(MA 2472) and was carried out during the tenure of a Canadian Heart Foundation Senior Research Fellowship. I should like to acknowledge the careful technical assistance of Miss Alice K. Fryer.

Department of Pharmacology DAVID M. PATON
University of Alberta
Edmonton 7, Alberta, Canada

May 13, 1970

REFERENCES

BOGDANSKI, D. F. & BRODIE, B. B. (1969). *J, Pharmac. exp. Ther.*, **165**, 181–189.
BOGDANSKI, D. F., TISSARI, A. & BRODIE, B. B. (1968). *Life Sci.*, 7, 419–428.
CRANE, R. K. (1965). *Fedn Proc. Fedn Am. Socs exp. Biol.*, **24**, 1000–1006.
EDDY, A. A., MULCAHY, M. F. & THOMSON, P. J. (1967). *Biochem. J.*, **103**, 863–876.
GILLIS, C. N. & PATON, D. M. (1967). *Br. J. Pharmac. Chemother.*, **29**, 309–318.
IVERSEN, L. L. (1963). *Ibid.*, **21**, 523–537.
IVERSEN, L. L. & KRAVITZ, E. A. (1966). *Molec. pharmac.*, **2**, 360–362.
KIPNIS, D. M. & PARRISH, J. E. (1965). *Fedn Proc. Fedn Am. Socs exp Biol.*, **24**, 1051–1059.
PATON, D. M. (1968). *Br. J. Pharmac.*, **33**, 277–286.
STEIN, W. D. (1967). *The movement of molecules across cell membranes.*, pp. 177–206, London: Academic Press.
TISSARI, A. H., SCHÖNHÖFER, P. S., BOGDANSKI, D. F. & BRODIE, B. B. (1969). *Molec. Pharmac.*, **5**, 593–604.
WHITE, T. D. & KEEN, P. (1970). *Biochim. Biophys. Acta*, **196**, 285–295.

Reduced variation of [^{3}H]noradrenaline uptake into rat submaxillary glands by atropine pretreatment

The submaxillary gland of the rat is useful for the study of peripheral adrenergic mechanism. It has a rich adrenergic innervation with a mean noradrenaline content of about 1·2 μg/g tissue, is paired so that it is always possible to get a matched control, and is easily accessible for different mechanical manipulations. The adrenergic nerves of the gland, with cell bodies in the superior cervical ganglion, and the preganglionic fibres in the cervical sympathetic trunk, are easily reached from the neck.

In the studies made in this laboratory using the preparation a serious problem was encountered in the great variation between different animals in the uptake of labelled noradrenaline (^{3}H-NA) or its analogues. A possible explanation for this could be that the secretory activity of the submaxillary gland and thus the blood flow through the organ varied widely between and within animals. The following experiment was made to see if a uniform increase or decrease of the secretory activity of the submaxillary gland could reduce the differences in uptake of labelled amines.

Male Sprague-Dawley rats, 170–270g, kept at 31°, received 1 μg/kg ^{3}H-NA (specific activity 8·45 Ci/mmol, NEN Chemicals) in a tail vein. One group of 8 rats was pretreated with atropine, 1 mg/kg intraperitoneally 30 min before the ^{3}H-NA injection. In another group, 8 rats were forced to chew dry wheat starch 5 min before and 5 min after the ^{3}H-NA injection. A third group, also of 8 rats, was not pretreated. Three h after the ^{3}H-NA administration the rats were killed. The hearts and the submaxillary + sublingual glands were immediately taken out, weighed and homogenized in ice-cold 0·4 N perchloric acid. The salivary glands from both sides were analysed together. Noradrenaline was separated on cation exchange columns and the tritium contents of the eluates were measured by liquid scintillation counting (Carlsson & Waldeck, 1963; Stitzel & Lundborg, 1966).

