

Effect of oesophageal perfusion with acid on basal gastric secretion

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The escape of acid gastric secretions from the stomach, in certain circumstances, is potentially destructive to the mucosae of the oesophagus and the duodenum. In the duodenum the pyloric sphincter plays a part in controlling gastric emptying, and further protection from the harmful effects of acid is offered by inhibitory mechanisms stimulated by duodenal acidification (Johnston and Duthie, 1965). In the oesophagus there is also a sphincter controlling reflux of gastric secretion, but it is not known whether any intrinsic mechanism exists which might influence the production of acid.

MATERIAL AND METHODS

The studies were performed on volunteer subjects to whom the nature and purpose of the experiment had been explained. There were 12 normal subjects (nine males and three females) whose ages ranged from 21 to 34 years. Eight patients with duodenal ulcer (two females, six males) aged 28-56 years were examined and the diagnosis was confirmed by operation in all cases. Sixteen patients (seven females, nine males) aged 41-64 years suffering from hiatus hernia were also studied. The diagnosis was made by barium meal examination and confirmed by manometric studies. Oesophagoscopy was also performed in these patients.

PROCEDURE The subjects were fasted overnight and next day a size 12F nasogastric tube together with a fine polythene tube of 1.9-mm internal diameter were passed into the stomach. The fine polythene tube, primed with water, was connected to a Statham strain gauge transducer and relayed to an oscilloscope. This system allowed respiratory pressure changes to be measured, and using a technique similar to that described by Fyke, Code, and Schlegel (1956), the polythene tube was withdrawn by intervals of 1 cm to identify the diaphragm and the lower oesophageal sphincter. When the position of the sphincter was established, the fine tube was withdrawn a further 10 cm and fixed in position. It was then disconnected from the strain gauge to provide a channel for the subsequent oesophageal perfusion.

Gastric secretions were aspirated by continuous suction using an electric pump, and samples were collected

in 15-minute periods. Great care was taken to ensure that all saliva was voided during this time. After collecting basal secretions for one hour, the effect of perfusing the oesophagus was studied for a further hour using tap water or hydrochloric acid (N/100 and N/10) infused at a rate of 20 ml per 15 minutes. These solutions were labelled with phenol red 15 mg per 100 ml. All gastric samples were filtered through glass wool and then titrated with N/100 sodium hydroxide using 0.4% Bromocresol green as indicator (pH 3.8). The phenol red concentration in the last four samples was estimated using 0.2 ml of gastric juice mixed with phosphate buffer at pH 10.0 and measuring optical density at 500, 560, and 600 μ as recommended by Allen (1950). This allowed calculations of the contamination of the gastric samples by the perfusate, and the results are expressed as the volume and milliequivalents of free acid after correction. In all patients with duodenal ulceration and hiatus hernia the maximum acid output was also determined using the histamine infusion test of Lawrie, Smith, and Forrest (1964).

RESULTS

CONTROL STUDIES Perfusion studies using tap water only were performed in five male subjects, three of whom had a duodenal ulcer. No symptoms were experienced and there was no significant change in the basal acid secretions.

EXPERIMENTAL STUDIES Five normal subjects had oesophageal perfusion tests using N/10 hydrochloric acid, and the results are shown in Figure 1 (top). All subjects experienced an increased production of saliva during perfusion though none had heartburn. With the start of perfusion there was an immediate increase in the volume of juice, which rose from the mean basal level of 70.9 ml per hour to 138.1 ml in the perfusion hour. In four of the subjects there was a small increase in the acid output, rising from a mean of 2.3 m-equiv in the basal hour to 3.1 m-equiv in the perfusion hour. In the remaining subject, who had a basal achlorhydria, there was no change in the acid output. Since the changes observed in acid secretion were small, the possibility arose that an experimental

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error might result from infusing acid whose concentration was considerably in excess of the resting gastric juice.

The experiment was therefore repeated in seven normal subjects using oesophageal perfusion of N/100 hydrochloric acid. The results shown in Figure 1 again illustrate an increase in the volume of juice from 47.5 to 80.8 ml per hour. Two subjects were achlorhydric throughout the test but the remainder showed stimulation of acid secretion, the mean rising from 0.5 m-equiv in the basal hour to a mean of 1.8 m-equiv during perfusion. There seemed little doubt therefore that the response to oesophageal perfusion of acid in normal subjects resulted in stimulation of gastric secretion affecting both the volume and acid output.

