significant difference between the acid secretory responses to db cyclic AMP (2.5×10^{-4} M) in the absence and presence of metiamide (up to 5×10^{-4} M). Student's 't' test on results from different preparations also indicated that metiamide did not inhibit acid secretion induced by db cyclic AMP ($n = 5$ for db cyclic AMP, 2.5×10^{-4} M, and for metiamide up to 5×10^{-4} M + db cyclic AMP 2.5×10^{-4} M). In contrast to db cyclic AMP, histamine or pentagastrin did not regularly stimulate acid secretion. However, marked stimulation of acid secretion by histamine or pentagastrin could be obtained in the presence of phosphodiesterase inhibitors. The order of effectiveness was triazolopyrimidine > theophylline > caffeine. In preparations treated with histamine 20 min after triazolopyrimidine (10^{-4} M) was added, sustained and dose-related responses to histamine (10^{-5} to 10^{-3} M) could be obtained. In the presence of triazolopyrimidine (10^{-4} M), $[H^+]$ secretion to a submaximal dose of pentagastrin (2×10^{-6} M) was about 80 μM as compared to that of about 100 μM in response to a submaximal dose of histamine (2.5×10^{-4} M). Triazolopyrimidine on its own caused slight stimulation of acid secretion by the isolated mouse stomach.

The present results are in agreement with the findings of Fromm, Schwartz & Quijano (1975), who showed that marked stimulation of acid secretion in the isolated rabbit gastric mucosa by db cyclic AMP was not inhibited by metiamide. The exact mode of action of phosphodiesterase inhibitors on the acid secretory responses to histamine and pentagastrin is not clear. In view of the evidence that triazolopyrimidine greatly potentiated the increase in cyclic AMP levels induced by biogenic amines in mouse cerebral slices (Nahorski & Rogers, 1975), the present results support the hypothesis that cyclic AMP may be involved in histamine or pentagastrin-induced acid secretion by the mouse stomach *in vitro*.

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The effects of intravenous secretin on the small intestinal vasculature of the cat

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Secretin, administered intravenously or intra-arterially, increases superior mesenteric arterial blood flow in the anaesthetized cat (Ross, 1970; Fasth, Filipsson, Hulten & Martinson, 1972). Since other gastrointestinal hormones such as glucagon and pentagastrin, when infused intravenously in low doses, alter capillary filtration coefficient in the cat small intestine (Richardson, 1975), the effects of intravenous secretin on the resistance, capacitance, and vascular exchange function of this tissue have been examined.

Eight cats (2.66-3.87 kg) were anaesthetized with α-chloralose (70 mg/kg i.v.) after halothane induction, and loops of sympathetically-innervated jejunum (62.6 ±18.4 g, mean ± s.d.) prepared for the measurement of blood flow, changes in tissue volume, and capillary filtration coefficient (CFC), by a modification (Richardson, 1974) of the plethysmographic technique of Folkow, Lundgren & Wallentin (1963).

Under control conditions, the systemic arterial mean pressure (BP) was 151.4 ± 4.2 (mean ± s.e. mean) mmHg, the heart rate (HR) 174.6 ± 10.0 beats/min, and the superior mesenteric venous outflow (SMVF) 55.7 ± 7.8 ml min^{-1} 100 g^{-1}, giving a calculated jejunal vascular resistance (JVR) of 3.15 ± 0.57 mmHg ml^{-1} min 100 g. The CFC, measured as the continuous volume increase resulting from raising the superior mesenteric venous pressure by 10 cm H_2O for 1 min was 0.060 ± 0.009 ml min^{-1} $mmHg^{-1}$ 100 g^{-1} ($n = 5$).

Natural secretin (Boots) was infused intravenously in a dose of 0.1 U kg^{-1} min^{-1} (Crick-Harper-Raper Units; 1 U = 62.5 ng) to five preparations, resulting in a significant (paired 't'-test; $P < 0.05$) increase in CFC of 38.8 ± 9.2% from 0.060 ± 0.009 to 0.083 ± 0.012 ml min^{-1} $mmHg^{-1}$ 100 g^{-1}. The jejunal volume (JV) rose by 0.27 ± 0.06 ml/100 g at the start of the infusion

($P < 0.05$) but changes in BP, HR, SMVF and JVR were variable and insignificant ($P > 0.30$).

When secretin was infused intravenously in a dose of 0.5 U kg^{-1} min^{-1} to five preparations, the CFC rose by 61.6 ± 10.9% from 0.060 ± 0.009 to 0.095 ± 0.011 ml min^{-1} $mmHg^{-1}$ 100 g^{-1} ($P < 0.02$), and the JV rose by 0.83 ± 0.25 ml/100 g ($P < 0.05$). These infusions resulted in falls in BP (3.4 ± 1.2%), rises in HR (13.5 ± 5.0%), rises in SMVF (17.4 ± 7.2%) and reductions in JVR (16.4 ± 5.5%), changes which were consistent, but not statistically significant ($P > 0.05$). The effects of secretin at this dose on CFC and JV were not modified by pretreatment with hexamethonium (5 mg/kg, i.v.: three experiments) or propranolol (0.1 mg/kg, i.v.: three experiments).

On six occasions in three preparations, intravenous injections of 0.02 to 20.0 U/kg secretin resulted in dose-dependent transient reductions in JVR (maximum: −67.3 ± 3.0%) and increases in JV (maximum: +1.61 ± 0.27 ml/100 g). Doses above 0.5 U/kg additionally caused dose-dependent falls in BP and rises in HR.

As well as reducing small intestinal vascular resistance, intravenous secretin causes an increase in tissue volume over the same dose range, indicating dilatation of capacitance vessels (Folkow *et al.*, 1963). Low dose infusions increase CFC and JV without significant effects on other variables: the rise in CFC indicates either dilatation of precapillary 'sphincters', leading to an increased functional exchange vessel area, or an increased vascular permeability, mechanisms which are not separable by this technique.

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Some preservatives in eyedrop preparations hasten the formation of dryspots in the rabbit cornea

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Three factors are important in the maintenance of the tear film between the replenishing action of the blink. Its adherence to the cornea is aided (a) by the surface microplicae on the epithelial cells, (b) by the surface-tension lowering layer of conjunctival mucus which overlies the epithelium and (c) by an outer layer of oil (secreted by the Meibomian glands) which delays evaporation. Since surface-active substances are often used as preservatives in eyedrop preparations, these experiments were undertaken to examine the effect of such substances on the stability of the rabbit tear film.

Dutch rabbits were anaesthetized with halothane (3%) in nitrous oxide-oxygen (3 : 1). Saline (3 drops of 0.9% w/v) was applied to both eyes at zero time and the excess fluid removed. The time taken for the development of a dry spot on each cornea was measured and was taken as the 'start-control' value (each eye to act as its own control). The tear film was immediately restored by blinking the eyelids three times. Three drops of preservative solution (lowest concentration, in 0.9% saline or suitable vehicle) were then applied, excess fluid removed and the drying time measured again. This procedure was repeated for successive increases in concentration of the preservative solution. Finally, the cornea was irrigated with saline and the eyelids repeatedly blinked for 10 min, before another control determination was made ('end-control').