be admirably adapted to serve constructively its best interests, requiring only further development along the general lines indicated. The problem now is almost wholly a financial one. Contributing as volunteer abstracters and section editors, and often as subscribers as well, biologists individually, both here and abroad, have from the beginning lent very impressive support. This, and the increasing material contribution from the organized societies of biologists, is indicative of the wide-spread determination to maintain and develop *Biological Abstracts*. But, as clearly foreseen from the beginning, such support, including subscription income, probably at best can not provide more than one third of the funds necessary to maintain *Biological Abstracts* adequately, even in the immediate future. At the same time, such support on a still broader basis is indispensable to the present efforts to secure the necessary additional permanent funds from other sources.

The adequate solution of the financial problem of *Biological Abstracts* is admittedly difficult. But in view of the investment made, the service already rendered and the great potentialities ahead, it is incredible that it should now fail for lack of adequate financial support.

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SPECIAL ARTICLES

EXPERIMENTAL DETERMINATION OF THE ANTICONVULSANT PROPERTIES OF SOME PHENYL DERIVATIVES[1]

THE introduction of bromides and later of phenobarbital may well be considered the two greatest steps forward ever made in the practical treatment of the convulsive state. In view of the prevalence of the condition and the urgent need for better means of controlling it, there have been surprisingly few attempts to survey the field for even more effective medication. One difficulty has been to devise a standard means of producing convulsions in animals for preliminary studies. The use of convulsant drugs (for example, in the hands of Keith,[2] Elsberg and Stookey[3]) have not been thoroughly satisfactory. Fulton and Keller[4] have compared the effect of various anesthetics on the excitability of the cerebral cortex to electrical stimulation. Krasnogorosky[5] has used an arrangement of electrodes somewhat similar to ours for the purpose of producing experimental convulsions, and Spiegel[6] has designed an apparatus for determination of the convulsive reactivity by gradual electrical stimulation of the brain with the skull intact, using electrodes placed upon the eyeballs. We are indebted to Dr. Frederic A. Gibbs for suggesting that a modification of these methods could be used for our purposes and to Dr. Paul Hoefer for help in devising one which has proved simple and practical.

As used at present, the stimulator consists of a 45-volt radio battery, discharging through a commutator operated by a motor and through a potentiometer of 50 ohms. One end of the potentiometer is wired through a 0–50 milliammeter to an occipital electrode and the sliding connection is wired to a mouth electrode. Thus, it is possible to apply shocks at various speeds and at various amperages (Fig. 1).

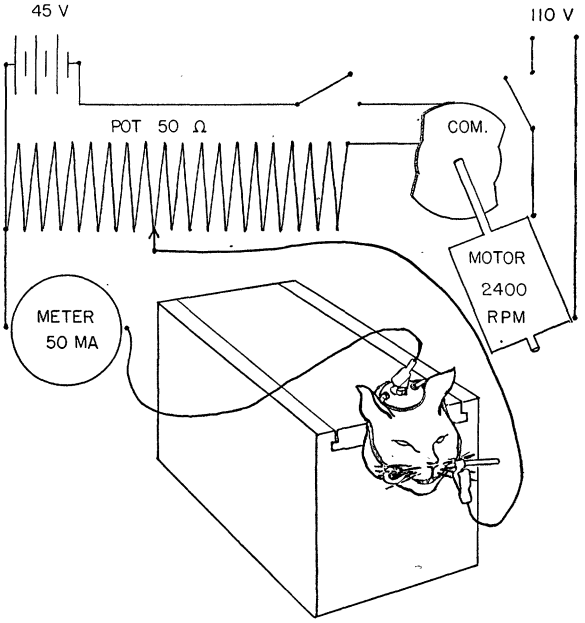

FIG. 1. Diagram of the wiring employed, permitting an interrupted current of determined amperage to be applied through an animal's head to determine the threshold for convulsions.

[1] From the Department of Neurology, Harvard Medical School, and the Neurological Unit, Boston City Hospital, Boston. This work was aided by a grant from Parke, Davis and Company.

[2] H. M. Keith, *Am. Jour. Dis. Child.*, 41: 532, 1931. Also, *Jour. Pharmacol. and Exper. Therap.*, 44: 449, 1932.

[3] C. A. Elsberg and B. P. Stookey, *Arch. Neurol. and Psychiat.*, 9: 613, 1923.

[4] J. F. Fulton and A. D. Keller, *Surg. Gynec. and Obstet.*, 54: 764, 1932.

[5] N. I. Krasnogorosky, International Physiological Congress, Leningrad, Moscow. August 9–17, 1935. Summaries of Communications, p. 213.

