Nutrient-induced spatial patterning of human duodenal motor function

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Andrews, Jane M., Selena M. Doran, Geoffrey S. Hebbard, Charles H. Malbert, Michael Horowitz, and John Dent. Nutrient-induced spatial patterning of human duodenal motor function. Am J Physiol Gastrointest Liver Physiol 280: G501–G509, 2001.—The spatiotemporal patterning of duodenal motor function has been evaluated comprehensively for the first time in humans, with a novel 21-lumen manometric assembly. In nine young, healthy volunteers (6 male, 3 female), duodenal motility was recorded during fasting and three 45-min intraduodenal (ID) nutrient infusion periods (Intralipid at 0.25, 0.5, and 1.5 kcal/min). Pressures were recorded along the length of the duodenum with an array of 18 sideholes at 1.5-cm intervals. Pressure patterns were compared for the final 20 min of each of the four periods. Compared with fasting, ID lipid was associated with regional variation in pressure wave (PW) sequences, with fewer proximally and more distally; this was not observed during fasting ($P < 0.001$). During fasting and all rates of lipid infusion, most (87–90%) PW sequences were short (1.5–4.5 cm), with a small number (2–4%) of 10.5 cm or longer. At all times, antegrade PW sequences occurred more frequently than retrograde sequences over all distances examined (3, 4.5, and >6 cm), and the proportion of antegrade sequences increased with greater PW sequence length ($P = 0.0001$). Increasing ID lipid rates appeared to produce dose-related suppression of PW sequences ($P < 0.001$). The frequency and spatial patterning of human duodenal motor function show substantial variability in response to different nutrient delivery rates. These complex patterns are likely to be involved in duodenal modulation of flow and gastric emptying rate.

THE HUMAN DUODENUM IS A SHORT but highly specialized region of the gastrointestinal tract. Its motor activity plays a role in retarding the rate of gastric emptying (31) and regulating the orderly delivery of chyme to the remainder of the small intestine (24). Rather than being merely a passive conduit, these mechanical functions appear to be highly modulated by luminal feedback control mechanisms (27, 31, 40). The duodenum also serves an important sensory function (23, 27, 29), containing both chemo- and mechanoreceptors (11), which when stimulated modulate the rate of gastric emptying directly by feedback onto gastric motor functions (1, 12, 17) and indirectly by varying duodenal resistance to gastric emptying (40). These effects are mediated by neural (1) and humoral means (14, 39). Absence or “malfunction” of the duodenum is associated with disordered gastric emptying and dyspeptic symptoms (21), due to the resulting mismatch between gastric emptying and subsequent digestion and absorption, attesting to the vital regulatory role of the duodenum.

Despite the recognized importance of the duodenum in humans, there is little detailed knowledge of its motor function in health. In part, this is a result of technical limitations. Most information on normal human upper gastrointestinal motility concentrates on the esophagus, stomach, and small intestine. The relatively few manometric studies (3, 4, 9, 31, 44, 45) that have focused on duodenal motility in humans are limited in their temporospatial resolution because of the relatively restricted number of recording sites placed in the duodenum. Scintigraphic studies are limited by the low spatiotemporal resolution of this technique (30), and fluoroscopic studies by the length of radiation exposure permissible in volunteers (31). In other regions of the gut, pressure patterns are known to vary over short distances (43); moreover, closely spaced pressure recordings have been found to be invaluable in defining some of the pressure-flow relationships in the esophagus (6). We have therefore sought to perform duodenal manometry with high spatiotemporal resolution.

Luminal manometry is the most direct method of assessing the forces applied to luminal contents by motor events, and closely spaced (1.5–2 cm) manometry gives better spatial resolution of these forces. High spatial resolution manometry has been facilitated by the recent development of fine-bore silicone rubber assemblies capable of recording intraluminal pressures concurrently from up to 21 channels. In this study, one such assembly, with an array of 18 sideholes...
at 1.5-cm intervals, was used to record duodenal pressures in healthy subjects along the whole length of the duodenum. High temporal resolution was obtained by employing a computer-based system recording data at 10 Hz.

