pressed above, although its possible significance in relation to the mechanism of sulfanilamide and PAB effects has apparently been overlooked. Other examples of antagonisms among narcotics could be cited. The whole problem needs further study.

In summary, both the stimulatory and inhibitory effects of PAB and sulfanilamide, as well as urethane, appear to be fundamentally related to the general problem of narcotic action, which does not necessarily involve a structural similarity between the molecules of the inhibitor and an intermediary of normal metabolism in the cell. This interpretation has some interesting implications with respect to the various effects of PAB in different organisms referred to above. Further study from the point of view discussed would appear justified on the basis of the evidence at hand.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A HEAD HOLDER FOR INTRACRANIAL OPERATIONS ON THE MONKEY

THE advantages of fixation of the head, apparent to any one undertaking intracranial operative procedures in experimental animals, are readily secured in carnivores by use of the Czermak type head holder. Adaptation of the Czermak holder for employment with monkeys has not proved satisfactory in our hands, and we have thought it worth while briefly to describe the apparatus devised for that purpose in this laboratory.

The essential instrument is the head holder (A) invented some years ago by Dr. A. R. Buchanan for use with the Horsley-Clarke machine on guinea pigs (Fig. 1). This consists of a cylindrical cross-bar (1) and two side arms (2) which slide onto the bar and can be tightened in place by set screws (3). The cross-bar is slotted and an interlocking piece fitted on the interior of the base of each arm, in order that the arms be aligned in the same plane. When employed with the stereotaxic instrument on the guinea pig, the Buchanan holder is applied by approximating the two arms until the shaped pins (4) fit into the meatuses. Finally the ear bars of the Horsley-Clarke machine are seated in the openings (5). When the Buchanan holder is used to fix a monkey's head, the ear plugs (D) are firmly inserted into the meatuses; these are the short, straight plugs described by Harrison.[1] The side arms are then approximated until the shaped pins are solidly set in the open ends of the ear plugs, and the arms held in place by tightening the set screws. Dorso-ventral rotation of the animal's head is prevented by introducing into the opened mouth a straight bar covered with rubber tubing (E), and making this fast on the side arms by the use of two common right angle clamps (C), as illustrated in the lower figure.

As shown by the sketch of the apparatus set up for operation, the Buchanan holder can be attached to a vertical bar (F), arising from the table, and adjusted to a convenient height by any suitable clamp. We have employed a universal clamp (G) to allow tilting to either side. For approaches through the convexity of the calvarium no further fixation of the head is needed. In lateral approaches involving exposures down to the zygoma, the distal part of the side arm forms an inconvenient bulge beneath the drapes.

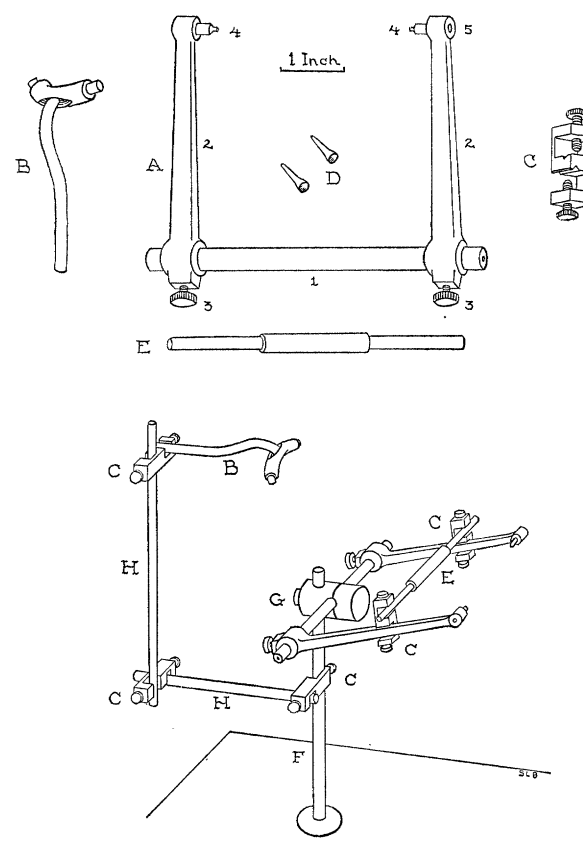

FIG. 1.

This might be obviated by constructing a side arm containing a right angle or one made so that it would lie flush with the ear.

For approach to the posterior fossa through the enlarged foramen magnum, we have found it necessary further to stabilize the head to prevent its dorsiflexion. For this purpose a simple nose piece (B) was contrived, the cross-bar of which, covered with

[1] F. Harrison, *Arch. Neurol. Psychiat.*, 40: 563, 1938.

rubber tubing, fits across the nose immediately below the eyes. As demonstrated in the figure, the nose piece can be mounted from the vertical rod (F) by means of two straight bars (H) and three right angle clamps (C). For the posterior approach the Buchanan holder is turned in the universal clamp until the side arms of the holder are almost vertical, in order to obtain proper exposure of the operative site. The nose piece (B) can then be adjusted.

The Buchanan holder in the size shown accommodates monkeys weighing up to 4 kilograms and, used without ear plugs, is also satisfactory for guinea pigs. In neither the monkey nor the guinea pig does the apparatus rupture the tympanic membrane or do apparent injury to the external ear.

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SODIUM DIPHENYLHYDANTOINATE AND EXPERIMENTAL EPILEPSY

SODIUM diphenylhydantoinate is a drug introduced by Putnam and Merritt in clinical practice for treatment of epileptic seizures on account of their particularly efficient anti-convulsant action with the least hypnotic effect. Primarily such results were obtained on cats with convulsions induced by electrical stimulation of the cerebral cortex.[1] Clinical investigations were performed later.[2]

In this article are discussed experiments performed in our laboratory with sodium diphenylhydantoinate in an experimental epileptiform seizure of the frog induced by quick cooling of the spinal cord. The results reported are a résumé of a more detailed paper in preparation.[3] The technic employed was recently reported[4,5] and now is usual in our laboratory. For the Brazilian frog (*L. ocellatus*) cooling of the isolated spinal cord of the preparation to a temperature below 8° C. produces an epileptiform seizure which lasts 20 to 40 seconds. For the American and European frog the cooling must be below 0° C.

The anti-convulsant action has been studied injecting sodium diphenylhydantoinate solution in the abdominal lymphatic sac before the isolated spinal cord preparations were started. The doses employed varied from 0.05–0.90 grams per kilogram of body weight. Doses from 0.05–0.09 grams did not avoid the production of the attacks, but sometimes they were less severe. Doses greater than 0.10 grams per kilogram commence to hinder the production of the convulsions and 0.15 grams prevent the epileptiform seizure in nearly all the frogs injected. This anti-convulsant effect was observed with no hypnotic effect, the frog jumping quite well in the laboratory. When the medulla was sectioned and the isolated spinal cord prepared, the flexor reflexes of the legs were as in the normal preparations. Such anti-convulsant action is still observed after 2 days elapse between the injection of the sodium diphenylhydantoinate and the cooling of the spinal cord. Hypnotic effects were obtained only with doses superior to 0.20 grams per kilogram. The lethal dose has not been determined, being superior to 0.90 grams.

Sodium diphenylhydantoinate acts on the spinal cord of the frog, hindering the epileptiform seizures induced by quick cooling with no hypnotic effects and disturbances of the spinal reflexes.

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