EXPERIMENTAL STUDIES ON ENCEPHALITIS

I. Transmission of St. Louis and Kansas City Encephalitis to Mice*

By LESLIE T. WEBSTER, M.D., and GEORGE L. FITE, M.D.

(From the Laboratories of The Rockefeller Institute for Medical Research)

Plate 2

(Received for publication, November 3, 1934)

An outbreak of encephalitis during August and September, 1933, in Missouri, centering in St. Louis where about 1,000 persons were affected, furnished an unusual opportunity for experimental studies on the nature of the disease. Attempts to transmit the encephalitis to laboratory animals were made promptly in St. Louis by Muckenfuss, Armstrong, and McCordock. Shortly after, the writers became interested in the possibility of transmitting the disease to a special breed of mice (1) which had proved highly susceptible to a virus associated with an encephalitis of sheep—louping ill (2). Consequently Dr. R. A. Muckenfuss was asked for sterile brain tissue from fatal cases in St. Louis and later a request for similar tissue from fatal cases in Kansas City was made to Dr. P. Stookey. They collected and generously sent us material, enabling inoculations to be begun September 1, 1933.

In November, 1933, Muckenfuss, Armstrong, and McCordock reported that a condition similar to the St. Louis disease had been transmitted to *Macacus rhesus* monkeys and maintained successfully for five passages (3). Following this, Webster and Fite reported that the encephalitis in both St. Louis and Kansas City was communicable by inoculation to mice, that the infectious agent was filtrable, highly virulent when instilled into the nasal passages of mice, and was neutralized by the serum of encephalitis convalescents from the 1933 epidemic but not by the serum of non-contacts (4). Further notes on the

* The writers gratefully acknowledge the aid of Dr. T. M. Rivers, both critical and suggestive, during the course of the work.

differentiation of the disease on an etiological basis (5, 6), on the presence of the disease in Paris, Illinois, in 1932 (5), and in New York in 1933 (5), and on the immunological properties of the virus (7) have been made by Webster and Fite; and reports of clinical and epidemiological data have been published by Hempelmann (8), Leake (9), and Bredeck (10). The aim of the present series of papers is to elaborate the preliminary reports from this laboratory and describe further experiments in detail.

Materials and Methods

The unusual feature in the technique of these experiments was the use of white-face, R. I. R., and Swiss mice. These specially bred animals have been described elsewhere in studies on inherited susceptibility and resistance to infectious diseases (1). They were reared in a breeding room in which environmental and dietary factors are uniform and in which no infectious diseases occurred. The mice had already proved highly susceptible to the neurotropic virus of sheep encephalitis, louping ill, developing a characteristic encephalitis (2) when inoculated either directly into the brain or into the nares. One strain of mice, the white-face, had proved equally susceptible to every microorganism and virus thus far tested,—*B. enteritidis*, *B. aertrycke*, *Pasteurella aviseptica*, *B. friedlaenderi*, pneumococcus, and louping ill virus. This, together with the Swiss strain, was therefore chosen for the present experiments.

Brain tissue from cortex, midbrain, and medulla was removed as soon as possible after the death of the patient, placed in 50 per cent glycerine and mailed to this laboratory where it was kept at +4°C. until tested. For injection about 2 gm. of tissue from different areas was placed in a mortar, ground with sterile alundum for 10 minutes, taken up in 0.85 per cent salt solution to make a 10 per cent suspension, and tested for anaerobic and aerobic bacteria. Intracerebral injections into the mice were made with a 0.25 cc. tuberculin syringe and short No. 26 gauge needles. The mice were anesthetized lightly and given the inoculum into the brain through the skull, lateral to the mid-dorsal line and posterior to the eye. They were then placed one to five per cage and observed for 21 days. Signs of disease were looked for daily; prostrate or dead animals were examined at once or kept at +4°C.

Transmission Experiments in Mice (Text-Fig. 1)

Specimen 1.—Brain tissue from a female patient aged 20 years who died at St. Louis City Isolation Hospital Aug. 21, 1933. Anatomical diagnosis: Encephalitis.[1] The first inoculation of tissue was made Sept. 1, 1933, into two white-

[1] We are indebted to Drs. Muckenfuss and McCordock for fixed tissue from, and histological diagnosis of the cases of encephalitis from St. Louis, and to Dr. Stookey for fixed tissue for microscopic study from the Kansas City cases.

face and two Swiss mice. All survived and were healthy after 21 days. A second inoculation was made Sept. 20 into two Swiss and two R. I. R. mice and a third inoculation Oct. 5 into four Swiss mice. All eight mice were living and well after 21 days.

