Factors controlling colonic motility: Colonic pressures and transit after meals in patients with total gastrectomy, pernicious anaemia or duodenal ulcer

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SUMMARY The motor responses of the proximal colon, sigmoid, and rectum to the ingestion of a standard meal have been compared in patients with total gastrectomy, pernicious anaemia, or duodenal ulcer. Colonic pressure activity increased during and after food in all the patients, but this was only once associated with propulsive activity. The results suggest that the postprandial pressure activity in the sigmoid colon is greater after total gastrectomy than in the other two groups. It is concluded that entry of food into the upper small intestine is the most important factor in initiating the colonic pressure response to food, since this response does not require the presence of the stomach, acid, antral gastrin, or of vagal innervation.

Abnormalities of colonic motility are important in the pathogenesis of a number of disorders, such as diverticular disease (Morson, 1963; Arfwidsson, 1964; Painter, Truelove, Ardran, and Tuckey, 1965), the irritable colon syndrome (Chaudhary and Truelove, 1962; Connell, Jones, and Rowlands, 1965), idiopathic megacolon, intractable constipation or diarrhoea, and the like; they are also important in the production of abdominal pain (Holdstock, Misiewicz, and Waller, 1969). Pressure activity in the human colon increases after meals, and eating is among the main physiological stimuli that affect colonic motility, but the factors which control this effect are largely unknown. It therefore was of interest to investigate the pathway through which the colonic response to meals is mediated. We have measured intraluminal pressures and transit in the colon of patients with pernicious anaemia, duodenal ulcer, or with total gastrectomy, and have compared their responses to a standard meal. The results suggest that entry of food into the small intestine is of major importance in initiating the postprandial increase of colonic pressure activity.

Patients and Methods

The number of patients studied in the three diagnostic groups and their clinical features are listed in Table I.

In the seven patients with total gastrectomy, the operation had been performed from six months to 13 years previously; they all enjoyed good general health and a good appetite at the time of the study. Six patients had a Roux-en-Y anastomosis and the seventh a jejunal reservoir. The pernicious anaemia group (nine patients)
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<table>
<thead>
<tr>
<th>Diagnostic Group</th>
<th>No. of Patients</th>
<th>Males</th>
<th>Females</th>
<th>Age (Mean ± SEM)</th>
<th>Range</th>
<th>Records Available for Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total gastrectomy</td>
<td>7</td>
<td>5</td>
<td>2</td>
<td>58 (±6-4)</td>
<td>22-84</td>
<td>4</td>
</tr>
<tr>
<td>Pernicious anaemia</td>
<td>9</td>
<td>1</td>
<td>8</td>
<td>65 (±4-5)</td>
<td>50-83</td>
<td>8</td>
</tr>
<tr>
<td>Duodenal ulcer</td>
<td>12</td>
<td>10</td>
<td>2</td>
<td>49 (±3-8)</td>
<td>25-66</td>
<td>8</td>
</tr>
</tbody>
</table>

Table I Clinical details of patients and records available for analysis

Fig. 1 Design of study.

consisted of either out-patients on maintenance B12 treatment, or of recently diagnosed and treated inpatients who had a rising haemoglobin level of > 9.0 g%. The diagnosis had been established in all by low serum B12 levels and achlorhydria to maximal stimulation with histalog; the majority had gastric autoantibodies, but none had evidence of neuropathy.

The 12 patients with duodenal ulcer were all inpatients admitted for surgery or convalescent from an episode of haematemesis and melena; none had clinical or radiological evidence of pyloric stenosis or a high resting gastric juice volume. Maximal histalog tests were performed on them by standard procedure with a dose of 1.5 mg/kg (Baron, 1963; Wormsley and Grossman, 1965).

Measurement and Analysis of Intraluminal Pressures and of Transit Times

Intraluminal pressures (IP) were measured simultaneously at three sites, one in the proximal and two in the distal colon. The proximal colon was defined for the purpose of this study as consisting of the caecum, ascending and transverse portions; measurements in the distal bowel were made in the sigmoid and the rectum.

