mortality ratio was 5/14 in the Phenergan-treated animals, compared to 11/14 in those receiving 0.55 - 0.6 mg per kg of epinephrine without Phenergan. In the group to which 1.2 - 1.5 mg per kg of epinephrine was administered, 8 of 11 Phenergan-treated animals died.

Our results, as well as those of Stone and Loew, do not lend support to Halpern's hypothesis that Phenergan opposes the formation of pulmonary edema by virtue of the property of inhibiting cellular permeability.

Summary. The antihistaminic drug, Phenergan (3277 R.P.), in doses of 20 or 40 mg per kg, failed to protect rats or guinea pigs against the pulmonary edema induced by injection of ammonium chloride, and also offered no protection against epinephrine-induced pulmonary edema in guinea pigs.

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Maintenance of Spontaneous Activity within the Cerebellum.*† (17352)

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The hitherto unsuspected widespread projection of the cerebellum[1] to the cerebral cortex and the ease with which facilitation[2] and suppression[3] of cortically and reflexly induced movements can be produced by cerebellar excitation emphasizes the need to answer the interesting but intricate question, what is the cerebellar influence on the rest of the nervous system? One approach to an answer is the study of mechanisms underlying the maintenance of the fast electrical activity of the cerebellum. The best study yet made on the nature of this electrical activity was that by Dow[4] who not only described it in great detail, but also studied the influence of various drugs on it and related the activity to muscular tone.

In the present study we have confirmed many of Dow's observations and extended the problem into an analysis of intrinsic cerebellar mechanisms which maintain what is probably the fastest electrical activity within the nervous system.

Methods. In mature cats, decerebrated, or placed under ether, nembutal, dial, chloralosane, or various combinations of the above mentioned anesthetics, the calvarium was removed to expose all parts of the cerebellum except the anterior one-half of anterior lobe and paraflocculus and flocculo-nodular lobe. Bipolar and monopolar silver wire as well as saline-cotton wick pick-up electrodes were used to introduce the cerebellar activity into Grass Model 111 amplifiers. The amplified electrical activity was observed and photographed on a five-inch cathode ray tube.

Results. The first question was: Does this fast electrical activity result from the driving of the cerebellum by extrinsic centers or is it something intrinsic to the cerebellum? As shown in Fig. 1a, the activity results from intrinsic mechanisms within the cerebellum. The electrical activity in this preparation was normal despite the fact that 5 days previous all afferent and efferent fibers (verified histologically) had been cut. Previously, Dow[4] reported fast electrical activity following "acute incomplete section of the cerebellar peduncles in four experiments" and Spiegel[5] also observed it

Further support for this observation is given

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2 Snider, R. S., and Magoun, H. W., *Med. Proc.*, 1948, **7**, 117.

3 Snider, R. S., Magoun, H. W., and McCulloch, W. S., *Med. Proc.*, 1947, **6**, 207.

4 Dow, R. S., *J. Physiol.*, 1938, **94**, 67.

5 Spiegel, E. H., *Am. J. Physiol.*, 1937, **118**, 569.

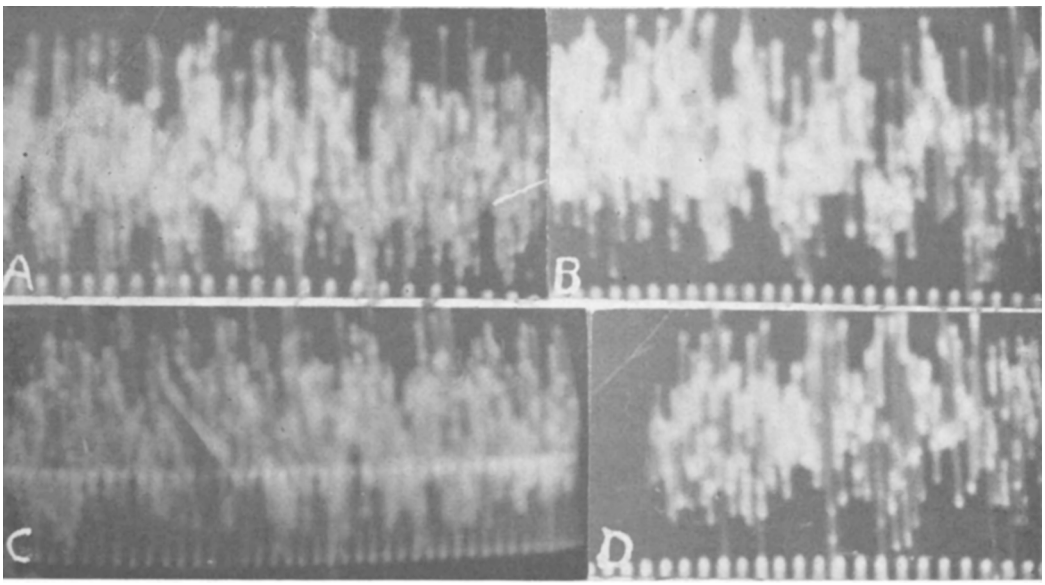

FIG. 1.

