Pancuronium bromide (10 mg/kg) had qualitatively similar effects.

These results demonstrate two effects of pancuronium bromide on heart rate *in vivo*; a short-lasting injection effect, which may be due to an indirect sympathomimetic action, and a longer-lasting potentiation of cardiac sympathetic responses which is at least partly due to blockade of neuronal NA uptake.

J.R.D. is an M.R.C. Student.

References

CLANACHAN, A.S. & MUIR, T.C. (1972). A technique for the study of muscle relaxants by stimulating the spinal motor nerve outflow in the pithed rat. *Br. J. Pharmac.*, **46**, 514–516.

COLEMAN, A.J., DOWNING, J.W., LEARY, W.P., MOYES, D.G. & STYLES, M. (1972). The immediate cardiovascular effects of pancuronium, alcuronium and tubocurarine in man. *Anaesthesia*, **27**, 415.

DOMENECH, J.S., GARCIA, R.C., SASIAIN, J.M.R., LOYOLA, A.Q. & OROZ, J.S. (1976). Pancuronium bromide: an indirect sympathomimetic agent. *Br. J. Anaesth.*, **48**, 1143–1148.

GILLESPIE, J.S., MacLAREN, A. & POLLOCK, D. (1970). A method of stimulating different segments of the autonomic outflow from the spinal column to various organs in the pithed cat and rat. *Br. J. Pharmac.*, **40**, 257–267.

HUGHES, R. & CHAPPLE, D.J. (1976). Effects of non-depolarizing neuromuscular blocking agents on peripheral autonomic mechanisms in cats. *Br. J. Anaesth.*, **48**, 59–67.

IVANKOVITCH, A.D., MILETICH, D.J., ALBRECHT, R.F. & ZAHED, B. (1975). The effect of pancuronium on myocardial contraction and catecholamine metabolism. *J. Pharm. Pharmac.*, **27**, 837–841.

Effects of castration on the mechanical response to motor nerve stimulation of the rat vas deferens

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Various drugs including adrenaline produce contraction of the rat vas deferens consisting of two elements, a sustained rise in tone and a super-imposed rhythmical contraction (Waddell, 1916). Following castration, the tonic contraction is lost but the tissues become more sensitive to rhythmical contraction (Martins & Valle, 1939).

Motor nerve responses of rat vas deferens also have two components, an early 'twitch' and a slower but better maintained 'secondary' contraction (Swedin, 1971; Ambache, Dunk, Verney & Zar, 1972). Since the time courses of the 'twitch' to nerve stimulation and of the rhythmical contraction found with agonist drugs are similar, the present study examined whether castration could produce differential effects on the two components of the nerve response and on the form of the response to noradrenaline (NA).

Male Wistar rats (250 g) were castrated under ether anaesthesia and tissues analysed 10–12 weeks post-operatively when the reduction in wet weight and in total noradrenaline content has reached equilibrium (Wakade, Garcia & Kirpekar, 1975). One group of castrates (10 weeks p.o.) were treated with testosterone propionate (2 mg/day, s.c. in corn oil) for 10 days and tissues taken on the 11th day. Vasa deferentia from castrates, testosterone treated castrates and untreated controls were isolated in Krebs' bicarbonate solution at 37°C and isometric tension recorded (Gillespie & McGrath, 1975). Frequency/response curves to field stimulation (1 ms pulses, 0.1–150 Hz, 30 s trains) and dose/response curves to NA (10^{-8}–10^{-3} M) were constructed for each tissue.

After castration, the 'secondary' response to nerve stimulation at all frequencies and the tonic response to NA were almost completely absent. The 'twitch' component at low frequencies ($\leqslant$2 Hz) was, however, virtually unaltered in height and NA produced rhythmical contractions. The response to a single pulse of field stimulation was as great in height but of shorter duration than in controls, the slower adrenergic phase (McGrath, 1977) being absent. At frequencies above 2 Hz the 'twitch' phase of the vas response was reduced compared with controls. All effects on the nerve response were consistent with the loss of the conventional adrenergic component and thus present another situation, analogous to the effect of post-junctional α-adrenoceptor blockade (Swedin, 1971), where the 'twitch' response can be isolated. This suggests a different post-junctional basis for the 'twitch' and 'secondary' responses.

