REFERENCES

ARMITAGE, S. G. (1952). *J. comp. physiol. Psychol.*, **45**, 146–52.

HARNED, B. K., HAMILTON, H. C. & BORRUS, J. C. (1940). *Am. J. med. Sci.*, **200**, 846–50.

LEONARD, B. E. & TONGE, S. R. (1969). *Life Sci.*, **8**, 815–25.

TONGE, S. R. & LEONARD, B. E. (1972). *Psychopharmacologia*, **23**, 86–90.

VINCENT, N. M. (1958). *Am. Psychologist*, **13**, 401–7.

WELCH, A. M. & WELCH, B. (1969). *Analyt. Biochem.*, **30**, 161–79.

WERBOFF, J. (1970). In: *Principles of Psychopharmacology*. pp. 343–53. London and New York: Academic Press.

WERBOFF, J. & GOTTLIEB, J. S. (1963). *Obst. Gynecol. Survey*, **18**, 420–3.

Some observations on the pulmonary artery of the guinea-pig

Qualitative as well as quantitative variations of drug actions on the pulmonary artery of several species have been previously reported with special interest in the biphasic response to acetylcholine (Gaddum & Holtz, 1933; Smith & Coxe, 1951). However, drug effects on the pulmonary artery of the guinea-pig have not been thoroughly documented and therefore the responses to several pharmacological agents on this blood vessel have been examined.

The blood vessel was removed from guinea-pigs (Hartley strain, 200–250 g) into Tyrode solution and cut spirally to produce a strip of 1·5–2 cm in length. The tissue was suspended in Tyrode solution (containing 17 mg^{-1} litre ascorbic acid), at 37°, aerated with 5% carbon dioxide in oxygen and allowed to equilibrate for 60 min. The initial tissue tension was 0·5 g and recordings of contractions and relaxations were measured isometrically using a pen recorder.

The blood vessel contracted to the following drugs (threshold ranges expressed as $\mu g\ ml^{-1}$ base for 8–10 experiments): histamine, 0·075–0·1; 5-HT, 5·0–6·0; acetylcholine, 4·5–5·5; carbachol, 30–35 and noradrenaline, 0·02–0·05. Contractions to acetylcholine produced a transient biphasic response (Fig. 1) unlike the other spasmogenic agents. This was increased in height, but not duration of contraction, by eserine salicylate ($10\ \mu g\ ml^{-1}$). Relaxation to lower doses of acetylcholine ($0{\cdot}2–1{\cdot}0\ \mu g\ ml^{-1}$) were produced on the artery previously contracted with noradrenaline in 4 of the 8 preparations examined. Acetylcholine-mediated relaxation was not affected by eserine salicylate ($10\ \mu g\ ml^{-1}$) in these experiments. Both contraction and relaxation produced by acetylcholine were completely abolished by atropine sulphate ($2\ \mu g\ ml^{-1}$).

The vasodilator response with low doses of acetylcholine and the vasoconstrictor response at higher concentrations confirms the findings on dog and cat pulmonary artery (Gaddum & Holtz, 1933) but is in contrast to the pure vasoconstrictor response to this drug in the same vessel of the calf (Eyre, 1971) and rabbit (Su & Beavan, 1965).