Specimen 2.—Brain tissue from a female patient aged 67 years who died at St. Louis City Isolation Hospital Aug. 28, 1933. Anatomical diagnosis: Encephalitis. The first inoculation was made Sept. 1, 1933, into two white-face and two Swiss mice, a second inoculation Sept. 20 into two Swiss and two R. I. R. mice, and a third and fourth inoculation Oct. 5 and Oct. 19 into four Swiss and four white-face mice respectively. All sixteen mice remained well throughout the 21 day period of observation.

Specimen 3.—Brain tissue from a female patient who died at St. Louis City Isolation Hospital Aug. 25, 1933. Anatomical diagnosis: Encephalitis. The first inoculation of tissue was made Sept. 1, 1933, into two white-face and two Swiss mice. The mice remained well and active for 4 days. One white-face mouse was hyperesthetic and tremorous on the 5th day and dead on the 6th day. The second white-face mouse had convulsions on the 6th day and was killed. One Swiss mouse was dead on the 6th day; the other Swiss mouse remained healthy. Brains from the two white-face mice were removed aseptically, emulsified, suspended in saline, cultured, and diluted as before. Each suspension was then given intracerebrally to two white-face and two Swiss mice Sept. 9. After a 3 day healthy period, the mice developed hyperesthesia, tremors, convulsions, became prostrate and died on the 4th or 5th days. Brains from one of these white-face and one of these Swiss mice were removed, prepared and injected Sept. 14 each into white-face and Swiss mice. Mice receiving the brain emulsion from the white-face mouse died in 4, 4, 4, 4, 3, 4, 4, 4 days respectively, while those receiving the brain emulsion from the Swiss mouse died in 6, 7, 8, 8, 9, 6, 6, 6, 7, 8 days. Further passages of this Strain 3 at 4 to 7 day intervals to the number of about 50 have now been made. No changes in its behavior have been noted. A second inoculation from the original human material was made Sept. 11 into two white-face and two Swiss mice. The Swiss mice died with characteristic signs on the 7th day, the white-face mice on the 11th and 16th days. The brain from one of the Swiss mice was prepared and injected Sept. 20 into one Swiss and two R. I. R. mice. All died on the 5th day. A third attempt to transmit the disease from the human material was made Oct. 5. Four Swiss mice were injected but all remained healthy.

Specimen 4.—Brain tissue from a male patient aged 3 years who died at the Children's Hospital, St. Louis, Aug. 21, 1933. Anatomical diagnosis: Encephalitis. The first inoculation was made Sept. 1, 1933, into two white-face and two Swiss mice. One white-face mouse, A, was well until the 6th day at which time it developed convulsions and was killed. The second white-face mouse, B, was well until the 9th day when it was found to be prostrate and was killed. The two Swiss mice remained well during the 21 day period of observation. Brains of the two white-face mice were removed and emulsions prepared for the second

passage. The emulsion from the white-face Mouse A was injected into two white-face and two Swiss mice on Sept. 9; the brain emulsion from the other white-face Mouse B was injected similarly on Sept. 14. Mice receiving the A emulsion died on the 4th day. A brain from one of these white-face mice was emulsified and injected into two white-face and two Swiss mice on Sept. 14. These mice died on the 3rd, 3rd, 3rd, and 4th days following injection. A brain from one second passage Swiss mouse was treated similarly and injected into three white-face and three Swiss mice on Sept. 14. Two of the inoculated white-face mice died on the 8th day; the other survived. The three Swiss mice died on the 6th, 6th, and 7th days respectively. A brain emulsion of the first passage white-face Mouse B was given to two Swiss and two white-face mice on Sept. 14. They died on the 5th, 6th, 8th, and 8th days respectively. The brain from one Swiss mouse was given to two R. I. R. and two Swiss mice on Sept. 20. These third passage mice died with characteristic signs on the 5th, 6th, 5th, and 5th days respectively. The material was then stored in 50 per cent glycerine until Nov. 9, when a fourth passage was made. Fifth to tenth passages were then made with fresh tissue and the material was again stored in glycerine on Jan. 5, 1934. The results were consistent and similar in every way to those obtained with Strain 3. A second successful attempt to transmit the disease from the human material to mice was made Sept. 11, 1933, at which time two white-face and two Swiss mice were injected. One white-face mouse and one Swiss mouse died on the 6th day; the other two remained healthy 21 days. From the brain of the white-face mouse an emulsion was made and injected into two R. I. R. mice and 1 Swiss mouse. These died promptly on the 5th day with characteristic signs of encephalitis. A third attempt to transmit the disease from the human material was made on Oct. 5 when four Swiss mice were injected, and a fourth attempt on Oct. 19 when four white-face mice were injected. All remained alive and well 21 days.