DUODENAL ULCER SUBJECTS Perfusion tests using N/10 hydrochloric acid were performed in eight patients with duodenal ulcer and the results are shown in Figure 2. One patient had no alteration of volume or acid output during perfusion, but in the remainder the volume rose from a mean of 109 ml to 198.6 ml per hour, and the mean acid output rose from 6.0 to 10.4 m-equiv per hour. During perfusion five of the patients experienced heartburn and all showed marked stimulation of acid secretion. Of the three patients without symptoms, one had no alteration of either volume or acidity of gastric content. Two others showed an increase in the volume of aspirate, but the effect on acid secretion was slight and occurred only towards the end of the perfusion hour. These results confirmed the observations in normal subjects, and the more dramatic response compared with normal subjects was regarded as a reflection of the greater secretory capacity of patients with duodenal ulcer.

HIATUS HERNIA Sixteen subjects were perfused using N/10 hydrochloric acid and of these seven did not experience any symptoms and nine experienced heartburn. The results in the seven asymptomatic patients are illustrated in Figure 3A. All but one patient showed an increase in volume during perfusion and the mean rate rose from 38 ml/hr to 85 ml/hr. Only one patient, however, showed a substantial increase in acid, the basal level rising from 0.6 to 2.9 m-equiv during the test hour. The relatively small changes in the remainder are indicated by the mean alteration from a basal of 1.1 to 1.5 m-equiv/hr during the test period. This contrasts with the results in nine patients who experienced heartburn during perfusion (Fig. 3B). One patient showed no increase in either volume or acid output, but in addition to a substantial increase in the volume of aspirate, acid secretion

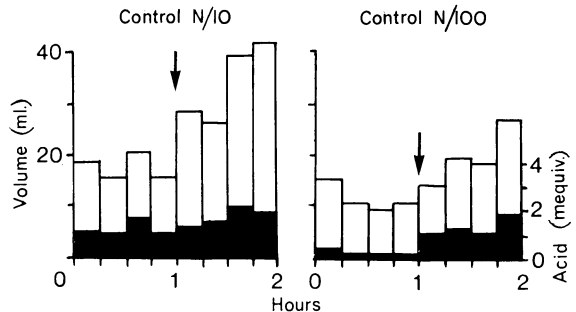


FIG. 1. The mean results in five normal subjects perfused with N/10 hydrochloric acid and seven normal subjects perfused with N/100 hydrochloric acid. The clear columns represent the volume of gastric aspirate and the black columns the acid output in consecutive 15-minute samples before and after oesophageal perfusion (indicated by the arrow). These and subsequent figures show results corrected for contamination by the fluid perfusing the oesophagus.

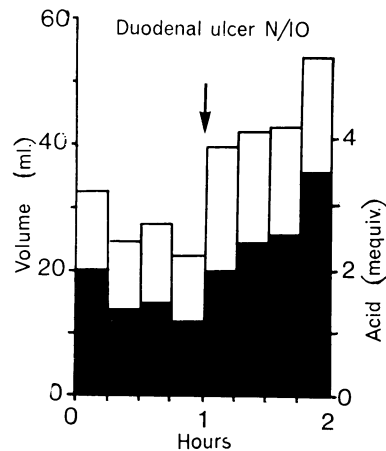


FIG. 2. The mean results in eight patients with duodenal ulcer perfused with N/10 hydrochloric acid. With the onset of perfusion (arrow) there is marked increase in the volume and acid output from the stomach. Five of these subjects experienced heartburn during the test.

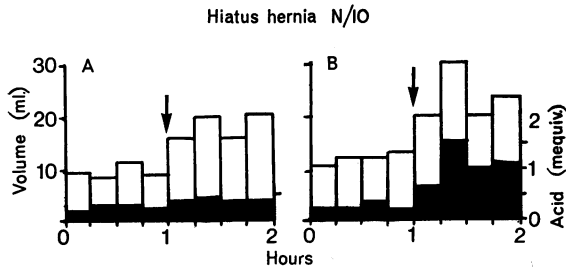


FIG. 3. In the diagram (A) are the mean results of seven patients with hiatus hernia who were asymptomatic on oesophageal perfusion with hydrochloric acid. In (B) are the mean results of nine patients with hiatus hernia who felt heartburn with oesophageal perfusion. Both groups show an increase in the volume of gastric aspirate, but only those in (B) showed any significant increase in the acid output.

