These results suggest that the uptake process operated most efficiently in the presence of blood and was inhibited by low frequency nerve stimulation. About half the NA taken up was retained unchanged and half was metabolized.

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Monoamines in the guinea-pig intestine

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Noradrenaline (NA) and 5-hydroxytryptamine (5-HT) are present in the mammalian small intestine (Erspamer, 1954 ; Shore, 1959). NA-containing axons, originating from prevertebral ganglia, occur in the myenteric and submucous plexuses and around blood vessels (Norberg, 1964).

TABLE 1. *Distribution of noradrenaline (NA) and 5-hydroxytryptamine (5-HT) in the guinea-pig intestine and the changes produced by extrinsic denervation (applying a probe cooled with liquid nitrogen on a nerve-vascular mesenteric bundle) and drug treatments. Values are in μg/g ± S.E. of mean of fresh tissue and are corrected for recovery. Number of experiments in parentheses.* ****P < 0·001, ***P < 0·005, **P < 0·01 *and* *P < 0·025

	Longitudinal muscle-myenteric plexus	Circular muscle-submucous plexus-submucosa-mucosa	
	NA μg/g	NA μg/g	5-HT μg/g
Duodenum	0·75 ± 0·18 (3)	0·52 ± 0·09 (3)	30·1 ± 6·9 (3)
Ileum	0·56 ± 0·06 (8)	0·54 ± 0·08 (8)	6·35 ± 0·86 (7)
Colon	1·33 ± 0·08 (8)	0·56 ± 0·07 (8)	2·35 ± 0·34 (8)
Taenia coli	0·82 ± 0·14 (6)	—	—
Rectum	0·91 ± 0·19 (5)	0·72 ± 0·08 (5)	1·51 ± 0·37 (4)
	Extrinsic denervation (5 days before)		
Ileum (control†)	0·56 ± 0·18 (4)	0·56 ± 0·07 (4)	8·90 ± 0·60 (4)
Ileum denervated)	0·03 ± 0·01 (4)****	0·06 ± 0·01 (4)****	10·0 ± 1·8 (4)
	6-Hydroxydopamine (35 mg/kg, I.V.‡)		
Ileum	0·22 ± 0·03 (4)***	0·11 ± 0·02 (4)**	6·46 ± 0·42 (4)
Colon	0·43 ± 0·17 (4)****	0·08 ± 0·03 (4)****	3·88 ± 1·10 (4)
	Reserpine (0·05 mg/kg, S.C., 3 days before)		
Ileum	0·08 ± 0·03 (3)***	0·09 ± 0·01 (3)*	3·44 ± 0·26 (3)
Colon	0·21 ± 0·07 (3)****	0·12 ± 0·02 (3)***	2·23 ± 0·35 (3)

† Taken from a non-denervated, neighbouring ileum loop.
‡ The drug was given in divided doses on the first and third day, and animals were killed on the sixth day.

Segments of small and large intestine from duodenum to rectum were studied. Amines were estimated fluorimetrically (Juorio, 1971). The intestinal wall was dissected, separating longitudinal muscle and myenteric plexus (10–20% of total weight of the wall for the ileum) on one side and circular muscle, submucous plexus, submucosa and mucosa on the other. NA and 5-HT were found as shown in Table 1. The longitudinal muscle-myenteric plexus of the colon had the highest NA concentration, which is probably accounted for by the occurrence of intramural adrenergic neurones in this part of the gut (Costa, Furness & Gabella, 1971). The ileum had the lowest concentration of NA, approximately in the same amount in both parts of the wall. Since a large portion of the circular muscle-submucosa-mucosa is made of epithelial cells, the NA concentration in the part of this preparation where axons are, is higher than in the

longitudinal muscle myenteric plexus. An almost complete disappearance of NA was obtained with extrinsic denervation. Reserpine (0·05 mg/kg) reduced, by about 80%, the NA content of both ileum and colon. Less than 0·2 μg/g of 5-HT were found in the longitudinal muscle-myenteric plexus of the ileum. Large amounts of 5-HT were found in the circular muscle-submucosa-mucosa. Its concentration decreases steadily from duodenum to rectum. 5-HT content of the ileum was not significantly affected by extrinsic denervation, nor by reserpine (0·05 mg/kg). Decrease of 5-HT was obtained with a higher dose of reserpine (1 mg/kg). Dopamine (DA) was found in concentrations 10–15% those of NA, which suggests that DA is mainly a precursor of NA.

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Depolarization and neuromuscular block in the rat

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The remarkable difference in sensitivity to decamethonium as a neuromuscular blocking agent between species is well known. In the cat which is particularly sensitive, neuromuscular block is produced by a maintained depolarization (Burns & Paton, 1951). However, rat muscles are particularly insensitive (Paton & Zaimis, 1949) and the characteristics of the paralysis *in vivo* (Derkx, Bonta & Lagendijk, 1971) and *in vitro* (Galindo, 1971) indicate that end-plate depolarization may not be the cause of the block.

In this study, isometric contractions of the rat diaphragm *in vitro* were recorded in response to nerve stimulation and the time course of neuromuscular block measured over a range of concentrations of decamethonium. In parallel experiments changes in potential in response to decamethonium were recorded from the end-plate region by means of external electrodes (Lu, 1970) and log dose-response curves obtained. Depolarization was found to occur at relatively low doses with a median effective dose of 4·7 μM. In contrast neuromuscular block required considerably larger doses.

A concentration of 50 μM decamethonium produced a depolarization which was 94–100% of maximal. In parallel experiments this dose produced no sign of neuromuscular block within the first hour. A higher concentration (100 μM) produced complete depolarization which declined within minutes to a residual value while several hours were required to produce complete paralysis. Progressively larger concentrations while producing no greater depolarization caused complete paralysis within minutes. Since both the time course and the concentration required for depolarization are so distinct from those required for neuromuscular block it appears that neuromuscular block by decamethonium in rat muscle *in vitro*, is not the result of a prolonged postsynaptic depolarization.

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