Specimen 5.—Brain tissue from a male patient who died at Deaconess Hospital, St. Louis, Sept. 1, 1933. Anatomical diagnosis: Encephalitis. The first inoculation was made September 6, 1933, into two white-face and two Swiss mice. One Swiss mouse was found prostrate and was sacrificed on the 8th day; the others remained well. A second passage was made from the brain of the positive mouse into two Swiss mice and one R. I. R. mouse on Sept. 20. They died on the 5th, 5th, and 6th days respectively. An emulsion for third passage was made from the brain of one of the Swiss mice and injected into four Swiss and four R. I. R. mice on Sept. 27. They died on the 5th, 5th, 5th, 6th, 4th, 5th, 5th, and 6th days respectively with typical signs of encephalitis. The material was then stored in glycerine until Nov. 9 when a fourth passage was made. Fifth to ninth passages were then made in rapid succession and the ninth passage material was again stored in glycerine. The results of these passages were similar in every way to previous tests with this Strain 5 and with Strains 3 and 4. Three additional unsuccessful attempts to transmit the disease from the human material to mice were made on Oct. 5 at which time four Swiss mice were injected, on Oct. 19

four white-face mice, and on Nov. 23 four Swiss mice. All animals remained well during the 21 day period of observation.

Specimen 6.—Brain tissue from a female patient aged 63 who died at St. Louis City Isolation Hospital Sept. 2, 1933. Anatomical diagnosis: Encephalitis. Four unsuccessful attempts were made to get positive results in mice with this material. On Sept. 6, 1933, two white-face and two Swiss were injected; on Sept. 20 two Swiss and two R. I. R.; on Oct. 5 four Swiss; and on Oct. 19 four white-face mice. All survived and were well during the period of observation.

Specimen 7.—Brain tissue from a female patient aged 75 who died at St. Louis County Hospital Aug. 29, 1933. Anatomical diagnosis: Encephalitis. Four unsuccessful attempts were made with this specimen at the same time and in the same manner as in the case of Specimen 6. All sixteen injected mice remained well.

Specimen 8.—Brain tissue from a male patient aged 73 who died at De Paul Hospital, St. Louis, Aug. 30, 1933. Anatomical diagnosis: Encephalitis. The first inoculation was made Sept. 8, 1933, into four white-face and four Swiss mice. One white-face mouse died on the 9th day and one Swiss mouse on the 11th day. The six remaining mice continued well throughout the 21 day period of observation. The brain from the Swiss mouse was prepared and injected into two R. I. R. and two Swiss mice. These second passage animals died on the 5th day. Brains from two of these animals were placed in glycerine and not tested until Nov. 9 and again on Nov. 15. The five injected animals remained well and no further attempts to recover the virus from the second passage material were made. The original human material was tested again, on Oct. 5, Oct. 19, and Nov. 23 by injecting four Swiss, four white-face, and four Swiss mice respectively. All remained well during the 21 day period.

Specimen 9.—Brain tissue from a female patient aged 70 who died at the Jewish Hospital, Kansas City, Sept. 25, 1933. Anatomical diagnosis: Encephalitis. Four unsuccessful attempts were made with this material to transmit the disease to mice. On Sept. 28, 1933, four Swiss mice were inoculated; on Oct. 6 four Swiss mice; on Oct. 19 four white-face mice; on Nov. 13 four white-face mice. All remained well and were discarded 18 days after the injection was made.