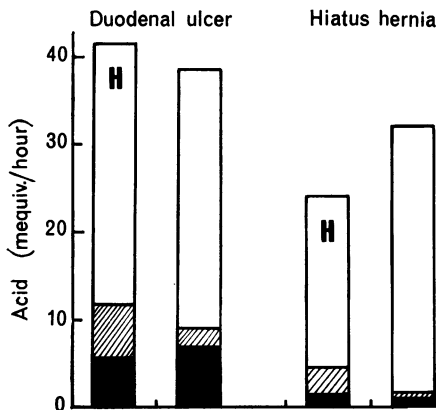


FIG. 4. The secretion of acid in patients with duodenal ulcer and hiatus hernia, comparing basal secretion (black), the response to oesophageal perfusion (hatched), and the maximum response to histamine (clear). Columns marked by H indicate the patients who felt heartburn during acid perfusion of the oesophagus. The response to oesophageal perfusion is greater in patients with heartburn, and is not related to the maximum secretory capacity of the stomach.

was stimulated in the remainder from a mean of 1.7 to 5.1 m-equiv per hour. These patients all showed evidence of oesophagitis, and were subsequently treated by operation.

The absent response to perfusion in the asymptomatic group of hiatus hernia patients could have been due to a much smaller acid secretory capacity and thus a comparison of the results of the histamine tests in these patients and those with duodenal ulcer is relevant. Figure 4 shows a comparison of the basal acid output, the response to oesophageal perfusion, and the maximum response to histamine. In patients with duodenal ulcer the response to perfusion is about 40% of the histamine-stimulated secretion in those who felt heartburn, but there is little stimulation in the three patients unaffected by the perfusion. Clearly this difference was not due to a lack of secretory capacity since the histamine response is similar in both groups. Patients with hiatus hernia feeling heartburn during perfusion had stimulation of the basal secretion to about 20% of the histamine-stimulated secretion and a response was seen in all but one patient. The most striking observation is the very small response to perfusion in asymptomatic hiatus hernia patients, even though the secretory capacity, as measured by histamine-stimulated secretion, is greater than in patients suffering from oesophagitis.

DISCUSSION

The method used for locating the cardiac sphincter and perfusing the oesophagus is similar to that described by Bernstein and Baker (1958), Tuttle, Bettarello, and Grossman (1960), and Bennett and Atkinson (1966). The previous use of this technique has been as an aid to the diagnosis of oesophagitis, but it has not, to our knowledge, been used to study the effects on gastric secretion. The interpretation of the results must take into account the changes in basal secretion which are known to depend upon psychic background and upon collection techniques. In control studies with water labelled with phenol red, the volume of gastric aspirate increased by less than 10% and the acid output was quite unaffected. This means that the perfusion of acid via the lower oesophagus into the stomach may increase the effectiveness of the collection to a slight degree. However, the changes in volume observed during the acid perfusion experiments are very much greater than in control studies, and must represent a real rather than an apparent increase in the volume of aspirate. In the majority of the patients studied it has been shown that perfusing the oesophagus with acid results in a true stimulation of basal acid secretion of the

stomach and this is usually accompanied by a marked increase in the volume of juice, which is almost doubled.

The effects on acid secretion are most marked in patients with duodenal ulceration, and it was of interest that five of these patients suffered from heartburn during the procedure. Of the remaining three patients with ulcer who had no symptoms during perfusion, one had no increase in either volume or acid output, and the others showed an increase in volume but only a small rise in acid output towards the end of the perfusion hour. The onset of heartburn in the symptomatic ulcer patients was immediate, and presumably due to the acid in contact with the oesophagus. Unfortunately none of these patients had an oesophagoscopy, so that it cannot be denied that oesophagitis may have existed.

The relationship between duodenal ulcer and heartburn on oesophageal perfusion is uncertain. It is well known that many patients with hiatus hernia suffer from associated peptic ulceration. Furthermore Pridie (1966) has recently demonstrated an hiatal hernia in 25% of patients with duodenal ulceration. Tuttle *et al.* (1960) demonstrated acid reflux into the oesophagus in 39 of 61 patients with duodenal ulcer (64%) and of these 33 (89%) experienced heartburn during acid perfusion. Bernstein and Baker (1955), in a group of 20 patients with symptoms suggestive of oesophagitis and a positive response to acid perfusion, found only 10 with confirmatory changes on endoscopy, and similar observations were made by Tuttle *et al.* (1960). This may be accounted for by the findings of Palmer (1955) who showed that the initial lesions in oesophagitis affect first the lamina propria and only later extend to the epithelium and the muscle. It is of interest that Lodge (1955) has shown experimentally in the rat that this is also the response to acid perfusion. Thus Tuttle *et al.* (1960) have argued that a positive response to perfusion where there is evidence of reflux is indicative of oesophagitis regardless of the endoscopic findings. Though formal proof of this hypothesis by histology is lacking, there is certainly sufficient evidence from the work quoted to support it.

