of NA in modulating intramural cholinergic nerves were investigated by measuring the inhibition of acetylcholine release. After denervation, NA was significantly more active in reducing Ach release both at rest and during transmural stimulation, the calculated activity ratios being both >5.

Concluding, both α- and β-receptors are involved in direct circular muscle relaxation and in the inhibition of peristaltic reflex. However, the different order of activity against peristalsis and carbachol-induced contractions indicated that α-receptors, not located in smooth muscle, are involved in peristaltic inhibition. The pattern of hypersensitivity observed in our preparations does not completely fit to any of the types of hypersensitivity described in other smooth muscle preparations supplied by an adrenergic motor innervation. In our preparations hypersensitivity is specific for adrenergic receptor stimulating agents and a mechanism involving contractile machinery outside the receptors can be excluded. Both muscular and nerve-mediated effects undergo sensitivity changes. Since IPNA and methoxamine are not taken up by adrenergic terminals, a postsynaptic mechanism seems to operate. However, the higher hypersensitivity to NA indicates that probably a presynaptic mechanism is also involved. Inasmuch as NA uptake is not highly effective at the intestinal neuroeffector junction (Bowman & Hall, 1970), the higher hypersensitivity to NA could be explained by the effectiveness of a presynpatic mechanism at the level of adrenergic nerve endings impinging on the intramural nervous structures.

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Evidence that substances capable of increasing the duodenal content exert a spasmogenic effect on the pylorus

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A series of natural and synthetic compounds were studied on the anaesthetized rat for their contracting activity on the gastroduodenal junction, by means of a technique described in a previous paper (Bertaccini, Impicciatore & De Caro, 1973). It was found that many substances (in particular two natural peptides, caerulein and bombesin) were endowed with a striking stimulant action on the pyloric sphincter. This activity, however, seemed to be unrelated to unspecific spasmogenic effects since many true spasmogenic (like bradykinin, physalaemin, histamine, etc.) and spasmolytic (like sodium nitrate, papaverine, atropine, etc.) compounds, failed to affect significantly the tone of the pyloric sphincter. Conversely substances endowed with stimulant activity on biliary or pancreatic secretion (like caerulein, some choleretic drugs, secretin, etc.) constantly exerted a strong contracting activity. It is therefore suggested that the contraction of the pylorus is a constant feature of substances capable of increasing the duodenal content and this might have a 'physiological' protective action towards the possible regurgitation into the stomach of alkaline duodenal juice. The spasmogenic activity was found to be direct on the smooth muscle and independent from the autonomic nervous system. In very preliminary experiments, performed in human volunteers we found that some of the most effective compounds behaved in man exactly as in the rat.

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