Pressures in the proximal colon were telemetered with radiocapsules (Rowlands and Wolff, 1960) which were localized by fluoroscopy and the characteristics of the pressure record (Misiewicz, Waller, Fox, Goldsmith, and Hunt, 1968a). Pressures in the sigmoid and rectum were measured with 7 x 10 mm air-filled balloons (Atkinson, Edwards, Honour, and Rowlands, 1957) connected by fine polyethylene tubing to transducers recording on a multi-channel penwriter (Sanborn). At sigmoidoscopy, the proximal balloon was placed at 20 to 25 cm and the distal at 10 to 15 cm from the anal margin. The pressure records were processed in an analogue to digital converter and analysed by computer (Misiewicz, Waller, Healy, and Piper, 1968b). Separate analyses were made for each 10-minute observation period and for the time interval during which the meal was eaten. Variables of motility derived from computer analysis included the motility index (MI) and percentage duration of activity, as defined previously (Misiewicz et al, 1968b). The motility index results were expressed as logarithms (to the base 10), because the distribution of these data was lognormal. Tests for significant differences between the 10-minute observation periods, or the meal period, were carried out with two-way analysis of variance.

Comparisons were always made at the same recording site, both between the various observation periods within each diagnostic category, and of the same observation period between the three groups of patients. Comparisons of the responses in the proximal with the distal colon were not considered meaningful, because of the different methods used to measure pressures at these sites (Misiewicz, 1968c; Misiewicz, Waller, and Holdstock, 1969b).

Colonic transit was measured with radiopaque pellets (Halls, 1965; Hinton, 1967; Hinton, Lennard-Jones, and Young, 1969) administered simultaneously with the radiotelemetering capsule. To detect propulsive activity, plain radiographs of the abdomen were taken at the start and finish of the study, the dose of radiation being minimized by the use of fast films exposed through intensifying screens (Kodak High Speed) and at low mA (Holdstock, Misiewicz, Smith, and Rowlands 1970). The skin dose did not exceed 60 mR/film. The results were expressed as change, or otherwise, of the position of the pellets and of the radiotelemetering capsule in relation to bony landmarks. Under the conditions of the study all the pellets were in the colon by the time the first radiograph was taken. In addition, mouth-to-anus transit times were measured by collecting the stools in cartons and counting the number of pellets in each stool specimen by fluoroscopy; the results were expressed as described by Hinton (1967).

Design of Study

The patients were given the radiotelemetering capsule and pellets on the evening before the test and fasted overnight. Half an hour after withdrawing the sigmoidoscope, basal activity was recorded for three consecutive 10-minute observation periods. An appetizing standard meal, comprising egg, toast and butter, tinned fruit, and tea, was then served. Recording of pressures continued during the meal, and for a further three 10-minute
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Table II  Variations in log motility index (means ± SEM)

<table>
<thead>
<tr>
<th>Site</th>
<th>Group</th>
<th>Observation Period</th>
<th>± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre-meal</td>
<td>Meal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Proximal colon
- Total gastrectomy
- Pernicious anaemia
- Duodenal ulcer

Sigmoid
- Total gastrectomy
- Pernicious anaemia
- Duodenal ulcer

Rectum
- Total gastrectomy
- Pernicious anaemia
- Duodenal ulcer

Results

INTRALUMINAL PRESSURES
The number of studies available for analysis is shown in Table I. Results of analysis of the pressure records are presented in Tables II and III, and the calculated differences between various observation periods are listed in Tables IV and V for MI and percentage duration of activity, respectively.

BASAL ACTIVITY
There were no significant differences within each of the three diagnostic groups between any of the three 10-minute pre-meal periods at any of the sites studied, indicating that the observations were adequately controlled. Nor were there any significant differences in mean activity during the 30-minute period before the meal between the three diagnostic groups at the three sites studied.

ACTIVITY DURING THE MEAL
The time taken to eat the standard meal was similar in the three groups, averaging 13·0 min...
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in the total gastrectomy, 12·4 min in the pernicious anaemia, and 10·0 min in the duodenal ulcer patients.

Stimulation of activity was prompt and within two to three minutes of the first mouthful of food; it continued throughout the meal in all the groups. The increase in colonic activity during the meal was significantly higher than the basal activity with respect to one or both variables of motility in all the groups, with the exception of the sigmoid in the pernicious anaemia patients (Tables IV and V). Comparisons between the three groups of patients showed no difference in activity at any site during the meal.

ACTIVITY AFTER THE MEAL

The increase in motor activity which began during the meal continued throughout the postprandial half-hour. One or both variables of motility were significantly higher than basal values at all three sites in each of the three groups of patients (Tables IV and V).

