## Contraction of rat vas deferens by cocaine

SIR,—During studies on isolated tissues, designed to examine the effect of drugs which inhibit uptake mechanisms on the potency of sympathomimetic amines, we have attempted to use cocaine on the isolated rat vas deferens.

Vasa deferentia from young adult rats were split longitudinally, to facilitate washing of drugs from the tissue, and were suspended in a 10 ml bath of Krebs solution (containing 200 $\mu$g/ml ascorbic acid) aerated with oxygen 95% and carbon dioxide 5% at 29°. Isotonic contractions were recorded using a modified Statham 10B strain gauge.

In 8 experiments in which $10^{-5}$M cocaine was left in the bath for 30 min before testing its effect on noradrenaline, adrenaline and phenylephrine, a small contraction to cocaine was observed. In another 7 experiments $10^{-4}$M cocaine caused a pronounced contraction of the tissue. After doses of cocaine, spontaneous activity of the preparation made it difficult to obtain quantitative results. In some preparations spontaneous activity was troublesome with high doses of noradrenaline or adrenaline before cocaine was added, and was intensified by the addition of cocaine. Tachyphylaxis to the cocaine contraction occurred even up to 60 min after the addition of the first dose. If responses to noradrenaline were obtained between the doses of cocaine the contraction to cocaine was restored. The restoration or maintenance of the cocaine contraction was dependent on the dose of noradrenaline used.

Cocaine, $10^{-4}$M, caused no initial contraction of 6 vasa taken from rats pretreated with reserpine (2 mg/kg on each of 2 days before the experiment). If responses to large doses of noradrenaline were then obtained, a contraction on the addition of cocaine was now observed. The size of the restored response depended on the amount of noradrenaline used. Spontaneous activity in all preparations from reserpinized animals was pronounced on the addition of cocaine. In both normal and reserpinized preparations, piperoxan ($10^{-4}$M), left in contact with the tissue for 15 min before the addition of cocaine, caused a complete block of the cocaine contraction.

The use of cocaine to inhibit uptake of amines into the adrenergic nerve terminals of the isolated rat vas deferens has not proved satisfactory since cocaine causes a contraction and initiates or exaggerates spontaneous activity. The contraction of the rat vas deferens by cocaine is probably due to an indirect sympathomimetic effect causing a release of noradrenaline. The contraction shows tachyphylaxis, does not occur in reserpinized preparations and is blocked by the $\alpha$-adrenergic blocking drug, piperoxan. Sympathomimetic effects of cocaine have been reported by workers on other tissues (Teeters, Koppanyi & Cowan, 1963; Maengwyn-Davies & Koppanyi, 1966).

Department of Physiology,
University of Queensland,
Brisbane,
Australia.

STELLA R. O'DONNELL
SALLY E. HECKER

June 19, 1967

### References

Maengwyn-Davies, G. D. & Koppanyi, T. (1966). *J. Pharm. exp. Ther.*, **154**, 481–493.
Teeters, W. R., Koppanyi, T. & Cowan, F. F. (1963). *Life Sci.*, **2**, 509–518.