Electrical activity of the cerebellum recorded from the pial surface with bipolar silver wire pick-up electrodes. 100/sec. time signal.

A. Cat under nembutal anesthesia. Five days previously all 6 cerebellar peduncles had been transected, thus interrupting all afferent and efferent fibers. Note normal activity.

B. Cat under nembutal anesthesia. Note electrical activity in cerebellar cortex dissected free of animal and lying on saline moistened gauze. Nuclear cells were not present.

C. Cat under nembutal anesthesia. Note "normal" electrical activity, despite the total bilateral destruction of cerebellar nuclei.

D. Cat under nembutal anesthesia. Note electrical activity similar to A, B, C, above. Cerebellar peduncles and cerebellar nuclei left intact.

in Fig. 1b which shows the electrical activity in a part of the cerebellum which was dissected free and was lying on a strip of gauze several centimeters from the animal. Such activity, however, does not continue for more than 2-4 minutes

Since the fast electrical activity can continue in the absence of all fiber connections with the rest of the nervous system, then it must be maintained by intrinsic mechanism within the cerebellum.

The next question was: What are the intrinsic mechanisms which maintain this electrical activity? The cerebellar cortex is an ideal preparation with which to work because the anatomy is simple, well known, and remarkably uniform in structure. Fig. 2 summarizes the present state of our information on the anatomy of this organ. Working on the assumption that this activity is maintained either by reverberating circuits, or spontaneous activity of cellular aggregates, or both, the following analysis has been made:

Reverberating Circuits. A glance at Fig. 2 indicates the possibility of two reverberating circuits: 1. Purkinje cell (A) to central cerebellar nuclei, (B) back to Purkinje cell. That this circuit cannot be the responsible one is shown by the experiment illustrated in Fig. 1c. Note that the activity appears normal despite the absence of all the central nuclei on both sides.

A second possible reverberating circuit is Purkinje cell (A) through Purkinje cell axon collateral (I) back to a second Purkinje cell. Thus, one Purkinje cell could fire another, then a third, etc., and back again. Although our experiments do not disprove the possibility of this circuit functioning in this manner, as can be seen below, there are other more tenable explanations.

Spontaneous activity of cellular aggregates. The most conspicuous cell in the cerebellar cortex is the Purkinje cell. The large soma,

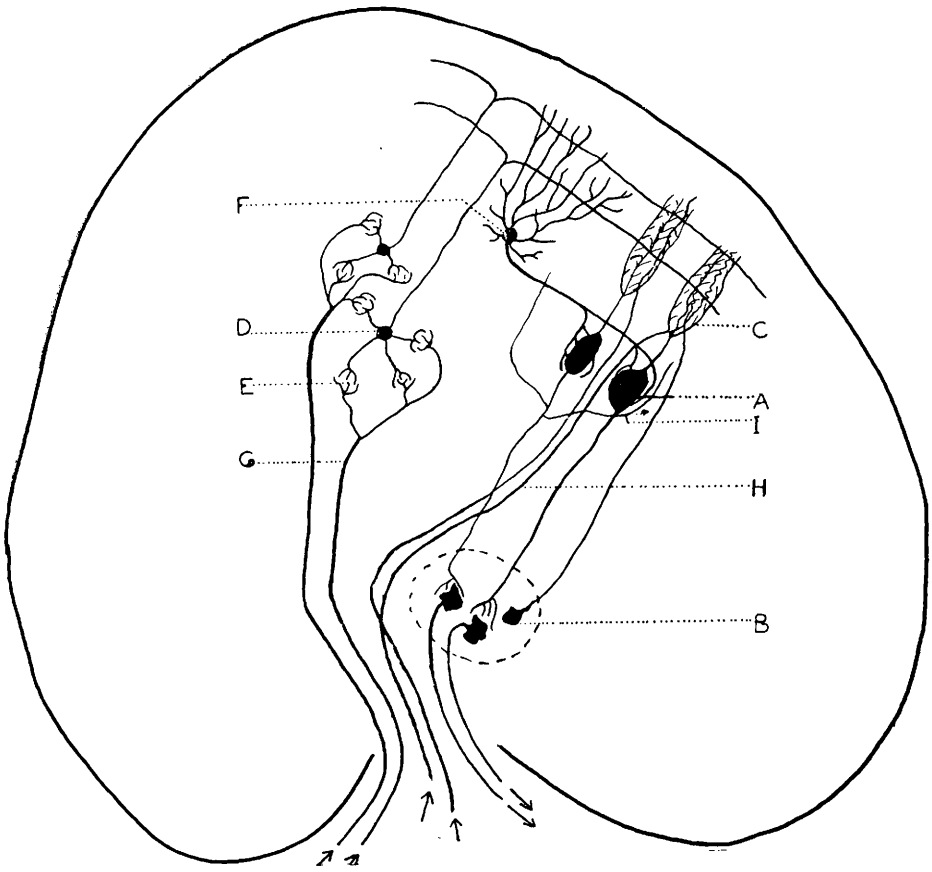

FIG. 2.

