therefore develop as rapidly as that to other centrally acting drugs including opiates.

In subsequent experiments using these techniques we observe significant differences in the rate and magnitude of development of cellular tolerance to ethanol of mice of different age and strain. We intend to use these differences to investigate the biochemical basis of cellular tolerance.

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The effects of (−)-isoprenaline, salbutamol and nylidrin on gastric acid secretion in conscious dogs with Heidenhain pouches

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β-Adrenoceptor agonists such as (−)-isoprenaline and salbutamol are potent inhibitors of pentagastrin-induced gastric acid secretion in the dog (Curwain, Holton & Spencer, 1972; Daly & Stables, 1977). However, histamine-induced secretion is reported to be unaffected by salbutamol, enhanced by low doses of isoprenaline and inhibited by high doses of isoprenaline (Curwain *et al.*, 1972). We have reinvestigated the effects of (−)-isoprenaline and salbutamol on gastric secretion and have also studied nylidrin, a β-adrenoceptor agonist claimed to stimulate gastric secretion (Geumei, Issa, El-Gindi & Abd-el-Samie, 1969).

Three male beagle dogs (13–18 kg) with well-established Heidenhain pouches were used. Submaximal gastric acid secretion was induced by continuous intravenous infusion of pentagastrin (1–4 μg kg^{-1} h^{-1})

Table 1 The effects of β-adrenoceptor agonists on gastric secretion induced by pentagastrin or histamine in conscious dogs with Heidenhain pouches

Secretory stimulant and β-adrenoceptor agonist	*n*	*Increased secretion*			*Decreased secretion*
		Incidence†	*Dose (ng kg^{-1} min^{-1})*	*% Increase**	*ED_{50} ± s.e.mean (effective dose range ng kg^{-1} min^{-1})*
versus pentagastrin					
(−)-Isoprenaline	30	0			5.7 ± 2.7 (1–10)
Salbutamol	27	0			82.4 ± 23.9 (30–300)
Nylidrin	12	1	300	40	999 ± 74 (300–3,000)
versus histamine					
(−)-Isoprenaline	15	2	100	96, 15	299 ± 105 (100–1,000)
Salbutamol	12	1	30	8	514 ± 84
		1	300	11	(300–1,000)
Nylidrin	9	3	300	10, 11, 17	11,500 ± 3,145 (3,000–10,000)

n = number of experiments.
† = incidence in 3 experiments at dose level shown.
* = values given are all significant by *t* test at $P < 0.05$.

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.

The gift of nylidrin by Troponwerke is gratefully acknowledged.

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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

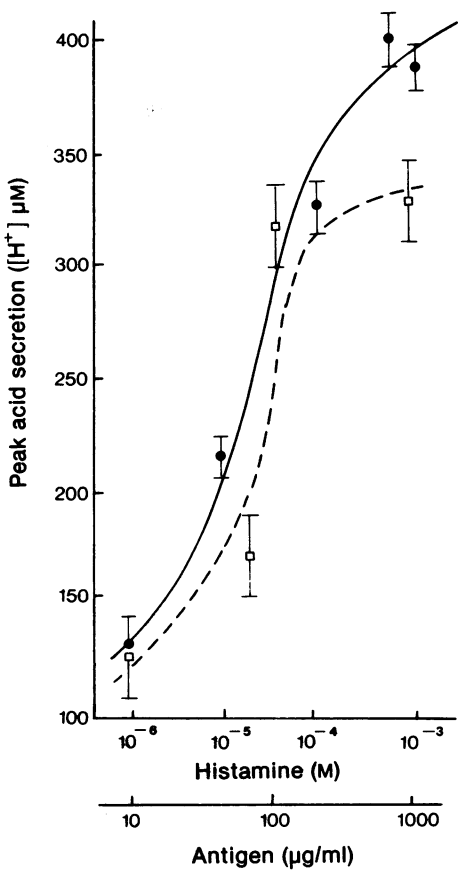

Figure 1 Effect of antigen on acid secretion in the sensitized mouse stomach (□) as compared with the effect of histamine on acid secretion in the non-sensitized mouse stomach (●). Each point shows the mean of four experiments and the vertical lines represent s.e. mean. Abscissae log scale.