The results in the two groups of patients with hiatus hernia are therefore important, for nine had a positive response to perfusion and seven had no response. In the former, oesophagitis was readily detected by endoscopy, and all had symptoms of sufficient severity to warrant operation. All but one of these patients had stimulation of acid secretion during perfusion, the mean level being about four times the basal level. This was in contrast to the patients with no heartburn on perfusion, where only one showed

a substantial increase in acid secretion, and the remainder showed only small increases or no change. The difference between those with a positive response to perfusion and the remainder can be partly related to the output of acid on perfusion, but other factors must play a part.

Previous observations on gastric secretion in patients with hiatus hernia have shown that the basal acid secretion is greater than normal in the majority of patients with significant symptoms. Casten, Bernhang, Nach, and Spinzia (1963) found that the 12-hour overnight secretion in 82% of patients with symptoms severe enough to warrant operation was greater than 20 m-equiv, whereas only 12% of those not requiring operation had an acid output of similar magnitude. Similarly in the present study, patients with marked symptoms on clinical evaluation, and as judged with the acid perfusion test, showed the greatest increases in basal secretion on oesophageal perfusion. Thus the differences in basal secretion noted by Casten *et al.* (1963) between patients with hiatus hernia requiring operation and those controlled by medical treatment may have been due to the frequency and severity of reflux and its stimulatory effect on gastric secretion.

The mechanism by which basal secretion is increased by oesophageal perfusion remains speculative. The concomitant stimulation of salivary secretion suggests a vagal reflex. Aylwin (1953) found an increase in salivary and oesophageal secretion in patients with hiatus hernia and oesophagitis, and this was associated with nocturnal gastric hypersecretion. These findings were attributed to a vagal reflex stimulated by irritation of the collecting tube. The present experiments demonstrate that the increase in basal secretion occurred only when acid perfusion had begun, which suggests that the acid was the stimulating factor. If this is the case, then in any situation leading to incompetence of the cardia, reflex of acid gastric contents into the oesophagus may simulate the circumstances of this experiment. The effect is then to stimulate gastric secretion and make more acid available for reflux, establishing a vicious cycle.

The response in the hiatus hernia patients without oesophagitis is not easily explained. Clearly some stimulation occurred as the volume of secretion extracted was almost doubled, but a significant increase in the acid output did not accompany this except in one case. It seems likely therefore that the increase in volume is accounted for by a change in the nonparietal component of gastric juice. With the symptomatic hiatus hernia patients the positive response to acid perfusion may be related to a more sensitive epithelial lining which elicits the response

to the stimulus with greater ease. The fact that oesophagitis occurred in these patients helps to support this hypothesis, and if the views of Palmer (1955) and Lodge (1955) on the early stages of oesophagitis are upheld, this could also explain the results in patients with duodenal ulcer. These preliminary observations are as yet incomplete and the effect of perfusion on the denervated and anaesthetic oesophagus would be of interest. Such denervation would, however, interfere with the gastric secretion and make interpretation of the results very difficult. We have made a few studies using local anaesthetics on the oesophageal mucosa, but like Hookman, Siegel, and Hendrix (1966), we have not found them of help in preventing heart-burn during perfusion and it seems likely that the pain endings lie deep in the submucosa and are not accessible to the local agent whereas the H⁺ ions of the acid have no difficulty in penetrating the mucosa and causing pain.

It is concluded that acid reflux into the oesophagus can set up a reflex stimulation of basal gastric secretion. When the reflex is associated with inflammation of the oesophagus the stimulation is more marked and a situation arises where a vicious cycle becomes established which will maintain or worsen the existing inflammation.

SUMMARY

When acid passes from the stomach into the

duodenum inhibitory mechanisms are stimulated which reduce further acid secretion. This study shows that when acid is in the oesophagus, there is no inhibition of gastric secretion. Instead there is stimulation of basal gastric secretion, particularly in subjects with duodenal ulcer and those with hiatus hernia and an associated oesophagitis.

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