Diagrammatic drawing of microscopic anatomy of cerebellum. Modified from Ranson, 1935, The Anatomy of the Nervous System. A, Purkinje cell body. B, Cell body in central cerebellar nuclei. C, Purkinje cell dendrites. D, Granule cell body. E, Glomerulus in which afferent fiber mossy terminal synapses with granule cell dendrite. F, Basket cell body. G, Afferent fiber terminating as mossy terminal. H, Incoming fiber terminating as climbing fiber. I, Purkinje cell axon collateral.

the elaborate branching dendrites, and the axonal connections to the central nuclei make it one of the important cells, and one of the first to be considered as a possible source of spontaneous activity. This cell is of further interest because of the spatial representation of other cellular components on its cell body and processes. The basket cell axons synapse around the cell body, while the granule cell (Fig. 2, D) axons and climbing fibers (Fig. 2, H) synapse on the Purkinje cell dendrites. Possible synapse points on Purkinje cell axons are not known. As is well known, granule cell axons connect with Purkinje cells along the longitudinal axis of the folium and basket cell axons connect with them along the transverse axis of the folium. In this manner, impulses coming from granule cells can be widely dispersed in the longitudinal and transverse planes of the cerebellar cortex and, from Purkinje cells, can be relayed in turn to the central cerebellar nuclei thence to centers within the brain stem. Thus, one cannot doubt the major role played by these cells in relaying the message through the cerebellar cortex. However, in order to study the role played by these cells in the maintenance of the fast electrical activity, according to the technics we were using, it would be desirable to selectively destroy them, leaving intact the other

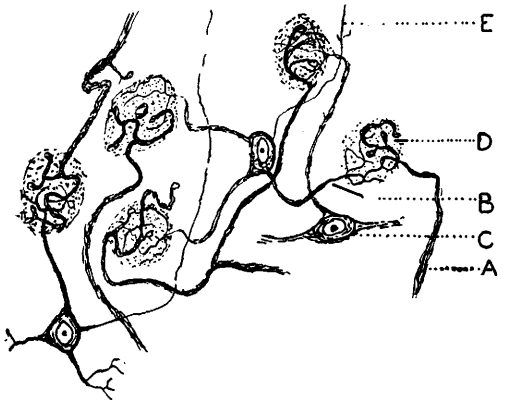

FIG. 3.
Outline drawing of microscopic anatomy of granule cell and granule cell glomerulus (modified from Cajal). A, Afferent fiber terminating as mossy fiber in protoplasmic glomerulus, D. C, Granule cell body. B, Dendrite of granule cell synapsing with afferent fiber in granule cell glomerulus. E, Granule cell axon.

cellular elements of the cerebellar cortex. We were not able to accomplish this technical procedure.

The Purkinje cell is not the only potential source of cellular elements for the maintenance of spontaneous electrical activity. A second possible source is the granule-basket cell combination in which the granule cell glomerulus deserves some comment. This non-nucleated protoplasmic structure located at the junction of the incoming mossy terminal with the dendritic terminals of the granule cells is approximately 15 μ in diameter. Fig. 3 illustrates the salient properties of the various parts of the granule cell. Note that the incoming afferent fiber (A) synapses within the glomerulus (D) on the way to the granule cell (C) dendrite (B). Note also that, except for a slightly granulated appearance, the protoplasm appears almost structureless.

To check the possibility of activity coming from the granule cell layer, we attempted to record directly from this layer with pick-up wire (26 gauge, insulated to tip). Although good activity could be recorded, and often better activity than that from the pial surface, which is approximately 250 μ from the granular layer, the answer is still equivocal because possible activity of nearby Purkinje cells may have spread to the needle tip or Purkinje cell axons passing nearby may have been conducting activity through the area to the underlying cerebellar nuclei. From this, one must conclude that if the intrinsic spontaneous electrical activity of the cerebellar cortex results from spontaneous activity of cellular aggregates, as seems likely, then the basket-granule cell Fig. 2 D,F (with glomerulus) combination appears to be a possible responsible agent. One thing is certain, either it is this cellular complex or it is the Purkinje cell itself which is responsible.

Summary. Evidence is presented to show: (a) that the fast electrical activity of the cerebellum is intrinsically maintained within this structure; (b) that it is not due to reverberating circuits through the cerebellar nuclei and back to the cerebellar cortex; (c) that it is probably due to the spontaneous activity of Purkinje cells and/or the granule-basket cell combination.

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Prevention of Secondary Infection due to *Pseudomonas aeruginosa* in Frostbitten Tissue. (17353)

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One of the major problems encountered in investigations on experimental frostbite is the prevention of infection of the frozen tissue. Without prophylactic treatment infection occurs in practically all cases of severe frostbite. The following report gives the results of the application of penicillin and sulfamylon*

* The sulfamylon hydrochloride powder was supplied by the Medical Research Department of Winthrop-Stearns, Inc.