

On the relationship between gastric pH and pressure in the normal human lower oesophageal sphincter

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SUMMARY The effect upon the lower oesophageal sphincter (LOS) of acid in the proximal stomach was investigated in 12 young healthy subjects. The cardia was perfused in turn with solutions at pH 7, 4, 3, 2, and 1, during successive withdrawals of three perfused pressure-recording catheters, openings of which were at the same axial level. Although there was considerable individual variation, there was a direct and significant relationship between LOS pressure and the acidity of the solution perfused. The results suggest that resting LOS pressure may be determined in part by the pH of the gastric content.

Cannon (1908) observed in cats that the gastric contents were rhythmically regurgitated into the oesophagus after ingestion of a neutral starch meal. The phenomenon was prevented by acidification of the meal. Moreover, he demonstrated that a greater intragastric pressure was required to produce gastro-oesophageal reflux when the gastric contents were acid than when they were not. Confirmatory observations, for this species, have been reported (Robson and Welt, 1959; Clark and Vane, 1961; Titchen and Wheeler, 1971). There is relatively little evidence for the existence of a similar mechanism in man. Giles *et al.* (1969a) described a rise in the maximum pressure recorded from the lower oesophageal sphincter (LOS) when the distal part of this zone was perfused with acid solutions. However, their results, obtained with a single unperfused recording catheter, were not entirely consistent. Constant perfusion of an end or side-opening catheter improves the accuracy of pressure measurements within the LOS (Pope, 1967; Winans and Harris, 1967). We have attempted to evaluate the effect of alterations in pH in the region of the gastric cardia using this type of manometric system. As the pressure recorded from the LOS is influenced by the radial position of the opening (Kaye and Showalter, 1971), we used a tube complex which included three recording catheters the openings of which were at the same axial level, and equidistant around the circumference of a circle.

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Methods

SUBJECTS

Twelve healthy, informed, freely consenting subjects, all either physicians or medical laboratory technicians, were studied. The group comprised 11 males and one female, with a mean age of 31 years (range 23-39 years). All subjects were free of oesophageal symptoms.

The tube complex (Fig. 1) consisted of a pH electrode and its recording lead, an infusion tube, and three recording catheters, the side-openings of which, measuring 1.60 × 2.30 mm, were located at the same axial level and were equidistant around the circumference of a circle. The recording and infusion catheters, made of stiff polyvinyl tubing with internal and external diameters of 1.12 and 1.65 mm respectively, were glued along their lengths to the centrally located pH recording lead. The tips of the infusion tube and pH electrode were, respectively, 6 and 5 cm distal to the recording openings. The infusion tube had nine lateral openings, at 0.5 cm intervals, beginning 0.5 cm distal to the recording openings. During all studies, the recording catheters were continuously perfused with distilled water at a constant rate of 8.4 μl/s by infusion pump (Harvard Apparatus Co., Inc., model 975). Pressures were recorded through external transducers (Statham P 23 DE) on a Gilson Macropolygraph. The fluids used for infusion were double distilled water (pH 7), and solutions at pH 1, pH 2, pH 3, and pH 4, obtained by appropriate dilutions of hydrochloric acid with double distilled water. These fluids were pumped through the infusion tube at a rate of 7.5 ml/min (Harvard, model 1201).

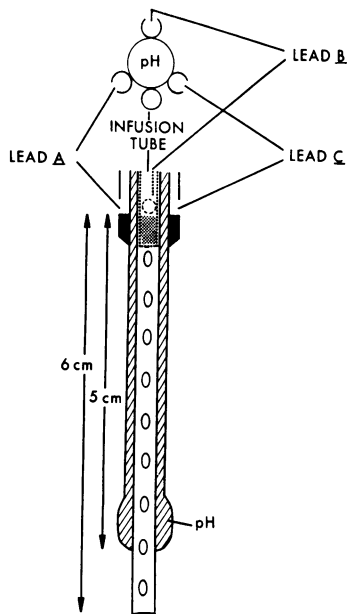


Fig. 1 Diagram of tube complex. Transverse and longitudinal sections are shown. Leads A, B, and C are pressure-recording catheters with their lateral openings at the same axial level.

Studies were carried out in the morning after an overnight fast. The tube complex was passed through the mouth into the stomach, without prior pre-medication or pharyngeal anaesthesia. Subjects lay supine on a couch, height of which was such that oesophagus and transducers were at approximately the same level. Respiration and swallowing were recorded by pneumatic cuffs applied around upper abdomen and neck. Pressure tracings of the LOS were obtained by measured withdrawals, in 0.5 cm steps, of the three recording openings, from stomach to oesophagus. The tube complex was maintained at each point until satisfactory baseline pressures had been achieved. Subjects were asked to avoid swallowing during withdrawals. Resting pressure profiles of the LOS were recorded during perfusion through the infusion tube of the various solutions, in the following order: (1) no infusion, (2) double distilled water, (3) pH 4, (4) pH 3, (5) pH 2, (6) pH 1. The original intention to perfuse these fluids in random order was abandoned when preliminary *in vitro* observations showed that, after the infusion tube had been filled with a strongly acid (pH 1) solution, effluent from the tube remained acid for at least 30 minutes after the beginning of perfusion with double-distilled water at a rate of 7.5 ml/min.

