the third, fourth, fifth, and sixth days of fever, and touch preparation slides of the inflammatory exudate were stained with Giemsa.

No inclusion bodies were found, but numerous minute, extra-cellular and intracellular pleomorphic, rickettsia-like organisms were observed. They were first seen in slides prepared from the inflammatory exudate produced by an unfiltered spleen suspension (shown to be sterile on ordinary aerobic media) from a guinea pig inoculated with one of the strains. It was later noted that the same findings could be duplicated with each of the four strains isolated from ticks.

Spleen tissue suspensions of each of the four strains were then filtered through new Berkefeld N filters and each filtrate was injected subcutaneously in 1 cc quantities into 3 normal guinea pigs and into 5 control animals recovered from infection with the original strain. Each filtrate was also tested aerobically on dextrose beef infusion broth, dextrose nutrient agar slants, blood agar pour plates, blood agar slants, blood broth, Noguchi's leptospira-media (3) and tularensis media, and anaerobically on media similar to those listed above except incubated under complete hydrogen tension in a McIntosh and Fildes jar. All culture media remained sterile during 2 weeks' incubation. The 20 control guinea pigs (5 to each filtrate) remained normal during 4 weeks' observation. On the other hand, the 12 normal guinea pigs inoculated with the filtrates (3 to each filtrate) all became febrile and developed characteristic skin lesions. The animals were sacrificed on the fifth and sixth days of fever; the spleens were enlarged, and 7 showed exudate. Giemsa-stained impression slides prepared from the skin lesions revealed the rickettsia-like organisms to be present in abundance in all guinea pigs of all 4 strains. Control slides prepared from the same material, but stained with Gram and Loeffler's alkaline methylene-blue failed to reveal any kind of organism.

These results indicated that the infectious agent is not a filterable virus in the recognized sense of the term.

#### DEMONSTRATION OF THE ORGANISM IN OTHER TISSUES

Repeated experiments have been performed in which guinea pigs have been readily infected by injecting bacteria-free filtrates of

infected spleen suspensions passed through Berkefeld N or W filters. When the filtrates are injected subcutaneously, the rickettsia-like organisms are readily demonstrated in the inflammatory exudate of the skin.

The organisms have also been demonstrated in great abundance in the cellular exudate frequently found covering the spleen. In addition, they have been shown in large numbers in the spleen substance and have been demonstrated infrequently in impression slides prepared from the tunicae and polar fat of the testes. Attempts to demonstrate them in the lungs, liver, blood, and scrapings of the abdominal wall have thus far been negative. They have not been observed to invade red blood cells. In the inflammatory exudate of the skin, the spleen substance, and the splenic exudate, the organisms were often found outside of cells, but in many cases were abundant within the cytoplasm. In each case pleomorphism was marked.

The organisms most commonly observed free from cells were small lanceolate rods, bipolar rods, diplobacillary forms, and occasionally segmented, filamentous forms. Measurements showed the individual, small lanceolate rod forms to be approximately  $0.25 \mu$  in diameter by  $0.4$  or  $0.5 \mu$  long. The bipolar forms were  $0.25 \mu$  by  $1.0 \mu$ , while the diplobacillary forms were approximately of the same diameter and about  $1.5 \mu$  long. Also frequently observed were chains consisting of 3 to 6 or even more minute rod or coccus forms. Individual bipolar or diplobacillary forms, as well as small spherical clusters (3 to  $12 \mu$  in diameter) of sharply stained rod-like forms were commonly observed in the cytoplasm of cells. Also many cells were packed with intracytoplasmic clusters or nests of less discrete organisms which appeared to be coccoid or granular. Many cells also showed large vacuoles in the cytoplasm. Sometimes the cytoplasm was entirely vacuolated with the nucleus pushed out to the edge of the cell wall. Bipolar forms or diplobacillary rods existing either as individual forms or in chains could be seen in the vacuoles. Frequently, too, these vacuolated cells contained clumps of the organisms.

Cell nuclei were not observed to be commonly invaded although in one instance, in which the slides were prepared from the splenic exudate, the nuclei of a number of cells appeared to be vacuolated, and sharply stained forms, indistinguishable from the bipolar forms commonly observed, could be seen in the vacuoles.

The organisms appear to be more slender than typhus rickettsiae, although it would be difficult to differentiate them from those of typhus when observed as individual forms. The individual forms also closely resemble *Bartonella bacilliformis*, and it is noteworthy that the picture of the cell-infection as a whole is remarkably similar to that described by Pinkerton and Weinman for "Carrion's disease" (4).

## STAINING REACTIONS

Repeated experiments have been performed to determine the staining characteristics of the organisms.<sup>2</sup> Impression slides prepared from selected tissues of guinea pigs and smears prepared from tissue cultures were employed.

The results may be summarized by stating that the organisms stain sharply and deeply with Giemsa and also well by Machiavello's method. With the ordinary dyes used to demonstrate bacteria (Gram, Loeffler's alkaline methylene blue, Pappenheim-Saathof methyl green-pyronine, 1 percent aqueous crystal violet, 1 percent aqueous methylene blue, 1 percent aqueous malachite green) the organisms may occasionally appear as faint shadow-like forms too poorly defined to be recognized with certainty, but as a rule they are not stained at all. The organisms are not acid-fast since they are unaffected by staining by the Ziehl-Neelsen method. The staining reactions are therefore like those of the rickettsiae.

## ATTEMPTS TO CULTIVATE THE ORGANISM ON LEPTOSPIRA MEDIA

In view of the remarkable similarity of the cell-infection picture to that described by Pinkerton and Weinman (4) for Carrion's disease, special efforts were made to cultivate the organism on Noguchi's leptospira medium (3) which is commonly used for the growth of bartonellae (3) (4).

The cultures were initiated from guinea pig heart blood, spleen tissue, and tissue culture suspensions. Three types of leptospira media were employed: (a) Noguchi's leptospira media (3) prepared with rabbit serum, (b) similar media with the substitution of guinea pig serum for rabbit serum, and (c) Anigstein's modified medium.<sup>3</sup> Also an experiment was carried out in which the culture tubes (Noguchi's rabbit serum media) were sealed with a layer of sterile vaseline.

In every experiment the media tubes in duplicate were incubated at 37.5° C. In 2 of the tests additional tubes were also incubated at 32° C. Transfers were made every 7 to 10 days and at each transfer guinea pigs were injected either subcutaneously or intraperitoneally with pooled material from the culture tubes. The dilution factor in transfer from tube to tube was approximately 1 to 3. In repeated experiments the organism failed to survive beyond the sixth subculture. Guinea pigs inoculated with the subcultures showed increasing incubation periods to the point of failure to produce reactions.

<sup>1</sup> The writer is indebted to Dr. F. D. Pease, of Missoula, Mont., for his kind assistance in preparing a number of paraffin section slides of infected skin tissues. In these, individual rickettsia-like forms located extracellularly, as well as individuals and clusters of organisms located in the cytoplasm, were readily found.

<sup>2</sup> Personal communications from Dr. Ludwik Anigstein, State Institute of Hygiene, Warsaw, Poland. This media differs from that of Noguchi in that tap water is substituted for physiological saline and the desired hemoglobin content is achieved by adding defibrinated blood.

In table 1 are shown the daily temperature records and the time of appearance of lesions in the skin of guinea pigs inoculated with the guinea pig serum leptospira cultures used in one of these experiments.

TABLE 1.—Record of daily temperatures and time of appearance of lesions in the skin of guinea pigs inoculated with guinea pig serum leptospira cultures. Each guinea pig was injected subcutaneously with 1 cc of the culture

Culture transfer ...	1		2		3		4		5		6	
Guinea pig number.	1	2	3	4	5	6	7	8	9	10	11	12
Days following date of injection												
1. ....	37.8	38.2	39.0	39.1	38.5	38.8	39.3	39.4	39.5	38.7	39.3	39.2
2. ....	39.0	39.5	39.0	39.0	38.8	38.6	39.0	39.0	39.0	38.6	39.5	39.6
3. ....	38.8	38.6	39.0	39.5	39.3	38.5	39.3	39.3	39.0	38.5	39.3	39.3
4. ....	39.3	39.0	38.5	38.8	39.0	38.8	39.5	39.2	38.4	38.7	39.3	39.0
5. ....	39.8	39.7	39.0	39.2	39.3	39.0	39.3	39.5	39.0	39.0	39.3	39.6
6. ....	39.6	39.9	38.5	39.0	39.2	39.2	39.4	39.5	39.0	38.7	39.4	39.4
7. ....	140.9	140.3	39.0	39.5	38.5	38.5	39.5	39.2	39.2	39.0	39.8	39.4
8. ....	140.4	40.3	140.5	140.3	38.8	39.1	39.3	39.6	39.0	39.2	39.2	39.0
9. ....	140.8	40.4	141.0	140.7	40.4	39.5	39.3	40.4	39.0	38.7	39.0	39.0
10. ....	140.5	40.5	140.6	141.0	40.3	39.7	39.5	140.7	39.3	39.3	39.0	39.4
11. ....	140.5	40.2	139.8	140.4	40.7	40.4	39.5	141.0	38.5	39.2	39.5	39.2
12. ....	139.2	39.1	139.6	140.4	141.2	141.3	39.5	140.8	39.0	39.0	39.7	39.7
13. ....	138.6	39.0	139.0	-----	140.4	140.0	39.2	140.6	39.0	39.0	39.2	39.3
14. ....	-----	38.7	139.0	-----	139.2	139.2	39.4	140.0	39.2	39.2	39.0	39.2
15. ....	-----	38.8	138.8	-----	138.7	-----	39.2	139.2	39.2	39.4	39.0	39.0
16. ....	-----	38.6	139.0	-----	39.0	-----	39.5	139.3	39.0	39.0	39.0	38.7
17. ....	-----	-----	-----	-----	138.8	-----	39.3	139.3	38.7	39.0	38.8	39.0
18. ....	-----	-----	-----	-----	-----	-----	39.4	139.3	39.0	38.5	39.0	39.2
19. ....	-----	-----	-----	-----	-----	-----	39.5	139.5	39.0	38.7	39.2	38.8
20. ....	-----	-----	-----	-----	-----	-----	39.4	139.2	38.4	38.7	39.4	38.6
21. ....	-----	-----	-----	-----	-----	-----	39.4	139.2	38.6	38.6	39.2	39.0
22. ....	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
23. ....	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
Result.....	( <sup>1</sup> )	( <sup>2</sup> )	( <sup>3</sup> )	( <sup>4</sup> )	( <sup>5</sup> )	( <sup>6</sup> )	( <sup>7</sup> )	( <sup>6</sup> )	( <sup>7</sup> )	( <sup>7</sup> )	( <sup>7</sup> )	( <sup>7</sup> )

- <sup>1</sup> Inflammatory exudate produced in skin (skin lesion).
- <sup>2</sup> Sacrificed on 13th day.
- <sup>3</sup> Sacrificed on 12th day.
- <sup>4</sup> Sacrificed on 15th day.
- <sup>5</sup> Rickottsia-like bodies found in skin lesion.
- <sup>6</sup> Animal found to be immune upon subsequent test.
- <sup>7</sup> Animal found to be not immune.

