Part II Effect of varying the size and frequency of meals[1]

N. BABOURIS, JANET FLETCHER, AND J. E. LENNARD-JONES

From the Department of Gastroenterology and Medical Research Council Gastroenterology Research Unit, Central Middlesex Hospital, London

EDITORIAL SYNOPSIS Careful comparisons of the gastric *p*H in duodenal ulcer patients show that with two-hourly feeds maximum acidity never rises as high as with four-hourly feeds, and there is less fluctuation in acid level throughout the day. The authors conclude that both size and frequency of meals may be of clinical importance in relation to the pain of duodenal ulcer.

'When hunger calls, obey, nor often wait till hunger sharpen to corrosive pain.' (*Kitchiner*, 1828)

Pain relieved by food is characteristic of duodenal ulcer and many patients learn to eat little and often. During the day, the acidity of the gastric contents in these patients is at its greatest some hours after a meal and it has been suggested that pain at this time coincides with the rapid passage of acid chyme into the duodenum (Dekkers, 1959). This experiment compares the effect on the acidity of taking a constant amount of food either in small two-hourly portions or in larger four-hourly meals.

METHOD

The criteria for selection of patients for study, and the methods of gastric sampling, measuring acidity, and of analysing the results have been described in Part I of this study on pages 113 to 117.

In this experiment, 12 patients chose a day's menu which they regarded as appetising and attractive, and without any medical restrictions upon the type or quantity of food taken. Having chosen a menu, each patient was asked to eat the foods which he had chosen in the same quantities on two days, the distribution of the food being varied in this way:

	Four-Hourly Feeds	*Two-Hourly Feeds*
8 a.m.	Breakfast	Breakfast less some milk and bread
10 a.m.	*No* snack	Hot milk drink and sandwiches (= bread and milk witheld at breakfast)
12 midday	Lunch	Lunch without pudding
2 p.m.	—	Pudding
4 p.m.	Tea	Tea
6 p.m.	*No* snack	Supper without pudding
8 p.m.	Supper	Pudding

(Order of test days alternated from patient to patient)

The approximate mean calorie content and composition of the meals is shown in Table I. Breakfast was the largest meal, the snacks at 10 a.m., 2 p.m. and 8 p.m. were smaller than the meals taken at 8 a.m., 12 midday, and 6 p.m. on the same day. Samples were withdrawn every half hour from 8 a.m. to 10 p.m. inclusive.

TABLE I

APPROXIMATE MEAN CALORIE CONTENT AND COMPOSITION OF MEALS TAKEN BY THE PATIENTS

Time	*Calories*		*Protein (g.)*		*Fat (g.)*		*Carbohydrate (g.)*	
	A	*B*	*A*	*B*	*A*	*B*	*A*	*B*
8 a.m.	800	540	27	18	33	23	100	68
10 a.m.	—	260	—	10	—	11	—	32
12 m.d.	620	370	26	20	31	20	59	27
2 p.m.	—	250	—	7	—	11	—	31
4 p.m.	520	520	9	9	21	21	75	75
6 p.m.	—	330	—	18	—	16	—	26
8 p.m.	570	240	25	7	25	8	60	34

A = four-hourly meals B = 2-hourly meals

RESULTS

The *p*H values of all the samples obtained have been analysed as follows[2]:

DISTRIBUTION OF SAMPLES IN DIFFERENT *p*H RANGES The distribution of samples from all the patients in different *p*H ranges is shown in Table II. There were more samples both of high and of low acidity with the four-hourly feeds than with the two-hourly feeds. This trend is consistent with the finding to be described that the acidity immediately after the larger four-hourly meals was lower, and the peak acidities during the four-hourly schedule were higher than during the two-hourly feeding programme.

MEAN ACIDITY The overall mean acidity for all the samples, determined from the arithmetic equivalents

This work was included in a thesis submitted by one of the authors J.E.L.-J.) to the University of Cambridge for the degree of M.D.

[2]Detailed results for each patient may be obtained on request from Dr. Lennard-Jones and have been published elsewhere (Lennard-Jones, 1964).

