dopamine concentration slowed down the conversion of tyrosine to dopa by a feedback mechanism resulting in a subsequent decrease in the concentrations of both noradrenaline and dopamine. When dopamine approached or reached the control level, the feedback effect of noradrenaline became dominant which by increasing the conversion of tyrosine to dopa restored a new balance on the one hand between catecholamines and tyrosine, and on the other hand between noradrenaline and dopamine. Since the deflection in tyrosine concentration after CS_2 was not so extensive as after DDC, and at least after the first or second exposures the increase in dopamine corresponded to the decrease in noradrenaline, CS_2 seems to be more suitable than DDC as an agent for the study of dopamine receptors.

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Blockade of adrenergic transmission by dehydroemetine

The synthetic amoebicidal drug, dehydroemetine, is effective as the natural alkaloid, emetine, in the treatment of amoebiasis and is better tolerated by the patient (Powell, Wilmot & others, 1967), but, as with emetine, gastrointestinal complications like diarrhoea and abdominal colic occur after injections of dehydroemetine in therapeutic doses (Herrero, Brossi & others, 1960). Ng (1966a,b) demonstrated an adrenergic neuron-blocking action for emetine and suggested that diarrhoea produced by this drug might reflect a reduction in intestinal sympathetic activity. I now report that dehydroemetine also has this adrenergic neuron-blocking action.

Segments of rabbit jejunum (Finkleman, 1930) were suspended in 70 ml aerated Tyrode solution (NaCl, 8·0; KCl, 0·2; $CaCl_2$, 0·2; $NaHCO_3$, 1·0; $MgCl_2$, 0·1; NaH_2Po_4, 0·5; Glucose, 1·0 g/litre) at 37°. The periarterial nerves were stimulated with square pulses (20 V; 0·5 ms) for 15 s every 3 min. Cats were anaesthetized with chloralose (80 mg/kg) and pentobarbitone sodium (5 mg/kg, i.v.). The cervical sympathetic nerve was stimulated with square pulses of 20 V and 0·5 ms for 10 s every 2 min, and isotonic contractions of the nictitating membrane were recorded on smoked paper.

Dehydroemetine (0·5–10 μg/ml) had no effect on the tone and pendular movements of the rabbit jejunum but antagonized the relaxation of tone and cessation of pendular movements produced by sympathetic stimulation. The inhibition of pendular movements produced by added noradrenaline (0·2–2 μg/ml) was either not affected or increased. Concentrations of dehydroemetine higher than 10 μg/ml reduced the tone of the intestine and the amplitude of the pendular movements in addition to antagonizing the effects of sympathetic stimulation. The sympathetic block was

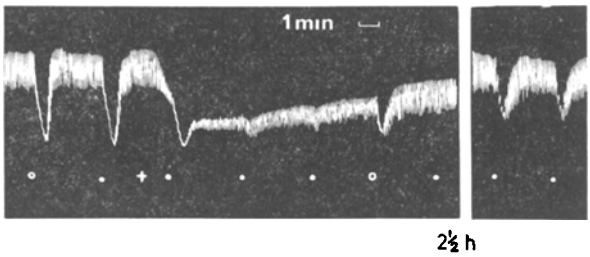

FIG. 1. Pendular movements of isolated rabbit jejunum. Dehydroemetine (17 μg/ml) added at (+) reduced the tone of the intestine, the magnitude of the pendular movements, and the effect of sympathetic stimulation (20 V, 0·5 ms, 50/s, for 15 s every 3 min, at the white dots). After the effect of sympathetic stimulation had been completely abolished, the effect of adding noradrenaline 1 μg/ml (open circles) persisted. Partial recovery from the effect of dehydroemetine occurred after repeated washing and stimulation over 2½ h.

slow to develop with the lower concentrations of the drug but developed more rapidly as the concentration was increased. The effect of dehydroemetine was not reversed by cocaine (0·2–20 μg/ml) but could be reversed by repeated washing and stimulation over 1–3 h. The longer recovery times were associated with the higher drug concentrations (Fig. 1).

Dehydroemetine (3–5 mg/kg) reduced the contractions of the cat nictitating membrane produced by preganglionic or post-ganglionic stimulation of the cervical sympathetic nerve. The blockade, once established, was persistent, no reversal being obtained during observations lasting 3–4 h, and the block was also not antagonized by 0·5 mg/kg cocaine given intravenously. At the height of the blockade produced by dehydroemetine, responses to noradrenaline (50 μg, i.v.) were either unchanged or slightly increased when compared with control responses.

The results show that dehydroemetine has an adrenergic neuron-blocking action which, however, differs from that of bretylium and guanethidine in that it is not antagonized by cocaine (Day, 1962).

A similar action has previously been observed with emetine (Ng, 1966b), and the diarrhoea which has been found to complicate parenteral administration of dehydroemetine in therapeutic doses might, at least in part, be due to this action.

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