Each study lasted 60 to 90 minutes. The amount of fluid infused over this period was approximately 350 ml.

LOS pressures were measured at end-expiration. Gastric end-expiratory baseline pressures were used as zero reference.

Results

Since pressure measurements were obtained simultaneously by three orifices located at the same axial level, maximum LOS pressure, for a given withdrawal, can be determined in two ways—either by taking the greatest mean pressure recorded by the three leads at a single point within the LOS (method A) or by considering each recording orifice independently, and taking the mean of the maximum pressures recorded by each, irrespective of the point at which they were measured (method B). Both methods have been used for expression of results, as a choice between the two is arbitrary.

The maximum LOS pressures, for each of the six withdrawals, are shown in the Table. The pressures measured during perfusion with distilled water were higher than those obtained when the infusion tube was unperfused. For this reason, the measurements obtained during distilled water perfusion have been used as baseline values for evaluation of pH effects. The maximum pressures obtained during perfusion with acid solutions, in relation to these baseline values, are shown in Figure 2. In order to determine whether acid perfusion influenced maximum sphincteric pressure, mean values for maximum pressure obtained during perfusion of the different solutions were regressed against pH. The slope of the regression line was significantly ($P = 0.012$ and 0.011 for methods A and B respectively) different from zero, which indicates that acid significantly increased maximum sphincteric pressure, and that this effect was proportional to the acidity of the perfusate.

Table Maximum LOS pressures obtained during different withdrawals from 12 subjects

Maximum pressure (mmHg)	Withdrawal					
	Unperfused	Distilled water	pH 4	pH 3	pH 2	pH 1
Method A	14.48	19.64	22.05	21.00	23.49	25.28
Method B	15.47	21.94	24.06	23.49	26.40	27.31

Figure 3 illustrates the effect of perfusion of acid solutions upon the LOS as a whole. All pressure measurements in a given individual were expressed in relation to the pressure inversion point (PIP), and in terms of their variation from the values obtained during distilled water perfusion. It is apparent that the pH4 solution had little effect upon any part of the LOS, while the other three more acid solutions

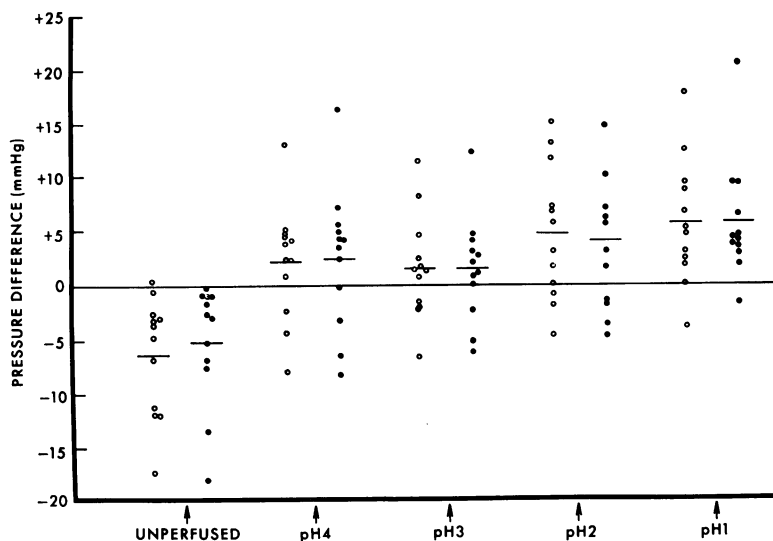


Fig. 2 Changes in maximum sphincteric pressure during perfusion of proximal stomach with acid solutions. All values, including those obtained when the infusion tube was unperfused, are expressed in relation to maximum sphincteric pressures observed during perfusion of double distilled water (pH 7). Pressures measured according to methods A and B (see text) are represented by closed and open circles respectively. Means are shown by horizontal lines.

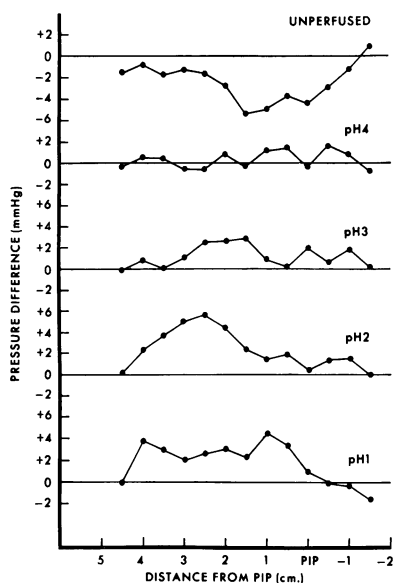


Fig. 3 Changes in pressure at various LOS levels during perfusion of proximal stomach with acid solutions. All values, including those obtained when the infusion tube was unperfused, are expressed in relation to pressures observed during perfusion of double distilled water. The PIP was used as a reference point for measurements in each of the 12 subjects. Positive values on the horizontal axis represent points distal to the PIP.

produced an increase in pressure throughout the greater part of the LOS, the most marked changes being in its distal portion.