The aims of this study were to 1) describe normal motor patterns in the human duodenum of healthy subjects and 2) examine the relationship between motor patterns and nutrient delivery.

METHODS

Subjects. Nine volunteers (6 male, 3 female), aged 21–39 years (mean 30 years), were recruited by advertisement. No volunteer had any history of upper gastrointestinal disease or surgery or was taking medication. The mean body mass index of the volunteers was 24.2 kg/m² (range 21.1–27.8 kg/m²); all volunteers were nonsmokers. Each subject gave written informed consent, and the protocol was approved by the Human Research Ethics Committee of the Royal Adelaide Hospital.

Protocol. After an overnight fast, each subject attended the motility laboratory between 8:30 and 9 AM. The manometric assembly (see Fig. 1) was introduced via an anesthetized nostril into the stomach. The position of the assembly was continuously monitored, taking advantage of the known transmucosal potential difference (TMPD) across the gastroduodenal junction (see below). The weighted tip of the assembly was allowed to pass into the duodenum by peristalsis. When the two most distal sideholes were located in the duodenum, a small (10-mL) balloon was inflated to speed the passage of the remainder of the assembly into the duodenum. Once the manometric assembly was correctly positioned, fasting motility was recorded until the occurrence of a duodenal phase III migrating motor complex of the interdigestive motor cycle (IDMC) (35). Within 5 min of duodenal phase III cessation, a graded infusion of a triglyceride (lipid) emulsion (Intralipid 10%, Kabi Pharmacia) into the proximal duodenum was commenced. It was diluted with normal saline to deliver 0.25, 0.5, and 1.5 kcal/min at 2 mL/min, for 45 min at each caloric rate. These caloric rates of intraduodenal (ID) lipid were selected because lipid at rates of 1 kcal/min and greater has been shown to stimulate pyloric motility and slow gastric emptying (17). Subjects were recumbent, and to minimize the occurrence of pressures arising external to the gut, they were requested to refrain from any avoidable movement during each of the four recording periods.

Positioning of manometric assembly. A small-gauge saline-filled cannula was inserted into the forearm of the subject to act as a reference electrode, enabling TMPD to be monitored as previously described (17). Initially, the two most distal sideholes of the assembly were perfused with saline and used to record TMPD. When these were both noted to be in the duodenum according to established TMPD criteria (17), the next two more proximal sideholes were used to record TMPD to monitor their passage across the gastroduodenal junction. Dual-point TMPD recording was made progressively from each more proximal pair of sideholes in this fashion, until only one sidehole remained in the antrum, with 19 in the duodenum. The TMPD gradient between the two most proximal sideholes was then monitored and maintained throughout the remainder of the study by adjustments in the position of the assembly as necessary.

Manometric recordings. The manometric assembly used (Fig. 1) had an external diameter of 4 mm. It was composed of 21 lumina of 0.5-mm internal diameter, 1 lumen being used for infusion of lipid into the proximal duodenum and 20 for manometry. An additional 0.9-mm lumen was used for inflation of the balloon at the tip of the assembly. The 4.5-cm interval between the first two manometric sideholes straddled the pylorus, the interval between the two most distal sideholes was 3 cm, and the remaining 17 intervals were 1.5 cm each. Thus the sidehole chain spanned the duodenum. The manometric channels were perfused at 0.15 ml/min with distilled degassed water or saline (while being used for TMPD recording), which gave pressure increase rates of at least 150 mmHg/s. Data were recorded online at 10 Hz with a Power Macintosh (7100/80, Apple, Cuppertino, CA) using software developed in-house (MAD, C. H. Malbert), written in LabView (National Instruments), and logged direct to disk for later analysis. In each subject, four separate data files were generated, one for the fasting period and one for each rate of ID lipid infusion.