Specimen 11.—Brain tissue from a male patient aged 70 who died at the General Hospital, Kansas City, Oct. 5, 1933. Clinical diagnosis: Encephalitis.[2] The first transmission experiment was made Oct. 9, 1933, by injecting four Swiss mice. All remained healthy during the 21 day period of observation. A second attempt was made with the human tissue on Oct. 19 by injecting four white-face mice. One with convulsions and later prostrate on the 8th day was killed and its brain prepared and injected Oct. 29 into two white-face and two Swiss mice. The other three white-face mice remained well. The second passage mice were all

[2] No record of histological study of brain tissue from this case has been located.

dead on the 3rd day. The brains from one white-face and one Swiss mouse were pooled and injected Nov. 4 into three Swiss mice. They were all dead on the 4th day. A fourth and fifth passage were made in Swiss mice Nov. 9 and Nov. 15. All died in 3 to 5 days. Brains of the fifth passage mice were preserved in glycerine until Dec. 16 when the sixth to ninth passages were made. This strain from Kansas City behaved in every way like the St. Louis strains and gave rise in the injected mice to the typical signs of encephalitis. A third attempt with the original human material was made Nov. 3. Four white-face mice were injected and one was prostrate and one was dead on the 6th day. The prostrate mouse was sacrificed, its brain removed and injected Nov. 10 into three Swiss mice. These were all dead on the 5th day. Their brains were removed and stored in glycerine.

Specimen 12.—Brain tissue from a female patient aged 68 who died at the De Paul Hospital, St. Louis, Sept. 3, 1933. Anatomical diagnosis: Encephalitis. One transmission experiment was made Oct. 16, 1933, by inoculating four white-face mice. The mice remained well.

Specimen 13.—Brain tissue from female patient who died at the Jewish Hospital, St. Louis, Sept. 3, 1933. Anatomical diagnosis: Encephalitis. One attempt to transmit the disease was made with this specimen on Oct. 16, 1933. Four white-face mice were injected but none showed any sign of disease for the 21 days following.

Specimen 14.—Brain tissue from male patient aged 65 who died at St. Louis County Hospital Sept. 6, 1933. Anatomical diagnosis: Encephalitis. One injection of the brain tissue was made on Oct. 16, 1933, into four white-face mice. All remained well.

Specimen 15.—Brain tissue from male patient aged 80 years who died at the St. Louis County Hospital Sept. 10, 1933. Anatomical diagnosis: Encephalitis. One injection of tissue into four white-face mice was made Oct. 16, 1933, with negative results.

Specimen 16.—Brain tissue from a female patient aged 75 who died at Barnes Hospital, St. Louis, Sept. 14, 1933. Anatomical diagnosis: Encephalitis. An injection of this material was made Oct. 16, 1933, into four white-face mice. Three remained well, but one, with tremors and convulsions on the 8th day, was sacrificed. Its brain, prepared and injected Oct. 25 into two white-face and two Swiss mice, was fatal to all four on the 4th day. Brains from these mice were pooled and a third passage made Oct. 30 into two white-face and two Swiss mice. All were in convulsions or prostrate on the 4th day. A fourth passage, Nov. 4, fifth passage, Nov. 8, and sixth passage, Nov. 15, were made successfully and the material preserved in glycerine. This strain behaved in every way like the others.

Specimen 17.—Brain tissue from male patient aged 65 years who died at the Jewish Hospital, St. Louis, Sept. 4, 1933. Anatomical diagnosis: Encephalitis. One injection of this material was made Oct. 16, 1933, into four white-face mice. All remained well during the 21 day period of observation.

Specimen 18.—Brain tissue from male patient aged 23 years who died at the Deaconess Hospital, Sept. 13, 1933. Anatomical diagnosis: Encephalitis. One attempt to transmit the disease with this specimen was made Oct. 16, 1933, in four white-face mice. The result was negative.

