liver porphyrins was observed when the incubation time was extended to 30 h. A similar response was seen after 34 h incubation although after 41 h the response was reduced but still marked (Table 1).

Thus a well-defined porphyrinogenesis could be demonstrated in the liver after the incubation of chick embryos with methsuximide. This supports the finding of Racz & Marks (1969) with this drug. 2-Methyl-2-phenylsuccinimide, a pharmacologically active anticonvulsant metabolite of methsuximide in the rat and man (Nicholls & Orton, 1971), increased the porphyrin content of chick embryo liver approximately six-fold (1·2 μg porphyrins/g liver) which is about eight times less than that observed after administration of methsuximide (10 μg porphyrins/g liver). Hydrolysed methsuximide, which does not possess anticonvulsant properties (Nicholls & Orton, 1971), had no porphyrinogenic activity.

It, therefore, appears that 2-methyl-2-phenylsuccinimide not only contributes to the pharmacological anticonvulsant activity of methsuximide but also to the porphyrinogenic activity.

Welsh School of Pharmacy,
UWIST, Cardiff, CF1 3NU, U.K.

T. C. ORTON
P. J. NICHOLLS

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Simultaneous measurement of skeletal muscle, pulmonary mechanical and vascular responses to bronchodilators in the cat

Lands, Arnold & others (1967) and Lands, Luduena & Buzzo (1967) proposed two types of β-adrenoceptors. Bronchodilatation and vasodepression produced by β-adrenoceptor stimulants are believed to be mediated via β_2-adrenoceptors. These drugs can also enhance normal physiological tremor in man (Marsden, Foley & others, 1967) by a mechanism believed to involve β_2-adrenoceptors in skeletal muscle (Bowman & Nott, 1970). Inhalation therapy with β-stimulants is free from effects on skeletal muscle, but effective bronchodilatation after oral administration carries with it the side effect of muscle tremor in some patients (Legge, Gaddie & Palmer, 1971). Lands' proposal is based on results obtained from experiments in different species and so far no work has been reported in which simultaneous recordings have been made for the effect of β-stimulants on skeletal and bronchial muscle in the same animal. Some such experiments are now reported.

Cats of either sex, 2·2–4·0 kg, were anaesthetized with chloralose (80 mg/kg intravenously) after induction with a 3% halothane nitrous oxide 3 litre min^{-1} oxygen 1 litre min^{-1} mixture. Arterial blood pressure (mm Hg) was monitored from a cannula in a common carotid artery. The left soleus muscle was prepared (Bowman & Nott, 1970) and submaximal tetanic contractions were elicited by rectangular pulses of 50 μs duration at twice the voltage necessary to elicit a maximal twitch. Tetani (6–10 Hz) were produced for 1 s every 10 s and peak tension (g) recorded using an Ether UFI 32 oz strain gauge connected to a Devices M–4 pen recorder. Area ($g\ s^{-1}$) under the tetanus was obtained by integration of the strain

Table 1. *Dose ratios for salbutamol and orciprenaline relative to (—)-isoprenaline (= 1) for their effects on skeletal, bronchial and vascular muscle in the anaesthetized cat.*

Tissue	Response measured	Salbutamol Mean dose ratio (range)	Orciprenaline Mean dose ratio (range)
Skeletal muscle	Reduction in tension of submaximal tetanus	12·1 (9·3–16·2)	23·8 (20·0–30·9)
	Reduction in area of submaximal tetanus	10·4 (9·7–11·4)	19·3 (16·3–27·4)
Bronchial muscle	Inhibition of 5-HT-induced increase in pulmonary resistance	9·0 (8·3– 9·9)	28·1 (10·6–47·2)
	Inhibition of 5-HT-induced decrease in pulmonary compliance	18·9 (14·9–21·4)	26·6 (6·0–43·9)
Vascular muscle	Decrease in diastolic blood pressure	26·0 (4·9–55·9)	28·7 (10·0–50·0)

gauge output. Pulmonary resistance (cm H_2O litre^{-1} s^{-1}) and compliance (ml cm H_2O^{-1}) were measured as described for the dog by Daly, Farmer & Levy (1971). The cats were artificially respired through a tracheal cannula using a stroke volume of 13 ml/kg and stroke frequency of 28/min.

5-Hydroxytryptamine (5-HT) (3–20 μg/kg, i.v.) produced adequate bronchoconstriction with negligible effects on skeletal muscle and this spasmogen was injected intravenously every 10 min throughout the experiment. When pulmonary resistance and compliance changes were constant a dose of β-stimulant was injected intravenously 1 min before a 5-HT challenge. Log dose-response curves were constructed for (—)-isoprenaline, salbutamol and orciprenaline for reduction in tension and area of the submaximal tetanus, for inhibition of the bronchoconstriction induced by 5-HT and also for lowering of blood pressure. Doses of either salbutamol or orciprenaline were administered alternately with isoprenaline at intervals of not less than 30 min. Comparisons were made in 3 cats for salbutamol and 4 cats for orciprenaline. In the text doses stated refer to the free base.

The β-adrenoceptor stimulants did not differentiate between the β_2-mediated responses of skeletal, bronchial and vascular muscle (Table 1), results that are in agreement with the proposals of Lands & others (1967).

Department of Pharmacology,
Allen and Hanburys Limited,
Ware, Hertfordshire, U.K.

G. H. APPERLEY
M. J. DALY

October 20, 1971

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