STUDIES ON ACUTE DISSEMINATED ENCEPHALOMYELITIS PRODUCED EXPERIMENTALLY IN RHESUS MONKEYS

IV. Disseminated Encephalomyelitis Produced in Monkeys with Their Own Brain Tissue*

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The rapid production in several laboratories (1–7) of acute disseminated encephalomyelitis in several species by the injection of homologous brain tissue in an emulsion with paraffin oil, aquaphor, and killed tubercle bacilli (for earlier studies without these adjuvants *cf.* references 8 and 9), an immunization procedure introduced by Freund and McDermott (10), has focussed attention on the possibility of autosensitization or autoantibody formation as a mechanism in the causation of certain demyelinating diseases. Since it was possible that individual differences existed among the brain antigens of individuals of a given species and therefore that injection of brain emulsions from one individual into another might be more or less comparable to the injection of a foreign antigen, it was considered of importance to establish whether or not encephalomyelitis could be produced in an animal by the injection of an emulsion of its own brain tissue. Accordingly, *rhesus* monkeys from which the right frontal lobe had been excised were given injections of emulsions with adjuvants prepared from their own individual brain tissue. These animals developed typical acute disseminated encephalomyelitis.

EXPERIMENTAL

Right frontal lobectomies were performed on six *rhesus* monkeys. The brain tissue removed, from 3.3 to 5.5 gm. per animal, was kept frozen in solid carbon dioxide until the animals had recovered. Emulsions of the brain tissue with aquaphor and paraffin oil containing heat-killed tubercle bacilli were prepared as previously described (2). Each animal received three 1 ml. intramuscular injections, a week apart, of the emulsion prepared from its own brain tissue. Animals were carefully observed for symptoms which could not be attributed to the effects of the surgery and were sacrificed and necropsied when their condition became such that they appeared unlikely to survive another day.

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RESULTS

Five of the six animals developed symptoms in from 4 to 28 days following the third inoculation. These included ptosis of an eyelid, dilatation of the

TABLE I

Production of Acute Disseminated Encephalomyelitis in Lobectomized Rhesus Monkeys Injected with Their Own Brain Tissue Plus Adjuvants

Monkey No.	Day signs first noted after 1st injection	Signs observed	Day of death	Necropsy findings*
2-86		None; found dead	19	Negative for encephalomyelitis; acute, suppurative cerebrospinal leptomeningitis and ventriculitis complicating cranial operation
2-87	41	Ptosis, left eyelid; blindness, dilated pupils	52	Positive; subacute and chronic perivascular and coalescent, demyelinating lesions found chiefly in optic nerves and sparsely in rest of brain
2-88	26	Trunk ataxia, intention tremor	26(S)	Positive; acute and subacute perivascular and coalescent, inflammatory and demyelinating lesions in brain most severe in brain stem and cerebellum
2-89	20	Dilated pupils; blindness, convulsive seizures	23(S)	Positive lesions as in 2-88; most marked in optic nerves and cerebrum and less intense in brain stem and cerebellum; sparse in spinal cord‡
2-98	18	Trunk ataxia; generalized tremors	19(S)	Positive; few acute and many subacute lesions as in preceding animals most marked in pons, and less extensive in cerebellum and cerebrum
3-00	23	Dilatation of pupils, generalized tremors	23(S)	Positive; acute and subacute lesions as in above animals of considerable severity in the brain stem and optic nerves, less marked in the cerebrum and least intense in the cerebellum; sparse lesions in the spinal cord

Animals received three 1.0 ml. intramuscular injections at weekly intervals.

S = sacrificed.

* All animals showed scars of right frontal lobectomy and secondary degeneration consequent to it.

‡ Right frontal lobectomy followed by local abscess formation, aspirated, instilled with penicillin, subsided before brain inoculation; local granulation tissue.

pupils, reduced vision or blindness, intention tremor, ataxia, and fine generalized tremors (Table I). One monkey in which complete blindness, dilatation of the pupils, and ptosis of the left eyelid were the only symptoms, showed numerous

lesions in the optic nerves (Fig. 1) and rare limited lesions in the cerebral white matter. In this animal death occurred 53 days after the first inoculation, 39 days after the last, and 11 days after the first symptoms. Inflammation was absent in the optic nerve lesions and absent or slight and limited to perivascular lymphocytes in the others. In the other four animals lesions were found in the cerebrum, cerebellum, brain stem, and optic nerves (Fig. 2) and in two in the spinal cord as well. These had died in from 5 to 19 days after the last inoculation and 1 to 3 days following the first symptom. The lesions were acute or subacute (Fig. 3), perivascular (Figs. 3 and 4), and frequently coalescent. Their characteristics were in every respect like those previously described in acute disseminated encephalomyelitis in the monkey (2, 11).

In the sixth monkey, found dead 6 days after the last inoculation, an acute suppurative cerebrospinal leptomeningitis and ventriculitis was encountered. In this animal no lesions were found in the brain or spinal cord and the acute leptomeningitis was probably a complication of the operation although no infection of the scalp wound was discovered and death occurred 29 days after the operation. There were tuberculous lesions in the lungs and liver.