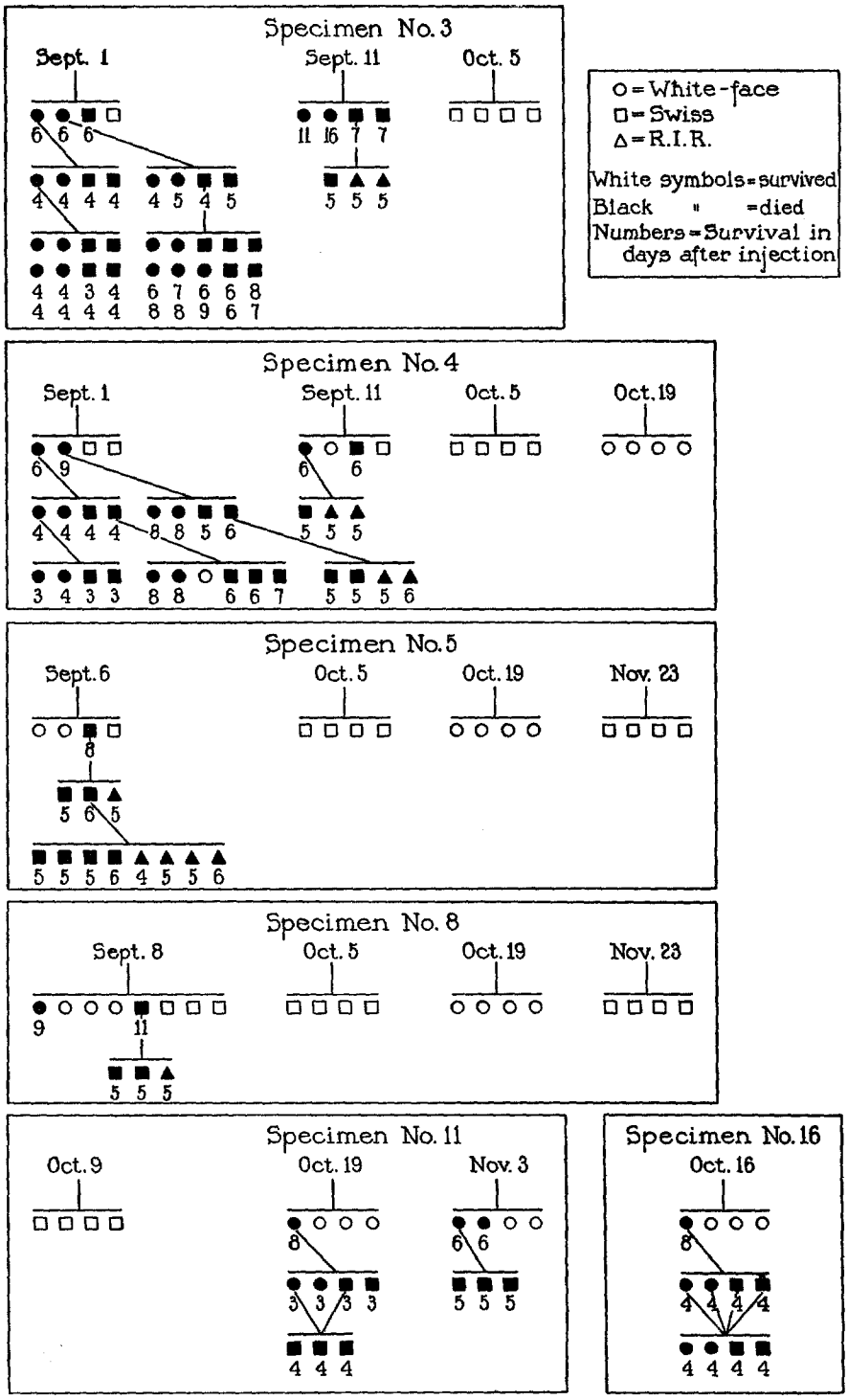
Specimen 19.—Brain tissue from male patient who died at the De Paul Hospital, St. Louis, on or about Sept. 15, 1933. Anatomical diagnosis: Encephalitis. One injection of this material Oct. 16, 1933, into four white-face mice was without effect.

Specimen 20.—Brain tissue from male patient aged 74 who died at St. Margaret's Hospital, Kansas City, Oct. 11, 1933. Anatomical diagnosis: Encephalitis. Two attempts were made to transmit the disease with this material, one on Oct. 14, 1933, when four Swiss mice were injected, and one on Oct. 19 when four white-face mice were injected. All of the animals remained healthy throughout the 3 week period of observation.

