Inhibition of motor transmission in the vas deferens of the rat by adrenergic neuron blocking agents and β-adrenoceptor blocking agents having local anaesthetic effects

Motor transmission in the guinea-pig vas deferens has been shown to be readily inhibited by adrenergic neuron blocking agents (Boyd, Chang & Rand, 1961; Bentley, 1965) but Ambache & Zar (1971) found it to be resistant to α-adrenoceptor blocking drugs. They suggested that the motor transmission may not be adrenergic and they pointed out that the actions of the adrenergic neuron blocking agents may be unspecific and possibly associated with their local anaesthetic effect. I have estimated the motor transmission blocking activities of guanethidine, bretylium, pronethalol, propranolol and procaine and compared the results with their published local anaesthetic activities, in order to determine whether these two properties were potency-related.

The vas deferens removed from Wistar rats (250–300 g) was cleared of mesenteric attachments, cut longitudinally and suspended under a tension of 1 g, in a 10 ml organ bath of McEwan solution (McEwan, 1956) at 35°. The solution was gassed with oxygen containing 5% carbon dioxide. The preparation was field stimulated by platinum electrodes at a frequency of 6 Hz with rectangular pulses of 0·5 ms at supramaximal voltage (25 V). Muscular contractions were recorded isometrically by a force transducer (Grass FTO3C). The reduction in the height of the electrically induced twitches was measured 3 min after adding the drug. Two or three doses of each drug which produced between 30 and 80% inhibition of twitches were selected.

The log dose-effect lines for the percentage inhibition of the electrically induced twitches of the isolated vas deferens by the drugs are shown in Fig. 1. Taking procaine as unity, the approximate relative potency was guanethidine 460, bretylium 70, pronethalol 6 and propranolol 5. In confirmatory experiments with the rabbit

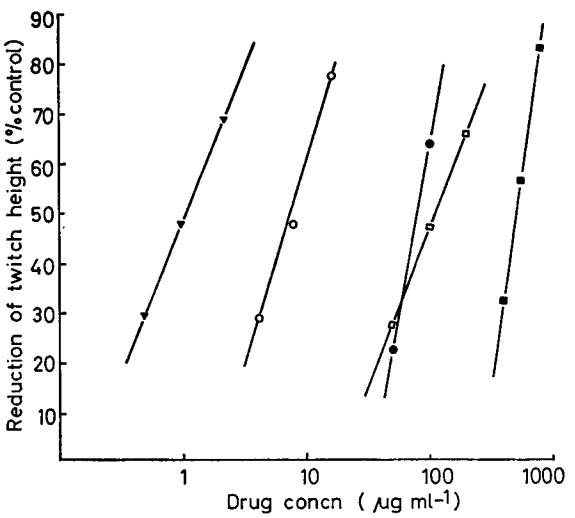

FIG. 1. Inhibition of electrically induced twitches of the vas deferens of the rat by guanethidine (▼), bretylium (○), pronethalol (●), propranolol (□) and procaine (■). Reduction in twitch heights expressed as a percentage of control twitches is plotted against the log-concentration (μg ml^{-1}) of each drug. Each point is the mean of five experiments.

isolated innervated jejunum preparation (Finkleman, 1930), the drugs had the same relative order of potency in inhibiting the pendular movement induced by periaterial nerve stimulation.

The order of potency of the drugs in inhibiting the electrically induced twitches of the rat vas deferens was guanethidine > bretylium > pronethalol > propranolol > procaine. On the other hand, the order of local anaesthetic potency of the drugs is known to be propranolol > pronethalol > procaine > bretylium > guanethidine (Morales-Aguilerá & Vaughan Williams, 1965; Gill & Vaughan Williams, 1964; Papp & Vaughan Williams, 1969; Davis, 1970; Bein, 1960). There was thus no correlation of local anaesthetic and motor transmission blocking activities, since guanethidine and bretylium, the least potent local anaesthetics, were the most potent inhibitors of responses to electrical stimulation. It does not seem reasonable, therefore, to attribute the blockade of the electrically induced twitches of the vas by the adrenergic neuron blocking agents directly to their trivial local anaesthetic action.

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Effect of reserpine on catechol-*O*-methyl transferase in rat submaxillary gland

Marsden, Broch & Guldberg (1971) showed that ligation of the excretory duct of the rat submaxillary gland, which induces an atrophy of the glandular acini without affecting the adrenergic nerves, reduced the activity of the catechol-*O*-methyl transferase (COMT) in the gland by 60%, while removal of the superior cervical ganglion reduced the COMT activity by 40%. Moreover, reserpine (5 mg kg^{-1}) was found to reduce the COMT activity of unoperated glands by up to 50% at 6 and 18 h after its administration. The effects observed were thought to be due to COMT being localized extraneuronally and being dependent on the presence of the substrate (noradrenaline) for full activity.

I have now assessed the effect of reserpine on the enzyme in ganglionectomized glands. Twenty Wistar rats of either sex, 200–250 g, were treated as described by Marsden & others (1971). The left superior cervical ganglion of 10 rats was removed, atrophy was induced in the other 10 rats by ligating the excretory duct on the left side. The right gland always served as control. The animals were then left for 14 days.