DISCUSSION

The successful production of acute disseminated encephalomyelitis in *rhesus* monkeys by the injection of a portion of their own individual brains which were previously removed surgically and incorporated with adjuvants, provides additional evidence for the hypothesis previously advanced that such pathological changes may be a result of sensitization or antibody formation to an individual's own brain tissue. It should be emphasized, however, that the procedure used for producing the encephalomyelitis is a highly artificial one, and the manner in which such a sequence of events could be initiated in instances of spontaneously occurring encephalomyelitides or in other related diseases is as yet completely unknown.

SUMMARY

Acute disseminated encephalomyelitis has been produced in *rhesus* monkeys by injection of their own brain tissue, removed surgically and incorporated with adjuvants.

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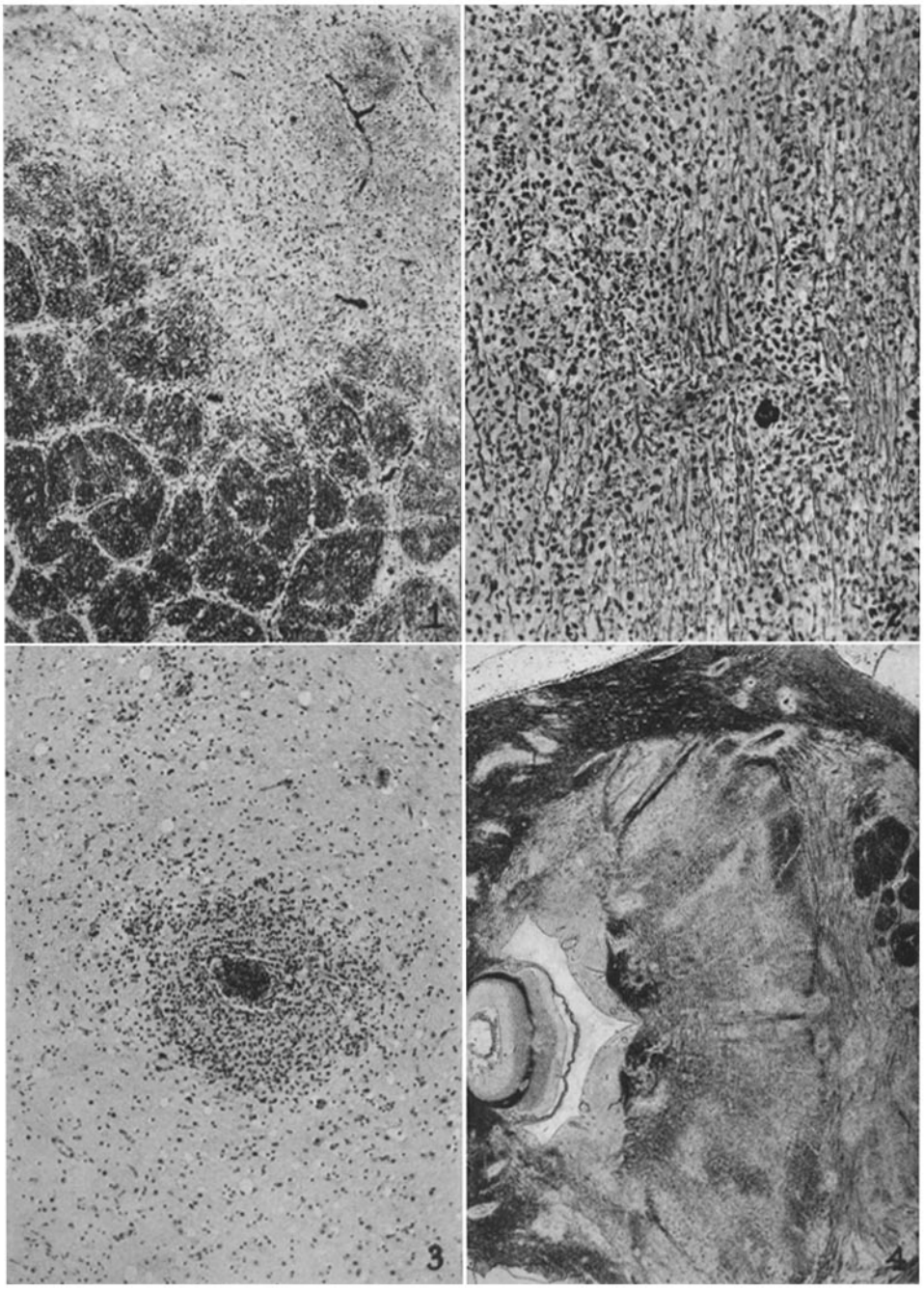
EXPLANATION OF PLATE 14

FIG. 1. Monkey 2-87. Coalescent area of demyelination in optic nerve. Mahon stain. × 56.

FIG. 2. Monkey 2-89. Partial preservation of axones in demyelinated area in optic nerve. Bodian stain. × 85.

FIG. 3. Monkey 3-00. Focal lesion in thalamus. Perivascular infiltration by lymphocytes and associated microglial proliferation. Hematoxylin-eosin stain. × 56.

FIG. 4. Monkey 2-98. Numerous perivascular foci of demyelination in pons. Mahon stain. × 4.5.



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