The experiments showed that brain tissue from clinical cases of encephalitis, with histological lesions characteristic of the disease, and free of bacteria, when injected intracerebrally into mice of special strains, gave rise in them to a characteristic picture of encephalitis. After an incubation period of 5 to 10 days, hyperesthesia and tremors were noted, progressing to convulsions, prostration, and death in 6 to 12 days. This encephalitis was reproduced in mice in series by injecting emulsions of bacteriologically sterile brain from the sick mice into the brains of normal mice (Text-fig. 1). No change in the clinical disease took place on passage except that the incubation period was soon shortened to 3 to 4 days and the duration of life to 4 to 6 days. Five of eleven specimens tested within 14 days of the death of the patient were positive—45 per cent (Table I). Retests of these were positive until the 29th day but were negative thereafter. One of three specimens was positive when first tested 32 to 36 days after the death of the patient; five not tested until the 36th to 43rd day were negative. Apparently the encephalitis-producing activity of the human tissue when preserved in glycerine is limited to about 32 days (Table I). Finally, the five active specimens from St. Louis cases and the one from Kansas City were identical in so far as could be determined in their effects on the mice.

Pathology of Encephalitis in Mice

Lesions in mice prostrate or dying of the disease were apparently limited to the central nervous system. Mononuclear leucocytes were



TEXT-FIG. 1. Successful transmission and maintenance of encephalitis (St. Louis and Kansas City) in mice.

TABLE I

Survival of Virus in Human Brain Tissue from Fatal Cases of Encephalitis (St. Louis and Kansas City)

Specimen No.	Date of death of patient	Date of inoculation of tissue	Interval between patient's death and inoculation of tissue	Results of inoculation
	1933	*1933*	*days*	
1	Aug. 21	Sept. 1	11	0
		" 20	30	0
		Oct. 5	45	0
2	" 28	Sept. 1	4	0
		" 20	23	0
		Oct. 5	38	0
		" 19	52	0
3	" 25	Sept. 1	7	+
		" 11	17	+
		Oct. 5	44	0
4	" 21	Sept. 1	11	+
		" 11	21	+
		Oct. 5	45	0
		" 19	59	0
5	Sept. 1	Sept. 6	5	+
		Oct. 5	29	0
		" 19	43	0
		Nov. 23	77	0
6	" 2	Sept. 6	4	0
		" 20	18	0
		Oct. 5	33	0
		" 19	47	0
7	Aug. 29	Sept. 6	8	0
		" 20	22	0
		Oct. 5	37	0
		" 19	51	0
8	" 30	Sept. 8	9	+
		Oct. 5	27	0
		" 19	41	0
		Nov. 23	76	0
9	Sept. 25	Sept. 28	3	0
		Oct. 6	11	0
		" 19	24	0
		Nov. 3	39	0
11	Oct. 5	Oct. 9	4	0
		" 19	14	+
		Nov. 3	29	+
12	Sept. 3	Oct. 16	43	0
13	" 3	" 16	43	0
14	" 6	" 16	40	0
15	" 10	" 16	36	0
16	" 14	" 16	32	+
17	" 4	" 16	42	0
18	" 13	" 16	33	0
19	" 14	" 16	32	0
20	Oct. 11	" 14	3	0
		" 19	8	0

collected about many small blood vessels throughout the brain, stem, and cord, especially near the meninges (Figs. 1 and 2). The cells were likewise present in the pia in the perivascular and neighboring spaces. Near them, glial cells were sometimes mobilized. Most striking, however, were the lesions in the lobus piriformis and cornu Ammonis of the cortex (Figs. 1, 3, and 4). Here the bands of pyramidal cells, normally very regular in their arrangement, showed areas of sudden widening, distortion, and nearly complete destruction. The pyramidal cells contiguous to the normal area were scattered, some with large ameboid outlines, others with pycnotic nuclei and shrunken cytoplasm. Glial cells and scattered mononuclear cells were conspicuous. Adjacent to this early lesion there were often areas in which no pyramidal cells remained, consisting of either a relatively homogeneous necrotic substance with an occasional shrunken glial cell, or leucocyte, or areas of definite thinning and softening. Thus far, no specific cellular pathology has been noted beyond certain intranuclear bodies in the choroid and glial cells of certain mice, which are being subjected to further study.

