Discrete excitatory mechanical responses can be obtained to single pulses (0·01–0·25 Hz). The accompanying electrical changes following single pulses are graded junctional depolarizations rather than spike potentials.

Following infusion of guanethidine  $(5 \times 10^{-5} \text{ M})$ , which raises tone and depolarizes the muscle membrane, supramaximal field stimulation using single pulses (1 ms, 8 Hz) causes a mechanical relaxation which is graded with frequency; the membrane potential in most cases remaining unchanged though on occasions a slight (<10 mv) hyperpolarization has been observed. The mechanical inhibition so obtained is abolished by tetrodotoxin (8  $\mu$ g) and by drugs reducing muscle tone, e.g. papaverine (0.6 mg) and is enhanced by perfusion with atropine ( $5 \times 10^{-7}$ M). The demonstration is intended to illustrate the electrical basis of the mechanical relaxation and the effect of drugs upon these.

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### Effects of salbutamol and terbutaline on physiological tremor in man

## A. RICHENS and JUDITH M. WATSON

Department of Clinical Pharmacology, St. Bartholomew's Hospital, London EC1

Sympathomimetic bronchodilator drugs produce an increase in physiological tremor as an adverse effect and it has been postulated that this may be due to their action on  $\beta$ -adrenoceptors in skeletal muscle (Bowman & Nott, 1969). Animal studies have shown that  $\beta_2$ -adrenoceptor agonists produce an increase in rate of relaxation of slow skeletal muscle and this may account for the feeling of weakness and tremulousness associated with acute stress (Bowman & Zaimis, 1958). In man, Marsden, Foley, Owen & McAllister (1967) have shown an increase in physiological tremor with isoprenaline and adrenaline which may be blocked by propranolol. We have studied the effects of two other sympathomimetic drugs, salbutamol and terbutaline, on physiological tremor, bronchial tone, blood pressure and heart rate in man.

Finger tremor was recorded with an accelerometer, frequency analyser and integrating circuit. Bronchodilatation was expressed as degree of protection against histamine-induced bronchoconstriction, as measured by F.E.V.<sub>1</sub>. Salbutamol (4 and 8 mg), terbutaline (5 and 10 mg) and placebo were administered orally to six normal healthy volunteers in a double-blind randomized trial. Readings were taken before and at intervals up to six hours after administration of drug.

Salbutamol (4 and 8 mg) and terbutaline (5 and 10 mg) produced a significant increase in physiological tremor, as compared with placebo (p<0.05). Terbutaline (5 and 10 mg) produced graded responses which were significantly different from each other at 2 h (p<0.02) but there was no significant difference between 4 and 8 mg of salbutamol.

Terbutaline (5 and 10 mg) and salbutamol (8 mg) produced a significant bronchodilatation (p<0.01). The terbutaline response was dose-dependent with a significant difference between doses at 1 h (p<0.02) but there was no significant difference between 4 and 8 mg of salbutamol.

In the higher doses, both drugs produced a significant increase in heart rate (p<0.05). Significant differences between the doses for each drug were produced at 1 and 3 h with salbutamol (p<0.02) and at 1.5 h, with terbutaline (p<0.05). Neither drug produced any significant change in blood pressure.

Terbutaline (10 mg) appeared to produce greater responses than salbutamol (8 mg) on tremor, bronchial tone and heart rate but the differences were not statistically significant.

The effects on physiological tremor of salbutamol and terbutaline followed a similar time course to their effects on bronchial tone.

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# The simultaneous measurement of blood flow and oxygen handling in normal and ischaemic areas of the myocardium in the dog (T)

R. J. MARSHALL and J. R. PARRATT

Department of Pharmacology, Royal College, University of Strathclyde and Department of Surgery, Western Infirmary, University of Glasgow

### An isolated, innervated, blood perfused cat heart preparation (T)

A. G. H. BLAKELEY, G. Powis and R. J. Summers

Department of Pharmacology, University of Glasgow, Glasgow G12 8QQ

### Microphotometric and microspectrographic identification of tissue components (T)

F. C. BOYLE

Department of Pharmacology, University of Glasgow, Glasgow G12 8QQ

## Measurement of electrical properties of the smooth muscle cell membrane of the rat anococcygeus (T)

K. E. CREED and J. S. GILLESPIE

Department of Pharmacology, University of Glasgow, Glasgow G12 8QQ

#### The rat anococcygeus muscle preparation in vitro and in vivo (T)

J. S. GILLESPIE, H. McCAFFERY and J. C. McGrath

Department of Pharmacology, University of Glasgow, Glasgow G12 8QQ

# Examination of the concept that sodium salicylate acts via an active metabolite (T)

PAMELA DAVISON and A. L. WILLIS

Department of Physiology, Stanford University, Stanford, California 94305

## Developing skeletal muscle fibres in tissue culture as a test system for the measurement of drug effects (T)

W. F. DRYDEN, A. L. HARVEY and B. HAMILTON

Department of Pharmacology, University of Strathclyde, Glasgow Gl 1XW