or histamine (0.3–0.5 μg kg^{-1} min^{-1}). When a plateau of stimulated gastric acid secretion had been established (−)-isoprenaline, salbutamol or nylidrin was infused concurrently with the secretory stimulant for 1 h and the percentage changes in acid secretion determined over a range of doses for each β-adrenoceptor agonist in each dog (Daly & Stables, 1977).

The results of these experiments are summarized in Table 1 from which it can be seen that (−)-isoprenaline, salbutamol and nylidrin inhibited both pentagastrin and, at higher dose levels, histamine-induced gastric secretion in the dog. Low dose levels of the β-adrenoceptor agonists occasionally increased secretion, more frequently after nylidrin than (−)-isoprenaline or salbutamol. In experiments on the non-stimulated Heidenhain pouch i.v. infusion for 1 h of (−)-isoprenaline (10 ng kg^{-1} min^{-1}), salbutamol (300 ng kg^{-1} min^{-1}) or nylidrin (3000 ng kg^{-1} min^{-1}) caused a slight but statistically insignificant increase in secretion.

It has been proposed that β-adrenoceptor agonists inhibit pentagastrin-induced gastric acid secretion in the dog by preventing the formation and/or release of histamine (Curwain, Holton, McIsaac & Spencer, 1974). Since, however, histamine-induced gastric secretion is also inhibited by higher doses of these drugs, they may act at more than one stage in the sequence of events culminating in secretion of acid by the parietal cell.

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Studies on antigen-induced acid secretion in the sensitized mouse stomach

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The physiological role of endogenous histamine and its relationship to other secretagogues in the regulation of gastric acid secretion is not fully understood. As a new approach to this problem, the present investigation examines the characteristics of antigen-induced histamine release and acid secretion in an isolated presensitized stomach.

For sensitization, female mice weighing between 15–20 g received intra-muscularly 0.1 ml of saline containing 2.5 mg egg albumin with pertussis vaccine and another i.m. injection of 0.05 ml 50 mg/ml egg albumin the next day. Three weeks later, peritoneal

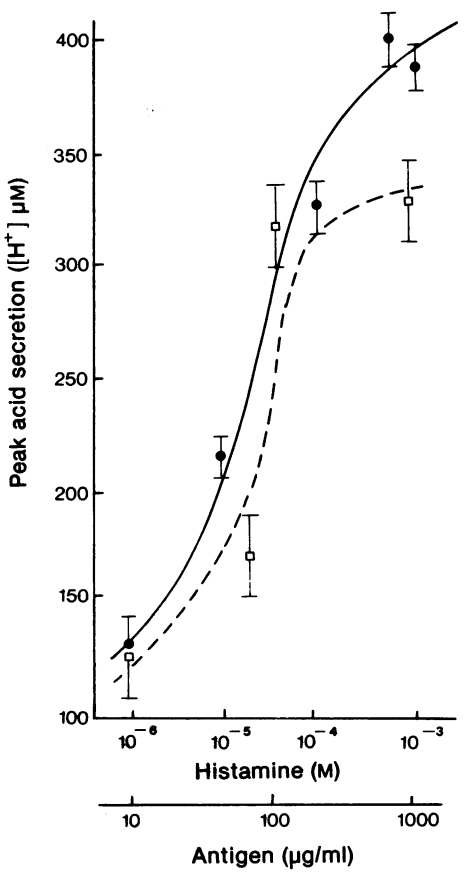

Figure 1 Effect of antigen on acid secretion in the sensitized mouse stomach (□) as compared with the effect of histamine on acid secretion in the non-sensitized mouse stomach (●). Each point shows the mean of four experiments and the vertical lines represent s.e. mean. Abscissae log scale.

exudate cells, isolated from these animals, were shown to be well sensitized by challenge *in vitro* with antigen and assay of the histamine released, using a guinea-pig ileum. Using a preparation (Wan, 1977) of an isolated perfused stomach from a mouse sensitized similarly 3–4 weeks before, the addition of a solution of the antigen induced a profuse secretion of acid.

