strip was $8 \pm 0{\cdot}98$ μg/g wet weight, compared with $20{\cdot}7 \pm 1{\cdot}63$ μg/g in the whole ileum segment. Histamine release with antigen was significantly greater in the strip, being approximately 10% of the total histamine content, as compared with about 2% in the full-thickness ileum preparation. As much as 36% of the total histamine was released by antigen in some strips.

The role of Auerbach's plexus in the anaphylactic response was investigated using tetrodotoxin. This substance in a concentration of 5×10^{-7} g/ml. eliminates the response to nicotine and DMPP in both strips and full-thickness loops, while leaving the histamine response unaffected. The anaphylactic dose response curve was unchanged in the presence of this concentration of tetrodotoxin in both strips and full thickness ileum. Some aspects of the role of the mast cells in the Dale–Schultz response were investigated using octylamine. The normal mast cell distribution was studied in spread strips and the dose-response curve for the disruption of mast cells with octylamine was assessed. Exposure of the strips to octylamine (10^{-3} g/ml.) for 1 min decreased the mast cell count by 95%, compared with control strips. The response of the muscle to small concentrations of histamine (10 ng/ml.) was still present after this treatment, but the anaphylactic response of the strips was eliminated entirely, while that of the full-thickness ileum was markedly reduced. The significance of these findings for the theory that part of the anaphylactic response is due to a direct antigen antibody reaction on muscle is discussed.

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Pharmacological studies of cinanserin in human isolated smooth muscle

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Cinanserin hydrochloride is 2'-(3-dimethylaminopropylthio) cinnamanilide hydrochloride. It has been shown *in vitro* and *in vivo* to antagonize 5-hydroxytryptamine (5-HT) (Krapcho, Spitzmiller, Turk & Fried, 1964; Krapcho & Turk, 1966; Rubin, Piala, Burke & Craver, 1964). It has been used successfully in patients with carcinoid syndrome but not in schizophrenia (Gallant & Bishop, 1969; Costello, 1966; Mengel & Lotito, 1968).

The actions of cinanserin on isolated strips of human smooth muscle have been studied. Specimens were obtained from surgical operations and set up in an isolated organ bath in aerated Krebs-bicarbonate solution at 37° C as described previously (Coupar, Hedges, Metcalfe & Turner, 1969; Coupar & Turner, 1969). Responses were recorded by a frontal writing lever on a kymograph.

Cinanserin (0·02–100 μg/ml. for 5 min) did not contract or relax the tissues studied. When antagonizing responses to 5-HT for pA_2 determinations (Schild, 1947), an incubation period of 2 min with the antagonist was used before adding 5-HT for a 1 min contact period. The dose cycle was 15 min. The anti-5-HT properties of cinanserin were compared with methysergide, and their interactions with acetylcholine studied.

TABLE 1. *Comparison of cinanserin and methysergide on human isolated tissue*

Organ	Muscle direction	Agonist	Response	Cinanserin No. expts.	Cinanserin Mean pA_2 (range)	Methysergide No. expts.	Methysergide Mean pA_2 (range)*
Stomach		5-HT	None				
		ACh	Contraction	4	4·6 (4·3–5·0)	7	P
Duodenum	Circular and longitudinal	5-HT	None				
		ACh	Contraction	2	4·35 (4·3–4·4)	1	P
Ileum	Circular	5-HT	Contraction	2	7·7 (7·6–7·8)	2	8·0 (7·7–8·4)
		ACh	Contraction	1	5·1	0	
	Longitudinal	5-HT	Contraction	3	5·5 (5·4–5·7)	0	
		ACh	Contraction	1	5·0	2	P
Appendix	Longitudinal	5-HT	None				
		ACh	Contraction	2	5·0	1	P
Colon	Circular	5-HT	Relaxation	2	7·25 (7·2–7·3)	0	
		ACh	Contraction	1	4·4	2	P
	Longitudinal	5-HT	None				
		ACh	Contraction	2	4·35 (4·2–4·5)	0	
Rectum	Circular	5-HT	Increased spontaneous activity				
		ACh	Contraction	1	5·4	1	P
	Longitudinal	5-HT	Contraction	1	<5·0	0	
		ACh	Contraction	1	4·9	0	
Bladder neck		5-HT	None				
		ACh	Contraction	3	4·15 (4·1–4·2)	1	P
Ureter	Circular	5-HT	None				
		ACh	None				
	Longitudinal	5-HT	Contraction (marked tachyphylaxis)				
		ACh	None				
Vein	Circular	5-HT	Contraction	3	7·9 (7·5–8·2)	2	8·2

* P denotes increased sensitivity of tissue to ACh.

Table 1 shows that cinanserin is slightly less active than methysergide against 5-HT although their potencies are of the same order. Cinanserin antagonizes acetylcholine in all tissues studied. In contrast, methysergide in doses of 5–800 μg/ml. increases the sensitivity of the tissues to acetylcholine. This phenomenon will be the subject of a separate communication.

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The influence of adrenocortical insufficiency on cardiac muscle

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In untreated adrenocortical insufficiency the heart is commonly subnormal in size and dry weight (Remington, 1951; Solomon, Travis & Sayers, 1959). No other consistent structural abnormality has been described.

Adrenalectomized animals and Addisonian patients are hypotensive (Ramey & Goldstein, 1957), largely because of a low cardiac output (Weiner, Verrier, Miller & Lefer, 1967). The left ventricular work index of hearts taken from rats adrenalectomized 14 days previously was only 28% of that of controls (Solomon *et al.*, 1959).

Since there are obvious functional changes in the heart after adrenalectomy, we have examined changes in the ultrastructure of the myocardium. Hearts removed from male rats (Wistar) weighing 200–400 g and adrenalectomized 10 days previously were compared with those from sham-operated controls. Adrenalectomized rats were maintained on 0·9% (w/v) NaCl solution.

The mean blood pressures in control and adrenalectomized rats were 120 ± 5 and 101 ± 6 mm Hg ($P<0{\cdot}02$) respectively. Plasma sodium concentration was not significantly different in the two groups (intact $150{\cdot}1 \pm 4{\cdot}6$; adrenalectomized $155{\cdot}3 \pm 3{\cdot}8$ mEq/l.). Plasma potassium concentration (intact, $4{\cdot}59 \pm 0{\cdot}18$ mEq/l.), however, was significantly increased ($P<0{\cdot}001$) in the adrenalectomized rats ($6{\cdot}81 \pm 0{\cdot}28$ mEq/l.). Blood volume in control rats was $8{\cdot}5 \pm 0{\cdot}3$ and in adrenalectomized rats $8{\cdot}3 \pm 0{\cdot}3$ ml./100 g body weight. There were no significant changes in the haemoglobin concentration, the packed cell volume or plasma calcium concentration.

Electron microscopy of pieces of left ventricular muscle showed a patchy disintegration of myofibrils. This process at times extended completely across some cells, adjacent cells remaining normal. Light micrographs of 1 μm sections from the same blocks showed some fibres which stained abnormally pale.

In longitudinal sections, gaps were seen between some filaments; others were no longer parallel, and had a splayed appearance. Particular areas showed extensive loss of both thick and thin filaments but the Z disks were often intact when only a few filaments were present. In some regions myofibrils were completely absent, only granular debris remaining among scattered but apparently normal mitochondria, transverse tubules and sarcoplasmic reticulum.