Data analysis. The analysis focused on the timing and patterning of pressure wave (PW) sequences, and as we were primarily interested in studying intraluminal pressures likely to be important in determining intraluminal flows, we elected not to take account of stationary PWs. Pressures were only included in the analysis when the assembly was correctly positioned according to established TMPD criteria (17). Pressures with a pattern characteristic of those arising external to the gut, due to straining or movement, were excluded. To make standardized comparisons between the four analysis periods (fasting and the 3 different lipid infusion rates), 20-min segments of each condition were selected. The last 20-min segment of phase II was selected as the fasting data because it superficially resembles postprandial motility (irregular frequent contractions) and can be reproducibly identified (retrospectively) in each subject. To allow each caloric rate of ID lipid some time to exert its effect, data analysis at each rate was restricted to the last 20 min of each lipid infusion (min 25–45).

The analysis was performed in a semiautomated fashion. Previously validated (25, 26), custom-written software (MAD) detected PWs and PW sequences in Labview 3.0.1 (National Instruments). Because pressures as low as 6 mmHg at the lower esophageal sphincter (33) and 4 mmHg at the pylorus (46) are known to impede flow, we chose to score PWs ≥6 mmHg. The analysis criteria were set so that a PW was first defined by its peak, as a rise in pressure from baseline of ≥6 mmHg lasting between 0.8 and 7 s. The onset
of the PW was then defined as the first point at which the PW was greater than baseline by 1%. On the basis of the slow wave frequency in the human duodenum, a PW sequence was defined as the occurrence of PWs in two or more adjacent channels, which had onsets within ±3 s of each other. PW sequences could therefore involve between 2 and 20 recording points (a span varying from 1.5 to 33 cm). Although this time window appears long, it encompasses sequences within the reported range for small intestinal propagation velocities (0.39–4.51 cm/s) (13). Moreover, it is known that contractions cause shortening of ~1–2 cm along the intestine (36), and while the intestine shortens, the interval between sideholes does not. In effect this window is likely, therefore, to include waves with a lower limit of propagation velocity of ~1 cm/s, which is also within the range quoted (20). PW sequences were then sorted manually by length and predominant direction of travel. The direction of travel of very short PW sequences involving only two sideholes (1.5 cm) was not considered. PW sequences were defined as traveling in either a purely or predominantly antegrade or retrograde direction by examining the time interval between each pair of sideholes that a PW sequence traversed. If a majority of these intervals was positive, it was scored as antegrade, if negative, retrograde. PW sequences that converged on or spread from a site were not analyzed separately and were likewise allocated a direction based on their predominant component. In this analysis, no account is taken of either “synchronous” PW sequences or those with bidirectional components of equal length.

This automated identification of PW sequences, and assignment of direction was validated by comparison with manual analysis of the first 2 min of the analysis period in eight (of 36) randomly selected 20-min recording periods from six subjects (4 during fasting and 4 during ID lipid).

For analysis of the regional occurrence and site of origin of PW sequences, the duodenum was divided into four 6-cm segments, composed of four continuous 1.5-cm intervals, as depicted in Fig. 1. Data from each interval were combined within segments and averaged. To maintain equal segment lengths, data from the last (17th) 1.5-cm interval were excluded from this analysis.

The total number of PW sequences, those traversing each segment, their start site, length, and predominant direction of travel during each of these 20-min periods were assessed and compared between fasting (late phase II of the IDMC) and during the three rates of ID lipid.

Statistical analysis was performed with repeated measures ANOVA in SuperANOVA (ABACUS Concepts). All observations were matched between subjects. $P < 0.05$ was regarded as significant. Data are presented as means ± SE, unless otherwise stated.