ABSENCE OF ANGIOMATOUS NODULES IN INOCULATED MONKEYS

The following experiment was performed to determine whether or not the infectious agent would produce angiomatous nodules, such as are caused by *Bartonella bacilliformis* in the eyebrows of monkeys.

A 10 percent suspension of guinea pig spleen was used as inoculum. One monkey was injected intradermally with 0.5 cc into each of 2 spots on the abdomen. In addition, this animal received an intradermal injection of 0.5 cc in each eyebrow. A second monkey and 2 control guinea pigs received 1 cc intraperitoneally. The guinea pigs reacted typically. Both of the monkeys remained normal during 30 days' observation and in no case did a lesion appear at the site of inoculation.

CULTIVATION IN TISSUE CULTURE

The organism has been readily cultivated and carried in transfer series in modified Maitland tissue cultures consisting of minced chick

embryonic tissues suspended in filtered human ascitic fluid or modified Baker's solution (5). Six series of cultures (all initiated with Berkefeld N or W filtrates) have been successfully carried through more than 12 passages (one series through 29) and the rickettsia-like organisms have been readily demonstrated in every series.

#### DISCUSSION

Cowdry (6) has defined the term "rickettsia" as follows: "Gram-negative, bacterium-like organisms of small size, usually less than half a micron in diameter, which are found intracellularly in arthropods, which may be more or less pleomorphic and stain rather lightly with aniline dyes, but which resemble in most of their properties the type species, '*R. prowazeki*'."

The infectious agent described here meets all the requirements set forth in this definition of "rickettsiae" with the exception that it has not as yet been demonstrated in tick tissues. However, like the causative agent of Rocky Mountain spotted fever, it has been isolated repeatedly from naturally infected ticks and has been transmitted by them (2).

In addition to the properties defined for a "rickettsia" this agent possesses the ability to pass filters that are impermeable to ordinary bacteria and to rickettsiae in general. Nevertheless, it does not seem that mere possession of the property of filterability can justify the classification of this agent as a filterable virus. Neither is it thought, on the basis of present information, that it can be classified as a bartonella (especially *Bartonella bacilliformis*) since it has not been observed to invade red blood cells, it apparently cannot be cultivated on cell-free media, and it does not produce angiomatic nodules when injected intradermally into the eyebrow of a monkey.

In 1926, Noguchi (7) reported the recovery of a filter-passing virus from one tick (*Dermacentor andersoni*) of a lot of 50 collected in the Saw Tooth Canyon, Mont.

The area where these ticks were collected is about 60 miles from the area where the infected ticks reported in the first paper of this series (1) were found. Noguchi found that his virus passed through Berkefeld N filters, did not grow on ordinary media, but could be carried on leptospira media through 7 subculture generations. He did not find microorganisms in his cultures, although the virus was shown to be present by guinea pig inoculation. In guinea pigs the reaction caused by the Noguchi virus was apparently not unlike the clinical picture produced by inoculation with the infectious agent reported by us (1). Noguchi was able to infect monkeys with his virus, while we have so far failed in doing so. He showed that adult ticks could be infected by feeding on infected guinea pigs and that

ticks partially fed on infected guinea pigs could later transmit the infection when allowed to complete their engorgement on fresh guinea pigs. He failed to infect one female tick and did not further try stage to stage transmission which Parker (2) has demonstrated for the infectious agent reported in this series of papers. Noguchi does not mention any microscopic examinations of preparations from guinea pig tissues such as smears from the spleen, tunicae, or the testes, in which preparations we have found numerous rickettsia-like organisms.

Comparison of Noguchi's findings with ours leads us to think that it is quite probable that the two infections are identical.

#### SUMMARY

Studies of a filter-passing infectious agent isolated from *Dermacentor andersoni* are reported and the possible identity of this agent with the filter-passing virus reported by Noguchi in 1926 is pointed out. This agent has been shown to be a minute gram-negative, pleomorphic rickettsia-like organism that occurs both intra- and extra-cellularly in the affected tissues of guinea pigs. It may be present in abundance in the spleen and splenic exudate and especially in the skin lesions of animals inoculated subcutaneously. It stains well with Giemsa and by the Machiavello method, but very faintly and usually not at all with the usual bacterial stains. It grows well in tissue culture but not on bacteriological media under either aerobic or anaerobic conditions and so far has not been maintained on Noguchi's leptospira medium or various modifications thereof.

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IV. HUMAN INFECTION<sup>1</sup>

By R. E. DYER, *Senior Surgeon, United States Public Health Service, National Institute of Health*

In preceding publications, Davis and Cox (1) have reported the isolation from ticks of a filter-passing agent, infectious for animals, Parker and Davis (2) have reported the experimental tick transmission of this infection, and Cox (3) has described the characteristics of the organism associated with the infection.

In May 1938, a member of the staff of the National Institute of Health, "X," spent a few days (May 12-16) at the Public Health Service laboratory in Hamilton, Mont., where this infection was being studied in animals, chiefly guinea pigs, and in tissue cultures. Many of the infected guinea pigs were handled by X in company with Y, one of the investigators engaged in the study of this virus at the Hamilton laboratory. X also assisted Y when the latter was making egg culture transfers. No accident is recalled by either X or Y which might explain an infection with this virus. X left the Montana laboratory on May 16 and returned to Washington, stopping 2 days en route at Laramie, Wyo., and reaching Washington on May 21. On May 26 and 27, X noticed occasional rather dull to sharp pains in the eyeballs, and in the evening of the 27th felt more than ordinarily tired. He afterwards thought that he might have had a slight fever on the evening of that day. The pains in the eyeballs persisted throughout the 28th, with an increasing feeling of malaise in the late afternoon. Temperature was taken at 8 p. m. and found to be 99.5° F. The following day, May 29, the temperature was 100.5° at 3 p. m., and 100° at 8 p. m. The temperature course is shown in figure 1. On the 28th, X felt slightly chilly at times, particularly in the afternoon. These chilly sensations became more pronounced on the 30th, and the patient took to bed during the evening of that day. Repeated mild to moderate chills persisted throughout the following 2 days. The chills ceased on June 2 and a drenching sweat was experienced about midnight. This sweat was repeated on each of the following 4 nights, becoming less in intensity each succeeding night. On June 2, tenderness developed in one tooth which persisted for 4 days. On June 7, the second joint of the third finger of the right hand became sore; no swelling was apparent. On the succeeding day, the first joint of the second finger of the same hand became tender with no swelling. The tenderness in the joints subsided in 3 days.

<sup>1</sup> From the Division of Infectious Diseases, National Institute of Health.

The appetite remained good throughout the illness and the bowels about normal with a little tendency to constipation. After convalescence was established the return to normal strength was fairly rapid, being gained about 10 days or 2 weeks after defervescence.

The pulse rate did not exceed 90 during the illness, showing a rate of 72-74 when the temperature was at the low point of the day and 84-90 at each day's temperature peak.

No other physical signs nor symptoms were noted during the entire illness.

Urinalyses during the illness showed nothing of importance, the only variation from normal being a slight trace of albumin in specimens taken at the height of fever.

Blood counts made during the illness were essentially negative. Count made on the 7th day of illness was as follows: Red cells

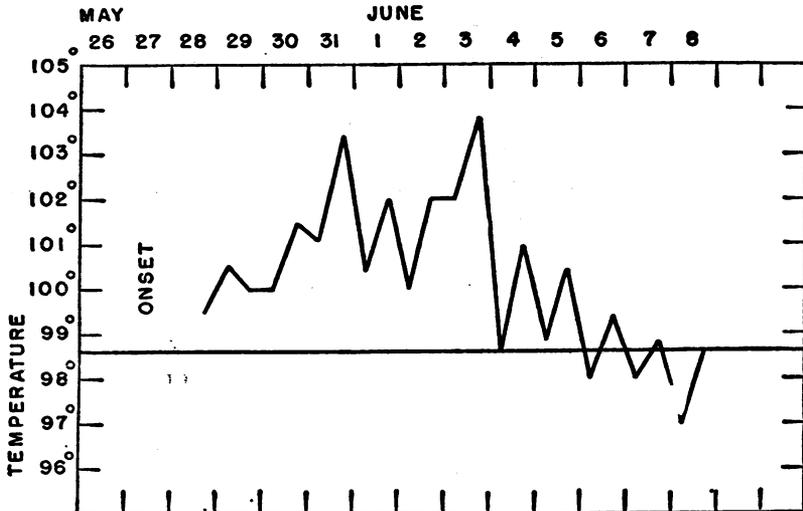


FIGURE 1.—Temperature chart, case X.

4,540,000, hemoglobin 85 percent, leucocytes 8,800, neutrophils 54 percent, juveniles 0, band 21, lymphocytes 18, mononuclears 4, eosinophils 2, and basophils 1. Blood cultures made on June 2, 3, and 7 were negative.

Agglutination tests on serum specimens taken at the height of illness and during convalescence were carried out against *B. typhosus*, *B. paratyphosus* A and B, *B. abortus*, *B. tularensis*, and *B. proteus* X19. All agglutination tests were negative with the exception of *B. proteus* X19, which was positive in low titers (complete 1:80, partial 1:160). Since X had had typhus fever 6 years previously, had been repeatedly vaccinated against spotted fever, and had a similar titer 1 year prior to this illness, the low agglutination of X19 is thought to have no significance in regard to the illness described here.

## ISOLATION OF THE VIRUS FROM CASE X

On June 3 (sixth day of illness), 5 cc of blood were drawn from X and injected intraperitoneally into a 500-gram guinea pig. This guinea pig developed a febrile reaction 8 days later. On the third day of fever, this animal was sacrificed and small amounts of its blood and spleen were injected into fresh guinea pigs. This injection resulted in establishing a definite infection in guinea pigs which has been readily maintained in these animals for 20 transfer generations. Blood has been used as the medium of transfer from guinea pig to guinea pig. All injections have been intraperitoneal.

Blood serum drawn from X shortly after defervescence gave definite protection, when tested in guinea pigs, against the X strain of virus, indicating that the infection established in animals was identical with the infection suffered by X. In these protection tests, 0.5 cc amounts of the serum being tested were mixed in conical vials with different amounts of blood serum drawn from a guinea pig at the height of its infection. The amounts of this guinea pig serum virus were 0.1, 0.25, 0.5, and 1.0 cc. The mixtures were allowed to stand at room temperature for 30 minutes and then injected intraperitoneally into guinea pigs. Control guinea pigs were inoculated with like amounts of the same serum virus.

