produced a small contraction initially, which displayed rapid tachyphylaxis.

Field stimulation resulted in frequency-dependent motor responses (max. 527 ± 60 mg; $n = 6$) which were blocked by guanethidine (1 μM) and phentolamine (1 μM). Higher concentrations of guanethidine (50 μM) raised muscle tone and field stimulation now caused relaxations which were unaffected by atropine, propranolol, or hexamethonium, but were prevented by tetrodotoxin (500 ng/ml). Isoprenaline did not lower the tone of the contracted tissue, but following incubation with indomethacin (Burnstock, Cocks & Crowe, 1978) high doses of ATP (> 100 μM) produced dose-related relaxations. In some preparations high concentrations of acetylcholine (40 μM) produced relaxations of the contracted muscle which were blocked by (+)-tubocurarine (2 μM).

Thus the pharmacology of the isolated anococcygeus muscle of the mouse most closely resembles that of the rat. In particular, it will be of interest to determine whether the relaxant effects of ATP and acetylcholine are mediated directly, or indirectly by release of inhibitory transmitter (Gibson & James, 1977).

C.V.W. is an MRC student.

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A comparison of the effects of agonist drugs on nerve-induced contractions of the rat bisected vas deferens

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The effects of drugs on the nerve-induced contraction of vas deferens have given rise to unexpected observations difficult to reconcile with straightforward adrenergic transmission. For example, Ohlin & Stromblad (1963) commented that 'classroom experiments... had soon to be abandoned since on addition of drugs known to affect sympathetic transmission the preparation did not behave according to the classical scheme' and it has been suggested that motor transmission in the vas may not be adrenergic, the adrenergic nerves having, instead, an inhibitory function (Ambache & Zar, 1971; Ambache, Dunk, Verney & Zar, 1972).

The properties of the smooth muscle and its response to nerve stimulation, however, vary along the organ. If rat vas is bisected transversely into equal lengths then a single field stimulus will produce a biphasic contraction in each portion but the first and second components will dominate in the prostatic and epididymal ends respectively. This first component is resistant to and the second component susceptible to 'classical' pharmacological manoeuvres which modify adrenergic transmission (Booth, Connell, Docherty & McGrath, 1978; McGrath, 1978).

The present study investigates whether a variety of drugs, which are known to affect neurotransmission in other tissues, will have similar or different effects on the nerve-induced (0.5 ms field stimulus) longitudinal, isometric contractions of isolated portions from the two ends of rat vas deferens isolated in Krebs' bicarbonate saline at 37°C (see McGrath, 1978).

α-Adrenoceptor agonists produced pre-junctional α_2-mediated inhibition and post-junctional α_1-mediated excitation which acted in physiological antagonism. In the prostatic portion inhibition dominated. In the epididymal portion the inhibitory effect was accompanied by a dominant excitatory effect manifest by potentiation and prolongation of the nerve-induced response followed, at higher concentrations by drug-induced contraction (see Docherty, MacDonald & McGrath, 1979).

Catecholamines: noradrenaline, adrenaline and dopamine produced effects qualitatively similar to the other α-adrenoceptor agonists, inhibition and excitation dominating in the prostatic and epididymal portions, respectively.

β-Adrenoceptor agonists: isoprenaline and salbutamol both inhibited responses in each portion. In the

prostatic but not in the epididymal portion this inhibition was antagonised by sotalol. At least part of this β-effect was post-junctional since phenylephrine-induced contractions were inhibited. Isoprenaline also produced an α_1-mediated excitation in the epididymal portion.

Other agonists: ATP and (D-Ala^2, D-Leu^5)-enkephalin, produced pre-junctional inhibition in each portion which was independent of adrenoceptors. The effect of ATP was greater on the prostatic portion while that of (D-Ala^2, Leu^5)-enkephalin was similar in each portion and could be reversed by naloxone.

With each of these examples the precision of the observations was increased by analysing separately the responses of the different portions. Furthermore the adrenergic and 'non-adrenergic' components need no longer be inextricably confused. These results may, therefore, justify the introduction of limited, double-blind classroom trials with a view to rehabilitation of the preparation.

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Mechanism of action of dopamine on the guinea-pig isolated gastroesophageal junction

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Domperidone has been shown to block central dopamine receptors but after peripheral administration it does not readily cross the blood brain barrier (Costall, Fortune & Naylor, 1979). This has led to the suggestion that its gastrointestinal effects are due to an interaction with a peripheral dopaminergic system (Van Nueten & Janssen, 1978). A selective effect of domperidone on dopamine-induced relaxations of the isolated longitudinal muscle strip of the guinea-pig gastroesophageal junction has been reported (Ennis, Schnieden & Cox, 1978). We have examined the ability of a series of dopamine antagonists to inhibit the response to dopamine on the gastroesophageal junction and phenylephrine on the isolated aortic strip using the pA_2 method of Arunlakshana & Schild (1959). These compounds had no effect on the relaxations of the gatroesophageal junction induced by either isoprenaline or noradrenaline. Whilst the relative order of potency for spiroperidol, domperidone and haloperidol on the gastroesophageal junction was that which would be predicted for an interaction with dopamine receptors (Table 1), pimozide and metoclopramide were ineffective. These results do not support the suggestion of a peripheral dopamine system in the gastrointestinal tract.

There appeared to be a close correlation between the ability to block the α_1 adrenoceptor of the aorta

Table 1 Comparison of pA_2 values for a series of dopamine receptor blocking drugs as antagonists of dopamine on the gastroesophageal junction and phenylephrine on the spiral aortic strip of the guinea-pig

	pA_2 value	
Antagonist	*Gastroesophageal Junction*	*Aortic Strip*
Spiroperidol	8.6 ± 0.3	8.8 ± 0.1
Domperidone	6.6 ± 0.1	7.4 ± 0.1
Haloperidol	6.1 ± 0.1	6.6 ± 0.1
Pimozide	No antagonism	No antagonism
Metoclopramide	No antagonism	No antagonism