DISCUSSION

Primary encephalitis breaks out occasionally in epidemic form. For example, lethargic or epidemic encephalitis did so following the influenza pandemic of 1917–18 in Europe and the United States; Japanese Type B encephalitis occurred during August and September, 1924 and 1933; and the encephalitis now under study was prevalent in St. Louis in August and September, 1933. Some infectious agent has been postulated as responsible for these epidemics but searches for the agent in the case of epidemic and Japanese Type B encephalitis, while eliminating the more common bacterial species and suggesting the presence of a virus, have not yet disclosed the presence of any specific agent. Still less clear is our understanding of the nature of the sporadic cases of primary encephalitis, which differ so widely in clinical and time and space patterns. The main problem is therefore whether the types of primary encephalitis referred to are one or many diseases and whether they, like certain types of encephalitis of animals, are to be regarded as infections, each one associated with a specific filtrable virus.

Transmission of the St. Louis encephalitis to *Macacus rhesus* monkeys for five passages by presumably bacteria-free suspensions of brain tissue from fatal human cases (3) is suggestive that this disease is a virus infection, but unfortunately the clinical disease of the passage monkeys becomes progressively less definite and finally disappears, even though a technique of massive inoculation is employed. It is of special interest, therefore, that the St. Louis and Kansas City diseases can be transmitted to mice in indefinite series by small injections of bacteria-free brain emulsions from fatal cases, and that a characteristic and consistent clinical and pathological picture results. From these experiments, it is inferred that at least one type of encephalitis is infectious in nature and incited by a virus agent.

CONCLUSIONS

1. Mice of special strains injected intracerebrally with a 10 per cent emulsion of bacteria-free brain tissue from fatal cases of encephalitis in St. Louis and Kansas City develop a characteristic and fatal encephalitis.

2. Transmission of the disease can be continued indefinitely by injecting the bacteria-free brain tissue from the infected mice into healthy mice.

3. In the injected mice there is a 3 to 4 day incubation period, followed by hyperesthesia, coarse tremors, convulsions, prostration, and death in from 4 to 6 days.

4. The lesions in the mice with experimental encephalitis consist chiefly of perivascular accumulations of mononuclear leucocytes throughout the brain, stem, cord, and the pia, and destruction of pyramidal cells in the lobus piriformis and cornu Ammonis.

5. The human encephalitis brain tissue preserved in glycerine from the time of death of the patient apparently loses its infectivity for mice in about 32 days.

BIBLIOGRAPHY

1. Webster, L. T., *J. Exp. Med.*, 1933, **57**, 793.
2. Webster, L. T., and Fite, G. L., *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 656.
3. Muckenfuss, R. S., Armstrong, C., and McCordock, H. A., *Pub. Health Rep., U. S. P. H. S.*, 1933, **48**, 1341.
4. Webster, L. T., and Fite, G. L., *Science*, 1933, **78**, 463.

5. Webster, L. T., and Fite, G. L., *Proc. Soc. Exp. Biol. and Med.*, 1933, **31,** 344.
6. Cox, H. R., and Fite, G. L., *Proc. Soc. Exp. Biol. and Med.*, 1934, **31,** 499.
7. Webster, L. T., and Fite, G. L., *Science*, 1934, **79,** 254.
8. Hempelmann, T. C., *Am. J. Pub. Health*, 1933, **23,** 1149; *J. Am. Med. Assn.*, 1934, **103,** 733.
9. Leake, J. P., *Am. J. Pub. Health*, 1933, **23,** 1140; *J. Am. Med. Assn.*, 1934, **103,** 728.
10. Bredeck, J. F., *Am. J. Pub. Health*, 1933, **23,** 1135; *J. Am. Med. Assn.*, 1934, **103,** 827.