## THE INFECTION IN GUINEA PIGS

The usual incubation period in the guinea pig following the intraperitoneal inoculation of 2 cc of blood virus is from 4 to 6 days. Extremes are 2 and 10 days. The temperature is continuous in most of these animals for from 2 to 8 days, averaging between 40° and 40.5°. The common febrile period is from 2 to 4 days. This strain has proved fatal in about one-third of the infected guinea pigs.

At autopsy, the only definite gross findings are an enlarged spleen and some congestion of the blood vessels of the tunica vaginalis testis. The enlargement of the spleen may vary from slight to 5 or 6 or more times the normal size. In appearance, the spleen resembles the spleen of guinea pigs with Rocky Mountain spotted fever. In addition to a little congestion of the vessels of the tunica covering the testicles, a thin exudate is usually present over this surface.

Rickettsia-like bodies may be readily demonstrated in the tunica exudate and also in smears made from the cut surface of the spleen.

The reactions in the guinea pigs and the appearance of the rickettsia-like bodies are, as far as can be judged, identical with those described by Cox (3) in his discussion.

## IDENTIFICATION OF THE X VIRUS

Cross immunity tests were entirely negative between the virus isolated from X and typhus (endemic and epidemic strains) and Rocky Mountain spotted fever (two strains, one isolated in Montana, the other in Washington, D. C.). The strain of virus isolated from *Dermacentor andersoni* with which Y had been working at the time of X's visit to the Montana laboratory was sent to Washington and tests between this strain and the strain isolated from X showed complete cross immunity.

One serum from a case of Rocky Mountain spotted fever which gave complete protection against Rocky Mountain spotted fever virus gave no protection against the X virus.

Two additional serums were tested for protective antibodies against the X virus with negative results. One of these was from a healthy individual who had had no contact with the X strain animals and the second was from an individual who had assisted in the taking of temperatures of guinea pigs inoculated with the X virus and had made many of the autopsies on these animals. This latter individual had an attack of typhus fever in 1935 and had been repeatedly vaccinated against Rocky Mountain spotted fever.

## POSSIBLE RELATION TO "Q" FEVER

In 1937 Derrick (4) and Burnet and Freeman (5) published accounts of a new disease recently noted by them in Australia, to which they give the name "Q" fever. The clinical features of this disease are similar to the attack of illness suffered by X. The description of the disease in guinea pigs, the association of rickettsia-like organisms with the disease, and the lack of agglutinations for *B. proteus* X19 correspond to the findings of Cox and Davis in their work and reported in this article for the X strain.

Dr. Burnet, in April 1938, sent mouse spleens infected with "Q" virus to X, who succeeded in establishing this disease in guinea pigs in the laboratory by the injection of these spleens. After the disease was established in guinea pigs, the routine maintenance of the strain was carried out by a technician. X recalls no contact with these animals from the latter part of April until he returned to work following his illness, his last definite contact with animals of the "Q" strain being on April 18, at which time he autopsied a guinea pig from this strain and inoculated other guinea pigs with blood from the autopsied animal. The strain of "Q" fever was lost during the month of July on account of certain difficulties with the supply of stock guinea pigs. Prior to the loss of this strain, it had been found that guinea pigs recovered from infection with typhus or Rocky

Mountain spotted fever were not immune to subsequent infection with the "Q" fever strain. However, 5 guinea pigs which had recovered from "Q" fever were subsequently found to be immune to the X strain.

The virus of "Q" fever was lost before further comparison of the "Q" and X viruses could be made. Altogether over 100 guinea pigs have been inoculated with the X strain virus, including those which had previously reacted to two strains of typhus and two strains of spotted fever and also including guinea pigs which had recovered from illnesses occasioned by enteritidis and other unidentified infections. None of these animals showed any signs of immunity to the X virus. In view of these facts, it would seem that the immunity of the recovered "Q" fever guinea pigs to the X virus was more than a chance circumstance and suggests a relationship between "Q" virus and X virus.

#### DISCUSSION

Assuming that the "Q" virus from Australia and the X virus are identical, it seems improbable that X was infected by his contact with animals infected with "Q" virus on April 18, 6 weeks before he became ill. The incubation period noted by Derrick in human cases of "Q" fever is 15 days or less. This stated period was apparently based on one case in which the incubation could be definitely determined.

With the identification of the X virus with the infectious agent reported by Davis and Cox and the more recent exposure of X to this strain in the Montana laboratory, it seems probable that X's illness was contracted in Montana, and was not an infection with the "Q" strain from Australia.

The possibility of the infectious agent isolated in Montana and the causative agent of "Q" fever being closely related, as the "one-way" cross immunity tests suggest, should not be overlooked. That the two diseases may not be identical is indicated by our failure to infect monkeys (4 attempts), while the Australian workers report monkeys as susceptible to "Q" fever. Epidemiologically, this latter disease has been found in Australia, particularly among workers in abattoirs and among dairy farmers. Such an epidemiological picture is not at variance with the picture of a "tick borne" infection, since it suggests a reservoir in animals and the existence of the infection in their arthropod parasites.

#### SUMMARY

A newly recognized agent recovered from ticks has been found capable of causing infection in man. The relationship of this infection to "Q" fever of Australia is suggested.

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## RIBOFLAVIN DEFICIENCY IN MAN

### A PRELIMINARY NOTE

By W. H. SEBRELL, *Surgeon*, and R. E. BUTLER, *Passed Assistant Surgeon*,  
*United States Public Health Service, National Institute of Health*

Eighteen adult women were given a daily ration similar to that used by Goldberger and Tanner (1), consisting of cornmeal, 9.5 oz.; cow-peas, 0.48 oz.; lard, 1.625 oz.; casein, 2.43 oz.; flour, 0.75 oz.; white bread, 3.6 oz.; calcium carbonate, 3 grams; tomato juice, 4 oz.; cod liver oil, 0.5 oz.; sirup, 4.75 oz.; sirup of iodide of iron, 2 drops. In addition, on the eighty-sixth day all were started on a weekly supplement of 30 mg. of crystalline ascorbic acid and 3.3 mg. of crystalline thiamin chloride (vitamin B<sub>1</sub>).

Ten of the 18 women developed a cheilosis (lesions of the lips) in from 94 to 130 days after the beginning of the experiment. These lesions began as a pallor of the mucosa of the lip in the angles of the mouth without involvement of the buccal mucosa. This pallor was soon followed by maceration, and within a few days superficial transverse fissures appeared, usually bilateral, and exactly in the angle of the mouth. These fissures extended somewhat downward from the angle and there was very little inflammatory reaction. The lesions remained moist and became covered with a honey-colored crust which could be scraped off without bleeding. In some instances the fissures continued to extend onto the skin for a distance of as much as one-half an inch. These lesions resemble those described as perlèche. At about the time the fissures were seen, the lips became abnormally red along the line of closure. This was due apparently to a superficial denudation of the mucosa. In addition to the cheilosis, there was also seen a fine, scaly, slightly greasy desquamation on a mildly erythematous base in the nasolabial folds, on the alae nasi, in the vestibule of the nose and on the ears.

Four of the 10 women with the cheilosis were treated with daily doses of 1 mg or 2 mg of synthetic crystalline riboflavin<sup>1</sup> for from 3 to 10 days, after which the daily dose was changed to 0.025 mg per kilo of body weight. All lesions completely disappeared after 5, 6, 20, and 47 days of treatment.

Another 4 women with the cheilosis were treated for 5 days with 100 mg of nicotinic acid daily. At the end of the 5 days the cheilosis in all 4 was definitely worse, and treatment with 1 mg of synthetic crystalline riboflavin daily was started. After 3 days the dose was changed to 0.025 mg per kilo of body weight. The lesions completely disappeared in 3 of the women after 12, 13, and 24 days of treatment. The fourth showed slow improvement and after 49 days the daily dose of riboflavin was increased to 0.05 mg per kilo of body weight. The symptoms then receded more rapidly and after 9 days the only visible lesion was a small fissure in the right angle of the mouth.

One woman with the cheilosis was treated with 100 mg of nicotinic acid daily for 43 days. At the end of this period the cheilosis was still present and treatment was started with 0.025 mg of synthetic crystalline riboflavin per kilo of body weight daily. The cheilosis completely healed in 10 days.

The remaining woman developed the typical skin lesions of pellagra, beginning 36 days after the start of the experiment. These lesions were allowed to progress for 40 days until the diagnosis could be made without question. After 30 days on 30 mg of nicotinic acid daily these lesions were completely healed. In spite of the continued administration of this quantity of nicotinic acid daily, the cheilosis appeared 21 days after the skin lesions of pellagra had completely healed, and 127 days from the beginning of the experiment. Three days after the cheilosis was seen the nicotinic acid was increased to 100 mg daily. The cheilosis increased in severity for several days and then decreased during the following month. However, at the end of this period the lesions were present and again were increasing in severity (45 days after beginning the increased dose of nicotinic acid). Treatment was then started with 0.025 mg of riboflavin per kilo of body weight daily. The lesions completely disappeared in 6 days.

The cheilosis and other symptoms are identical with those seen experimentally by Goldberger and Tanner (1) and Wheeler (2), and they appear to be similar to lesions described by Stannus (3) in association with pellagra in Nyasaland and to some of the lesions described by Landor and Pallister (4) in Malaya as avitaminosis B<sub>2</sub>. Although their appearance is also similar to lesions described by Aykroyd and Krishnan (5) in India as angular stomatitis due to vitamin B<sub>2</sub> deficiency, there is some question as to the identity of the two conditions

<sup>1</sup> Furnished by Merck and Co., Inc., and reported by them to be synthetic in origin.

since Aykroyd and Krishnan (6) report beneficial therapeutic results with a yeast preparation treated to destroy flavin.

### CONCLUSIONS

A clinical syndrome in which a cheilosis (lesions on the lips in the angles of the mouth) is one of the early prominent symptoms has been produced experimentally. Under the conditions of this experiment the symptoms are alleviated by the administration of small doses of crystalline synthetic riboflavin, but are not benefited by 100 mg of nicotinic acid daily. The conclusion, therefore, seems warranted that the condition is a manifestation of riboflavin deficiency. It is suggested that the term ariboflavinosis be added to the nomenclature of the vitamin deficiency diseases as a designation for the clinical condition due to riboflavin deficiency.

