Effect of calcium on acid secretion by the isolated rat gastric mucosa

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Changes in plasma Ca^{++} levels have been shown to affect gastric acid secretion in man and other species (Barreras, 1973). These effects may be caused indirectly via hormonal mechanisms or by a direct action on the parietal cells. We have therefore investigated the effects of various external Ca^{++} concentrations on secretory responses to histamine and to pentagastrin using the isolated rat gastric mucosa (Hearn & Main, 1975).

Ca^{++} concentrations were adjusted over the range of 0.0 to 7.2 mM, in both mucosal and serosal solutions, keeping other cations constant. Drugs were added serosally and acid output recorded via an electrode in the unbuffered mucosal solution. An initial control response (in 3.6 mM Ca^{++}) was compared with the mean of two responses, 90 min apart, in the presence of altered Ca^{++}.

When the control conditions (3.6 mM Ca^{++}) were maintained throughout the 450 min experimental period, a progressive decrease in basal secretion rate was seen. This trend was increased by 7.2 mM Ca^{++} and reversed by 0.9 or 0.0 mM Ca^{++}. The effects were readily reversed on washing with 3.6 mM solutions.

Ca^{++} produced similar effects on acid responses to histamine (25×10^{-6} M, 45 min contact). In control experiments, the responses increased slightly ($+0.55 \pm 0.46$ μmol $cm^{-2}\,h^{-1}$, mean change ± s.e. mean), while lowering Ca^{++} to 1.8 or 0.9 mM produced larger changes ($+3.68 \pm 0.41$, $P < 0.002$ and $+4.67 \pm 1.04$, $P < 0.01$ respectively). In the presence of Ca^{++}-free solutions, with EDTA (0.5 mM) in serosal solution only, test responses were not significantly altered from control ($+0.42 \pm 0.84$, $n = 8$ for all groups).

Using the same experimental design, consistent responses to pentagastrin (1.8×10^{-8} M, 30 min contact) were obtained. Control responses to pentagastrin and histamine did not differ significantly (1.18 ± 0.24, $n = 25$ and 2.01 ± 0.47, $n = 32$, respectively). Under control conditions, there was a mean fall in the test responses to pentagastrin of -0.17 ± 0.08 μmol $cm^{-2}\,h^{-1}$ with a larger decrease of -0.61 ± 0.35 being produced by 7.2 mM Ca^{++} ($n = 6$). A significant increase in size of responses was observed with both 0.9 mM and Ca^{++}-free solutions ($+0.95 \pm 0.29$, $P < 0.05$, $n = 6$ and $+1.04 \pm 0.15$, $P < 0.002$, $n = 7$ respectively).

Raising Mg^{++} concentrations from 1.2 to 2.4 and 4.8 mM (keeping Ca^{++} constant at 3.6 mM) caused a potentiation of responses to histamine, the results being significant only for 2.4 mM solutions ($+4.97 \pm 1.79$, $P < 0.05$, $n = 5$).

These results demonstrate that, in the rat *in vitro*, lowering external Ca^{++} increases both basal and stimulated acid secretion by a direct effect on the secretory mucosa. They provide little support for the hypothesis that pentagastrin acts via Ca^{++}-dependent histamine release within the mucosa, since changing the Ca^{++} concentration had similar effects on the responses to histamine and pentagastrin.

J.B.P. is an M.R.C. Student.

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The effects of some gastrointestinal hormones and metoclopramide on cardiovascular dopamine receptors

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During investigations of the pharmacology of metoclopramide, a drug known to accelerate gastric emptying and stimulate intestinal motility in animals (Jacoby & Brodie, 1967) and man (James & Hume, 1968), we have considered the possibility of an interaction between metoclopramide and various hormones which affect gastrointestinal motility. Metoclopramide blocks cardiovascular dopamine receptors (Day & Blower, 1975) and some actions of secretin may be mimicked by dopamine (Furuta, Hashimoto, Iwatsuki & Takeuchi, 1973). We have therefore investigated the effects of secretin, glucagon, cholecystokinin and the synthetic peptide pentagastrin on cardiovascular dopamine receptors in anaesthetized rats.

Anaesthetized male Wistar rats were prepared as previously described (Day & Blower, 1975). After α- and β-adrenoceptor blockade, the intravenous

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