**RESULTS**

The study was well tolerated by all volunteers, with no adverse effects noted. Recordings were satisfactorily completed in nine subjects for all four analysis periods (fasting, 0.25, 0.5, and 1.5 kcal/min). In one volunteer, a duodenal phase III episode occurred toward the end of the 0.5 kcal/min lipid infusion; in this case, the 10 min preceding phase III were used for analysis, and the values doubled to simulate a 20-min period. In the remaining eight volunteers, complete data sets were obtained, yielding matched data from nine subjects for all four analysis periods. An example of the motor patterns recorded is presented in Fig. 2.

Segments (2 min) of data from 8 of the 36 analysis periods were manually analyzed, and the results from manual analysis and automated analysis were compared with respect to how well each technique applied the analysis criteria. According to the criteria, there were 101 PW sequences; manual analysis detected 64 PW sequences and the computerized analysis detected 103. There was concordance between the two analysis methods for directional information in 93% of instances. The discrepancy in the number of PW sequences was nearly all accounted for by errors in the manual analysis. Two categories of variation between the automated and manual analyses accounted for most (37/39) of these discrepancies: 1) eight longer PW sequences scored manually were divided (correctly) by the automated analysis into 23 shorter PW sequences, where a wave within the PW sequence failed to meet the strict analysis criteria, and 2) 22 short (21 of 1.5 cm and 1 of 3 cm) PW sequences ignored in the manual analysis (because of low but above threshold PWs) were correctly identified by the automated method. In two cases, the automated analysis appeared to have incorrectly scored a 1.5-cm PW sequence where none existed according to the criteria. From this review, the automated analysis had an accuracy of >98% in identification of PW sequences.

**Number of PW sequences.** The greatest number of PW sequences occurred during fasting. There was a progressive suppression of PW sequences as the rate of delivery of ID lipid increased ($P < 0.001$ for linear contrast effect), so that at the highest rate of ID lipid (1.5 kcal/min) the number of PW sequences was reduced by 60% compared with fasting (see Fig. 3).

**Distribution of sequence lengths.** Despite the large differences in the total number of PW sequences among the 20-min analysis periods (see above and Fig. 3), PW sequence length was not affected by ID lipid ($P = 0.44$) (see Figs. 4 and 5, bottom). The vast majority (87–90%) of PW sequences traversed 1.5–4.5 cm. PW sequences that traversed 6–9 cm accounted for 5–10%, and those 10.5 cm and longer made up only 2–4% of all sequences. Although long PW sequences comprised only a small proportion of the total, their occurrence was such that during the 20-min analysis periods most volunteers had at least one PW sequence that spanned a substantial portion of the duodenum (as shown in Fig. 2E).

**Site of PW sequences.** The number of PW sequences that traversed each of the four duodenal segments is shown in Fig. 5, top. These varied significantly by both duodenal segment and rate of ID lipid infusion (by ANOVA, $P = 0.0016$ for effect by segment, $P = 0.0086$ for effect by rate, and $P = 0.0009$ for interaction between segment and rate). These differences were largely brought about by regional variation in the occurrence of PW sequences along the duodenum during all three rates of lipid infusion. During ID lipid, fewer PW sequences occurred proximally, compared with distally, and this effect was greatest as the rate of ID lipid increased. In contrast, during fasting the rate of occur-
rence of PW sequences was similar across the four duodenal segments.

The regional variation (by duodenal segment) in the occurrence of PW sequences was largely accounted for by variation in the site of origin of PW sequences. Site of origin varied by both duodenal segment and rate of ID lipid (by ANOVA, \( P < 0.01 \) for segment, \( P < 0.01 \) for rate, and \( P = 0.056 \) for interaction). Again the same trends (as described above) were noted, with fewer PW sequences starting proximally, particularly at the higher rates of ID lipid.

In contrast, as shown in Fig. 5, bottom, the distance traveled by PW sequences was not different between fasting and ID lipid at any rate of ID lipid infusion. PW sequences that started proximally tended to be slightly longer than those starting more distally.