### REFERENCES

- (1) Goldberger, Joseph, and Tanner, W. F.: A study of the pellagra-preventive action of dried beans, casein, dried milk, and brewers' yeast, with a consideration of the essential preventive factors involved. *Pub. Health Rep.*, 40: 54 (1925).
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- (4) Landor, J. V., and Pallister, R. A.: Avitaminosis B<sub>2</sub>. *Trans. Roy. Soc. Trop. Med. and Hyg.*, 29: 121 (1935).
- (5) Aykroyd, W. R., and Krishnan, B. G.: Stomatitis due to vitamin B<sub>2</sub> deficiency. *Indian J. Med. Res.*, 24: 411 (1936).
- (6) Aykroyd, W. R., and Krishnan, B. G.: The treatment of stomatitis caused by diet deficiency. *Indian J. Med. Res.*, 25: 643 (1938).

## DEATHS DURING WEEK ENDED DECEMBER 10, 1938

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

	Week ended Dec. 10, 1938	Correspond- ing week, 1937
<b>Data from 88 large cities of the United States:</b>		
Total deaths.....	8,805	18,552
Average for 3 prior years.....	18,702	-----
Total deaths, first 49 weeks of year.....	397,853	422,441
Deaths under 1 year of age.....	517	1,558
Average for 3 prior years.....	1,534	-----
Deaths under 1 year of age, first 49 weeks of year.....	25,641	27,116
<b>Data from industrial insurance companies:</b>		
Policies in force.....	68,233,468	70,452,399
Number of death claims.....	11,995	12,820
Death claims per 1,000 policies in force, annual rate.....	9.2	9.5
Death claims per 1,000 policies, first 49 weeks of year, annual rate.....	9.2	9.7

<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 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 Dec. 17, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median*

Division and State	Diphtheria				Influenza				Measles				
	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	
<b>NEW ENG.</b>													
Maine.....	140	23	2	2	.....	.....	.....	.....	1	30	5	42	42
New Hampshire.....	0	0	0	0	.....	.....	.....	.....	.....	.....	.....	96	12
Vermont.....	0	0	0	1	.....	.....	.....	.....	.....	177	13	130	59
Massachusetts.....	6	5	5	15	.....	.....	.....	.....	.....	250	212	61	195
Rhode Island.....	0	0	1	1	.....	.....	.....	.....	.....	8	1	1	9
Connecticut.....	18	6	5	5	21	7	.....	.....	4	204	68	5	93
<b>MID. ATL.</b>													
New York.....	11	27	43	43	10	14	10	19	.....	336	836	128	584
New Jersey.....	23	19	16	24	6	5	11	20	.....	36	30	690	96
Pennsylvania.....	16	32	37	46	.....	.....	.....	.....	.....	34	67	2,275	327
<b>E. NO. CEN.</b>													
Ohio.....	26	34	22	65	.....	.....	6	60	.....	12	16	267	129
Indiana.....	41	27	17	33	18	12	57	46	.....	15	10	50	39
Illinois.....	32	48	30	48	9	14	17	21	.....	23	34	935	34
Michigan.....	17	16	17	17	3	3	.....	4	.....	167	155	305	42
Wisconsin.....	0	0	1	4	78	44	51	25	.....	331	186	141	141
<b>W. NO. CEN.</b>													
Minnesota.....	2	1	1	6	2	1	2	.....	.....	785	399	.....	41
Iowa.....	29	14	12	15	16	8	4	2	.....	227	111	4	12
Missouri.....	14	11	35	51	81	62	44	55	.....	5	4	976	112
North Dakota.....	30	4	1	5	89	12	18	10	.....	2,615	354	11	11
South Dakota.....	23	3	0	0	8	1	.....	.....	.....	1,228	163	.....	5
Nebraska.....	15	4	3	6	.....	.....	.....	.....	.....	31	8	.....	13
Kansas.....	22	8	7	12	31	11	4	1	.....	6	2	23	23

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Dec. 17, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Diphtheria				Influenza				Measles			
	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median
<b>SO. ATL.</b>												
Delaware	0	0	0	0					80	4	2	2
Maryland <sup>2,3</sup>	19	6	22	19	28	9	16	12	264	85	5	43
Dist. of Col. <sup>4</sup>	91	11	10	10	25	3					6	5
Virginia	91	47	24	44	316	164			35	18	127	87
West Virginia	42	15	18	37	42	15	49	52	70	25	237	16
North Carolina <sup>2</sup>	94	63	35	53	9	6	11	11	403	270	434	434
South Carolina	11	4	7	9	1,246	448	359	410	31	11	71	30
Georgia <sup>2</sup>	12	7	25	25	130	77			17	10		
Florida <sup>2</sup>	19	6	20	15	16	5	4	4	56	18	35	6
<b>E. SO. CEN.</b>												
Kentucky	25	14	18	36	75	42	24	25	18	10	101	14
Tennessee	41	23	11	30	85	47	96	93	65	36	119	76
Alabama <sup>2</sup>	43	24	23	26	168	93	258	88	76	42	12	12
Mississippi <sup>2</sup>	26	10	17	17								
<b>W. SO. CEN.</b>												
Arkansas	38	15	23	15	356	140	134	44	64	25	17	10
Louisiana <sup>2</sup>	78	32	27	27	24	10	54	14	64	26	3	3
Oklahoma	33	16	21	17	203	99	98	53	88	43	5	4
Texas <sup>2</sup>	50	50	48	88	325	385	490	288	22	20	36	36
<b>MOUNTAIN</b>												
Montana	0	0	0	2	68	7		14	2,302	238	1	2
Idaho	0	0	3	0			3	2	846	80	11	11
Wyoming	244	11	0	0					399	18	1	4
Colorado	58	12	7	8	112	23			34	7	61	11
New Mexico	161	13	6	6					250	21	49	49
Arizona	89	7	2	3	2,392	189	73	46	63	5	5	3
Utah <sup>2</sup>	0	0	1	0	332	33			181	18	69	12
<b>PACIFIC</b>												
Washington	19	6	1	3	3	1		3	503	160	38	38
Oregon	15	3	2	1	117	23	31	31	86	17	10	31
California <sup>2</sup>	42	49	28	43	29	34	32	41	787	929	71	137
Total	30	735	654	1,021	100	2,047	1,965	1,671	198	4,816	7,631	5,048
50 weeks	23	28,770	26,697	36,393	62	62,720	288,665	153,510	648	739,887	283,762	369,544

Division and State	Meningitis, meningococcus				Poliomyelitis				Scarlet fever			
	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median
<b>NEW ENG.</b>												
Maine	0	0	0	1	0	0	1	1	67	11	45	29
New Hampshire	0	0	0	0	0	0	0	0	31	3	7	11
Vermont	0	0	0	0	0	0	0	0	54	4	35	16
Massachusetts	1.2	1	0	2	0	0	0	0	137	116	207	207
Rhode Island	0	0	2	1	8	1	0	0	77	10	31	17
Connecticut	3	1	0	0	3	1	0	0	207	69	77	55
<b>MID. ATL.</b>												
New York	1.6	4	9	5	0	0	0	1	160	398	410	453
New Jersey	0	0	2	1	1.2	1	1	1	104	87	94	129
Pennsylvania	0.5	1	3	3	1	2	0	1	147	286	428	428

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Dec. 17, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Meningitis, meningo-coccus				Poliomyelitis				Scarlet fever			
	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37, median
<b>E. NO. CEN.</b>												
Ohio.....	0.8	1	4	4	0.8	1	1	4	257	332	274	485
Indiana.....	3	2	0	2	0	0	0	1	245	163	167	183
Illinois.....	0	0	5	4	0.7	1	0	1	231	349	512	512
Michigan <sup>1</sup> .....	2.2	2	1	1	0	0	0	1	531	492	335	320
Wisconsin.....	0	0	0	1	0	0	0	1	310	174	140	247
<b>W. NO. CEN.</b>												
Minnesota.....	0	0	0	0	2	1	2	0	275	140	111	137
Iowa.....	4	2	0	1	2	1	0	1	212	104	233	94
Missouri.....	0	0	1	1	0	0	1	1	152	116	230	140
North Dakota.....	0	0	0	0	0	0	0	0	214	29	24	59
South Dakota.....	0	0	0	0	0	0	0	0	234	5	31	31
Nebraska.....	0	0	0	1	8	2	0	0	119	31	25	29
Kansas.....	2.8	1	1	1	0	0	1	1	403	144	160	160
<b>SO. ATL.</b>												
Delaware.....	0	0	0	0	0	0	0	0	220	11	12	12
Maryland <sup>1,2</sup> .....	0	0	0	0	0	0	1	1	158	51	71	76
Dist. of Col. <sup>4</sup> .....	0	0	0	1	0	0	0	0	67	8	16	16
Virginia.....	0	0	4	2	0	0	1	0	85	44	58	75
West Virginia.....	11	4	3	2	0	0	1	0	185	66	71	74
North Carolina <sup>2</sup> .....	0	0	1	2	1.5	1	0	0	97	65	50	68
South Carolina.....	2.8	1	2	1	8	3	0	0	33	12	15	8
Georgia <sup>2</sup> .....	0	0	1	1	1.7	1	1	1	32	19	43	33
Florida <sup>2</sup> .....	0	0	0	1	0	0	1	0	0	0	13	5
<b>E. SO. CEN.</b>												
Kentucky.....	5	3	5	3	0	0	1	1	145	81	72	71
Tennessee.....	9	5	5	2	0	0	0	1	108	60	45	61
Alabama <sup>1</sup> .....	0	0	10	2	1.8	1	1	1	20	11	20	22
Mississippi <sup>2</sup> .....	0	0	4	1	2.6	1	1	1	54	21	9	17
<b>W. SO. CEN.</b>												
Arkansas.....	2.5	1	1	1	2.5	1	2	0	99	39	25	15
Louisiana <sup>1</sup> .....	2.4	1	0	0	0	0	2	1	61	25	15	15
Oklahoma.....	0	0	3	2	4	2	1	1	82	40	76	27
Texas <sup>2</sup> .....	0.8	1	6	1	0.8	1	3	0	96	114	99	122
<b>MOUNTAIN</b>												
Montana.....	0	0	0	0	0	0	1	0	300	31	23	37
Idaho.....	0	0	0	0	0	0	0	0	137	13	11	11
Wyoming.....	0	0	0	0	0	0	0	0	155	7	12	12
Colorado.....	5	1	0	0	0	0	0	0	136	28	43	66
New Mexico.....	0	0	2	0	0	0	0	0	346	28	15	20
Arizona.....	38	3	1	0	0	0	0	0	101	6	9	13
Utah <sup>2</sup> .....	0	0	0	0	0	0	0	0	352	35	96	37
<b>PACIFIC</b>												
Washington.....	3	1	1	1	0	0	0	3	182	58	35	44
Oregon.....	0	0	0	0	0	0	3	1	239	47	76	59
California <sup>1</sup> .....	3	4	3	3	0.8	1	5	7	189	223	172	252
Total.....	1.6	40	80	80	0.9	23	32	50	171	4,234	4,806	4,831
50 weeks.....	2.2	2,740	5,226	5,226	1.4	1,680	9,391	7,197	145	179,436	214,311	214,311

See footnotes at end of table.