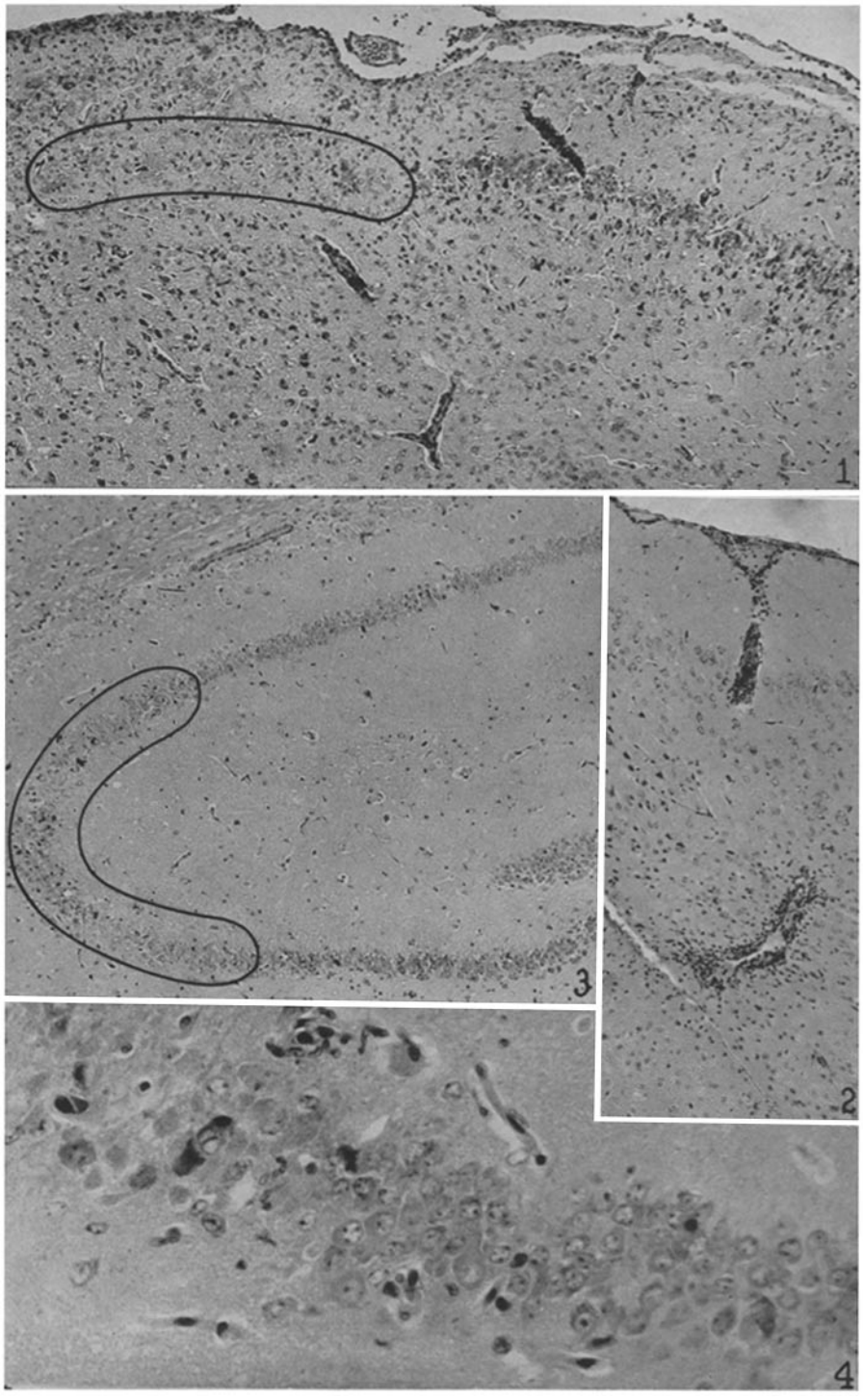
EXPLANATION OF PLATE 2

FIG. 1. Lobus piriformis. Perivascular and subpial accumulations of mononuclear cells and destruction of pyramidal cells (outlined area), with scattered glial cells and leucocytes. Hematoxylin and eosin stain. × 100.

FIG. 2. Lobus piriformis. Perivascular, mononuclear leucocyte infiltration. Hematoxylin and eosin stain. × 100.

FIG. 3. Cornu Ammonis. Specific destruction of pyramidal cells (outlined area), with little or no surrounding reaction. Hematoxylin and eosin stain. × 100.

FIG. 4. Cornu Ammonis. Destruction of pyramidal cells. Normal cells (right); ameboid and pycnotic cells (center and left); cell destruction (left). Hematoxylin and eosin stain. × 420.



(Webster and Fite: Encephalitis. I)