did not contract the muscle. On the contrary it was found that bromocriptine antagonized the effects of NA and was equipotent in this respect with the α-adrenoceptor blocker phentolamine. Bromocriptine (100 ng/ml) also reduced the responses of the anococcygeus muscle to field stimulation. This effect was not due to a non-specific depression of muscle activity since the responses to carbachol were unaffected.

The dopamine antagonist pimozide also antagonized the actions of NA but was 8 times less effective than bromocriptine or phentolamine.

The above results seem to confirm that DA can act on peripheral α-adrenoceptors. Further, supposedly selective DA agonists can also interact with α-adrenoceptors, and may produce opposing effects. Indeed bromocriptine, rather than possessing only weak α-blocking properties (Thorner, 1975) was equipotent with phentolamine. It would seem therefore that the results of experiments using these drugs to elucidate the role of DA in the peripheral nervous system should be interpreted with caution.

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Potentiation of cardiac sympathetic nerve responses *in vivo* by pancuronium bromide

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In clinical use pancuronium bromide can produce cardiovascular stimulation (Coleman, Downing, Leary, Moyes & Styles, 1972), part of which has been explained by a vagolytic action (Hughes & Chapple, 1976). Two effects on the cardiac sympathetic innervation have however been postulated; an indirect sympathomimetic action (Domenech, Garcia, Sasiain, Loyola & Oroz, 1976), and blockade of neuronal noradrenaline (NA) uptake (Ivankovitch, Miletich, Albrecht & Zahed, 1975).

We have now found that pancuronium bromide, in doses producing neuromuscular blockade (Clanachan & Muir, 1972), potentiates cardiac sympathetic responses in the pithed rat.

Rats were pithed (Gillespie, MacLaren & Pollock, 1970) and ventilated with 100% oxygen. Heart rate was extracted from carotid arterial pressure using a Devices instantaneous ratemeter. The pithing rod electrode was placed for optimal stimulation of the sympathetic outflow to the heart (C6–T1, 0.05 ms pulses, supramaximal voltage).

In the absence of sympathetic stimulation, pancuronium bromide (2 mg/kg, i.v.) produced a short-lived increase in heart rate (22.7 ± 2.5 bts/min) which returned to baseline within 5–10 minutes. When cardiac sympathetic tone was induced by continuous stimulation at 0.1 Hz, pancuronium bromide (2 mg/kg i.v.) produced an increase in heart rate (52.8 ± 9.3 bts/min) which was significantly larger than in the absence of stimulation ($P < 0.001$), and was maintained until stimulation was terminated. This suggests two effects of pancuronium on heart rate; a short-lived increase following injection and independent of nerve stimulation, and secondly, a longer-lasting potentiation of sympathetic nerve responses.

Pancuronium bromide (2 mg/kg) potentiated the cardiac acceleration produced by single pulses and by trains of up to 5 pulses at 1 Hz. With longer trains of pulses ($\geqslant 10$) no significant potentiation was found. Pancuronium bromide (2 mg/kg) also significantly potentiated the response to 20 pulses at 0.01–0.5 Hz. Potentiation was inversely related to both pulse number and frequency.

The cardio-acceleration response to a single pulse was significantly potentiated in both height and duration by pancuronium bromide (0.1–10 mg/kg). These effects were dose-related. Potentiation of response height was maximal at 2 mg/kg and of duration at 10 mg/kg. The above effects of pancuronium could be reproduced in adrenalectomized rats or during neuromuscular blockade with gallamine (20 mg/kg).

The NA uptake blockers cocaine (0.5 mg/kg) and desipramine (0.05 mg/kg) potentiated and prolonged the cardio-acceleration responses to a single pulse of sympathetic stimulation and to intravenous NA, and inhibited the corresponding response to tyramine.

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.

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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