*Cases of certain diseases reported by telegraph by State health officers for the week ended Dec. 17, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued*

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough		
	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37 median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37 median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases
<b>NEW ENG.</b>											
Maine.....	0	0	0	0	6	1	2	1	280	46	25
New Hampshire.....	0	0	0	0	0	0	1	1	0	0	9
Vermont.....	0	0	0	0	0	0	1	1	1,103	81	17
Massachusetts.....	0	0	0	0	1	1	4	3	266	228	217
Rhode Island.....	0	0	0	0	0	0	1	1	345	45	-----
Connecticut.....	0	0	0	0	3	1	1	1	258	88	43
<b>MID. ATL.</b>											
New York.....	0	0	0	0	4	9	6	9	254	632	375
New Jersey.....	0	0	0	0	1	1	3	3	552	460	152
Pennsylvania.....	0	0	0	0	4	8	12	20	236	460	320
<b>E. NO. CEN.</b>											
Ohio.....	1	1	2	2	10	13	1	4	167	216	64
Indiana.....	38	25	102	3	5	3	0	4	18	12	11
Illinois.....	4	6	28	3	5	8	1	6	327	404	73
Michigan <sup>1</sup> .....	3	3	0	0	8	7	4	10	294	272	179
Wisconsin.....	18	10	5	17	2	1	0	0	670	376	153
<b>W. NO. CEN.</b>											
Minnesota.....	75	38	21	6	6	3	0	0	24	12	30
Iowa.....	45	22	63	1	29	14	1	1	20	10	28
Missouri.....	9	7	2	2	4	3	5	2	12	9	22
North Dakota.....	37	5	7	4	15	2	0	0	30	4	44
South Dakota.....	15	2	3	6	8	1	0	0	0	0	35
Nebraska.....	15	4	0	2	0	0	0	1	8	2	1
Kansas.....	3	1	11	7	0	0	0	5	67	24	81
<b>SO. ATL.</b>											
Delaware.....	0	0	0	0	0	0	0	1	0	0	23
Maryland <sup>1,2</sup> .....	0	0	0	0	19	6	3	6	102	33	59
Dist. of Col. <sup>4</sup> .....	0	0	0	0	8	1	0	1	191	23	10
Virginia.....	0	0	0	0	0	0	2	12	119	62	67
West Virginia.....	0	0	0	0	3	1	1	5	67	24	44
North Carolina <sup>1</sup> .....	0	0	1	0	3	2	4	6	402	269	192
South Carolina.....	0	0	0	0	3	1	2	2	89	32	23
Georgia <sup>2</sup> .....	0	0	0	0	19	11	3	9	24	14	15
Florida <sup>3</sup> .....	0	0	0	0	3	1	7	3	0	0	6
<b>E. SO. CEN.</b>											
Kentucky.....	2	1	4	0	5	3	0	9	36	20	57
Tennessee.....	2	1	1	1	2	1	1	6	97	54	24
Alabama <sup>1</sup> .....	0	0	0	1	0	0	1	3	124	69	9
Mississippi <sup>1</sup> .....	0	0	1	1	18	7	0	1	-----	-----	-----
<b>W. SO. CEN.</b>											
Arkansas.....	5	2	1	1	10	4	2	5	25	10	19
Louisiana <sup>1</sup> .....	2	1	0	0	32	13	12	12	22	9	14
Oklahoma.....	16	8	0	0	4	2	1	7	8	4	16
Texas <sup>1</sup> .....	4	5	8	1	22	26	24	24	76	90	123
<b>MOUNTAIN</b>											
Montana.....	58	6	15	18	19	2	1	2	145	15	37
Idaho.....	53	5	20	1	0	0	0	0	0	0	6
Wyoming.....	22	1	11	2	0	0	0	0	44	2	14
Colorado.....	24	5	6	3	15	3	3	1	214	44	11
New Mexico.....	12	1	0	0	12	1	3	6	185	15	9
Arizona.....	13	1	0	0	0	0	0	1	63	5	16
Utah <sup>1</sup> .....	0	0	0	0	0	0	0	0	111	11	18

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Dec. 17, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough		
	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37 median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases	1933-37 median	Dec. 17, 1938, rate	Dec. 17, 1938, cases	Dec. 18, 1937, cases
<b>PACIFIC</b>											
Washington.....	6	2	12	12	0	0	0	1	47	15	87
Oregon.....	36	7	9	9	5	1	2	2	56	11	20
California <sup>1</sup> .....	3	4	14	8	1	1	13	13	88	104	308
Total.....	7	174	347	175	7	163	128	237	181	4,402	3,106
50 weeks.....	11	14,050	10,444	7,116	11	14,025	14,827	17,201	167	203,913	-----

<sup>1</sup> New York City only.

<sup>2</sup> Period ended earlier than Saturday.

<sup>3</sup> Typhus fever, week ended Dec. 17, 1938, 46 cases as follows: Maryland, 1; North Carolina, 2; Georgia, 12; Florida, 5; Alabama, 12; Louisiana, 1; Texas, 9; California, 4.

<sup>4</sup> Rocky Mountain spotted fever, week ended Dec. 17, 1938, District of Columbia, 1 case.

### 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	Menin- gitis, menin- gococ- cus	Diph- theria	Influ- enza	Ma- laria	Mea- sles	Pel- lagra	Polio- mye- litis	Scarlet fever	Small- pox	Ty- phoid and para- typoid fever
<i>September 1938</i>										
Puerto Rico.....	0	42	57	2,663	3	-----	0	0	0	20
<i>November 1938</i>										
Alabama.....	11	118	213	435	46	25	2	119	0	18
California.....	5	189	203	33	1,988	4	6	1,055	11	35
Georgia.....	2	140	114	134	54	40	4	125	1	23
Idaho.....	0	0	9	-----	171	-----	1	43	4	20
Maryland.....	1	41	22	2	181	2	0	121	0	18
Michigan.....	3	101	4	3	318	-----	5	1,616	33	22
Minnesota.....	2	36	7	-----	618	-----	1	367	28	7
New Jersey.....	2	40	36	-----	65	-----	3	281	0	7
New York.....	16	68	-----	12	1,164	-----	8	968	0	43
Pennsylvania.....	12	206	-----	4	236	1	19	1,018	0	62
Tennessee.....	9	118	129	52	24	18	2	246	1	19
Texas.....	1	330	765	297	-----	58	3	363	-----	103

<i>September 1938</i>		<i>November 1938—Continued</i>		<i>November 1938—Continued</i>	
	Cases		Cases		Cases
Puerto Rico:		Chickenpox:		Dysentery—Contd.	
Chickenpox.....	2	Alabama.....	93	Maryland.....	63
Dysentery.....	6	California.....	2,099	Michigan (amoebic)....	3
Hook worm disease.....	116	Georgia.....	75	Michigan (bacillary)....	57
Mumps.....	4	Idaho.....	71	Minnesota (amoebic)....	1
Ophthalmia neonato- rum.....	3	Maryland.....	179	Minnesota (bacillary)....	3
Fuerperal septicemia....	6	Michigan.....	1,686	New Jersey (bacillary)....	1
Tetanus.....	7	Minnesota.....	506	New York (amoebic)....	6
Tetanus, infantile.....	2	New Jersey.....	1,097	New York (bacillary)....	106
Whooping cough.....	92	New York.....	2,084	Pennsylvania (amoebic)	1
<i>November 1938</i>		Pennsylvania.....	3,857	Pennsylvania (bacil- lary).....	3
Actinomycosis:		Tennessee.....	206	Tennessee (amoebic)....	4
California.....	1	Diarrhea:		Tennessee (bacillary)....	9
Anthrax:		Maryland.....	63	Dysentery:	
New Jersey.....	1	Dysentery:		Alabama (amoebic)....	1
Pennsylvania.....	1	Alabama (amoebic)....	17	California (amoebic)....	77
Botulism:		California (bacillary)....	15	Georgia (amoebic).....	15
California.....	5	Georgia (amoebic).....	14	Georgia (bacillary)....	14
				Encephalitis, epidemic or lethargic:	
				Alabama.....	2
				California.....	12
				Michigan.....	1

Summary of monthly reports from States—Continued

November 1938—Continued		November 1938—Continued		November 1938—Continued	
Encephalitis, epidemic or lethargic—Continued.	Cases	Puerperal septicemia:	Cases	Trichinosis—continued.	Cases
New York	14	Tennessee	1	New York	3
Pennsylvania	4	Rabies in animals:		Pennsylvania	1
Texas	1	Alabama	31	Tularaemia:	
Food poisoning:		California	177	Alabama	1
California	77	Minnesota	10	California	3
German measles:		New Jersey	65	Georgia	2
California	115	New York <sup>1</sup>	10	Michigan	5
Idaho	1	Relapsing fever:		Minnesota	1
Maryland	11	California	2	New York	1
Michigan	38	Rocky Mountain spotted fever:		Pennsylvania	1
New Jersey	31	New Jersey	1	Typhus fever:	
New York	64	Scabies:		Alabama	25
Pennsylvania	32	Maryland	3	California	5
Tennessee	36	Septic sore throat:		Georgia	103
Granuloma, coccidioides:		California	25	Maryland	1
California	7	Georgia	38	New York	2
Hookworm disease:		Idaho	6	Undulant fever:	
Georgia	1,364	Maryland	25	Alabama	3
Impetigo contagiosa:		Michigan	5	California	26
Maryland	27	Minnesota	15	Georgia	1
Tennessee	13	New Jersey	9	Maryland	4
Jaundice, epidemic:		New York	73	Michigan	16
California	2	Tennessee	16	Minnesota	4
Maryland	6	Tetanus:		New Jersey	1
Michigan	4	Alabama	6	New York	17
Leprosy:		California	3	Pennsylvania	12
California	2	Georgia	1	Tennessee	1
Mumps:		Michigan	1	Vincent's infection:	
Alabama	21	Maryland	1	Maryland	6
California	2,099	Michigan	1	Michigan	12
Georgia	24	New Jersey	1	New York <sup>1</sup>	75
Idaho	18	New York	5	Tennessee	7
Maryland	135	Tennessee	2	Whooping cough:	
Michigan	211	Trachoma:		Alabama	143
New Jersey	242	California	55	California	650
Pennsylvania	1,645	Michigan	1	Georgia	30
Tennessee	46	Minnesota	1	Idaho	8
Ophthalmia neonatorum:		Pennsylvania	1	Maryland	136
California	1	Tennessee	2	Michigan	1,163
Maryland	1	Trichinosis:		Minnesota	191
New Jersey	22	California	3	New Jersey	1,243
New York <sup>1</sup>	9	Maryland	1	New York	2,477
Tennessee	1			Pennsylvania	1,489
				Tennessee	102

<sup>1</sup> Exclusive of New York City.