**Direction of PW sequences.** The predominant direction of travel of PW sequences is shown in Fig. 6. Direction varied by the length of PW sequences but not by rate of ID lipid infusion. At all lengths and all rates of ID lipid, antegrade PW sequences were more frequent than retrograde sequences. As the length of PW sequences increased, a greater proportion of sequences were antegrade for all conditions tested (proportion antegrade: 3 cm, 39.9 ± 3%; 4.5 cm, 62.0 ± 4%; ≥6 cm, 66.0 ± 4%; \( P = 0.0001 \) for linear effect).

**DISCUSSION**

This is the first study to present high temporospatial resolution pressure recordings from the full length of the human duodenum, and it provides an important base on which a better understanding of duodenal mechanics can be built. Potentially important differences between the fasting and fed states have been demonstrated. The major findings are 1) a greater number of PW sequences occurs during phase II of the IDMC compared with during ID lipid infusion; 2) the frequency of duodenal PW sequences shows a regional variation during ID lipid infusion that is not seen during fasting, with fewer PW sequences proximally than distally; 3) the suppression of PW sequences associated with ID lipid appears to be dose related; 4) regardless of their site of origin or whether nutrient was being delivered, most duodenal PW sequences were relatively short, traversing only a mean distance...
of ~3 cm; and 5) the majority of PW sequences of all lengths was purely or predominantly antegrade under all conditions tested, with a linear trend for a greater proportion of PW sequences to travel in an antegrade direction as PW length increased. Thus rather than being a passive conduit, there is substantial spatial variation and complexity in the patterning of duodenal pressures.

The progressive decrease in the number of PW sequences during the study could be causally related to either time or lipid infusion rate. Although volume differed between fasting and lipid infusion, it was the same during three infusions and could not therefore account for the progressive change observed. Although the order of the lipid infusions was not randomized, a number of lines of evidence (18, 19, 21, 22, 32, 41) lead us to suggest that the caloric rate of infusion is the important variable. In particular, dose-dependent changes in small intestinal motility have been clearly demonstrated in both dogs (41) and minipigs (18), suggesting that dose will have a similar effect in humans, although to assess this with confidence a repeat study with the caloric rates given in random order would be necessary.

The occurrence of phase III of the IDMC during the 0.5 kcal/min lipid infusion in one subject raises the likelihood that in this subject, at that time, a postprandial motility pattern had not yet been induced. At the time of this phase III activity, the subject would have received ~25 kcal lipid, which in caloric terms corresponds to a period of ~10–15 min after ingestion of a meal, if one accepts a rate of gastric emptying of ~1.5–2.5 kcal/min (19), which is entirely consistent with the knowledge that ingestion of a meal takes ~10–20 min to interrupt the small intestinal IDMC in progress at the time of eating (35). Presumably, a time lag exists between the first presence of small intestinal nutrients and IDMC interruption, during which sufficient mucosal receptors and quanta of small intestinal hormones are recruited to induce a “fed” motor pattern. Moreover, the fact that the duration of IDMC interruption is proportional to the caloric load of a meal (see Ref. 35 for review) also adds additional biological plausibility to the dose-related suppression of duodenal PW sequences. Additionally, the extent of small intestine exposed to nutrients determines the magnitude of small intestinal nutrient-mediated feedback (22), and as the dose of nutrient given increases, so will the area of intestine exposed to it because of saturation of absorption capacity (21). Thus an interrelationship is provided between dose and extent of small intestine exposed, which may account for the progressive suppression of PW sequences we observed with increasing dose of lipid.

Lipid infusion rate was not randomized because without long delays (~2 h after each dose) waiting for the reemergence of phase III as a marker of fasting motility, it would not be possible to give lower caloric

