ly the effect of ISO on vasopressin release, was much smaller than those which had been equieffective after i.v. injection. This action of ATR was not due to a residual effect on nicotinic receptors, which may occur after high doses, since the ganglionic blocking agent trimethidinium (TRI) had no effect on the ISO-induced vasopressin release, whereas mecamylamine (MEC) even slightly increased it.

Based on these data, we conclude that neurons with muscarinic receptors, which are accessible from the ventricular system, contribute to the ISO-induced vasopressin release. It may be speculated that the hypothalamic nuclei, which regulate the release of vasopressin, are informed of the ISO-induced changes in angiotensin plasma levels and blood pressure via different neuronal pathways. Muscarinic synapses may be a part of one of these pathways.

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A study of vasoactive intestinal polypeptide (VIP) stimulated intestinal fluid secretion in rat and its inhibition by indomethacin

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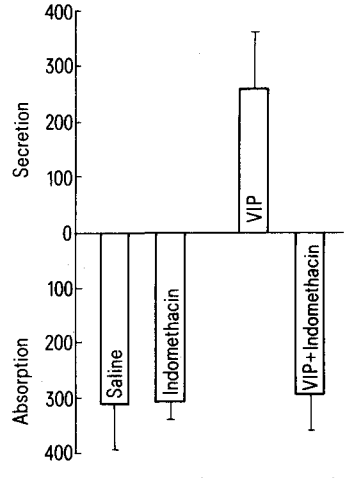
Summary. 4 groups of rats were studied under anaesthesia to assess the effect of VIP and the influence of the prostaglandin synthetase inhibitor indomethacin in isolated bowel loops. VIP produced a highly significant increase in the luminal fluid content and this was completely inhibited by addition of indomethacin.

Porcine VIP is a linear polypeptide with 28 amino acid residues closely related to secretin and glucagon[1]. In humans it occurs at particularly high concentrations in bowel and brain[2] and has been implicated in the watery diarrhoea hypokalaemic achlorhydria (WDHA) syndrome[3]. It is unique[4] among the gut hormones in sharing with prostaglandins[5-7] cholera enterotoxin[8-10] and probably other bacterial toxins, the ability to increase intestinal secretion of fluid[11], activate adenyl cyclase, increase intracellular cAMP in gastric[12] and intestinal mucosa[13] and produce changes in electrolyte secretion. The causal interrelationships and their physiological significance are complex, uncertain and different mechanisms probably operate in each of the above cases - even cAMP itself produces secretory effects resembling prostaglandins[14,15].

Potent inhibitors of prostaglandin synthesis such as aspirin and indomethacin (1-(p-chlorobenzoyl)-5-methoxy-2-methyl-indole-3-acetic acid)[16-18] produce a short-lived[9] inhibition of enterotoxin-induced secretion. This appeared particularly relevant once it was thought that the normal lag seen during induction of secretion could represent an endogenous process such as prostaglandin synthesis. The present work was undertaken to establish whether VIP increased intestinal secretion in the rat and whether it was inhibited by indomethacin.

Methods. Female Wistar rats (200-250 g) were anaesthetised with 0.1 ml/100 g i.p. pentobarbitone-Na (Sagatal 60 mg/ml) after 18-h fast with unrestricted water. The jugular vein was catheterised (Portex polythene gauge 52) and infused with pentobarbitone (12 mg/40 ml) in half strength physiological saline at 0.03 ml/min. A mid-line abdominal incision followed tracheostomy (Portex polythene PP 205) and the small bowel was tied off with double ligatures into segments approximately 5 cm long from the ligament of Treitz to the caecum. Handling was kept to a minimum and care taken not to occlude the major vessels. Krebs-bicarbonate solution (0.5 ml) was injected without undue distension into each segment using a Gillette 25 G needle. The abdomen was closed and the animal kept warm under a 60 W lamp while pentobarbitone saline with or without added VIP (140 ng/min) was infused for 45 min. Animals receiving indomethacin (Sigma Chemical Co.) were given 1 mg in 0.5 ml anaesthetic fluid over 1 min before the abdomen was opened initially and also 15 min before the infusion of VIP. After 45 min of infusion the abdomen was re-opened and the segments removed. They were first weighed then opened, blotted dry and weighed again. The mean weight gain (+) or loss (−) of the segment, assuming there to be little or no measurable



Intestinal fluid absorption or secretion was recorded as µl/45 min per g wet wt of the sac. There are 5 animals in each group (7 sacs per animal). Bars represent SE of mean.

luminal fluid initially, was calculated in µl/g wet wt for 45 min. There were 5 rats in each group. The results of these experiments are given in the figure.

