392P Proceedings of the

After treatment of the uteri from untreated mature, oestrogen treated immature and ovariectomized rabbits with the  $\alpha$ -adrenoceptor blocking agent, phentolamine (0·1–1·0  $\mu$ g/ml), all three catecholamines caused relaxation. Treatment of uteri from immature and ovariectomized animals with the  $\beta$ -adrenoceptor blocking agent propranolol (10–40 ng/ml) caused the inhibitory responses to adrenaline and noradrenaline to be converted to the excitatory type seen in the adult.

Thus it is concluded that both  $\alpha$ - and  $\beta$ -adrenoceptors are present in the uteri of mature and immature rabbits. The type of response obtained can be altered by choosing a catecholamine with a greater or lesser degree of  $\alpha$ - or  $\beta$ -agonist activity, by varying the level of oestrogen influence, or by the use of the appropriate type of adrenoceptor blocking agent.

† Present address: Pfizer Ltd., Sandwich, Kent.

## REFERENCES

AHLQUIST, R. P. (1948). A study of adrenotropic receptors. *Am. J. Physiol.*, **153**, 586-600. GRUBER, C. M. (1933). The autonomic innervation of the genito-urinary system. *Physiol. Rev.*, **13**, 497-609.

MARSHALL, JEAN M. (1969). Adrenergic innervation of the female reproductive tract: anatomy, physiology and pharmacology. *Ergebn. Physiol.*, **62**, 6-67.

## Effect of adrenalectomy upon some rat heart enzymes

B. A. CALLINGHAM and LAURA DELLA CORTE\*, Department of Pharmacology, University of Cambridge

One effect of adrenalectomy in the rat is an increase in the monoamine oxidase (MAO) activity of the heart (Avakian & Callingham, 1968) and, to a lesser extent in other organs (Caesar, Collins & Sandler, 1970). This increase in activity can be prevented by the administration of hydrocortisone to the adrenalectomized animals.

In an attempt to determine the nature of this effect, we have examined some of the enzymes found in rat heart homogenates, particularly those in the mitochondrial fraction where the bulk of the MAO is found. The possibility that morphological changes occur has been examined by means of electron microscopy of tissue sections and of mitochondrial pellets.

Adrenalectomized rats were maintained on sodium chloride solution (0.9% w/v) following operation and were killed between 10 and 42 days later. The hearts of these animals and of controls were homogenized in modified Chappell-Perry medium (Chappell & Perry, 1954) in which the editic acid (EDTA) is replaced by ethyleneglycol bis aminoethyl tetra acetic acid (EGTA) and magnesium ions omitted. Oxygen electrode measurements of the resulting mitochondrial fractions following differential centrifugation showed little or no uncoupling of phosphorylation when either succinate or pyruvate and malate were used as substrates. The mitochondria were therefore largely undamaged. Electron microscopy confirmed this.

MAO and NADH<sub>2</sub>-cytochrome-C reductase, both located in the outer membrane of the mitochondrion, significantly increased activity in whole homogenates and in mitochondria from the hearts of adrenalectomized rats. In our experiments MAO activity was 100% and NADH<sub>2</sub>-cytochrome-C-reductase 32% higher than control values in mitochondrial fractions. The increase in MAO activity was seen using several substrates, e.g. tyramine, dopamine and benzylamine. In contrast there was no

increase in the inner membrane marker, succinic dehydrogenase, or in malic dehydrogenase, which is found both on the inner membrane and in the space between inner and outer membranes. No increases could be found in the activity of any other enzyme studied, including fumarase in the mitochondrial matrix and the microsomal enzyme DPN-nucleocidase. Lactate dehydrogenase was also unaffected.

The effect of adrenalectomy on the mitochondrion appears to be restricted to those enzymes in the outer membrane. Furthermore intact mitochondria are not essential. If the hearts are homogenized in distilled water there is an increase in MAO activity. But the further increase as a result of adrenalectomy is the same as that produced in Chappell-Perry medium.

It appears that the effects produced in the heart mitochondria after adrenolectomy of the rat and those produced by extraction of the tissue in hypotonic media are exerted at different sites in the mitochondrial membrane.

L.D.C. is a British Council Scholar.

## REFERENCES

AVAKIAN, V. M. & CALLINGHAM, B. A. (1968). An effect of adrenalectomy upon catecholamine metabolism. Br. J. Pharmac. Chemother., 33, 211 P.

CAESAR, P. M., COLLINS, G. G. S. & SANDLER, M. (1970). Catecholamine metabolism and monoamine oxidase activity in adrenalectomized rats. *Biochem. Pharmac.*, 19, 921-926.

CHAPPELL, J. B. & PERRY, S. V. (1954). Biochemical and osmotic properties of skeletal muscle mitochondria. *Nature, Lond.*, 173, 1094–1095.

## Changes in catechol-O-methyl transferase activity in the rat submaxillary gland after surgical and pharmacological procedures

O. J. Broch, Jun., H. C. Guldberg and C. A. Marsden\*, Department of Pharmacology University of Bergen, Bergen, Norway

Monoamine oxidase (MAO) in the sympathetically innervated submaxillary gland has an intra- and extraneuronal localization (Iversen, Glowinski & Axelrod, 1966; Almgren, Andén, Jonason, Norberg & Olson, 1966). Jonason (1969) suggested, from indirect evidence, that catechol-O-methyl transferase (COMT) was localized outside the adrenergic nerves in the gland. To obtain information on the localization of COMT in the submaxillary gland the activity of the enzyme was measured in postganglionically sympathectomized and ligated glands and after reserpine and desipramine.

The excretory duct of one of the submaxillary glands was ligated in six rats and the superior cervical ganglion removed on one side of another nine. Five rats were ligated and post-ganglionically sympathectomized on the same side. Fourteen days later the glands were removed; MAO (Snyder & Hendley, 1968) and COMT activities (Broch & Guldberg, 1970) were determined in whole gland homogenates with the unoperated side acting as control. Small pieces of the glands were processed for fluorescence histochemistry of monoamines. Other rats were treated with reserpine (5 mg/kg intraperitoneally). Desipramine (25 mg/kg) was given subcutaneously three times at intervals of 8 hours. The rats were killed 24 h after the onset of drug administration.

Control glands showed a network of fluorescent adrenergic fibres around the acinar cells. In the atrophied gland the acinar cells were reduced in volume but the adrenergic fibres were unaffected. In sympathectomized glands there were no fluorescent