During withdrawals of the tube complex from stomach to oesophagus with the infusion tube unperfused, the pH consistently rose to, and remained at, levels above 4 in all subjects. These observations corroborated the historical evidence for sphincteric competence.

Discussion

The results of this study show, in support of Giles *et al.* (1969a), that exposure of the cardia and of the distal portion of the gastro-oesophageal junctional zone to solutions of low pH has a significant influence upon the resting pressures recorded from the lower oesophageal sphincter. The observation that sphincteric pressures were higher when the infusion tube was perfused with double-distilled water than when it was unperfused was unexpected. The mechanism of this effect is not clear. It may, however, be relevant to note that, during the withdrawal studies, relaxation and contraction within the lower oesophageal sphincter, not initiated by deglutition, were seen occasionally. This would suggest that significant amounts of infused fluid leaked back into the distal oesophagus, so that the assumption made by us, and by Giles *et al.* (1969a), that the proximal openings of the infusion tube would be occluded as they were drawn from the stomach into the sphincter, may not be entirely valid. Giles *et al.* (1969a) found in five subjects that infusion of saline through their infusion tube had no effect upon maximum sphincteric pressure. This discrepancy between the two studies may be explicable in terms of differences in method. For example, Giles *et al.* recorded

pressures from the LOS with a single unperfused catheter, and did not infuse fluids through their infusion catheter at a constant rate.

The effect of acid infusion, as compared with distilled water infusion, was quite small. It was nevertheless statistically significant; the fact that pressures throughout the greater part of the LOS, as opposed to those at a single point—that is, maximum LOS pressure—were higher during infusion of acid solutions than control values, would indicate that the effect is real. At first sight, however, it might appear that the physiological relevance of this is somewhat dubious. However, it is well established that gastrin has a marked influence upon resting LOS pressure (Giles *et al.*, 1969b; Castell and Harris, 1970; Cohen and Lipschutz, 1971), and that inhibition of release of gastrin, and probably of other hormonal agents (Brown *et al.*, 1978), by acidification of the gastric contents is followed by a decrease in resting LOS pressure (Castell and Levine, 1971). The circumstances of this study were such that the effect of acid, *per se*, upon LOS pressure may well have been partially masked by its additional effect of inhibition of hormonal release. It is likely that the LOS response to acid would have been greater, perhaps substantially so, if it had been possible to exclude changes in sphincteric pressure secondary to variation in rates of hormonal release.

As previously noted, clearing of a strongly acid solution from the infusion tube by perfusion of a less acid solution took at least 30 minutes. In consequence, the solutions used in this study were not perfused in random order, but rather LOS withdrawal tracings were obtained during perfusion of progressively more acid solutions. Although our results are entirely consistent with the conclusion that LOS pressure was proportional to the acidity of the perfusate, alternative interpretations of the data require consideration. Firstly, it could be argued that the observed increase in LOS pressure was merely a function of time. As there is no systematic evidence that LOS pressure increases during the course of motility studies—that is to say, increases as a consequence of the presence of a tube within the LOS—this possibility seems unlikely. Secondly, it is conceivable that LOS pressure changes were related to gastric distention, the degree of which would have increased during the study as a consequence of fluid infusion. However, assuming that the asymptomatic subjects whom we studied had normal rates of gastric emptying, it is unlikely that a strong distention stimulus would have been applied by infusion of approximately 350 ml of fluid over a 60 to 90 minute period. Moreover, any effect that distention may have had in the promotion of gastrin release (Grossman, 1960, 1961, 1962) would probably have

been more than offset by the counteractive influence of increasing acidity of the perfusate during the study period.

Giles *et al.* (1969a) found, in five subjects whose gastro-oesophageal junctional areas were perfused in random order with solutions at pH 1, 2, 3, and 4, that only during perfusion with the pH 3 solution were maximum LOS pressures significantly greater than control values. We, in contrast, observed, over the same pH range, that maximum LOS pressure was proportional to the acidity of the solution perfused. As Giles *et al.* pointed out, the optimal pH for peptic activity in gastric juice is close to 3, so that a maximal sphincteric effect at this same pH might seem teleologically reasonable. On the other hand, if this effect of acid upon LOS pressure is truly mediated through some type of acid-sensitive receptor in the region of the cardia, then it is likely that, in accord with our findings, the greatest effect would be observed with the most strongly acid solution. However, firm conclusions regarding the physiological significance of this effect, and the mechanism by which it is produced, require studies in which the influence of other important variables, such as circulating hormone levels, can be properly controlled.

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