Discussion. The results showed a net mean (±SEM) absorption of fluid in the saline control of -308 ± 89.2 and in control pre-treated with indomethacin -309.6 ± 37.1 (groups 1 and 2). Experimental animals receiving VIP (group 3) secreted fluid into the gut 255 ± 114.9 but this effect was completely reversed -292 ± 66.3 in the final group receiving indomethacin and VIP (group 4). Unpaired 2-tailed Student's test showed highly significant difference between groups 3 and 4 ($t = 4.14$, $p < 0.005$). The model demonstrates that in vivo parenteral porcine VIP produces a net secretion of fluid into the small bowel of rat (probably by increasing jejunal secretion and decreasing ileal absorption). Indomethacin 5 mg/kg has no direct effect on the net absorption normally at rest but when given 15 min before the infusion of VIP it completely inhibits the onset of net secretion. In other studies longer term and more localised in vivo studies on rat jejunum, indomethacin alone has been shown to produce a slight decrease in secretion[9].

Despite this effect implying the direct involvement of prostaglandins, there is little corroborative evidence. For example, VIP has not been able to release prostaglandins in 2 in vitro systems studied: guinea-pig lung perfusion and platelet aggregation[19] (unpublished observation). There is dissociation between hyperprostaglandinemia and circulating VIP in the WDHA syndrome[20], while during cholera enterotoxin-induced secretion VIP rather than prostaglandin-like substances are released from the mucosa[21,22]. Finally there is evidence against indomethacin operating solely through inhibition of prostaglandin synthesis as in vitro studies at concentrations high enough to inhibit synthesis did not prevent the accumulation of cAMP[9,23].

The mechanism whereby indomethacin inhibits cholera enterotoxin and now VIP-stimulated secretion thus remains somewhat obscure. Further work with this model and direct measurement of prostaglandin concentrations, adenyl cyclase activity and intracellular cAMP together with ion fluxes may be able to resolve the difficulties.

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A quantitative study of the catecholamine-fluorescence in the ganglion paracervicale uteri of the rat

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Summary. In the ganglion paracervicale uteri of the rat, there are principle neurons which are able to take up offered catecholamines. Normally there is an inverse relationship between their size and their mean catecholamine-fluorescence. A comparison with the catecholamine-fluorescence of depleted and repleted adrenergic perikarya in the ganglion cervicale superius is made.

The paracervical ganglion of the rat is said to consist of cholinergic perikarya, small, intensely fluorescent cells (SIF-cells), and adrenergic perikarya which are responsible for the innervation of at least part of the female genital tract[2,3]. Whereas there is no dispute about the existence of the SIF-cells and cholinergic perikarya in this ganglion, Baker et al.[4] doubted the existence of paracervical principle neurons, as they showed, there was no dopamine beta-hydroxylase, a noradrenaline synthesizing enzyme[5], in these cells.

The aim of this study was to reconsider the adrenergic nature of these principle neurons by testing their ability to take up offered catecholamines and to release catecholamines after treatment with reserpine. Changes in cellular catecholamine content were estimated by means of formaldehyde induced fluorescence and compared to those in the superior cervical and nodose ganglia.

Methods. a) Animals. 16 female Sprague-Dawley derived albino rats weighing 200–220 g were housed in cages under conditions of constant light:dark cycles (12 h), constant humidity and temperature with food and water ad libitum. They were divided into 4 groups:

group C: 4 controls, no treatment, excised ganglia treated with formaldehyde gas;

group U: 2 controls, no treatment, excised ganglia not treated with formaldehyde gas;

group R: 5 animals treated with reserpine 10 mg/kg b.wt i.p., 24 h before excision of samples;

group D: 5 animals treated with reserpine 10 mg/kg b.wt i.p. 24 h + nialamide 1000 mg/kg b.wt i.p. 2 h + L-DOPA-methylester 7.5 mg/kg b.wt i.p. 20 min before excision of samples.

The animals were sacrificed in ether anaesthesia by decapitation and the right superior cervical and nodose ganglia as