Fig. 4. The frequency distribution (%) of length of PW sequences is shown for late phase II and the 3 rates of intraduodenal (ID) lipid infusion. No differences were found between fasting and ID lipid.
rates after high caloric rates on the same day without the risk of carryover effects. This would necessitate either a 4-day study (introducing other potential problems such as standardizing diet over this period) or a protocol so long that few subjects would have completed it. The changes in motility can be safely said not to represent simply a time effect, because during the study period (3–5 h) in healthy subjects the cyclical recurrence of phase III would have occurred if lipid were not present. Moreover, prolonged infusion of saline would not be expected to interrupt the IDMC (20). Although all subjects began receiving lipid in phase I, suppression of duodenal PWs by ID lipid (at 1.1 kcal/min) has been previously reported (17) in humans in differing phases of the IDMC, making it unlikely that the phase of the IDMC during which lipid commenced affected our results. In addition, after subjects received 20–30 kcal of lipid infusion, phases of the IDMC were no longer relevant, because one is then examining postprandial motility.

Previous studies of human duodenal motor function have had to choose between closely spaced pressure recordings of part of the duodenum or broader sidehole spacing to cover the whole organ largely because of technical limitations on the number of recording points. Without the 1.5-cm spacing and total organ coverage used in the current study, a substantial proportion of the PW sequences would not have been categorized correctly, because 74–82% of PW sequences were only 1.5–3 cm in length. With broader sidehole spacing, some spatially unrelated short PW sequences that occurred close together in time would be misclassified as a single longer sequence, and the infrequent, longer PW sequences could not have been reliably identified. With our approach, it is possible to resolve the PW onset patterns accurately in both time and space, which is likely to have important consequences for propulsion. Moreover, we used an unusually rigorous process to continuously document assembly position, by monitoring TMPD at two points. This ensures complete confidence that the highest recording point in the duodenum was, in fact, within this region without reliance on PW criteria. This somewhat circu-

Fig. 5. Top: numbers (means ± SE) of PW sequences traversing each segment are shown, by rate of ID lipid. By ANOVA, there is an effect by segment ($P = 0.0016$) and rate of ID lipid ($P = 0.0086$) and an interaction between both ($P = 0.0009$). Compared with fasting, ID lipid caused a dose-related reduction in the occurrence of PW sequences overall and a differentially greater reduction of proximal PW sequences. During fasting, the rate of occurrence of PW sequences was similar along the length of the duodenum. Bottom: length (means ± SE) of PW sequences is shown. ID lipid had no effect on the mean length of PW sequences (by ANOVA, $P = $ not significant). However, there was an effect by segment on PW sequence length (by ANOVA, $P = 0.0001$), mainly because PW sequences in segment I were slightly longer than those starting in other segments.

Fig. 6. The predominant direction of travel of PW sequences is shown for the 4 conditions tested (mean proportion for each length examined). Proportions are used because of the large differences in the total number of PW sequences between the 4 conditions (see Fig. 3). Direction varied by the length of PW sequences but not rate of ID lipid infusion (ANOVA, $P = 0.0001$ for length, $P = 0.0001$ for direction, $P = 0.02$ for interaction direction by length, $P = $ not significant for rate of ID lipid). At all distances evaluated and all rates of ID lipid, the proportion of antegrade PW sequences was higher than retrograde sequences ($P < 0.002$ for all comparisons of antegrade vs. retrograde).
lar method for confirmation of assembly position has been used in other studies and suffers from problems of definition of what is "truly" an antral or duodenal PW. In addition, it leads to uncertainties about assembly position when PWs are not occurring frequently.

The criteria-based, automated analysis used in our study enabled the processing of large amounts of data from multiple channels with high temporal resolution, which is an approach not practical with manual analysis. Given the importance of high spatiotemporal resolution of pressures to gaining an understanding of duodenal mechanics, some form of automated analysis is vital to progress in this field. The automated analysis used here performed well compared with the analysis criteria, both in its ability to identify PW sequences and correctly assign direction. The discrepancies between the manual and automated analyses were virtually all due to inaccuracies in the manual interpretation. The automated method is consistent and reproducible, allowing accurate comparisons to be made between recordings. Although manual analysis has been previously held up as the "gold standard," with large amounts of data, human error due to misjudgment and fatigue is increasingly likely, and although discretion in analysis based on experience holds some appeal in theory, it leads to inconsistency in data handling, rendering data sets noncomparable.