Isoprenaline (50 ng-$2{\cdot}5\ \mu g\ ml^{-1}$) had neither an effect on the uncontracted nor contracted (produced by carbachol) artery strip (10 experiments) but at doses $> 5\ \mu g\ ml^{-1}$ slow contractions were produced. This contractile response was abolished by pretreatment with doses of phentolamine mesylate ($0{\cdot}5\ \mu g\ ml^{-1}$ for 5 min; Fig. 1) and phenoxybenzamine hydrochloride ($0{\cdot}5\ \mu g\ ml^{-1}$ for 5 min) that abolished the response to submaximal concentrations of noradrenaline ($0{\cdot}1–0{\cdot}2\mu g\ ml^{-1}$) but not affected by propranolol hydrochloride ($1\ \mu g\ ml^{-1}$) or atropine sulphate ($1\ \mu g\ ml^{-1}$). None of these agents affected base-line tension nor responses to acetylcholine, histamine and 5-HT at these concentrations. Salbutamol ($5–150\ \mu g\ ml^{-1}$) had no effect on the uncontracted or contracted preparation (4 experiments). Theophylline ($> 200\ \mu g\ ml^{-1}$), dibutyryl adenosine 3′,5′-monophosphate ($> 250\ \mu g\ ml^{-1}$) and sodium nitrite ($> 15\ \mu g\ ml^{-1}$) relaxed the uncontracted artery and also relaxed

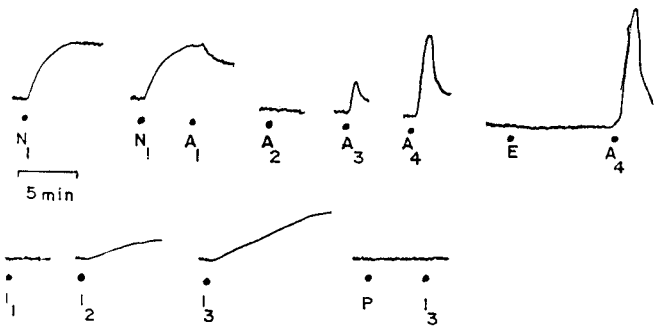

FIG. 1. Responses of the guinea-pig pulmonary artery to several pharmacological agents. noradrenaline, N (0·2 μg ml^{-1}); acetylcholine, A_1 (0·2 μg ml^{-1}), A_2 (4·5 μg ml^{-1}), A_3 (7·5 μg ml^{-1}) and A_4 (15·0 μg ml^{-1}); eserine sulphate, E (10 μg ml^{-1}); isoprenaline, I_1 (1μg ml^{-1}), I_2 (7·5 μg ml^{-1}), I_3 (12·5 μg ml^{-1}); phentolamine mesylate, P (0·5 μg ml^{-1}).

contractions produced by isoprenaline (10 experiments). Prostaglandin E_1 ($> 0{\cdot}75$ μg ml^{-1}) relaxed both histamine and isoprenaline induced contractions but did not influence base-line conditions even with doses up to 7·5 μg ml^{-1}.

This study confirms the absence of β-adrenoceptors in the artery recently described by Okpako (1972a, b). The discovery of an α-adrenoceptor response to isoprenaline, as confirmed by α-blockade with phentolamine and phenoxybenzamine, is not in agreement with the data of Okpako, however. Eyre (1971) has also described an α-adrenocepter response to isoprenaline in the pulmonary artery of the calf, during β-adrenoceptor blockade with propranolol.

This study further demonstrates the occurrence of dose-dependent biphasic pharmacological responses and the importance of careful choice of dosage to approximate "physiological" responses *in vitro*.

The work was supported by U.S. PHS Grants HE-14534 and HE-14179.

Yale University Lung Research Center ALAN J. LEWIS
and J. B. Pierce Foundation Laboratory,
290 Congress Avenue,
New Haven, Connecticut, U.S.A.

October 2, 1972

REFERENCES

EYRE, P. (1971). *J. Pharm. Pharmac.*, **23**, 899–900.
GADDUM, J. H. & HOLTZ, P. (1933). *J. Physiol., Lond.*, **77**, 139–158.
OKPAKO, D. T. (1972a). *J. Pharm. Pharmac.*, **24**, 40–46.
OKPAKO, D. T. (1972b). *Br. J. Pharmac.*, **44**, 311–321.
SMITH, D. J. & COXE, J. W. (1951). *Am. J. Physiol.*, **167**, 732–737.
SU, C. & BEAVAN, J. A. (1965). *Life Sci.*, **4**, 1025–1029.