have received little attention (although both IF and hydrogen ion are produced by the parietal cell), and we report here our findings in patients with duodenal ulcer.

Patients, methods, and results

Forty-four patients (34 men and 10 women) with endoscopically proved duodenal ulceration were investigated using standard gastric acid secretion study techniques. Gastric juice was collected in 15-minute aliquots and IF concentration was estimated by radioimmunoassay.² Two series of studies were carried out, one on basal gastric secretion (details can be supplied on request) and one on pentagastrin-stimulated secretion. For the pentagastrin study a control test was performed in 13 patients: 30-minute basal secretion was followed by pentagastrin infusion (6 µg/kg/h) for 120 minutes. A further 16 patients (test group) underwent the same procedure but cimetidine (2 mg/kg/h) was added from a separate syringe during the second hour of pentagastrin infusion.

In controls the characteristic pattern of IF output stimulated by pentagastrin infusion is shown in the figure.^{3,4} A steady state of IF secretion was achieved 60 minutes after the start of the infusion, there being no statistical difference between the IF output in sample 6 and subsequent collections. The pattern of IF secretion in the cimetidine-treated group was different: both IF and acid secretion at the end of the cimetidine infusion were about a quarter of the pre-cimetidine levels. The smaller IF and acid outputs were contributed to by a lower volume of secretion and a reduced concentration of both substances. Mean IF outputs (±SE of mean) in samples 6, 9, and 10 were 1871±270, 262±75, and 411±98 U/15 min respectively (6 v 9 and 6 v 10: $P < 0.01$, Wilcoxon test); mean IF concentrations were 20.5±2.3, 8.2±2.1, and 11.5±1.6 U/ml ($P < 0.01$). The corresponding values for acid output were 10.3±1.5, 2.3±0.5, and 2.3±0.6 mol/l ($P < 0.01$); for acid concentration 106.3±32.7, 62.8±31.1, and 62.0±31.4 mol/l ($P < 0.01$); and for volume of secretion 91.5±11.9, 35.0±7.8, and 35.9±7.4 ml ($P < 0.01$). (Similar results were obtained under basal conditions.)

Effect of cimetidine on pentagastrin-stimulated IF output. Results are means ± SE of mean.

Discussion

This study shows that cimetidine reduces IF output under basal and pentagastrin-stimulated conditions in patients with duodenal ulcer. Of special interest was the reduction in IF concentration in both parts of the study, which indicates that cimetidine has an action on IF over and above that of reducing the volume of gastric secretion. Burland *et al*⁵ studied the effect of cimetidine on IF release in eight normal volunteers and claimed that there was no significant reduction in IF secretion. They used a lower dose of cimetidine, however, which produced a smaller reduction in mean acid output than we achieved. The most important difference between the studies was the timing of cimetidine infusion. Burland *et al* investigated the effect of cimetidine during the early period of pentagastrin infusion, when preformed IF is rapidly released into gastric juice. We tested the effect of cimetidine after this initial rapid release phase had ended—during the period of IF synthesis.

IF secretion in patients with duodenal ulcers is therefore greatly reduced by cimetidine infusion, but this is unlikely to interfere with vitamin B₁₂ absorption in most patients. Nevertheless, the effect of

long-term cimetidine administration on IF secretion and vitamin B₁₂ absorption needs to be measured to confirm the safety of this new drug during prolonged treatment.

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Oesophageal bolus extraction by balloon catheter

Here I describe a simple technique of relieving sudden onset complete obstruction of the oesophagus by a bolus, which has been used in two patients.

Method and case reports

A well-lubricated 26 F Simplicast Foley catheter is passed through the mouth with the patient sitting upright. No sedation or surface anaesthesia is used. In the stomach the balloon is inflated with 8 ml of air, this allowing it to pass up through the cardia. On withdrawing the catheter the bolus is removed, resulting in immediate relief of symptoms.

Case 1—A 70-year-old woman presented with a three-hour history of total dysphagia. She gave no other history and the results of physical examination were normal. Bolus obstruction was diagnosed, but conventional methods (including fizzy drinks and passing a soft rubber tube) failed to dislodge it. The method described above was used, a large meat bolus produced, and she could then swallow normally again. Findings on subsequent oesophago-gastroduodenoscopy were normal.

Case 2—A 74-year-old man presented with a four-day history of total dysphagia. He had a history of productive cough and smoked one and a half ounces of tobacco weekly. Examination showed finger clubbing but no other abnormality, while a chest x-ray film showed a left hilar mass. A diagnosis of oesophageal bolus obstruction secondary to extrinsic compression from a bronchial carcinoma was made. After passing a 26 F Foley catheter, food debris was recovered, and the procedure was repeated four times until no more was obtained. The patient was immediately able to swallow sloppy foods. At subsequent oesophago-gastroduodenoscopy a resistance to the endoscope was found at 36 cm. Fibreoptic bronchoscopy confirmed the presence of a tumour of the left main bronchus, biopsy specimens of which showed a well-differentiated squamous cell carcinoma. He remained symptom-free for three months.