**PLAGUE INFECTION IN GROUND SQUIRRELS IN SAN BENITO COUNTY, CALIF.**

Under date of December 15, 1938, Doctor W. M. Dickie, Director of Public Health of California, reported plague infection proved in 10 *beecheyi* squirrels received at the laboratory December 11, 1938, from a ranch 6 miles north and 9 miles east of Hollister, San Benito County, Calif.

## CASES OF VENEREAL DISEASES REPORTED FOR OCTOBER 1938

These reports are published monthly for the information of health officers in order to furnish current data as to the prevalence of the venereal diseases. The figures are taken from reports received from State and city health officers. They are preliminary and are therefore subject to correction. It is hoped that the publication of these reports will stimulate more complete reporting of these diseases.

## Reports from States

	Syphilis		Gonorrhea	
	Cases reported during month	Monthly case rates per 10,000 population	Cases reported during month	Monthly case rates per 10,000 population
Alabama.....	1,978	6.83	290	1.00
Arizona.....	188	4.56	110	2.67
Arkansas.....	846	4.13	309	1.51
California.....	1,800	2.92	1,379	2.24
Colorado.....	115	1.07	90	.84
Connecticut.....	189	1.09	119	.68
Delaware.....	290	11.11	57	2.18
District of Columbia.....	579	9.23	460	7.34
Florida.....	813	4.87	78	.47
Georgia.....	2,877	9.33	464	1.50
Idaho.....	3,122	.45	11	.22
Illinois.....	3,192	4.05	1,548	1.96
Indiana.....	328	.94	105	.30
Iowa.....	265	1.04	163	.64
Kansas.....	169	.91	76	.41
Kentucky.....	744	2.55	288	.99
Louisiana.....	466	2.19	14	.07
Maine.....	35	.41	37	.43
Maryland.....	1,133	6.75	290	1.73
Massachusetts.....	400	.90	416	.94
Michigan.....	1,130	2.34	608	1.26
Minnesota.....	226	.85	187	.71
Mississippi.....	2,123	10.49	2,495	12.33
Missouri.....	858	2.15	136	.34
Montana.....	48	.89	20	.37
Nebraska.....	47	.34	72	.53
Nevada.....	21	2.08	10	.99
New Hampshire <sup>1</sup> .....				
New Jersey.....	908	2.09	280	.64
New Mexico.....	74	1.75	24	.57
New York.....	5,370	4.14	1,965	1.52
North Carolina.....	6,506	18.63	744	2.13
North Dakota.....	35	.50	33	.47
Ohio.....	2,336	3.47	373	.55
Oklahoma.....	477	1.87	348	1.37
Oregon.....	73	.71	185	1.80
Pennsylvania.....	1,615	1.59	164	.16
Rhode Island.....	109	1.60	58	.85
South Carolina <sup>1</sup> .....				
South Dakota.....	20	.29	30	.43
Tennessee.....	1,392	4.81	442	1.53
Texas.....	1,560	2.53	848	1.37
Utah.....	12	.23	22	.42
Vermont.....	21	.55	14	.37
Virginia.....	2,310	8.54	360	1.33
Washington.....	237	1.43	274	1.65
West Virginia.....	460	2.47	151	.81
Wisconsin.....	42	.14	101	.35
Wyoming.....	2	.09		
Total.....	44,441	3.50	16,248	1.28

## Reports from cities of 200,000 population or over

Akron, Ohio <sup>1</sup> .....				
Atlanta, Ga.....	268	8.93	87	2.90
Baltimore, Md.....	617	7.39	188	2.25
Birmingham, Ala.....	392	13.32	52	1.77
Boston, Mass.....	153	1.92	152	1.91
Buffalo, N. Y.....	112	1.86	44	.73
Chicago, Ill.....	2,186	5.96	1,064	2.90
Cincinnati, Ohio.....	234	4.95	90	1.90
Cleveland, Ohio.....	334	3.54	91	.96
Columbus, Ohio.....	45	1.44	11	.35

See footnotes at end of table.

Reports from cities of 200,000 population or over—Continued

	Syphilis		Gonorrhea	
	Cases reported during month	Monthly case rates per 10,000 population	Cases reported during month	Monthly case rates per 10,000 population
Dallas, Tex.....	226	7.44	124	4.08
Dayton, Ohio.....	58	2.62	0	.....
Denver, Colo.....	74	2.46	48	1.59
Detroit, Mich.....	577	3.18	293	1.61
Houston, Tex. <sup>1</sup> .....	.....	.....	.....	.....
Indianapolis, Ind.....	23	.60	34	.88
Jersey City, N. J.....	27	.83	10	.31
Kansas City, Mo.....	61	1.41	4	.09
Los Angeles, Calif. <sup>1</sup> .....	.....	.....	.....	.....
Louisville, Ky.....	71	2.09	253	7.46
Memphis, Tenn.....	325	11.13	70	2.40
Milwaukee, Wis. <sup>1</sup> .....	.....	.....	.....	.....
Minneapolis, Minn.....	71	1.42	69	1.38
Newark, N. J.....	325	7.15	180	3.96
New Orleans, La.....	16	.33	19	.39
New York, N. Y.....	3,968	5.30	1,416	1.89
Oakland, Calif.....	27	.86	26	.83
Omaha, Nebr.....	25	1.12	29	1.30
Philadelphia, Pa.....	470	2.34	.....	.....
Pittsburgh, Pa.....	286	4.06	24	.34
Portland, Oreg.....	48	1.50	86	2.68
Providence, R. I.....	53	2.04	25	.96
Rochester, N. Y.....	38	1.11	56	1.64
St. Louis, Mo.....	193	2.29	57	.98
St. Paul, Minn.....	39	1.36	21	.73
San Antonio, Tex.....	103	3.94	59	2.26
San Francisco, Calif.....	117	1.70	172	2.50
Seattle, Wash.....	120	3.10	164	4.24
Syracuse, N. Y.....	60	2.66	13	.58
Toledo, Ohio <sup>1</sup> .....	.....	.....	.....	.....
Washington, D. C.....	579	9.23	460	7.34

<sup>1</sup> No report for current month.

<sup>2</sup> Not reporting.

WEEKLY REPORTS FROM CITIES

City reports for week ended December 10, 1938

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	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Small-pox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
<b>Data for 90 cities:</b>											
5-year average.....	250	233	60	1,056	700	1,363	13	356	32	1,023	.....
Current week <sup>1</sup> .....	189	174	51	1,108	556	1,078	18	285	27	1,653	.....
<b>Maine:</b>											
Portland.....	0	.....	0	0	4	1	0	0	0	3	33
<b>New Hampshire:</b>											
Concord.....	0	.....	0	0	0	0	0	0	0	0	4
Manchester.....	0	.....	0	0	0	2	0	0	0	0	7
Nashua.....	0	.....	0	0	1	0	0	1	0	0	4
<b>Vermont:</b>											
Barre.....	0	.....	0	0	1	1	0	0	0	0	1
Burlington.....	0	.....	0	1	0	1	0	0	0	1	7
Rutland.....	0	.....	0	0	0	0	0	0	0	0	2
<b>Massachusetts:</b>											
Boston.....	0	.....	1	12	6	39	0	9	1	39	217
Fall River.....	0	.....	0	1	1	0	0	0	0	0	26
Springfield.....	0	.....	0	64	0	2	0	1	0	10	30
Worcester.....	2	.....	0	0	7	7	0	2	0	40	63
<b>Rhode Island:</b>											
Pawtucket.....	0	.....	0	0	0	1	0	0	0	13	16
Providence.....	0	.....	0	0	4	3	0	2	1	31	68
<b>Connecticut:</b>											
Bridgeport.....	1	.....	0	0	1	1	0	2	0	1	47
Hartford.....	0	.....	0	1	5	0	0	0	0	7	39
New Haven.....	1	.....	3	0	3	0	0	0	0	14	42

<sup>1</sup> Figures for South Bend, Ind., and Tacoma, Wash., estimated. Reports not received.

