

stimulus. In normal transmission there is a large safety factor, and the amount of ACh released is always sufficient to ensure that transmission to all fibres is complete. In the normal electromyogram (e.m.g.) all potentials are therefore of the same height. Myasthenic nerve endings release only about one-fifth as much ACh as normal endings, so the safety factor is diminished. Hence the decline in ACh release is reflected by a progressive decrease in the e.m.g. potential because fewer muscle fibres respond. The degree of neuromuscular failure is measured by expressing the height of the fourth response as a percentage of the first.

This decline in e.m.g. is a characteristic feature of myasthenia gravis and may be used diagnostically (Fig. 1).

Repeated observations of the e.m.g. response and calculation of the percentage of neuromuscular transmission have been used to follow the changes produced by anticholinesterase therapy and hence to determine the optimal dose and frequency of administration and to detect the occurrence of overtreatment. This technique has also enabled observations to be made on the complications that may arise during concurrent treatment with other drugs such as suxamethonium and streptomycin.

Automatic control of isolated smooth muscle with digital print-out of contraction size

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Muscle contraction displaces the core of a differential transformer. The output of the transformer is rectified, smoothed, backed off, and fed to a digital voltmeter (Solartron LM 1440.2). An electric typewriter, driven by its control unit (LU 1469), prints out the voltmeter reading on instruction from the tissue bath control unit. The typewriter tabulates the results; for assays a separate column is used for each drug solution.

The control unit uses camshaft timers and is designed to provide time sharing of the analogue/digital converter and print-out facilities between three different experiments.

Perfusion of the cerebral ventricular system in conscious dogs

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Using a modification of a technique described by Manuilov (1958) (Fig. 1), stainless steel guide tubes are screwed into the skull of an anaesthetized dog so that their tips lie just above each lateral ventricle. At the same operation a guide tube is bracketed on to the occipital protuberance with its tip through the lip of occipital bone adjoining the atlanto-occipital membrane. Three weeks postoperatively, while the animal is conscious, needles are inserted percutaneously into the guide tubes. When a free flow of cerebrospinal fluid has been established it is possible to perfuse the ventricular system for periods of up to 4 hr without producing any behavioural changes provided the rate of flow of fluid is less than 0.35 ml./min. A recirculatory perfusion system has been employed as the small external volume allows cerebrospinal fluid from another dog to be used as the perfusing fluid. Using this system it has been possible to study the rate of removal of various infused substances.

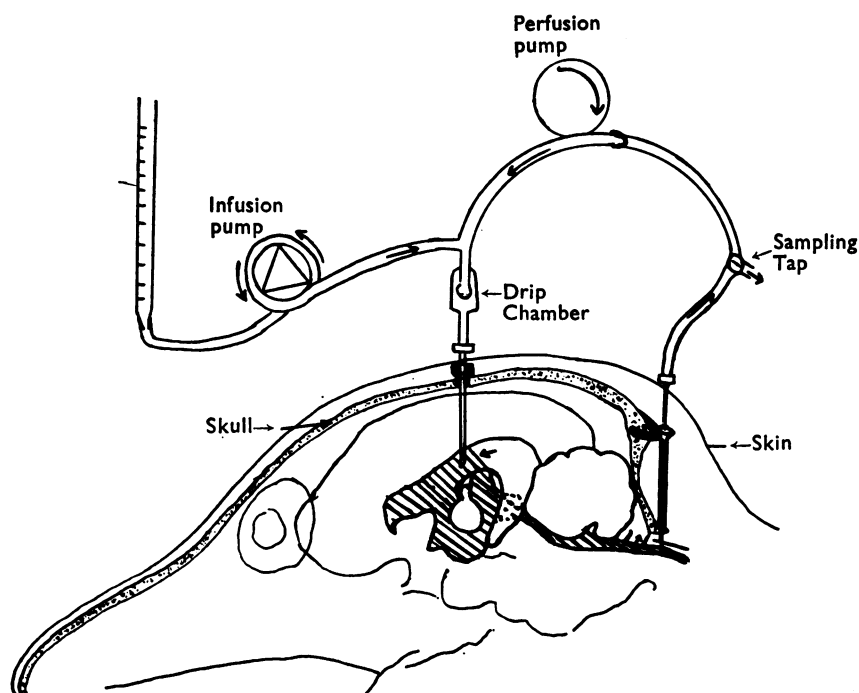


FIG. 1. A recirculatory perfusion system of the cerebral ventricular system of the dog.

Perfusion experiments of this type in conscious unrestrained dogs can be undertaken at intervals of two weeks without any subsequent ill effects.

REFERENCE

MANUILOV, I. A. (1958). *Sechenov Physiol. J. USSR* (English Transl.), **44**, 458.

An action of ouabain to promote smooth muscle contraction unrelated to membrane ATPase inhibition

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A concentration of 10^{-8} M ouabain causes contracture of uterine muscle isolated in a modified Krebs bicarbonate solution (Daniel & Robinson, 1960) and maintained at 17° – 19° C. In 1964, Daniel proposed that this contracture was due to inhibition of membrane ATPase.

It has been shown that smaller concentrations (10^{-5} to 5×10^{-4} M) of ouabain potentiate the responses of the isolated rat uterus to a variety of agonists. Furthermore, the potentiation of any one agonist by ouabain is not prevented by the antagonists of the others. Both the contracture produced by the higher concentrations of ouabain and the potentiation of the responses to other agonists produced by the lower concentrations are, however, prevented by low doses of a number of complexing agents (8 hydroxyquinoline, 1 : 10 phenanthroline, ATP, and other nucleotides).

Like ouabain, ZnCl_2 (10^{-4} M) causes potentiation of the responses of the uterus to the same agonists, and in higher concentrations will produce contracture. Furthermore,