Our results provide further evidence that anti-inflammatory agents reduce glycoprotein levels in inflamed tissue (Houck & Jacob, 1965).

Research Laboratories,
Istituto De Angeli S.p.A.,
Via Serio 15, Milan, Italy.

GERMANO COPPI
GRAZIANO BONARDI

January 12, 1968

References

Boas, N. F. (1953). *J. biol. Chem.*, **204**, 553–563.
Bolognani, L., Coppi, G., Della Berta, F. & Zambotti, V. (1961). *Nature, Lond.*, **190**, 913–914.
Bolognani, L., Coppi, G. & Zambotti, V. (1958). *Boll. soc. ital. Biol. sper.*, **34**, 1950–1951.
Coppi, G. (1966). *Archs int. Pharmacodyn. Thér.*, **162**, 422–431.
Delaunay, A. & Bazin, S. (1965). International symposium on non-steroidal anti-inflammatory drugs, editors Garattini, S. and Dukes, M. N. G., pp. 25–34. Amsterdam: Excerp. Med. Found.
Houck, J. C. & Jacob, R. A. (1965). *Ibid.*, pp. 44–51.
Marazzi-Uberti, E. & Turba, C. (1966). *Archs int. Pharmacodyn. Thér.*, **162**, 378–397.
Marazzi-Uberti, E., Turba, C. & Erba, G. (1966). *Ibid.*, **162**, 398–412.
Svennerholm, L. (1958). *Acta chem. scand.*, **12**, 547–554.
Turba, C. & Marazzi-Uberti, E. (1966). *Archs int. Pharmacodyn. Thér.*, **162**, 413–421.

Effects of some sympathomimetic amines on the response of the rabbit isolated ear artery to noradrenaline and electrical stimulation

SIR,—The site of uptake of noradrenaline in the rabbit ear artery has been shown to be situated on the outer perimeter of the smooth muscle layer (de la Lande & Waterson, 1967). These authors have also shown that cocaine applied to the outer surface of the artery potentiated the effects of extraluminally injected noradrenaline and had little effect on the intraluminal noradrenaline. Cocaine was also shown to potentiate the electrically induced vasoconstriction (de la Lande & Rand, 1965). Since sympathomimetic amines are known to potentiate noradrenaline in other smooth muscle (Bentley, 1965) and to block the uptake of noradrenaline in heart (Burgen & Iversen, 1965), it seemed important to investigate the effects of these amines on the vascular smooth muscle in relation to the hypothesis postulated by de la Lande & Waterson (1967).

Central ear arteries, 4–5 cm long, isolated from anaesthetized (25% urethane, i.v.) rabbits weighing 1·5–2·5 kg were perfused in a 400 ml bath by the method of de la Lande & Harvey (1965) with Krebs bicarbonate solution at 37°, aerated with 95% oxygen and 5% carbon dioxide. Perfusion pressure and perfusion rate were maintained at 20–30 mm Hg and 4–5 ml/min respectively. Intraluminal injections were given through the rubber tubing at the proximal end of the artery. In some experiments a 20 ml bath was used to facilitate a quick washout. Constriction of the artery in response to noradrenaline added intra- or extraluminally was recorded with a mercury manometer on a smoked drum. A Grass model S4-D stimulator delivering pulses of 0·5 msec duration alternatively at a frequency of 5 or 10 shocks/sec for 5 sec each 2 min was used for periarterial nerve stimulation. The drugs used were: (−)-noradrenaline bitartrate (Koch-Light); (±)-amphetamine sulphate (L. Light & Co); metaraminol bitartrate (Merck Sharp & Dohme) and tyramine hydrochloride (Calbiochem).

The results showed that the artery was much less sensitive to extraluminal than to intraluminal noradrenaline, which is in agreement with the findings of Cannell, de la Lande & Waterson (1966). Of the sympathomimetic amines

TABLE 1. EFFECTS OF SYMPATHOMIMETIC AMINES ON THE RESPONSE OF THE EAR ARTERY TO INJECTED NORADRENALINE. The figures represent the % change in presence of the drug. + (increase), — (decrease).

Drugs	Intraluminal	Extraluminal
Amphetamine 1×10^{-6}	11·3 (−)	62·1 (+)
	7·5 (−)	65·0 (+)
	12·4 (−)	135·2 (+)
Metaraminol 1×10^{-7}	11·3 (−)	72·2 (+)
	7·2 (−)	131·4 (+)
	7·3 (−)	130·5 (+)
Tyramine 1×10^{-5}	212·1 (+)	51·0 (+)
	172·3 (+)	32·6 (+)
	176·5 (+)	58·4 (+)

TABLE 2. EFFECTS OF SYMPATHOMIMETIC AMINES ON THE RESPONSE OF THE EAR ARTERY TO THE ELECTRICAL STIMULATION. The figures represent the % change in presence of the drug. + (increase), — (decrease).

Drugs	5 shocks/sec	10 shocks/sec
Amphetamine, 1×10^{-6}	28·0 (+)	48·0 (+)
	148·1 (+)	75·0 (+)
	35·0 (+)	60·4 (+)
Metaraminol, 1×10^{-7}	22·0 (+)	14·5 (+)
	108·1 (+)	105·0 (+)
	143·3 (+)	147·0 (+)
Tyramine 1×10^{-5}	12·1 (−)	26·0 (−)
	32·0 (−)	46·4 (−)
	22·2 (−)	21·4 (−)

tested, amphetamine 1×10^{-7}, 1×10^{-6}; metaraminol, 1×10^{-8}, 1×10^{-7} and tyramine 1×10^{-6} applied to both surfaces of the artery caused little or no change in the sensitivity of the artery to intraluminally injected noradrenaline, but with tyramine, 1×10^{-5}, a two-fold potentiation was noted. The application of amphetamine, 1×10^{-6}, metaraminol, 1×10^{-7} or tyramine, 1×10^{-5} to the outer surface of the artery caused a much greater potentiation of extra- than intraluminally applied noradrenaline (Table 1). Amphetamine, 1×10^{-6} and metaraminol, 1×10^{-7}, both caused approximately a two-fold increase in the response to electrical stimulation of the periarterial nerves but tyramine 1×10^{-5} caused a small depression (Table 2). From these findings it is concluded that sympathomimetic amines potentiate both extra-luminal noradrenaline and noradrenaline released by nerve stimulation by blocking the uptake mechanism in the sympathetic nerve endings in a way similar to cocaine as shown by de la Lande & Waterson (1967).

Department of Physiology,
Monash University,
Clayton,
Victoria,
Australia.

G. A. BENTLEY
A. H. M. HUSSAIN

January 25, 1968

References

Bentley, G. A. (1965). *Br. J. Pharmac. Chemother.*, **25**, 243–256.
Burgen, A. S. V., & Iversen, L. L. (1965). *Ibid.*, **25**, 34–49.
Cannell, V., de la Lande, I. S. & Waterson, J. G. (1966). *Ibid.*, **28**, 255–272.
de la Lande, I. S. & Harvey, J. A. (1965). *J. Pharm. Pharmac.*, **17**, 589–593.
de la Lande, I. S. & Rand, M. J. (1965). *Aust. J. exp. Biol. med. Sci.*, **43**, 639–656.
de la Lande, I. S. & Waterson, J. G. (1967). *Nature, Lond.*, **214**, 313–314.