TABLE II

DISTRIBUTION OF SAMPLES IN DIFFERENT *p*H RANGES

*p*H	⩽1·5	1·6-2·0	2·1-2·5	2·6-3·0	3·1-3·5	>3·5	Total
2-hourly	118	99	31	25	25	43	341
4-hourly	140	81	23	16	27	52	339

and converted back to the logarithmic scale, was similar on the two days, corresponding to *p*H 1·66 with two-hourly feeds and *p*H 1·63 with four-hourly feeds. The mean *p*H at half-hourly intervals through the day is shown in Figure 1. Meals of different sizes on the two days were taken at 8 a.m., 12 midday, and 8 p.m.; the acidity tended to fall to a lower level and rise more slowly after the larger meals at these times. Immediately after the small meals at 10 a.m., 2 p.m., and 6 p.m., at which times the level of acidity was rising, the acidity fell and then began to rise again. Meals of equal size were taken at 4 p.m. The greatest levels of acidity were found at 12 midday, 3.30 p.m., and 6 p.m.; these peak acidities were lower with two-hourly than with four-hourly feeds.

DIFFERENCES BETWEEN CORRESPONDING *p*H VALUES

The *p*H value of each sample obtained during the four-hourly feeding schedule has been subtracted from the *p*H value of the sample obtained from the same patient at the corresponding time during the two-hourly feeding schedule. The mean difference for each patient during different periods of the day was calculated and the means of these results for all the patients are shown in Table III. A positive difference indicates that the acidity of the two-hourly samples was less than the acidity of the four-hourly samples, and conversely a negative sign indicates that the acidity of the two-hourly samples was greatest during that period.

The acidity was least after the larger of the two meals taken at 8 a.m., 12 midday, and 8 p.m. It was reduced by the small meals at 10 a.m. and 6 p.m., but not significantly reduced by the snack at 2 p.m. Between 4.30 and 6 p.m. the acidity was lower on the day with two-hourly feeds even though the two meals taken at 4 p.m. were the same.

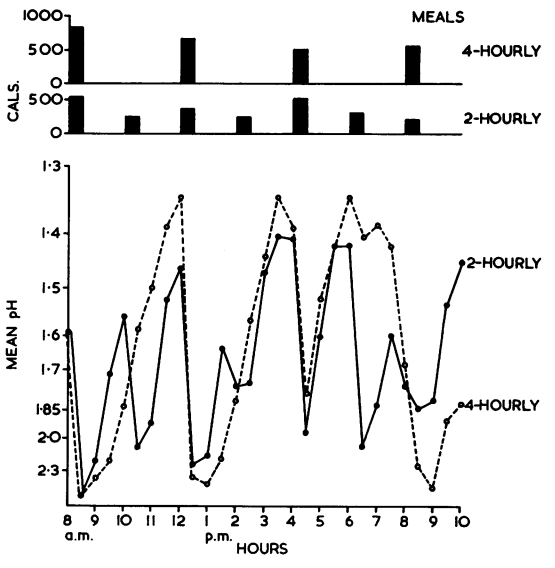

FIG. 1. *Mean acidity at half-hourly intervals through the day. The height of the columns indicates the approximate mean calorie content of the meals.*

The differences were greatest immediately after meals and diminished thereafter. Thus, differences at 9, 9.30, and 10 a.m.; 10.30 and 11 a.m.; 12.30, 1, and 1.30 p.m.; 6.30 and 7 p.m.; and 8.30 and 10 p.m. reach statistical significance ($P < 0.05$). The overall mean difference between samples on the two test days was only =0·01 *p*H unit because positive and negative differences were approximately equal and cancel out.

DISCUSSION

The mean acidity of the gastric contents with the two feeding schedules was the same. The difference between the schedules lay in the deviations from this mean. When meals were taken every four hours, there were large deviations on each side of the mean, low acidity after each meal rising to high levels of

TABLE III

MEAN DIFFERENCES BETWEEN *p*H OF SAMPLES TAKEN DURING TWO-HOURLY SCHEDULE AND *p*H OF SAMPLES TAKEN FROM SAME PATIENT AT CORRESPONDING TIMES DURING FOUR-HOURLY SCHEDULE

