in the presence of phenylephrine but in two of these the relaxation changed to a contraction as the experiment proceeded.

The relaxation of the colon appeared to involve typical β-adrenoceptors because it was antagonized by propranolol (10^{-7}–10^{-6} g/ml) but not by phentolamine (10^{-6} g/ml). In three tissues the relaxation produced by noradrenaline was converted to a contraction by propranolol.

The contraction observed in the presence of phenylephrine and noradrenaline was antagonized by phentolamine in nine out of twelve preparations whilst propranolol was without effect in six preparations. In two experiments phentolamine converted the response to noradrenaline from a contraction to a relaxation.

Contractions of the alimentary tract involving α-adrenoceptors are well documented (Lee, 1970) and in adult humans they have been reported in the oesophagus (Ellis, Kauntze & Trounce, 1960) and at the ileocaecal junction (Gazet & Jarrett, 1964). Preliminary observations suggest that the α-adrenoceptors in foetal colon are neurogenic because the contractions were antagonized by tetrodotoxin (10^{-7} g/ml, five tissues); they were also antagonized by atropine (5×10^{-8} g/ml, ten tissues), suggesting that the neurones may be cholinergic.

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Differential effect of alterations in the calcium and magnesium concentrations on the responses to sympathomimetic amines in the perfused rat mesentery

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Perfusion of the rat mesenteric artery preparation with different Krebs solutions containing either reduced concentrations of calcium, magnesium, or zero calcium and magnesium, modifies responses to tyramine and noradrenaline (Leach & Zumani, 1969). In these experiments the rat mesenteric artery preparation (modified from the method described by McGregor, 1965) was perfused with normal and modified Krebs solution and the responses to a series of four sympathomimetic amines, noradrenaline 200 ng, octopamine 50 μg, metaraminol 20 μg and tyramine 100 ug, were studied. Tachyphylaxis to tyramine did not occur in any of the perfusion solutions under the experimental conditions used.

Perfusion with a Ca^{2+}- and Mg^{2+}-free solution potentiated the responses to tyramine by 600%. Similarly, the potentiation of the response to octopamine was 200% and to metaraminol, 80% and to noradrenaline, 40%.

Experiments in which the Mg^{2+} concentration was varied from one-sixteenth to twice normal in a calcium-free Krebs solution demonstrated that, as the concentration

of magnesium was increased, the degree of potentiation of sympathomimetic responses compared to controls was decreased. Similar procedures in which the Ca^{2+} was used in Mg^{2+}-free solution showed that increasing the Ca^{2+} concentration also inhibited the degree of potentiation of the responses. However, at equimolar concentrations, the degree of potentiation of the sympathomimetic responses was less with the reduced Mg^{2+} than with the reduced Ca^{2+} solution.

Perfusion with either Ca^{2+}- and Mg^{2+}-free Krebs or with normal Krebs containing cocaine (50 ng/ml) antagonized the response to tyramine and had no effect on the response to octopamine, but potentiated the responses to metaraminol and noradrenaline. Perfusion with normal Krebs solution in the presence of ouabain 10^{-5} M, potentiated the responses to metaraminol and noradrenaline, but abolished the responses to tyramine and octopamine. Substitution with Ca^{2+}- and Mg^{2+}-free solution showed that ouabain had no effect on the tyramine response or on the responses to the other three amines. In the presence of a Krebs solution containing half the normal Mg^{2+} and no calcium, ouabain again had no effect. However, in the presence of solutions containing half the normal calcium and no magnesium, ouabain reduced the response to tyramine. Perfusion with 12 mM K^+ Krebs abolished the ouabain action indicating that ouabain was probably affecting the sodium-potassium ionic transfer system, possibly at the neuronal level.

Assuming that all the sympathomimetic amines, to which an indirect action is attributable, must enter, that is be taken up into, the adrenergic neurone before they effect a release of noradrenaline (Iversen, 1966), it would seem that there is probably more than one transport mechanism involved. These results may indicate the nature of the mechanism by which noradrenaline is released by the indirectly acting sympathomimetics.

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Myocardial effects of indoramin hydrochloride, a new hypotensive agent

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Indoramin, (3-(2-(4-benzamidopiperid-1-yl)ethyl)indole hydrochloride, Wy 21901), is a new potent hypotensive agent which combines α-adrenoreceptor blocking and cardio-inhibitory properties (Alps, Hill, Johnson & Wilson, 1970) and appears to provide a new mechanism of action for the treatment of hypertension in man. Like propranolol, indoramin causes bradycardia, reduced myocardial contractile force and decreased cardiac output in anaesthetized cats (Alps, Johnson & Wilson, 1970). It reduced the force and rate of contraction of the isolated rabbit heart and showed a potent local anaesthetic action (Alps, Hill, Johnson & Wilson, 1970). Because of these findings it seemed important to examine the electrophysiological effects of indoramin on the heart. Isolated canine myocardial strips were used in these experiments since in