Three h after the ^{3}H-NA injection a mean 1·58 ng/g (variance 0·297) ^{3}H-NA was found in the submaxillary + sublingual glands. Neither after pretreatment with atropine (1·41 variance 0·041) nor with dry wheat starch (1·50 variance 0·304) was this

amount significantly changed. The variance of the observations, however, was significantly reduced by atropine pretreatment ($P < 0{\cdot}01$). The hearts of the control rats contained a mean 4·58 ng/g of ^{3}H-NA 3 h after the injection and about the same in the rats pretreated with dry wheat starch (4·56). After atropine pretreatment, the content of ^{3}H-NA in the hearts (5·52) was significantly increased ($P < 0{\cdot}001$). The variance of the observation was not changed by pretreatment. As alterations in body temperature might influence the results, rectal temperature was recorded immediately before killing, and did not differ between groups.

Atropine, 1 mg/kg, completely abolishes the secretory response of the submaxillary gland by parasympathetic stimulation in the rat (Ohlin, 1965). Also the sympathetic nerves can mediate reflexly evoked secretory responses, although these are comparatively small (Ohlin, 1968). It is thus probable, that the secretory activity of the glands after atropine treatment is less variable than in the glands of the control rats. As the blood flow through the gland is correlated with the secretory activity (see Burgen & Emmelin, 1961), the variations in blood flow should also be reduced by atropine.

The uptake into an organ of exogenously administered noradrenaline is dependent on two major factors: the density of the adrenergic nerve terminals and the blood flow through the organ (Kopin, Gordon & Horst, 1965). In the present experiment reduced variations in blood flow through the glands is the most probable explanation for the smaller variance of the ^{3}H-NA values found after atropine.

Chewing dry wheat starch increases the salivary secretion (Hillarp, 1949). This treatment, when performed 5 min before and 5 min after the ^{3}H-NA injection, did not change the variation of the ^{3}H-NA content of the glands. Probably the stimulation was not maximal and perhaps not equally strong in all rats giving variations in blood flow and in uptake of ^{3}H-NA.

If atropine reduces and starch chewing stimulates secretory activity and blood flow, a decrease in ^{3}H-NA uptake by the salivary gland after atropine and an increase after starch chewing would be expected. Contrary to this, the average uptake was not influenced by these procedures; possibly other factors influencing ^{3}H-NA uptake are simultaneously affected.

Atropine pretreatment increased the content of ^{3}H-NA found in the hearts. Increased heart rate and blood flow through the heart, leading to a greater uptake of administered ^{3}H-NA, could account for this difference.

The results of this experiment indicate that atropine pretreatment can diminish uptake by the submaxillary glands by reducing variations in secretory activity and blood flow. When using labelled substances in the study of adrenergic transmission in the submaxillary glands, such pretreatment can be valuable.

This work was supported by the Faculty of Medicine, University of Göteborg. The technical assistance of Mrs. Marianne Olofsson is gratefully acknowledged.

Department of Pharmacology, OLLE ALMGREN
University of Göteborg,
Göteborg, Sweden.

April 2, 1970

REFERENCES

BURGEN, A. S. V. & EMMELIN, N. G. (1961). Monographs of the Physiological Society. No. 8. Editors: BARCROFT H., DAVSON, H. and PATON, W. D. M.
CARLSSON, A. & WALDECK, B. (1963). *Acta pharmac. tox.*, **20**, 47–55.
HILLARP, N·-Å. (1949). *Acta anat.*, **8**, 190–200.
KOPIN, I. J., GORDON, E. K. & HORST, W. D. (1965). *Biochem. Pharmac.*, **14**, 753–759.
OHLIN, P. (1965). *Acta Univ. Lund II*, **23**, 1–12.
OHLIN, P. (1968). *Q. Jl exp. Physiol.*, **53**, 19–22.
STITZEL, R. E. & LUNDBORG, P. (1966). *Br. J. Pharmac. Chemother.*, **29**, 99–104.