	Time Period						
	8.30-10 a.m.	*10.30-12 m.d.*	*12.30-2 p.m.*	*2.30-4 p.m.*	*4.30-6 p.m.*	*6.30-8 p.m.*	*8.30-10 p.m.*
Mean difference (S.E.)	−0·56 (±0·22)	+0·69 (±0·14)	−0·64 (±0·18)	+0·06 (±0·10)	+0·45 (±0·17)	+0·70 (±0·20)	−0·69 (±0·25)
Significance of difference	0·05	<0·001	<0·01	—	<0·02	<0·01	<0·02
Individual times at which mean difference significant	9.00 (<·05) 9.30 (<·01) 10.00 (<·01)	10.30 (<·01) 11.00 (<·01)	12.30 (·01) 1.00 (<·02) 1.30 (<·01)			6.30 (<·001) 7.00 (<·01)	8.30 (<·05) 10.00 (<·05)

acidity before the next meal. With two-hourly feeds, deviations were smaller; the acidities were not so low after meals, and did not rise so high before the next meal, as with four-hourly feeds. The lowest acidities, which were found soon after the larger four-hourly meals, are unlikely to be of clinical importance. The fact that the maximum acidities found during the day were lower with two-hourly than with four-hourly feeds may be clinically important and may be the reason why some patients adopt a regime of small frequent meals.

The acidity of the gastric contents after a meal depends mainly on the diluting and buffering power of the food, the rate of acid secretion, and the rate of gastric emptying. A large meal buffers more acid than a small one. In animals, the stimulus to acid secretion increases with the size of the meal (Ivy, Lin, and Langberg, 1957; Alphin and Lin, 1962) and, in man, acid secretion in response to an inert liquid meal depends on the volume of the meal (Hunt and Macdonald, 1952). The rate of emptying in man of simple test meals increases with their volume, a fixed proportion of the total volume being emptied each minute (Hunt and Spurrell, 1951). Varying the size of a meal may thus affect all the important factors controlling the acidity of the gastric contents.

Several investigators have investigated the effects on intragastric acidity of dietary regimes with different frequency of feeds, but Schüle (1895) alone has studied a feed of constant size and composition given whole on one occasion and divided into portions on another. He measured the acidity of gastric samples after 300 ml. of boiled milk given as a single drink or as 60 ml. every 15 minutes. In two of his three subjects the acidity was lower during the period of repeated small drinks than after the single large drink.

It can be argued that patients with duodenal ulcers should take meals infrequently because Dekkers (1959) has shown that pain does not occur when the stomach is empty but when acid chyme is passing rapidly into the duodenum. The present experiment shows that by giving frequent feeds the acidity of the chyme does not reach so high a value as when less frequent meals are taken. It seems possible that altering the size of feeds may affect not only the concentration, but also the rate at which acid enters the duodenum, the present observations do not yield information on this point. The effects of altering the size and frequency of feeds on the rate of gastric emptying and on the acidity within the duodenal bulb require further study. The relative merits of frequent and infrequent feeding can only be assessed by controlled therapeutic trial.

SUMMARY

The acidity of the gastric contents in 12 patients with duodenal ulcer has been measured, using a sampling technique, while they took on two days an identical freely-chosen diet, divided on one day into four-hourly portions and on another day into two-hourly portions. The mean acidity of the gastric contents on the two days was the same but variations on each side of the mean were less when the smaller meals were given two-hourly. The maximum acidity found during the two days was thus lower with the two-hourly than with the four-hourly feeds and this reduction in peak acidity with frequent feeding may have clinical relevance.

We thank Dr. F. Avery Jones, Dr. T. D. Kellock, and Dr. E. N. Rowlands for their help and encouragement. We are very grateful to Miss P. B. Wilcox for her help with the *p*H measurements.

REFERENCES

Alphin, R. S., and Lin, T. M. (1962). Response of chronic denervated gastric pouches of rats to food and histamine. *Amer. J. Physiol.*, **203**, 641-643.

Dekkers, H. J. N. (1959). Further experiments on pain in duodenal ulcer and its relation to gastric emptying. *Proc. 1st. Wld. Congr. Gastroent.*, **2**, 826-832.

Hunt, J. N., and Macdonald, I. (1952). The relation between the volume of a test-meal and the gastric secretory response. *J. Physiol. (Lond.)*, **117**, 289-302.

——, and Spurrell, W. R. (1951). The pattern of emptying of the human stomach. *Ibid.*, **113**, 157-168.

Ivy, A. C., Lin, T. M., and Langberg, G. (1957). Gastric secretory response to various amounts of food (dose-response curve). *Amer. J. Physiol.*, **188**, 71-75.

Kitchiner, W. (1828). *The Art of Invigorating and Prolonging Life . . . or, the Invalid's Oracle: Containing Peptic Precepts.* Whittaker, London.

Schüle, A. (1895). Untersuchungen über die Secretion und Motilität des normalen Magens. *Z. klin. Med.*, **28**, 461-504.