Comparisons of activity during the postprandial half-hour between the three diagnostic groups showed a similar response of the proximal colon and rectum, but some aspects of sigmoid activity in the total gastrectomy group differed from the sigmoid activity of patients with pernicious anaemia or duodenal ulcer. The motor response

### Table IV Comparison of observation periods: log MI

<table>
<thead>
<tr>
<th>Site</th>
<th>Group</th>
<th>Periods Compared (Differences of Means ± SE of Differences)</th>
<th>Meal v. Mean of (Pre-meal 1, 2, 3)</th>
<th>Meal v. Mean of (Post-meal 1, 2, 3)</th>
<th>Mean of (Post-meal 1, 2, 3) v. Mean of (Pre-meal 1, 2, 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal colon</td>
<td>Total gastrectomy</td>
<td>11·3³ ± 5·2</td>
<td>-5·2 ± 5·2</td>
<td>16·5³ ± 3·7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pernicious anaemia</td>
<td>15·2² ± 5·1</td>
<td>1·4 ± 5·1</td>
<td>13·8³ ± 3·6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duodenal ulcer</td>
<td>28·8³ ± 5·8</td>
<td>16·6³ ± 5·8</td>
<td>12·2³ ± 4·1</td>
<td></td>
</tr>
<tr>
<td>Sigmoid</td>
<td>Total gastrectomy</td>
<td>24·0³ ± 5·5</td>
<td>-17·7³ ± 5·5</td>
<td>41·7³ ± 3·9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pernicious anaemia</td>
<td>9·8 ± 5·1</td>
<td>-4·1 ± 5·1</td>
<td>13·9³ ± 3·6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duodenal ulcer</td>
<td>29·4³ ± 4·5</td>
<td>9·6³ ± 4·5</td>
<td>19·8³ ± 3·2</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>Total gastrectomy</td>
<td>14·4³ ± 4·4</td>
<td>0·2 ± 4·4</td>
<td>16·2³ ± 3·1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pernicious anaemia</td>
<td>8·7³ ± 3·6</td>
<td>3·5 ± 3·6</td>
<td>5·2³ ± 2·5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duodenal ulcer</td>
<td>18·2³ ± 5·0</td>
<td>7·7 ± 5·0</td>
<td>10·5³ ± 3·6</td>
<td></td>
</tr>
</tbody>
</table>

Table V Comparison of observation periods: percentage activity

¹ p < 0·05  ² p < 0·01  ³ p < 0·001
Fig. 2 Total gastrectomy patient. Simultaneous pressure records from the sigmoid, rectum, and right colon (top) before, and after, a meal. Pressure scale in cm H₂O. Δ P is the change in intraluminal pressure. Marked increase of activity in sigmoid after a meal.
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Fig. 3  Duodenal ulcer patient. Simultaneous pressure records from the sigmoid, rectum and right colon (top) before, and after, a meal. Pressure scale in cm H2O. Note change of baseline (arrowed) in telemetered record from right colon.
of the sigmoid in total gastrectomy patients is clear on inspection of the pressure records (Figs 2a and b), but in the other diagnostic groups the response although clearly present, was less striking (Figs 3a and b). Data for the sigmoid colon for MI and percentage duration of activity which are summarized in Figs 4 and 5 and in Tables II to V, suggest that the sigmoid response may have been greater and longer sustained in the total gastrectomy group than in the other patients. At the time of peak activity after the meal, i.e., during the second post-meal period, (Figs 4 and 5), the percentage duration of activity was greater in the total gastrectomy than in the pernicious anaemia patients (\(p<0.05\)), though just failing to reach the conventional levels of significance on comparison with the duodenal ulcer group.

Colonic motor response to meals may be defined as the difference between levels of motor activity in half-hours before and after the meal. Comparisons between the three diagnostic categories carried out in this way show a significantly greater sigmoid response in the total gastrectomy patients than in others, whilst there are no significant differences between the responses of patients with duodenal ulcer or pernicious anaemia (Table VI). The validity of this comparison depends on there being no significant difference in the levels of basal motility between the three groups, and this was so in the present study. However, basal percentage duration of activity tended to be low in the total gastrectomy group (Fig 5), although no such difference was apparent with respect to MI (Figure 4).

There were no differences between the responses to the meal of the proximal colon or the rectum between any of the three groups of patients.

**EFFECT OF ACID SECRETION ON POSTPRANDIAL MOTILITY**

Acid secretion of the duodenal ulcer patients was in the usual range for this condition (mean basal hour 6.5 m-equiv; SE ± 1.8; mean peak hour 45.1 m-equiv; SE ± 4.8). There was no correlation between maximal acid output and the increase in variables of sigmoid motility, regardless of whether correlations were made with the period of highest motor activity, or with the overall differences between pre- and postprandial activity in individual patients.

