Pieces of ileum from adult female guinea-pigs were suspended in Tyrode solution, at 30° C, gassed with air. Responses to acetylcholine approximately 50% of maximum were obtained; these were potentiated by addition of cephalin (10 μg–1 mg/ml.) to the bathing solution. The cephalin used in our experiments was a crude extract consisting of phosphatidylethanolamine and phosphatidyl-L-serine, and each of these phospholipids likewise potentiated the acetylcholine response. Phosphatidylethanolamine was approximately as effective as cephalin in this respect, but phosphatidyl-L-serine had much less activity. With each of these phospholipids a slight inhibition usually preceded the potentiation of the acetylcholine response. When larger concentrations (>250 μg/ml.) of the phospholipids were used the potentiation was often accompanied by a direct contractile effect.

A reverse sequence to the above events was observed with phosphatidylcholine (lecithin). In contrast to cephalin and its constituents the predominant effect of this phospholipid was inhibition of the acetylcholine response. A subsequent batch of lecithin (a crude extract from egg yolk) produced different results, but a sample of chromatographically pure synthetic dipalmitoyl phosphatidylcholine confirmed the original observations.

The effects of the phospholipids were not specific for acetylcholine, as cephalin, phosphatidylethanolamine and phosphatidyl-L-serine also potentiated the responses to histamine, 5-hydroxytryptamine, tetramethylammonium, potassium and barium ions, and to transmural stimulation. Lecithin inhibited these responses. High (up to 5 times normal) concentrations of Ca^{++} in the bathing solution prevented the potentiation by cephalin of responses to acetylcholine and transmural stimulation, whilst inhibition by lecithin was unaffected or increased. Conversely, low (1/3 to 1/10 of normal) Ca^{++} concentration increased the potentiation by cephalin but prevented the inhibition by lecithin.

Rojas & Tobias (1965) reported that at physiological pH, phosphatidylethanolamine binds Ca^{++} whilst phosphatidylcholine (lecithin) weakly repels Ca^{++}. Although the modes of action of cephalin and lecithin on the guinea-pig ileum are at present unclear, some pharmacological involvement is indicated between these compounds and calcium ions.

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A non-adrenergic component to the inhibitory innervation of the fundus of the rat stomach

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Inhibitory innervation which does not have the characteristics of adrenergic innervation has been described for the taenia of the guinea-pig caecum (Burnstock,

Campbell & Rand, 1966; Akubue, 1966), for rabbit ileum (Tweeddale, 1965) and for the rabbit portal vein (Hughes & Vane, 1967).

Evidence for the existence of an inhibitory innervation to the fundus of the rat stomach, which cannot be accounted for in terms of a classical adrenergic innervation, is now presented.

Strips of rat fundus (Vane, 1957) were stimulated between parallel platinum wires (Birmingham & Wilson, 1963) in Krebs solution at 32° C containing 5-hydroxytryptamine (3×10^{-7}M), hyoscine (1×10^{-6}M) and sodium metabisulphite (5×10^{-3}M). Trains of stimuli (5 shocks/sec; pulse duration 0·2 msec) induced relaxation which was reduced but not abolished by adrenergic neurone blockade (bethanidine 1×10^{-5}M; guanethidine 1×10^{-6}M) or by pretreatment with reserpine (5·0 mg/kg intraperitoneally 48 hr and 2·5 mg/kg 24 hr before the experiment).

When the whole fundus was set up in a similar bathing fluid so that the periarterial nerves of the coeliac artery could be stimulated by placing the artery over platinum electrodes, stimulation at 10 shocks/sec at 0·1 msec pulse width induced relaxation which was completely abolished by bethanidine (1×10^{-5}M).

The vagus nerves to the fundus were stimulated by placing the distal end of the oesophagus over platinum electrodes. When this oesophagus-fundus preparation was kept in Krebs solution containing 5-hydroxytryptamine to maintain tone and hyoscine (1×10^{-6}M) to prevent contractile responses, stimulation evoked relaxation. This inhibitory response was reduced but not abolished by adrenergic neurone blockade (bethanidine, 1×10^{-5}M; guanethidine, 1×10^{-5}M; dimethylphenyl piperazinium, 1×10^{-6}M).

Coeliac artery-fundus preparations and oesophagus-fundus preparations were taken from rats which had been pretreated with reserpine; depletion of catecholamines was verified by spectrophotofluorometry and fluorescence microscopy. For the coeliac artery-fundus preparation, the response to periarterial stimulation was abolished, whereas for the oesophagus-fundus preparation stimulation of the oesophagus still elicited an inhibitory response in the presence of hyoscine.

These results support the main findings of Paton & Vane (1963), namely that there are excitatory cholinergic nerves in the vagus and inhibitory adrenergic nerves around the coeliac artery. However, they also demonstrate that the fundus of the rat stomach receives a substantial non-adrenergic inhibitory innervation.

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