injections of either EL or PH themselves; (3) alterations in the chemical composition of saliva.

Our experiments showed that: (1) chronic administration of PH, but not of EL, produced enlargement of the main salivary glands; (2) chronic treatment with EL did not modify, whilst chronic treatment with PH reduced, glandular sensitivity to single injections of EL; (3) amylase activity of saliva from chronically EL-treated rats exceeded amylase activity of saliva obtained from controls or chronically PH-treated rats, regardless of the inducer employed; (4) in our experimental conditions not only was PH a stronger agonist than EL on a molar basis, but it also produced a saliva chemically different from the one evoked by EL.

The possible role of these modifications in determining the therapeutic effect of PH and EL was discussed.

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Effects of salbutamol on gastric acid secretion and gastrin liberation after feeding in conscious Heidenhain pouch dogs

B.P. CURWAIN*, L.P. FIELDING & C. RUSSELL

Departments of Physiology and Surgery, St Mary's Hospital Medical School, London W2 1PG

The main finding to be presented is that salbutamol decreases gastric acid secretion in response to feeding in conscious dogs with Heidenhain pouches. This result was to be expected since this drug has been shown to decrease acid secretion in response to pentagastrin (Curwain, Holton & Spencer, 1972). Since the response of the Heidenhain pouch to feeding is due to endogenous gastrin, there remained the possibility that secretory inhibition was partly due to interference with gastrin release. For this reason we have measured plasma gastrin concentrations during the response to food and during administration of salbutamol.

Six healthy bitches with well-established Heidenhain pouches were used. After an overnight fast, a standard meal of cooked, minced ox liver (20 gm/kg) plus 5-10 gm NaCl was given. Venous blood samples were taken every 15 min and plasma gastrin concentration was measured by radioimmunoassay. Gastric secretion was collected and acid measured by titration. Salbutamol sulphate (0.2 $\mu g\ kg^{-1}\ min^{-1}$ i.v.) was given for 30 min beginning 60 min after feeding during the secretory plateau. The acid secretory rate and plasma gastrin concentrations were compared with those in control experiments in which no salbutamol was given.

Acid secretory rate was significantly reduced during the two 15 min periods following the end of salbutamol infusion. The mean reductions were 58% and 51% respectively, $P < 0.05$ (t test for paired data). A mean reduction of 26% ($0.05 > P < 0.1$) was seen in the second 15 min period during the infusion of salbutamol. There were no significant changes in plasma gastrin concentration during the acid secretory inhibition.

In another series of experiments salbutamol (0.2 or 0.4 $\mu g\ kg^{-1}\ min^{-1}$) was given for 10 min before feeding and for 30 min afterwards. Acid secretion was significantly reduced in the first hour after the meal (mean reduction = 43.9% ± 12.4% s.e., $P < 0.05$). Total gastrin output during the first 60 min after feeding was not significantly altered by salbutamol. However, the pattern of gastrin liberation was different. In the control experiments peak plasma gastrin concentration occurred in the first 15 min after feeding after which it fell to a plateau maintained for the next 30 minutes. In the salbutamol experiments the peak was absent and the plateau of gastrin concentration was higher than but not significantly different from that in the control experiments.

We conclude that salbutamol decreases the gastric acid secretory response to feeding in the conscious Heidenhain pouch dog. The mechanism by which the initial gastrin response is altered during salbutamol remains to be elucidated.

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Preliminary data on the inhibition of pentagastrin stimulated gastric secretion induced by some natural and synthetic peptides

G. BERTACCINI*, R. DE CASTIGLIONE & MARIANNINA IMPICCIATORE

Department of Pharmacology, University of Parma, 43100 Parma, Italy

In previous papers cholecystokinin (CCK) and caerulein were found to inhibit gastric secretion induced by pentagastrin in man and dogs (Stening, Johnson & Grossman, 1969; Brooks, Agosti, Bertaccini & Grossman, 1970). This probably depended on a competitive antagonism between gastrin and these two peptides which, as partial agonists, competed with gastrin for an active site in the secretory process. On the basis of these results we synthesized and submitted to thorough pharmacological examination a series of caerulein-like peptides (Bertaccini, 1969) in the hope of finding some compounds endowed with the same inhibitory activity but devoid of the stimulant effect of the natural peptides. Among 25 compounds examined on Heidenhain pouch dogs two substances were found of considerable interest: an heptapeptide similar to the C-terminal heptapeptide of caerulein but with a nor-leucine instead of the methionine residue (Boc-Tyr(SO_3H)-Thr-Gly-Trp-Nle-Asp-Phe . NH_2) and a pentapeptide with the following structure: (H-Tyr(SO_3H)-Trp-Met-Asp-Phe . NH_2). The first compound is endowed with a striking inhibitory activity but retains a certain stimulant cholecystokinetic effect. The second is less active as an inhibitor but it is almost completely devoid of stimulant activities. The heptapeptide showed a remarkable effect also in a few human volunteers. In another series of experiments also the natural peptide Bombesin (Pyr-Gln-Arg-Leu-Gly-Asn-Gln-Trp-Ala-Val - Gly - His-Leu-Met . NH_2) which is completely different from gastrin and CCK both from a chemical and a pharmacological point of view was shown to inhibit significantly the hypersecretion induced by pentagastrin. The mechanism of action is probably connected with a release of gastrin and/or of cholecystokinin provoked by bombesin as shown by Erspamer, Melchiorri, Sopranzi, Torsoli, Corazziari & Improta (1973); Torsoli, Corazziari, Habib, Melchiorri, Delle Fave & Improta (1973). Of course a direct effect of bombesin cannot be excluded.

The present data were discussed and the possibility that an antisecretory effect may be present also in a caerulein-like compound lacking the tyrosyl-sulphate group in position seven is pointed out.

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