The response curve to doses of antigen or histamine shown in Figure 1 illustrates that acid secretion rate induced by antigen was comparable to that with histamine, except that the maximal acid secretion for histamine was higher. Antigen-induced acid secretion was inhibited by metiamide (5×10^{-5} M) or atropine (5×10^{-6} M) by about 50% and sodium cromoglycate (5×10^{-5} M) by about 33%, but not by the potent phosphodiesterase inhibitor ICI 63197 (10^{-4} M). Although the histamine concentration in the gastric effluent and the serosal solution bathing the sensitized mouse stomach did not correlate with antigen-induced acid secretion, the present evidence still suggests that endogenous histamine released in the anaphylactic mouse stomach is involved in gastric acid secretion. However, the possibility that antigen could also release gastrin and acetylcholine, which would induce acid secretion, should not be excluded.

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Influence of 2-2'-pyridylisatogen tosylate on responses produced by ATP and by neural stimulation on the rat gastric corpus

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The ATP-induced relaxation of the isolated guinea-pig taenia caeci can be antagonized by 2,2'-pyridylisatogen tosylate (PIT) while a similar response to field stimulation remains unaffected (Spedding, Sweetman & Weetman, 1975). In the isolated guinea-pig terminal ileum, PIT potentiated contractile responses to applied ATP and to field stimulation (Kazic & Milosavljevic, 1977). Using the rat gastric corpus, we found that ATP produced a biphasic response consisting of a relaxation followed by a contraction. Vagal or field stimulation produced a similar reponse in the presence of atropine, The influence of PIT on these responses has been studied.

A strip of gastric corpus was bathed at 36°C in Krebs–Hensleit solution containing barium chloride (10^{-3} M), to elevate tone, and atropine sulphate (3×10^{-6} M). For most experiments a cumulative dosing technique was used for the application of ATP to the preparation. The contractions which are normally apparent after a single dose of ATP were absent. The relaxations produced by such applications of ATP (5×10^{-5} M to 5×10^{-2} M) were antagonized by incubating the tissue with PIT (5×10^{-5} M to 5×10^{-4} M) for 30 minutes. The extent of this antagonism was dependent upon the dose of PIT and the duration of its incubation with the tissue. After 90 min incubation the antagonism was apparently irreversible. When relaxations of the tissue were induced with either noradrenaline (10^{-7} M to 10^{-5} M) or isoprenaline (10^{-7} M to 10^{-5} M) PIT (10^{-4} M) was without antagonistic effect. Incubation periods of both 30 min and 2 h were used.

Sequential doses of ATP produced biphasic responses at concentrations $\leqslant 5 \times 10^{-4}$ M; higher doses produced relaxation only. Pre-incubation of the tissue with indomethacin (10^{-5} M) (a prostaglandin synthesis inhibitor, Vane, 1971) for 10 min antagonized the contractile part of the biphasic response to ATP while the relaxation was unaffected. Again relaxations produced by ATP could be antagonized by PIT (10^{-4} M, duration of incubation 30 min).

Cumulative frequency (0.5–20 Hz) response curves were produced to field stimulation (100 v, pulse width 2.0 ms). Relaxations produced by such stimulations were not antagonized by incubation with PIT (10^{-4} M) for either 30 min or 2 hours. Sequential stimulation of the vagi at 10 v and 30 v (pulse width 2.0 ms, 20 Hz for 90 s) produced a biphasic response which was not antagonized by incubation with either PIT (10^{-4} M) or indomethacin (10^{-5} M) for 30 min or 2 hours.

This study demonstrates differences between the response to applied ATP and neural stimulation and so does not support the view that ATP is the non-adrenergic, non-cholinergic inhibitory transmitter in the rat stomach (Burnstock, 1972). A biphasic response to applied ATP was observed. The selective effect of PIT on the phase of relaxation could be