[6] E. A. Spiegel, "Quantitative Determination of the Convulsive Reactivity by Electrical Stimulation of the Brain with the Skull Intact." *Jour. Lab. and Clin. Med.* (to appear).

In practice, cats have been used as test animals, confined in cat boxes. One electrode is a stout wire bit placed in the animal's mouth, the other a metal plate between the ears, upon an area of fur which has been thoroughly moistened with soap solution. The two electrodes are kept in place by a simple bridle of string. Experiment shows that convulsions are produced at a slightly lower amperage if the speed of the commutator is increased up to 80 contacts per second (the limit available with the apparatus employed) than at lower speeds. The current is turned on for 10 seconds for each test; if the stimulus is above threshold, a convulsion will often begin in less than half this time. As there are no means of predicting accurately what the resistance of the circuit will be, the slider is adjusted to the desired milliamperage after the switch is closed.

The animals appear to be unconscious while the current is flowing, though naturally rigid. The method appears to involve no undue cruelty, and indeed is similar to that used for executing stray animals by some animal protective societies. A convulsion is marked by the persistence of tonic and clonic movements for a variable interval after the current is turned off, dilation of the pupils and subsequent stupor. Each animal has a characteristic threshold—usually between 6 and 15 milliamperes under the conditions stated—which seldom varies spontaneously more than 10 per cent. on any one day, and usually less than 25 per cent. from one day to another. If 5 minutes is permitted between shocks when no convulsion is produced, and an hour after each convulsion before the next shock, several determinations of threshold may be made daily.

The apparatus would probably be almost as efficient and somewhat simpler if a transformer of the "Variac" type were used on an alternating current line through a milliammeter. The difference in effectiveness between a 60-cycle current and the 80 shocks per second used at present can not be great.

The anticonvulsant effect of most of the common drugs has been studied by this apparatus, continuing the work of Spiegel.[6] Under the conditions of the experiment, it is easy to demonstrate that a dose of sodium bromide sufficient to prevent a cat from walking (about 2 gm) will raise the convulsive threshold only about 50 per cent., while a dose of phenobarbital producing similar symptoms (about 0.1 gm) may treble or quadruple it. Cats so protected may survive shocks of an intensity which proves fatal to untreated animals. Comparable doses of other familiar barbiturates have little anticonvulsant activity. This, and the fact that Harrison, Mason and Resnik[7] have produced evidence that the conjugated phenols are responsible for the motor depression of uremia suggested a search among phenyl derivatives as well as among standard hypnotics.

Accordingly, a large number of the less toxic phenol compounds was studied. They included phenyl, cresyl and tolyl sulfonates, benzoates, ketones and esters of such radicals as carbamic, malic, barbituric acids and hydantoin. The compounds which appear to have the greatest anticonvulsant activity combined with the least relative hypnotic effect of those tested so far are diphenylhydantoin, acetophenone and benzophenone.[8]

Whether the drugs found most effective under the conditions of the test will also prove of value in clinical practice remains to be seen. The experimental method appears, however, to constitute at least a provisional index of their activity.

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[6] R. T. Harrison, M. F. Mason and H. Resnik, *Jour. Clin. Invest.*, 15: 463, 1936.

[8] H. H. Merritt, T. J. Putnam and D. M. Schwab. Material in preparation.

EXTRACTION OF THE NITROGENOUS MATERIALS FROM DRIED GRASS[1]

As a part of a quantitative study of the nutritionally essential amino acids in the more important forage plants, it was considered highly desirable if not absolutely necessary to find a method for removing all the protein from such materials.

It is the object of this paper to report that extraction of the air-dry grass in a Soxhlet apparatus with 90 per cent. formic acid brings most of the sample into a solution which includes *all* the nitrogen. This procedure was developed as a result of some experiments in which several reagents were tested by agitating samples of grass at room temperature with successive small portions of each reagent. Ninety per cent. formic acid was found most effective, removing about 88 per cent. of the total nitrogen. Since repetition of this treatment removed further small quantities of nitrogen, it was decided to try the Soxhlet method of extraction. When the charge was mixed with a suitable material to facilitate percolation, such as 50-mesh ground glass, the Soxhlet extraction was completed in three to eight hours. Aliquots of two such extracts, representing 0.2 g of grass, contained 5.21 and 5.07 mg of nitrogen or an average of 100.8 per cent. of that present in the grass. Such extracts are being examined to determine their usefulness in a study of the nutritionally essential amino acids.

It is interesting to note that in a material containing

[1] Contribution from the Bureau of Plant Industry in cooperation with the Bureau of Animal Industry. The possibility of using formic acid as a protein solvent was suggested by Dr. H. W. Titus, of the latter bureau.