

Histamine output from the rat isolated gastric mucosa during acid secretion stimulated by pentagastrin, methacholine and dibutyryl cyclic adenosine 3',5'-monophosphate

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Histamine has been implicated as a local mediator of the action of gastrin in stimulating acid secretion but its role in the action of other secretagogues is less certain. We have used an isolated rat gastric mucosal preparation to correlate changes in histamine output with H^+ -secretion.

The muscle overlying the non-antral glandular region of the stomach was removed as described by Hearn & Main (1975). Two pieces of mucosa (1 cm^2) were mounted in organ baths containing 35 ml of buffered serosal solution. Acid secretion was recorded via an electrode in the unbuffered mucosal solution. Histamine released into the serosal solution, collected over 30 min periods, was assayed fluorometrically after condensation with o-phthalaldehyde by the method of Hakanson, Rönnberg & Sjölund (1972). An initial control response to a secretagogue at 120 min, (30 min contact, 3.6 mM Ca^{++}) was compared with the mean of two responses, at 270 and 360 min, in the presence of altered Ca^{++} (0.0 to 7.2 mM).

In experiments using paired tissues from 24 rats, one half was exposed to pentagastrin ($1.8 \times 10^{-8}\text{ M}$), the other kept as a non-stimulated control. The latter showed a steady decline in basal histamine output, falling from $267 \pm 23\text{ ng}$ (mean \pm s.e. mean, $n=6$), at 90 to 120 min, to $119 \pm 20\text{ ng}$, at 420 to 450 minutes. (Secretagogue-induced changes in histamine output were therefore calculated with respect to the extrapolated basal value).

Under control conditions, pentagastrin produced a mean increase of $1.18 \pm 0.24\text{ }\mu\text{mol cm}^{-2}\text{ h}^{-1}$ in acid secretion and $48 \pm 5\text{ ng}$ in histamine output. Methacholine ($5 \times 10^{-7}\text{ M}$) produced increases of $8.14 \pm 1.26\text{ }\mu\text{mol cm}^{-2}\text{ h}^{-1}$ in acid secretion and $28 \pm 4\text{ ng}$ in histamine output ($n=22$). Changing

external Ca^{++} -concentrations produced effects on methacholine-induced acid secretion similar to those previously reported with pentagastrin (Main & Pearce, 1977) but had no effect on histamine output associated with either secretagogue.

The effect of dibutyryl cAMP ($0.11 \times 10^{-3}\text{ M}$) in the presence of theophylline ($2 \times 10^{-3}\text{ M}$) was investigated on 6 preparations. Although consistent large acid-secretory responses were produced throughout the experiments, serosal histamine output was not altered during the responses ($+9.68 \pm 3.13\text{ }\mu\text{mol cm}^{-2}\text{ h}^{-1}$ and $-8 \pm 8\text{ ng}$ respectively).

These results support the hypothesis that pentagastrin stimulates acid secretion via mobilization of endogenous histamine whereas dibutyryl cAMP and theophylline act directly within the parietal cell, beyond the histamine-receptor mechanism. Although methacholine may act partly via histamine, the greatly reduced ratio of Δ -histamine: Δ - H^+ suggests a mainly direct effect. In contrast, Rangachari (1975) found similar ratios of histamine to acid during stimulation with pentagastrin and acetylcholine in the bullfrog. Our results are compatible with the observation that, in the rat isolated whole stomach preparation, metiamide did not inhibit acetylcholine-induced secretion in concentrations which blocked gastrin (Bunce, Parsons & Rollings, 1976).

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References

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