**PROPULSIVE ACTIVITY AND TRANSIT TIMES**

Propulsion of the radiotelemetering capsule was observed on only one occasion in this study, in a duodenal ulcer patient with a normal bowel habit, whose pressure record is shown in Figure 3. At the start of the study the radiocapsule was in the right colon (Fig 6a), whilst one and three-quarter hours later it had moved to the region of the splenic flexure (Figure 6b). Although the
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radiopaque pellets were partially obscured by residual contrast medium from a recent barium meal, inspection of the films suggested that they and the barium had shared in the movement. Sudden shift of an otherwise stable baseline (arrowed in Fig 3b) suggests the onset of propulsive activity, but as signal strength of the radiotelemetering capsule (Misiewicz, 1968c) was not being measured, it is not possible to decide with certainty when the movement occurred.

The results of measurements of transit with pellets and radiotelemetering capsules are summarized in Table VII and show that transit times of both markers were similar. Transit time was shortest in the patients with total gastrectomy and slowest in those with pernicious anaemia, although these differences were not significant.

Discussion

The gastro-colic reflex as described by Hurst (1919) clearly means extensive propulsive activity (mass movement) of the colon, whilst Barclay (1935) was able to differentiate between propulsive and non-propulsive colonic motor activity. Clinically, gastro-colic reflex implies defaecation after a meal, usually breakfast. The ‘working’ of a colostomy after meals is another example of the reflex. Increased colonic pressure activity during and after meals has been shown to take place without the stomach. Moreover, if patients are immobile, as in our studies, increased pressure activity was not associated (except in one patient) with propulsion. For these reasons the term ‘gastro-colic’ reflex seemed inappropriate to describe the changes observed in this study, and the term colonic pressure response to food is used instead. The occurrence of colonic propulsion or of defaecation in the postprandial period may depend on other factors, such as faecal loading of reflexogenic areas, or somatic activity (Holdstock et al, 1970).

Results of this study show that the colonic pressure response to food is similar in patients with total gastrectomy, pernicious anaemia, or duodenal ulcer in the proximal colon and rectum, whilst the response of the sigmoid is, in some respects, greater in the total gastrectomy group than in the other two diagnostic categories. These findings can be interpreted in the light of known clinicopathological changes after total gastrectomy, in pernicious anaemia, or in duodenal ulcer. In the absence of a gastric reservoir food enters the small intestine directly, without dilution by, or mixing with, gastric secretions. Mechanical distension of the upper small intestine is therefore likely. Secondly, patients with total gastrectomy have had a truncal vagotomy and often have steatorrhoea, both of which may affect the intestinal transit rate. Thirdly, they are unable
to secrete antral gastrin in response to food. Patients with pernicious anaemia secrete no gastric acid or intrinsic factor but there is no reason to implicate the latter in the control of motility. On the other hand gastrin is localized in specific cells of the antral mucosa (McGuigan, 1968), which does not share in the mucosal atrophy of the gastric body (Morson, 1966). Secretion of antral gastrin in pernicious anaemia may therefore be normal or high, especially as there is no acidification of the antrum to inhibit the release of the antral hormone.

Our patients with duodenal ulcer had a normal or raised acid output, and were therefore likely to acidify the duodenum at least intermittently (Rhodes and Prestwick, 1966; Watson, Watt, Paton, Glen, and Lewis, 1966). Gastric emptying is faster in patients with duodenal ulcer than in normals (Griffiths, Owen, Campbell, and Shields, 1968), but it is not known how it compares with the rate of gastric emptying in patients with pernicious anaemia. At the time of writing there was no information on the postprandial levels of circulating gastrin in patients with duodenal ulcer but it is likely to be normal or high.

Since the response of the gastrectomized patients was as marked as, if not greater than, that of the other groups, it is unlikely that gastrin is the major factor mediating the colonic pressure response to food. This conclusion agrees well with previous studies in vitro and in vivo of the effect of gastrin and pentagastrin on the human gastrointestinal tract (Bennett, Misiewicz, and Waller, 1967; Misiewicz, Holdstock, and Waller, 1967; Misiewicz et al, 1969b). Although it could be argued that gastrin inhibits colonic muscle, such an effect has never been demonstrated. Truncal vagotomy may occasionally be followed by diarrhoea, but our patients with total gastrectomy had a normal bowel habit and the sigmoid is not innervated by the vagus.

Although acidification of the duodenum is known to trigger the release of intestinal hormones and to affect various aspects of gastro-intestinal function, eg, gastric secretion or motor activity (Johnston and Duthie, 1966; Misiewicz et al, 1967, 1969b), it is unlikely that acidification of the duodenum stimulated colonic activity, since the colonic motor response to food was of the same order in patients with pernicious anaemia and in those with duodenal ulcer. Moreover, in the latter group there was no correlation between output of acid and the colonic response to food. This conclusion is further supported by previous observations (Misiewicz et al, 1967 and 1969b).