## City reports for week ended December 10, 1938—Continued

State and city	Diph- theria cases	Influenza		Meas- les cases	Pneu- monia deaths	Scar- let fever cases	Small- pox cases	Tuber- culosis deaths	Ty- phoid fever cases	Whoop- ing cough cases	Deaths, all causes
		Cases	Deaths								
New York:											
Buffalo.....	0		1	12	7	27	0	2	0	28	123
New York.....	32	14	3	31	71	79	0	60	6	194	1,491
Rochester.....	0	0	0	5	3	8	0	1	0	12	50
Syracuse.....	0		0	0	7	1	0	0	0	31	55
New Jersey:											
Camden.....	2		0	0	2	2	0	0	0	1	36
Newark.....	1	2	0	3	2	23	0	1	0	45	95
Trenton.....	1		0	0	2	5	0	0	0	3	39
Pennsylvania:											
Philadelphia.....	4	5	3	9	21	42	0	26	3	145	489
Pittsburgh.....	2	2	2	1	13	9	0	11	0	27	171
Reading.....	0		0	0	2	1	0	1	0	2	33
Scranton.....	1			0		10			0	19	
Ohio:											
Cincinnati.....	6	1	0	1	8	11	0	7	0	4	149
Cleveland.....	4	11	1	3	12	65	0	3	1	53	184
Columbus.....	8	2	2	1	2	8	0	3	0	4	81
Toledo.....	1		0	2	1	22	0	3	0	15	60
Indiana:											
Anderson.....	1		0	0	1	6	0	0	0	0	12
Fort Wayne.....	1		0	0	3	3	0	1	0	0	33
Indianapolis.....	6		2	8	15	34	12	1	0	7	109
Muncie.....	0		0	0	0	3	0	0	0	0	8
South Bend.....											
Terre Haute.....	5		0	1	0	2	0	0	0	0	27
Illinois:											
Alton.....	0		0	0	1	3	0	0	0	0	5
Chicago.....	16	5	3	17	45	150	0	35	3	393	780
Elgin.....	0		0	0	0	6	0	0	0	3	7
Moline.....	2		0	0	2	3	0	0	0	6	22
Springfield.....	0		0	0	4	1	0	0	0	0	22
Michigan:											
Detroit.....	12	3	2	6	16	139	0	7	1	147	270
Flint.....	1		0	32	5	36	0	0	0	2	31
Grand Rapids.....	0		1	4	1	21	0	1	0	6	30
Wisconsin:											
Kenosha.....	0		0	0	0	6	0	0	0	22	10
Madison.....	0		0	0	0	3	0	0	0	2	10
Milwaukee.....	1		0	7	7	50	0	1	1	147	107
Racine.....	0		0	1	0	1	0	0	0	7	16
Superior.....	0		0	0	0	3	0	0	0	0	10
Minnesota:											
Duluth.....	0		0	1	3	4	0	1	0	2	24
Minneapolis.....	0		0	66	9	11	0	0	0	13	108
St. Paul.....	0	1		85	16	24	0	0	0	12	65
Iowa:											
Cedar Rapids.....	0			0		0			12	0	
Davenport.....	1			0		6	1		0	0	
Des Moines.....	0		0	0	0	10	0	0	0	0	43
Sioux City.....	0			96		4			0	3	
Waterloo.....	5			0		14	1		0	0	
Missouri:											
Kansas City.....	3		1	5	15	28	1	2	0	3	116
St. Joseph.....	0		0	0	6	1	0	1	0	10	24
St. Louis.....	4	1	0	0	11	25	2	6	1	9	202
North Dakota:											
Fargo.....	0		0	130	3	1	0	0	0	0	11
Grand Forks.....	2			0		0			0	2	
Minot.....	0		0	19	0	0	0	0	0	0	6
South Dakota:											
Aberdeen.....	6			1		0			0	0	
Nebraska:											
Omaha.....	0		2	0	2	2	2	0	0	0	58
Kansas:											
Lawrence.....	0	9	0	0	0	3	0	0	0	0	5
Topeka.....	0	1	1	1	3	4	0	0	0	7	23
Wichita.....	1		0	0	6	7	0	1	0	0	35
Delaware:											
Wilmington.....	1		0	0	2	5	0	0	0	0	30
Maryland:											
Baltimore.....	5	3	1	63	18	9	0	10	0	24	223
Cumberland.....	0		0	0	0	1	0	0	0	4	13
Frederick.....	1		0	1	0	1	0	0	0	0	7
Dist. of Col.:											
Washington.....	9	4	1	1	12	7	0	10	0	20	181
Virginia:											
Lynchburg.....	2		0	1	1	0	0	1	0	6	8
Norfolk.....	0	3	0	0	5	2	0	1	0	1	20
Richmond.....	3		1	0	4	4	0	3	0	0	48
Roanoke.....	2		0	0	1	2	0	1	0	0	16

City reports for week ended December 10, 1938—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths all causes
		Cases	Deaths								
<b>West Virginia:</b>											
Charleston	1	1	0	1	2	3	0	0	0	0	13
Huntington	2			0		3	0	0	0	0	
Wheeling	0		1	0	1	1	0	0	0	6	21
<b>North Carolina:</b>											
Gastonia	0			0		0	0	0	0	0	
Raleigh	0	0	0	0	1	0	0	0	0	0	12
Wilmington	1	0	0	0	0	0	0	0	0	6	13
Winston-Salem	2		0	15	2	1	0	1	0	2	14
<b>South Carolina:</b>											
Charleston	1	36	0	0	6	3	0	0	0	0	22
Greenville	1	0	0	0	0	0	0	0	0	1	14
<b>Georgia:</b>											
Atlanta	0	21	3	0	9	6	0	1	1	0	74
Brunswick	1		0	1	0	0	0	1	0	0	4
Savannah	0	21	2	0	1	0	0	1	1	1	40
<b>Florida:</b>											
Miami	0		0	0	2	0	0	2	1	0	39
Tampa	2	1	1	1	2	1	0	0	0	2	26
<b>Kentucky:</b>											
Ashland	1		0	0	2	2	0	0	0	0	12
Covington	0		0	0	1	1	0	0	0	0	14
Lexington	0		0	0	3	0	0	2	0	0	22
Louisville	0	1	1	2	7	8	0	6	0	3	77
<b>Tennessee:</b>											
Knoxville	1	16	3	0	1	1	0	1	0	1	24
Memphis	3		3	1	8	6	0	3	0	3	86
Nashville	4	2	0	0	3	2	0	1	1	2	44
<b>Alabama:</b>											
Birmingham	1	4	0	0	3	9	0	6	0	0	69
Mobile	1		1	0	3	1	0	0	1	0	21
Montgomery	2			0		4	0		0	0	
<b>Arkansas:</b>											
Fort Smith	2	2		0		0	0		0	0	
Little Rock	1		0	0	6	3	0	2	0	0	9
<b>Louisiana:</b>											
Lake Charles	0		0	0	1	0	0	0	0	0	8
New Orleans	0	9	3	9	23	8	0	11	1	8	170
Shreveport	0		0	0	5	3	0	3	0	0	36
<b>Oklahoma:</b>											
Oklahoma City	0		0	3	2	5	0	0	0	0	53
Tulsa	1			0		6	0		0	0	
<b>Texas:</b>											
Dallas	4	1	1	0	8	7	0	3	0	0	71
Fort Worth	0		0	0	1	10	0	0	2	1	24
Galveston	0		0	0	3	4	0	2	1	0	19
Houston	8	1	0	0	5	4	0	3	0	0	78
San Antonio	1	2	3	1	10	0	0	5	1	0	79
<b>Montana:</b>											
Billings	0		0	4	1	0	0	0	0	0	13
Great Falls	0		0	1	1	0	0	0	0	0	5
Helena	0		0	0	0	0	0	0	0	0	6
Missoula	0		0	0	0	0	0	0	0	0	1
<b>Idaho:</b>											
Boise	0		0	0	0	0	0	0	0	0	10
<b>Colorado:</b>											
Colorado Springs	0		0	0	0	6	0	1	0	2	11
Denver	3		1	0	5	2	0	2	0	26	95
Pueblo	0		0	0	2	5	0	1	0	3	10
<b>New Mexico:</b>											
Albuquerque	0		0	0	2	0	0	1	0	0	15
<b>Utah:</b>											
Salt Lake City	1		0	4	3	9	0	1	0	1	40
<b>Washington:</b>											
Seattle	0		3	0	6	6	0	1	0	2	105
Spokane	0		0	2	2	2	0	0	1	0	30
Tacoma											
<b>Oregon:</b>											
Portland	0		0	3	4	7	1	1	0	0	58
Salem	0	3		0		3	0		0	0	
<b>California:</b>											
Los Angeles	16	16	0	12	24	55	0	15	0	33	423
Sacramento	1		0	3	2	1	1	1	1	4	23
San Francisco	1	1	0	476	16	13	0	8	1	13	177

## City reports for week ended December 10, 1938—Continued

State and city	Meningitis. meningococcus		Polio- mye- litis cases	State and city	Meningitis. meningococcus		Polio- mye- litis cases
	Cases	Deaths			Cases	Deaths	
Massachusetts:				Alabama:			
Worcester.....	2	1	0	Birmingham.....	1	0	2
New York:				Mobile.....	0	0	1
Buffalo.....	1	1	0	Louisiana:			
New York.....	0	0	2	New Orleans.....	1	0	0
New Jersey:				Colorado:			
Newark.....	1	0	0	Denver.....	0	1	0
Pennsylvania:				Oregon:			
Philadelphia.....	1	0	0	Portland.....	0	0	1
Missouri:				California:			
Kansas City.....	0	1	0	Los Angeles.....	1	0	0
South Carolina:				San Francisco.....	0	0	1
Charleston.....	0	0	2				
Tennessee:							
Nashville.....	1	0	0				

*Encephalitis, epidemic or lethargic.*—Cases: New York, 1; Minneapolis, 1; Topeka, 1; San Francisco, 2.

*Pellagra.*—Cases: Washington, 1; Charleston, S. C., 1; Atlanta, 7; Savannah, 1; San Francisco, 1.

*Typhus fever.*—Cases: Philadelphia, 1; Charleston, S. C., 1; Atlanta, 1; Savannah, 2; Nashville, 2; San Antonio, 1.

## FOREIGN AND INSULAR

### GERMANY

*Vital statistics—First half of 1938.*—Following are vital statistics for Germany for the first half of 1938:

	Number	Rate per 1,000 inhabitants		Number	Rate per 1,000 inhabitants
Marriages.....	333, 776	8. 8	Deaths.....	465, 479	12. 15
Live births.....	728, 530	20. 0	Deaths under 1 year of age.....	44, 798	16. 2
Still births.....	17, 861				

<sup>1</sup> Per 1,000 live births.

### GREAT BRITAIN

*England and Wales—Infectious diseases—13 weeks ended October 1, 1938.*—During the 13 weeks ended October 1, 1938, cases of certain infectious diseases were reported in England and Wales as follows:

Disease	Cases	Disease	Cases
Diphtheria.....	13, 488	Puerperal pyrexia.....	2, 228
Dysentery.....	419	Scarlet fever.....	19, 794
Ophthalmia neonatorum.....	1, 309	Smallpox.....	8
Pneumonia.....	5, 619	Typhoid fever.....	397

*England and Wales—Vital statistics—Third quarter 1938.*—During the third quarter ended September 30, 1938, 158,228 live births and 102,602 deaths were registered in England and Wales. The following statistics are 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 September 30, 1938*

Annual rates per 1,000 population:

Live births.....	15. 30
Stillbirths.....	0. 58
Deaths, all causes.....	9. 90
Deaths under 1 year of age.....	14. 1
Deaths from:	
Diarrhea and enteritis (under 2 years of age).....	15. 70
Diphtheria.....	.05
Influenza.....	.04
Measles.....	.01
Scarlet fever.....	.01
Typhoid fever and paratyphoid fever.....	.00
Whooping cough.....	.01

<sup>1</sup> Per 1,000 live births.

