Injections are made with a 100 μl. Hamilton syringe fitted with a 26 g×$\frac{3}{8}$ in. needle (Gillette) reduced to an effective length of $\frac{1}{4}$ in. with a rubber stop. The syringe is clamped in a "rack-work X" block (C. F. Palmer) to facilitate perpendicular penetration of the skull. The injection site is the midline, on a line drawn through the anterior base of the ears. To check the location of the injection site, 20 μl. of a 1 in 5 dilution of Indian ink in 0.9% NaCl was injected. Pathological evidence showing distribution of ink throughout the aqueducts and ventricles will be presented.

The pyrexia following injection of standard pyrogen ('E' Pyrogen, Organon) can be expressed numerically as the "temperature index", which is a simplified integral of the temperature changes seen during the 60 min after injection. The response (temperature index) to 'E' Pyrogen is proportional to the log of the dose, and when a constant dose of 'E' Pyrogen (2.5 μg/kg) is used, the responses obtained with prior administration of antipyretic drugs are proportional to the log of the dose of antipyretic drug. Relative potencies of antipyretic drugs may be assessed, and in our experiments these are expressed as the dose of drug necessary to reduce the response of 2.5 μg/kg of 'E' Pyrogen to that of 0.25 μg/kg in the absence of the drug.

The results show that the method is reliable and has a high degree of sensitivity, making it a useful screening procedure for antipyretic activity.

Electromyography in the diagnosis and treatment of myasthenia gravis

D. V. ROBERTS and A. WILSON, *The Physiological Laboratory and Department of Pharmacology, University of Liverpool*

When a motor nerve is stimulated, the release of acetylcholine (ACh) from the nerve endings is not always the same but decreases progressively from the first to the fourth

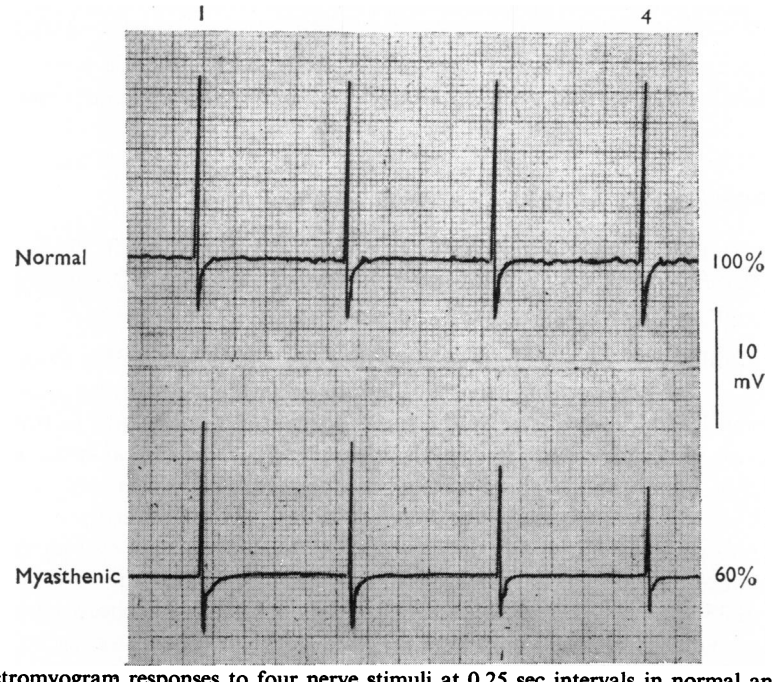

FIG. 1. Electromyogram responses to four nerve stimuli at 0.25 sec intervals in normal and myasthenic subjects. Neuromuscular transmission is measured by expressing the amplitude of the fourth response as a percentage of the first.

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

R. P. STEPHENSON, *Department of Pharmacology, University of Edinburgh*

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

G. W. ASHCROFT, R. C. DOW and A. T. B. MOIR (introduced by T. B. B. CRAWFORD), *Medical Research Council Unit for Research in Brain Metabolism, Department of Pharmacology, University of Edinburgh*

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.