indicating that the maximum response had been obtained. Omitting the highest dose tested, the mean response for each drug was linearly related to the log dose. The common regression coefficient

$$(b) = \frac{\text{response}}{\log_{10} \text{dose}},$$

was obtained by the method of Snedecor & Cochrane (1969). b = 2.06, (fiducial limits 1.20, 2.92 at $P = 0.05$). None of the regression coefficients for the four drugs differed significantly from the common regression coefficient. The molar potency ratios with reference to histamine were NαMeH 2.3 ± 0.22 s.e. mean $N\alpha Me_2H$, 0.85 ± 0.26 s.e. mean, 5MeH 0.43 ± 0.27 s.e. mean.

We have therefore confirmed that NαMeH is a more potent stimulus for gastric acid secretion than histamine but the potency ratio in the guinea pig is less than that observed in cats and dogs.

We have also shown that in the guinea pig $N\alpha Me_2H$ is an approximately equipotent and 5MeH is a less potent H_2-receptor agonist than histamine.

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Effects of atropine on gastric secretion and mucosal blood flow in conscious dogs.

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Atropine is known to decrease gastric acid secretion in the dog (Gregory & Tracy, 1961) rat (Johansson, Lundell & Svensson, 1971) and cat (Svensson & Emas, 1974), and is still used clinically as an anti-secretory and spasmolytic drug. For therapeutic use an anti-secretory drug is likely to be more beneficial if it does not greatly reduce the ratio of gastric mucosal blood flow (MBF) to secretory rate.

We have examined the effects of atropine on MBF and acid secretion in six dogs with Heidenhain pouches. Food was withheld but water allowed for 18 h before experiments. Submaximal gastric acid secretion was induced by pentagastrin (1-4 $\mu g\ kg^{-1}\ h^{-1}$) or bethanechol (60 $\mu g\ kg^{-1}\ h^{-1}$). Atropine was given during the secretory plateau. Secretion was collected over 15 min periods and acid output measured by titration. MBF was estimated by radioactive aniline clearance (Curwain & Holton, 1973). Effects on acid secretion and MBF were calculated as follows: Measurements for the three 15 min periods preceding the dose of atropine were compared with the mean of the three values from 15-60 min after atropine. Results are expressed as percentage changes ± s.e. mean.

In four experiments in four dogs atropine sulphate (100 μg/kg i.v.) decreased pentagastrin-stimulated acid secretory rate (62.8 ± 12.4) and MBF (44.5 ± 18). The concentration of acid secreted decreased by 14.8 ± 3.7 and 23.5 ± 7.5 respectively 45 and 60 min after atropine, but the pH of the secretion was less than 3.0. The ratio of MBF to secretion rose (39.3 ± 12.8) during secretory inhibition.

Atropine sulphate (100 μg/kg i.v.) also decreased acid secretion stimulated by bethanechol. In three experiments in three dogs secretion decreased by a mean of 83.0 ± 11.0. In one of these experiments the pH of the secretion remained less than 3.0 and the ratio of MBF to secretion rose by 56% during secretory inhibition. In the other two experiments acid concentration fell so much that the pH was above 3.0. Under these conditions aniline clearance does not measure MBF.

In twelve further experiments smaller doses of atropine (1-25 μg/kg i.v. or s.c.) inhibited secretion in response to both stimuli but were more

effective against bethanechol. In the seven experiments in which the pH of the secretion remained below 3.0 the ratio of MBF to secretory rate rose (55.0 ± 16.6). We conclude that atropine does not inhibit acid secretion by decreasing MBF.

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The effect of atropine on pentagastrin-induced gastric acid secretion and mucosal blood flow in the conscious rat

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Atropine is known to decrease gastric acid secretion in response to a variety of stimuli (Hirschowitz & Sachs, 1969; Johansson, Lundell & Svensson, 1971). In the present series of experiments the effect of atropine 100 μg/kg i.v. was investigated for its effect on pentagastrin-induced gastric acid secretion and gastric mucosal blood flow in the conscious rat.

Male and female Wistar rats were provided with either vagally innervated (Pavlov) pouches or vagally dennervated (Heidenhain) pouches using established surgical procedures (Svensson, 1970). Three weeks later indwelling vascular catheters (Weeks, personal communication) were implanted. Drugs were dissolved in sterile pyrogen-free saline and administered via the jugular catheter. Acid secretion was collected by pouch perfusion and measured every 15 min by titration to pH 7.4 using an automatic titrator. The results were expressed in $\mu Eq\ H^+\ min^{-1}$. Blood samples (0.01 ml) were withdrawn via a catheter in the carotid artery. Mucosal blood flow (MBF) in ml min^{-1} was estimated using the radioactive aniline clearance method developed for the conscious dog (Curwain & Holton, 1973) and adapted for use in the conscious rat. 18 h before each experiment food was withdrawn but water and Tyrode's solution allowed. Pentagastrin dose-response curves for each rat were determined and the dose which produced secretion at about 50% maximum was used for the rest of the study. A steady plateau of acid secretion and MBF was first obtained using pentagastrin. The ratio of mucosal blood flow to acid secretion was steady at $0.09 + 0.011$ ml $(\mu EqH^+)^{-1}$. The effect of atropine was calculated from the mean secretory rate and MBF of the three samples at 30, 45 and 60 min after atropine compared with the three samples immediately before giving atropine. The results are expressed as percentages s.e. mean.

In eleven experiments on three rats with Pavlov pouches and three rats with Heidenhain pouches atropine caused a 75.8 ± 2.95% fall in acid secretion with only a 39.8 ± 3.17% fall in MBF. No significant difference was found between the extent of inhibition in the two types of pouches. Acid secretion and MBF after atropine were significantly different from their pre-atropine levels. The percent decrease in MBF was also significantly different from the percent decrease in acid secretion.

An increase in the ratio of MBF to secretory rate was always seen, indicating a primary effect on the secretory apparatus and not blood flow.

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