## YUGOSLAVIA

*Communicable diseases—4 weeks ended November 6, 1938.*—During the 4 weeks ended November 6, 1938, certain communicable diseases were reported in Yugoslavia as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Anthrax.....	41	4	Paratyphoid fever.....	25	-----
Cerebrospinal meningitis.....	11	4	Poliomyelitis.....	17	3
Diphtheria and croup.....	932	58	Scarlet fever.....	404	3
Dysentery.....	117	14	Sepsis.....	12	5
Erysipelas.....	257	9	Tetanus.....	46	20
Favus.....	8	-----	Typhoid fever.....	703	50
Measles.....	1	-----	Typhus fever.....	5	-----



Bombay Presidency.....	22	154	767	1,223	394	452	378	254	248	267	391	330	270	324			
Bombay.....	9	81	277	749	174	213	196	101	126	95	161	141	140	136			
Calcutta.....	436	144	144	70	23	19	26	22	7	39	24	21	23	20	34	41	41
Coimbatore.....	15	88	202	101	15	7	8	1	1	1	1	1					
Madras.....	6	33	46	34	5	3											
Central Provinces and Berar.....	5,640	6,878	14,427	27,968	8,884	5,486	5,395	4,620	3,463	1,670	1,455	862	678	418	391	240	
Chittagong.....	2	1	2	3													
Delhi.....	74	64	14	1													
Howrah.....	187	127	156	103	32	15	40	50	26	28	37	25					
Jodhpur.....	3																
Madras Presidency.....	802	1,160	3,013	1,998	410	528	493	411	525	403	370	212					
Madras.....	352	477	1,601	860	170	188	213	160	228	190	153	100					
Madras.....	1	2	3	2		1		1			1	1	1	1	2	2	
Megapatam.....																	
Northwest Frontier Province.....	284	555	419	468	27	32	2	53	12	6	6	2					
Orissa Province.....	425	332	223	52	0	3		3	3	1	6	8	15		1	1	
Gopalpur.....																	
Punjab.....	2,319	673	542	88	8	6	1										
Rangoon.....	1	1						1		1							
Sind State.....	57	242	221	61	1												
India (French):.....																	
Chandernagor Territory.....		11	8					1							1		
Karikal Territory.....																	
Pondichery Province.....		2									3						
Yanaon.....			2														
India (Portuguese): Damao.....								7									
Indochina (French):.....																	
Annam Province.....	615	698	923	440	84	1						7					
Tonkin Province.....	1,669	1,383	461	23	7					61	15	1					
Hanoi.....	1,193	82	34	4													
Japan:.....																	
Fukuoka Prefecture—Wakamatsu.....			2							3							
Hiroshima Prefecture—Fukuyama.....			8							3							
Okayama Prefecture.....			4														

On vessels:—Continued

S. S. *Kverfyng* at Bangkok from Swatow and Hong Kong. 1 case. Aug. 5, 1938  
 S. S. *Kikkawa Maru* at Fukuoka from Shanghai. 57 cases. July 26, 1938  
 S. S. *Mau Sang* at Hong Kong from Sandakan. 1 case. July 16, 1938

On vessels: S. S. *Tak Sang* at Hong Kong from Shanghai and Swatow. 1 case. June 5, 1938S. S. *Kikkawa Maru* at Fukuoka from Shanghai. 57 cases. July 26, 1938S. S. *Mau Sang* at Hong Kong from Sandakan. 1 case. July 16, 1938

Cholera also reported present early in June in South Afghanistan, Afghanistan.

\* Information dated Nov. 30, 1938, stated that cholera had appeared in villages near Yunnanfu, China. In one village of approximately 1,000 persons, 500 were said to have died.

† Imported.

**CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued**

**PLAGUE<sup>1</sup>**

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

Place	Week ended—												
	September 1938			October 1938			November 1938						
	3	10	17	24	1	8	15	22	29	5	12	19	26
Argentina. (See table below.)													
Belgian Congo.....	C	3	2	3									
Bolivia (see also table below):													
Santa Cruz Department.....	C		10										
Tarifa Department.....	C		98										
Brazil. (See table below.):													
British East Africa:													
Kenya.....	C	10	4	9	1	1	1	1	1	1	1	1	1
Uganda.....	C	17	19	89	45	19	9	23	16	15	14	4	9
British East Africa:	D	16	17	61	44	20	9	23	16	15	14	4	8
Ceylon:													
Colombo.....	C	4	1	1	1	1	1	1	1	1	1	1	1
Plague-infected rats.....	D	4	1	1	2								
China, <sup>1</sup>													
Dutch East Indies:	C	130	135	157	120	25	34	32					
Java and Madura.....	D	128	135	157	120	25	34	32					
Ecuador:													
Guayaquil.....	C	2		1							1	1	
Plague-infected rats.....	D	1									1	3	
Egypt: Asyut Province.....	C	7											
Hawaii Territory: Plague-infected rats:													
Hawaii Island—Haleakala District:													
Hanalei Mill Sector.....										1	5		
Paeonian Sector.....													
India.....													
Bassein.....	C	218	68	488	1								8
Bombay Presidency.....	D	224	32	275	400	315	302	330	450	320	606	351	512
Central Provinces and Berar.....	C	4	2	4	96	135	146	121	200	182	211	157	225
Bombay Presidency.....	D	0	2	2	49	27	11	31	21	12	13	13	47
Central Provinces and Berar.....	D	0	11	27	13	4	19	8	20	6	4	8	22
Bombay Presidency.....	D	0	9	14	27	13	4	19	8	6	4	8	15
Central Provinces and Berar.....	C	42	1	126	109	119	68	116	160	46	144	73	155

	C	D	1	2	3	4	1	2	3	4	1	2
Cochin.....			1	2	3	4	1	2	3	4	1	2
Plague-infected rats.....			2	30	49	55	62	110	86		2	1
Madras Presidency.....		24	61	21	22	32	27	42	31		2	1
C.....		15	97	13	22	32	27	42	31		2	1
D.....			1		2							
Bangoon.....			1		2							
C.....			1		2							
D.....												
Madagascar. (See table below.)												
Peru. (See table below.)												
Senegal: At Four subdivision.....		1										
Tunisia: Tunis.....												
C.....												
D.....												
Union of South Africa (see also table below)												
C.....		21				2						
D.....												
Cape Providence—Fort Elizabeth.....												
C.....												
D.....												
United States:†												

Place	May 1938	June 1938	July 1938	August 1938	September 1938	October 1938	Place	May 1938	June 1938	July 1938	August 1938	September 1938	October 1938
Argentina: Salta Province.....				1	1		Peru	1		1	4	7	6
Bolivia (see also table above).....		4	6	4	103		Libertad Department.....				1	1	
Brasil:							Lima Department.....					3	6
Ceara State.....	1			4			Union of South Africa.....			1			
Fernambuco State.....	16	5	22	53	60		Cape Province.....	19					
Madagascar (central region).....	13	5	20	51	60		Orange Free State.....	7	5				

† Including plague in the United States and its possessions.  
 † According to information dated Aug. 12, 1938, 23 deaths from plague occurred in Kirin Province, China, up to Aug. 10, 1938, and 16 deaths from plague occurred in South Hin-An Province from July 28 to Aug. 8. Information dated Aug. 25, 1938, states that 17 cases of plague had occurred in South Hsingan Province and that 10 cases of plague with 10 deaths were reported in Northern Kirin Provinces between July 29 and Aug. 10.  
 ‡ 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 insect hosts are published currently in the Public Health Reports. The following summarizes recent reports for 1938: *Arizona*.—Insects, Sept. 27; *California*.—Ground squirrels, May, June, July, August, October, Dec. 11; insects, May, June, July, August, Oct. 12, 26; *Idaho*.—Ground squirrels, May, June, insects, May, June, July; *Montana*.—Ground squirrels, June; insects, May, June, *New Mexico*.—Prairie dogs, August, September, insects, August, September; *Oregon*.—Ground squirrels, May, insects, May; *Utah*.—Ground squirrels, June; insects, May, July; *Wyoming*.—Ground squirrels, June, July; insects, June, July, August.  
 † For the period Sept. 8 to Oct. 7.







Place	May 1933	June 1933	July 1933	August 1933	September 1933	October 1933	Place	May 1933	June 1933	July 1933	August 1933	September 1933	October 1933
Angola.....	13		35	62			Mexico (see also table above)—Con-	4					
Belgian Congo.....	251		292	163	185		tr. Chihuahua State—Ciudad Ju-						
Bolivia.....							rez. Coahuila State—Piedras Ne-						
Chuhambaba Department.....	5	4	2	32	41		bras. Mexico, D. F.....	1			1	2	
Chuquisaca Department.....	6	5	5	32	46		Michoacan State.....	10					
La Paz Department.....	1			27	44		Nuevo Leon State—Monter-	5					
Oruro Department.....	1	4	2				rey. Queretaro State.....	4			3		
Potosi Department.....	1	1	5	18	17		San Luis Potosi State.....	1			16	3	
Santa Cruz Department.....	1						Sonora State.....				1		
Tarija Department.....	1						Morocco.....	46	3	4	1	78	
Chosen (Korea).....	8	226	124	68	60	3	Portugal (see also table above).....	3	2		4	3	1
Colombia.....							Salvador.....						
Guaymas and vicinity.....							Union of South Africa:						
France.....							Cape Province.....				1	1	
Guinea.....	2				1		Natal.....				25	1	
Greece.....	3	4	5				Orange Free State.....				1	18	
Hainan.....							Transvaal.....		2	2	33		
Indochina (French) (see also table above).....							Uruguay—Montevideo.....	8	5	3			
Ivory Coast.....	511	409	409	206	113	166	Venezuela.....				3	3	1
Mexico (see also table above):	90	89	89	48	35	25							
Aguascalientes State—Aguasca-				10									
lientes.....	1				2								

1 For the period Aug. 1 to Sept. 7, 1933.

2 For the period Sept. 8 to Oct. 7, 1933.

3 For 3 months.





CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

TYPHUS FEVER—Continued

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

Place	May 1938	June 1938	July 1938	August 1938	September 1938	October 1938	Place	May 1938	June 1938	July 1938	August 1938	September 1938	October 1938
Belgium; Brussels.....					2		Mexico (see also table above)— Continued.....						
Bolivia.....	C						Hidalgo State.....	C			4	1	
Cochabamba Department.....	4	8	1	1			Mexico State.....		7			4	
La Paz Department.....	17	2	2	11	16		Mexico D. F.....	C	5		5	10	
La Paz.....		6	2	11	21		Queretaro State.....	C			1	1	
Oruro Department.....	8	4	3	17			San Luis Potosi State.....	C	2				
Potosi Department.....	9	4	1	2	5		Morocco (see also table above).....	1,264					
China; Manchuria—Harbin.....	9		22	1	12	2	Portugal.....	222	35	3	3	2	
Chosen (Korea).....	65			3			Rumania.....	22	6	10	5	8	
Ozobdovakia.....	1				4		Turkey.....	38	6	12	4	17	13
Greece.....							Latvian.....	3		4		5	2
Gustamala.....	2	11	108	20	6	3	Union of South Africa.....						
Latvia.....							Cape Provinces.....	4	37	98	62	165	
Lithuania.....	25	3	1				Natal.....				1	4	
Mexico (see also table above):.....							Orange Free State.....	2	2	10		7	
Agua Calientes State.....	3						Transvaal.....	3			1		
Guanajuato State.....	3												

1 For the period Aug. 1 to Sept. 7, 1938.

2 For the period Sept. 8 to Oct. 7, 1938.

