Chronic Epilepsy in the Monkey Following Multiple Intracerebral Injections of Alumina Cream. (18970)

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Previous studies have indicated that subcortical intracerebral injections of small quantities of alumina cream were occasionally effective in producing seizures and electroencephalographic (EEG) abnormalities in the monkey(1,2). A new technic based on simultaneous multiple intracerebral injections of alumina cream is here described.

Method. Eight injections (0.1 ml each) of alumina cream were made into the exposed sensori-motor cortex of one cerebral hemisphere in each of 5 *Macaca mulatta,* and into both hemispheres of an additional animal. Hypodermic needles (gauge 26) were inserted almost perpendicularly to the surface of the cortex in 8 standard positions (Fig. 1) to a depth of 3 to 11 mm and 0.1 ml of alumina cream was injected slowly into each site. An estimation of the amount retained in each hemisphere was noted and found to vary from 0.4 to 0.6 ml. The animals were observed for periods up to 6 months during which time serial EEG's were recorded. The brains were examined post-mortem and the position of the lesions plotted.

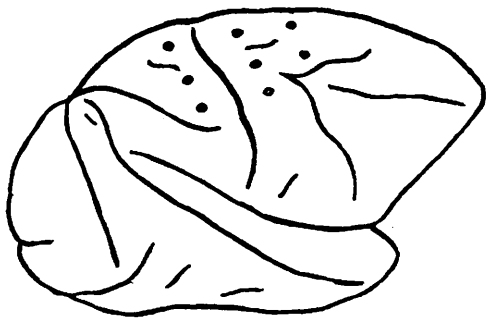

FIG. 1. Diagram of lateral aspect of cerebral hemisphere of *Macaca mulatta* in which the injection sites in the sensori-motor area are indicated by heavy dots.

Results. Five of the 6 monkeys exhibited motor seizures 3-4 weeks following injection. These were usually limited to the contralateral side of the body in 4 of the 5 monkeys injected unilaterally. The convulsive activity was characterized initially by frequent, almost continuous muscle twitching of variable intensity involving the upper and/or lower extremity, and appeared to be accentuated after excitement and movement. Associated loss of consciousness was not observed. In some animals prolonged rhythmic clonic movements of the contralateral extremities became a predominant feature. After a period of several weeks this type of spontaneous motor activity was less evident. Generalized seizures with apparent loss of consciousness occurred infrequently. A moderate degree of paresis was usually present in the limbs of the side contralateral to the injected hemisphere. The monkey injected bilaterally exhibited the most severe reaction: *status epilepticus* for 3 weeks which despite ample luminal sodium treatment terminated in death.

EEG's showed considerable spike, sharp, and slow wave activity which was most prominent over the injected hemisphere. In the later stages metrazol administered intravenously (0.1 ml 10%) accentuated the spike activity and occasionally precipitated associated contralateral clonic movements. When a single dose failed to evoke this response, 3-4 repeated injections proved effective.

Examination of the brain at post-mortem revealed that in all instances an adherent dural scar was present over the entire injected cortical area. Histologically the lesions resembled those described previously(2). The

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2. Kopeloff, N., Whittier, J. R., Pacella, B. L., and Kopeloff, L. M., *EEG Clin. Neurophysiol.,* 1950, v2, 163.

cerebral lesions produced by the injected alumina cream extended from the cortex into the adjacent underlying white matter along the needle track in the "arm-leg" zone. In the animal which failed to develop convulsive attacks a lesion extending into the superior pole of the underlying putamen and adjacent internal capsule was evident.

Discussion. Our findings indicate that multiple intracerebral injections of alumina cream into one hemisphere caused a more rapidly developing convulsive state than that usually induced by a disc containing alumina cream(1). The motor manifestations were initially constant, focal, variable in intensity, and associated with some weakness of the contralateral limbs. In this respect they resembled the form of motor epilepsy in man described as *epilepsia partialis continua* (Koshewnikow)(3).

The only animal which failed to exhibit convulsive movements after the multiple injection treatment of one cerebral hemisphere had received the deepest injections (11 mm), and the finding of a lesion extending into the superior putamen and internal capsule in this case may be significant. It might be inferred that under these conditions abnormal motor activation from the overlying cortical-subcortical zone was not possible because of interruption at the basal ganglia level.

Summary. 1. Chronic experimental epilepsy was induced in 4 of 5 monkeys (*Macaca mulatta*) by multiple intracerebral injections of alumina cream in the sensori-motor area of one cerebral hemisphere. 2. The early motor convulsive manifestations in the epileptic animals resembled those described in man as *epilepsia partialis continua* (Koshewnikow). 3. In an additional monkey treated by multiple intracerebral injections of alumina cream into both hemispheres death in *status epilepticus* occurred 3 weeks after the onset of seizures. 4. EEG's showed marked spike, sharp, and slow wave activity which was most prominent over the injected hemisphere.

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Effect of Hyaluronidase on Electrolytes (Sodium and Potassium) of Dog Synovial Fluid. (18971)

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The action of hyaluronidase as shown by Duran-Reynals(1), is that of depolymerizing a mucopolysaccharide hyaluronic acid, which occurs in high concentration in synovial fluid.

Since hyaluronic acid has been shown to be in a depolymerized state in synovial fluid of arthritic joints(2), and since electrolytes seem to be primarily involved in arthritis(3-5), tests were undertaken to determine the effect of hyaluronidase on the sodium and potassium content of synovial fluid.

Materials and methods. Twenty mongrel dogs were anesthetized by intraperitoneal injection of 100 mg of sodium phenobarbital per

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