# Effect of stimulation of vagus nerves on gastric tissue histamine concentration in albino rats

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*Summary.* 2 different time schedules were applied in order to stimulate vagus nerves around the oesophagus at the region of the cardio-oesophageal junction. The result shows a significant reduction in gastric tissue histamine concentration following vagal stimulation, the reduction being more when the duration of stimulation was longer.

That the vagal and adrenal pathways are involved, and that they play important roles in the production of stress induced gastric ulcers, is evident from a number of observations[2-7]. But our knowledge on the sequence of events following stimulation of either of these pathways is incomplete. Histamine, an important constituent of mast cells, is known to be a potent stimulator of gastric glands[8]. A strong correlation exists between mast cell population and histamine concentration of tissues[9]. In rats, about half of the whole body histamine formation presumably takes place in the stomach wall[10]. We had suggested that the adrenal pathway acts on gastric glands through histamine liberated from the mast cells[11,12]. That the vagal activity also leads to release of histamine from mast cells is indicated from our observations[13-15]. Moreover, Metiamide, a histamine blocker, has been shown to block the vagal response to gastric secretion[16]. The present experiment is planned to study the effect of direct stimulation of vagus nerves on the gastric tissue histamine concentration.

*Materials and methods.* 24 colony-bred albino rats of either sex, weighing 100-140 g, housed in separate cages were divided into 3 groups. All the animals in different groups were fasted for 24 h before starting any experiment, only water was allowed. The 1st group of animals comprising of 10 rats were anaesthetized with ether. The anaesthesia was maintained for 30 min, following which they were sacrificed by cutting the carotids; their stomachs were taken out, opened along the greater curvature, cleaned and processed for extraction of histamine. The 2nd and 3rd groups of animals comprising of 7 rats each were anaesthetized with ether, their abdomens opened with a long incision and the cardio-oesophageal region mobilized. The lower oesophagus was slightly distended from inside by introducing a polythene tube of appropriate size with a small piece of glass rod attached to its lower end. A specially designed ring electrode was positioned around the distended lower oesophagus so that the electrode lay in intimate contact with the vagal fibres, which run close to the oesophagus in this area.

Square wave pulses of 10 V, 5 msec duration and 10/sec were used for stimulating the vagal fibres. The schedule that was followed in order to stimulate the vagal fibres in the 2nd group of animals was 5 min stimulation, 5 min rest followed by 5 min stimulation and 5 min rest. The animals were then sacrificed by cutting the carotids; their stomachs removed, opened along the greater curvature, cleaned and processed for histamine extraction. In the 3rd group of animals the procedure followed was the same as in the 2nd group, except that the 2 stimulation periods were 10 min each.

The stomach tissue was weighed dry, cut into fine pieces in 2 ml/g of tissue of N hydrochloric acid and ground up with a little sand in a mortar. 10 ml of distilled water per g of tissue was added during grinding. The extract was put in a conical flask and boiled for 1 min. Before assaying, it was filtered and neutralized with N NaOH and made up to a given volume[17]. Histamine concentration was estimated by the standard biological assay method, using terminal portion of ileum of 24 h-fasted, medium-sized guinea-pig in a thermostat organ bath at 37 °C. Atropinized Tyrode's solution was used as bath fluid, and the presence of histamine was confirmed by mepyramine maleate, 0.2 ml $2.5 \times 10^{-6}$ M. 3 point assay was performed in order to calculate histamine concentration which was expressed in µg/g of tissue.

*Results.* The results, which are summarized in the table, show that vagal stimulation at the region of cardio-oesophageal junction leads to a reduction in gastric tissue histamine concentration, the reduction being more with increased duration of stimulation.

*Discussions.* It has been suggested that in rats about half of the whole body histamine formation takes place in the stomach wall[10]. A strong positive correlation between mast cell population and histamine content in the tissues has also been shown to be present[9]. In view of our earlier observation of decrease in stainable gastric mucosal mast cell population following over activity of vagus in stress[13], it appears from the present findings that the vagal stimulation leads to liberation of histamine from the mast cells and thereby the gastric tissue histamine concentration is reduced. With longer duration of vagal stimulation, more mast cells are degranulated and the gastric tissue histamine concentration is further reduced. Our earlier observation[15] of absence of any significant change in gastric tissue histamine concentration following subdiaphragmatic vagotomy in pylorus ligated rats further supports the view derived from the present experiment.

Effect of vagal stimulation on gastric tissue histamine concentration in albino rats

| Serial No. | Experimental situation | No. of animals | Mean gastric tissue histamine concentration in µg/g ± SD |
|---|---|---|---|
| 1 | Normal | 10 | 11.49 ± 1.41 |
| 2 | Vagal stimulation with schedule 1 (5-5-5-5) | 7 | 5.40 ± 2.73 |
| 3 | Vagal stimulation with schedule 2 (10-5-10-5) | 7 | 1.80 ± 1.13 |
| Statistical analysis | | | |
| Between experimental situations | | | t-values |
| Normal and schedule 1 | | | 6.04* |
| Normal and schedule 2 | | | 15.07* |
| Schedule 1 and schedule 2 | | | 3.60* |

*Significant at 1% level.