The rapid entry of food into the small intestine may therefore be of major importance in initiating postprandial colonic pressure activity whilst the less marked sigmoid response of patients with duodenal ulcer or pernicious anaemia may be due to the slower arrival of the ingested meal in the jejunum.

A stimulus to the upper small intestine could affect the colon in several ways, eg, by a spinal reflex, through the intramural nervous plexus, by the release of polypeptide hormones, such as secretin or cholecystokinin-pancreozymin, or other biogenic substances, eg 5-hydroxytryptamine (5HT), bradykinin, or prostaglandins. The chemical or mechanical effects of ileal contents entering the caecum may likewise be important. Several mechanisms may be active simultaneously. Thus the rapid increase of colonic motor activity within a few minutes of the first mouthful of food suggests a nervous pathway, whereas the maintenance of the response after the meal may be humoral. It may be relevant that activity during the meal was similar in the three study groups, whilst only in the total gastrectomy group was there a further increase in activity in the post-prandial period.

Persistence of colonic response to food in patients with lesions of the lower spinal cord (Connell, Frankel, and Gutman, 1963) is against the importance of a spinal reflex pathway. The increased activity of the right colon after food in our studies suggests that mechanical or chemical stimuli of ileal contents may be responsible. On the other hand, distension or changes of osmolarity and pH in the colonic lumen have been shown to be relatively ineffective stimulants of distal bowel motility (Hardcastle and Mann, in press), and pressure activity after meals occurs in the defunctioned limb of double-barrelled colostomies, indicating that the response is not wholly dependent on stimuli originating in the bowel lumen (Hardcastle, Misiewicz, and Kiley, in preparation).

In the dog, the ideal response to feeding is conducted by the intramural plexus (Douglas and Mann, 1940), but these authors were unable to show a similar effect in the colon. However, clinical and experimental evidence in man indicates that intramural nerves are essential to the normal functioning of the colon, and they can mediate peristaltic activity in response to local...
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That a humoral mechanism is implicated in the colonic response is suggested by the observations of Frigo, Crema, and Benzi (quoted by Torsoli, Ramorino, and Crucoli, 1968), who reported increased colonic activity after feeding in cross-circulation experiments on cats. Of the possible hormonal mediators other than gastrin, secretin and cholecystokinin-pancreozymin have obviously to be considered, and have been isolated in pure form (Jorpes and Mutt, 1961; Jorpes, Mutt, and Toscko, 1964). Most studies in man have so far been made with relatively impure preparations, which have been noticed in passing to stimulate the small intestine in man (Burton, Evans, Harper, Howat, Oleseney, Scott, and Varley, 1960), but their effect on the colon is not known. In vitro, cholecystokinin-pancreozymin seems to have little effect on isolated strips of human colonic muscle (Misiewicz and Waller, unpublished observations). The possible role of secretin as the agent causing diarrhoea in pathological states has been studied (Zollinger, Tompkins, Amerson, Endhal, Kraft, and Moore, 1968), but little is known of its effect on colonic motility, although changes in the colonic mucosa have been reported (Johansen, Hadorn, and Anderson, 1968).

The presence of a Roux-en-Y or jejunal reservoir type of reconstruction in the total gastrectomy patients suggests that entry of food into the upper jejunum, rather than the duodenum, can initiate the colonic response. As none of the patients had symptoms of dumping, the level of plasma kinin was unlikely to be high (Zeitlin and Smith, 1966), and bradykinin is known to relax isolated human colonic muscle strips, except in high concentrations (Fishlock, 1966). For similar reasons, it is not likely that 5HT was the mediator of the colonic response (Misiewicz, Waller, and Eisner, 1966). Of other possible mediators, various prostaglandins can cause diarrhoea when secreted by certain tumours (Williams, Karim, and Sandler, 1968; Sandler, Karim, and Williams, 1968) but increased rate of intestinal transit after oral prostaglandin E$_2$ was not associated with a marked increase in colonic pressure activity (Misiewicz, Waller, Kiley, and Horton, 1969a).

None of these agents therefore qualifies as the obvious transmitter for the colonic pressure response to eating. However, the present observations indicate that this response does not require the presence of the stomach, gastrin, acid, or of the vagus nerve but depends in some way on entry of food into the upper small intestine. This raises the question whether the rate of gastric emptying is relevant to the regulation of colonic function in health and disease. That this may be so is indicated by the recent findings of Connell and McKelvey (1970) that vagotomised diarrhoea is associated with rapid gastric emptying.

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References


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