Comment

Balloon catheter extraction of boluses that are obstructing the oesophagus has not been reported. Investigating patients with "spasm at the entrance of the oesophagus," Brown Kelly passed a metal urethral catheter with a finger stall tied to its end.¹ He then inflated this and withdrew the catheter, concluding that no organised adhesions were present in this condition. In addition, he found that the manoeuvre produced improvement in symptoms. Hydrostatic² and pneumatic³ dilatation of the lower oesophagus has been used in the treatment of achalasia, and more recently disruption of postcricoid oesophageal webs using a Foley catheter has been recorded.⁴ In the presence of a bolus obstruction, surface anaesthesia was deliberately omitted to

avoid possible tracheal aspiration. Elective fiberoptic oesophagogastro-duodenoscopy was performed later.

Apart from a neurological cause or hysteria, total dysphagia of sudden onset is invariably caused by a bolus, itself usually secondary to underlying disease. The oesophageal lumen will usually permit the passage of the Foley catheter. If it does not, rigid oesophagoscopy should be performed under general anaesthesia. The bolus may then be removed under direct vision, and the stenosis inspected and biopsied. Further management depends on the nature of the stricture.⁵ Most of these patients are old and frail and need quick relief of their distressing and dangerous total dysphagia. An advantage of catheter extraction is that this can be accomplished easily, safely, and without general anaesthesia.

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Effect of cimetidine on absorption of oral benzylpenicillin

The widespread use of cimetidine for treating duodenal and gastric ulcers¹ and peptic oesophagitis raises the question of possible undiscovered side effects. We investigated whether the inhibition of gastric acid secretion would affect the absorption of acid-labile drugs. Benzylpenicillin was chosen since its absorption is increased by achlorhydria.²

Subjects, methods, and results

Five healthy volunteers, three men and two women aged 21–30 years and weighing 59–87 kg, were studied. After an overnight fast 600 mg sodium benzylpenicillin in 100 ml water was administered. Venous blood samples were taken every 15 minutes and urine collected hourly for six hours. Free fluids were allowed after four hours. The experiment was repeated after 24 hours of cimetidine treatment using 1000 mg/day plus 400 mg one hour before the penicillin. Serum and urine samples were assayed in duplicate using the conventional agar plate diffusion method.

Blood penicillin concentrations followed a similar curve in all five subjects, with peak levels of 1.08–2.45 mg/l (mean ($\pm$ SD) 1.93 $\pm$ 0.54 mg/l) between 30 and 90 minutes. By four hours the serum concentrations had fallen to a mean of 0.16 $\pm$ 0.21 mg/l. Over six hours 24.1 mg to 78.9 mg of penicillin was excreted in the urine, over 80% in the first four hours.

After cimetidine the peak serum penicillin concentration in one subject increased from 1.8 mg/l to 4.1 mg/l and 6.0 mg/l on repeating the experiment. The concentration at four hours was three times the control value. Urinary penicillin excretion (see figure) showed an eightfold rise from 49.4 mg to 386.3 mg after cimetidine, and 417.3 mg on repetition. In four subjects no significant increase in absorption occurred, although the mean serum concentration at four hours was slightly increased (0.55 $\pm$ 0.32 mg/l). The peak serum penicillin concentrations on cimetidine were 1.55–2.60 mg/l, and urinary excretion was 27.3–73.5 mg.

Comment

The absorption of penicillin has been shown to be largely unchanged in most subjects given oral cimetidine. Gastric juice at pH 2 rapidly destroys benzylpenicillin.³ In most subjects given cimetidine the pH of gastric juice remains below 3 while fasting, since the drug diminishes the volume of gastric juice⁴ as well as the basal and maximal acid secretions.⁴ A few subjects have transient achlorhydria after oral cimetidine, and in these increased absorption of penicillin

Urinary excretion of benzylpenicillin before and after cimetidine. Shaded area represents mean value $\pm$ 2 SD before cimetidine.

would be predicted, similar to that in the newborn and in pernicious anaemia.² This would seem the likely explanation for the large increase in penicillin absorption in one subject after cimetidine. A sparing effect of cimetidine on orally administered pancreatic enzymes has recently been shown in chronic pancreatitis,⁵ but in this study the gastric pH was also increased by the buffering effect of a meal.

Increased absorption of acid-labile substances is a predictable side effect in some patients taking cimetidine, and this should be kept in mind when other drugs are given concurrently.

We wish to thank the doctors and medical students who volunteered as subjects for this study.

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Haemodialysis during cyclophosphamide treatment

The administration of cytotoxic drugs to patients with lymphomas with inadequate renal function is an uncommon problem, but may become more frequent with an increasing incidence of renal complications owing to improved survival. In patients on haemodialysis, drugs such as cyclophosphamide that are not rapidly cleared from the plasma may be removed in the dialysate, resulting in a reduced therapeutic effect. We report details of a patient receiving intermittent courses of intravenous cyclophosphamide and vincristine with oral prednisone while being treated with haemodialysis, in whom cyclophosphamide concentrations were measured in the plasma and dialysate.