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## Effect of suppression of endocrine or exocrine pancreatic function in hemorrhagic shock[1]

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*Summary.* Somatostatin did not influence the pathologic consequences of hemorrhagic shock, but pancreatic duct ligation prevented the post-oligemic decline of arterial pressure and formation of toxic factors. These results indicate that pancreatic acinar cells release myocardial depressant factor and are important in the pathophysiology of shock.

Somatostatin (SRIF) has been shown to inhibit pituitary growth hormone secretion both in vivo and in vitro[3-5] and suppresses a glucose induced rise in plasma insulin[6]. These findings and those of others[7-10] demonstrate that SRIF, at concentrations as low as 1 ng/ml, inhibits pancreatic islet cells. The pancreas has also been implicated as a key organ in the pathophysiology of shock[11-13]. Circulatory shock is characterized by a prolonged pancreatic ischemia which results in pancreatic autolysis and in the elaboration of a cardiotoxic peptide, myocardial depressant factor (MDF). Atrophy of exocrine pancreatic tissue prevents MDF formation in bowel ischemia shock[14]. This relationship between pancreatic function and shock lethality suggests that modification of the endocrine pancreas by SRIF or of the exocrine pancreas by duct ligation, might alter the response of animals to circulatory shock. This study was undertaken to evaluate such procedures on the hemodynamic and biochemical sequelae of hemorrhagic shock in cats.

*Materials and methods.* Male cats (3.0–3.5 kg) were anesthetized with sodium pentobarbital (30 mg/kg) i.v. Catheters were placed in the right carotid artery and left jugular vein for monitoring mean arterial blood pressure (MABP) and central venous pressure (CVP). Catheters were also placed in the right femoral artery and vein. The superior mesenteric artery was isolated, and a non-cannulating flow probe was placed around the artery near its origin for measurement of superior mesenteric artery flow (SMAF), using a Statham model SP 2202 electromagnetic flow-meter. All pressures, SMAF, and lead III of the electrocardiogram (ECG) were continuously recorded on a Grass oscillographic recorder. An electronic servomechanism, modified from the design of Culpepper et al.[15] was used to maintain MABP at 40 mm Hg during the oligemic period. All cats were given heparin (1000 U/kg) 20 min prior to time 0.

Cats were randomly placed in one of the following groups: A) sham hemorrhagic shock + vehicle (0.9% NaCl); B) hemorrhagic shock + vehicle (0.9% NaCl); C) sham hemorrhagic shock + SRIF; D) hemorrhagic shock + SRIF; E) hemorrhagic shock + pancreatic duct ligation. The duct ligation was performed 40–49 days prior to induction of shock as previously described[14]. Cats in groups C and D received both an initial i.v. injection of 24 µg/kg of somatostatin in 1 ml 0.9% NaCl just prior to bleeding, and an infusion of 1 µg/kg/min throughout the oligemic period. Cats given vehicle received an equivalent volume of 0.9% NaCl. Following drawing of the initial blood sample (i.e., time 0), hemorrhaged cats were bled into a plexiglass reservoir gassed with 95% $O_2$ + 5% $CO_2$, via the femoral arterial catheter. When MABP fell to 40 mm Hg, the servomechanism was activated. After 120 min of oligemia, the shed blood was reinfused and the animals observed for an additional 120 min. Hemodynamic measurements were made every 30 min, and 5-ml blood samples were drawn at 0, 120, 180 and 240 min. Following centrifugation of the blood, the plasma was decanted for the determination of plasma protein concentration and cathepsin D activity. 10 ml of 0.9% NaCl was given to replace each 5 ml of blood lost by sampling. At the termination of each experiment, 25 ml of arterial blood was drawn for assay of MDF activity. MDF activity of deproteinized plasma[16] eluted from a Biogel P-2 column[17], was assayed using isolated cat papillary muscles bathed in Krebs-Henseleit solution according to the method of Lefer et al.[18]. Plasma cathepsin D was assayed according to the method of Anson[19] using bovine hemoglobin as substrate. The biuret method of Gornall et

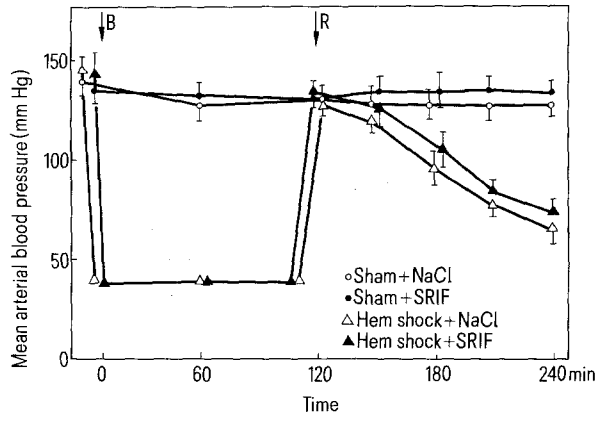


Fig. 1. Mean arterial blood pressure (MABP) during the 4-h experimental period in 6 cats given SRIF or NaCl. All points are mean values±SEM. No significant differences were observed between control values of 4 groups of animals. The MABP of the hemorrhage + NaCl and hemorrhage + SRIF were significantly less than the corresponding sham hemorrhage groups at 180, 210 and 240 min ($p < 0.01$).