All of the above effects of castration were reversed by testosterone treatment as has previously been demonstrated for other parameters in the vas deferens including responsiveness to agonists, tissue weight loss

and total NA content (Martins & Valle, 1939; Wakade *et al.*, 1975; Sjostrand & Swedin, 1976). It is, therefore, concluded that the effects of motor nerve stimulation and of NA on rat vas deferens are normally under the control of testosterone and that this should be borne in mind when using this tissue to analyse adrenergic mechanisms.

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References

AMBACHE, N., DUNK, LINDA P., VERNEY, J. & ZAR, M.A. (1972). Inhibition of post-ganglionic motor transmission in vas deferens by indirectly acting sympathomimetic drugs. *J. Physiol. (Lond.)*, **227**, 433–456.

GILLESPIE, J.S. & McGRATH, J.C. (1975). The effects of lysergic acid diethylamide on the response to field stimulation of the rat vas deferens and the rat and cat anococcygeus muscles. *Br. J. Pharmac.*, **54**, 481–488.

McGRATH, J.C. (1977). Adrenergic motor responses to single pulse stimulation in the rat vas deferens. *J. Physiol.* in the press.

MARTINS, T. & VALLE, J.R. (1939). Endocrine control of the motility of the male accessory genital organs. *Endocrinology*, **25**, 80–90.

SJOSTRAND, N.O. & SWEDIN, G. (1976). Influence of age, growth, castration and testosterone treatment on the noradrenaline levels of the ductus deferens and the auxiliary male reproductive glands of the rat. *Acta physiol. scand.*, **98**, 323–338.

SWEDIN, G. (1971). Studies on neurotransmission mechanisms in the rat and guinea-pig vas deferens. *Acta physiol. scand.* supplement 369.

WADDELL, J.A. (1916). The pharmacology of the vas deferens. *J. Pharmacol. Exp. Ther.*, **8**, 551–559.

WAKADE, A.R., GARCIA, A.G. & KIRPEKAR, S.M. (1975). Effect of castration on the smooth muscle cells of the internal sex organ of the rat: influence of the smooth muscle on the sympathetic neurons innervating the vas deferens, seminal vesicle and coagulating gland. *J. Pharmacol. Exp. Ther.*, **193**, 424–434.

Behavioural studies in the monkey (*Macaca mulatta*) with sotalol and with (+)-, (±)- and (−)-propranolol

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In a previous study Clancy, Nicholson & Wright (1977) described the effect of metoprolol and oxprenolol on delayed differentiation behaviour in the monkey. Accuracy of response was impaired over the dose range (5–30 mg/kg), and with 20 mg/kg and above total response time was increased. In the present paper we have extended these studies to sotalol and to (+)-, (±)-, and (−)-propranolol.

Five male monkeys (*Macaca mulatta*) of mean body weight 11.6 kg were used. The task (Nicholson, Wright & Ferres, 1973) involved the recognition of like and unlike pairs of visual stimuli, and the monkeys were required to press a lever if the stimuli were like and to refrain from pressing the lever if the stimuli were unlike. Each monkey was tested after the intraperitoneal injection of 5, 10 and 15 mg/kg of each isomer of propranolol hydrochloride, and 5, 10, 15 and 20 mg/kg sotalol hydrochloride. The drug vehicle (saline) was injected on four occasions. A random order of injection was used, and each injection was separated by at least 7 days. Performance was tested 1 and 4 h after injection. The data were analyzed by analysis of variance with reference to the overall effect of the drugs over the dose range, and the effect of individual doses of each drug.

It was not possible to differentiate between effects on total response time (TRT). Over the dose range 5–15 mg/kg the increase at 1 h for each drug was similar ($P < 0.01$), and there were no effects at 4 hours. Increase in TRT was dose related. With 15 mg/kg of each isomer of propranolol the increase at 1 h was very highly significant ($P < 0.001$), and with (−)-propranolol persisted to 4 h ($P < 0.05$). With 20 mg/kg sotalol the increase was very highly significant ($P < 0.001$) at 1 and 4 hours.

Accuracy of response was impaired over the dose range 5–15 mg/kg with sotalol ($P < 0.05$), (+)-propranolol ($P < 0.01$) and (±)-propranolol ($P < 0.001$), and with (+)-propranolol persisted to 4 h ($P < 0.01$). Impaired accuracy was related to dose. With 10 and 15 mg/kg (+) and (±)-propranolol the effect was highly significant ($P < 0.01$), and with 15 mg/kg sotalol the effect was significant ($P < 0.05$). With (−)-propranolol accuracy was not impaired over