High-resolution manometric recordings in the esophagus combined with fluoroscopy have led to a clear understanding of the mechanics of flows and the significance of intraluminal pressures in creating these flows (6), and, given the tubular nature of both the esophagus and duodenum, it is reasonable to propose that the relationship between flow and spatiotemporal pressure patterns will be similar in these two organs. We thus believe that the duodenal pressure patterns observed in the present study are likely to be the major determinants of duodenal intraluminal flow. Because duodenal motor characteristics differ somewhat from the esophagus, the exact relationship of pressure and flow still needs to be studied directly in the duodenum. However, it is likely that the short PW sequences we recorded are analogous to "mixing" contractions described previously (3, 4) and that longer PW sequences are responsible for movement of intraluminal contents in both directions over greater distances as observed by Borgstrom and Arborelius (3, 4). In the dog, pulsatile flow at the pyloric level is transformed within ~5 cm to smoother flow in the duodenum (24). This is due to the resistive characteristics of the duodenum, and it is likely that retrograde PW sequences noted in the current study are one of the mechanisms that contribute to this resistive function.

Castedal et al. (9) have also recorded pressures at 1.5-cm intervals, but only from the first 6 cm or so of the duodenum. They (9) found that a significant number of PW sequences had bidirectional components, rather than being simply unidirectional. Our recordings in the current study have confirmed this and have defined the spatial relationships of these pressure patterns to the rest of the duodenum. The finding of Castedal et al. (9) that predominantly retrograde PW sequences exceeded the proportion of predominantly antegrade sequences in any comparison was not confirmed in our study. This may be due to differences in the analysis technique used, because Castedal et al. (9) examined direction of travel by start site, whereas we examined direction of travel by length and rate of ID lipid infusion. Other differences in methodology between the study of Castedal et al. (9) and ours include their restriction in analysis to sequences of ≥6 cm and their use of peaks rather than PW onset times to establish propagation patterns. Another recent high-resolution manometric study (38) in the duodenum has confirmed our finding of regional variation in duodenal motor patterning and also found the motor response to vary by stimulus. Borgstrom and Arborelius (4) recorded pressures from a greater proportion of the duodenum but with much lower spatial resolution. Compared with that study (4), during fasting we found a higher proportion of predominantly antegrade PW sequences [current study vs. that of Borgstrom and Arborelius (4), 51% vs. 40%, respectively] and a lower proportion of "static" PW sequences (synchronous or equal directional components) [current study vs. that of Borgstrom and Arborelius (4), 19% vs. 31%, respectively]. During ID lipid infusion, we observed a far higher proportion of predominantly antegrade PW sequences [current study vs. Borgstrom and Arborelius (4), 61% vs. 19%, respectively] and a much lesser proportion of predominantly static PW sequences [current study vs. Borgstrom and Arborelius (4), 15.5% vs. 51%, respectively], with the proportion of retrograde PW sequences being similar between our study and that of Borgstrom and Arborelius (4) at 23.5% and 29%, respectively. These differences are likely to arise primarily from the different spatial resolution in manometric recordings between these two studies, as discussed earlier.

Some investigators (31, 37) have asserted that duodenal flows are intermittent and bidirectional. This is consistent both with the pattern of occurrence of intraluminal pressures we recorded and with our hypothesis that intraluminal pressures determine flow. This hypothesis would ideally be addressed by concurrent high-resolution recordings of both intraluminal pressures and flows. At present this is not possible in human volunteers, although a number of groups (2, 5, 16, 42) are working on potential methodology to enable this. Given the intermittent nature of duodenal flows, in seeking to understand the relationship between pressures and flows it is important to use techniques that enable sufficient temporospatial resolution of the data.

Some limited data exist in which duodenal flows and pressures or movement of contents have been found to interrelate. A combination of concurrent high-resolution manometry with scintigraphy led Samsom et al. (34) to conclude that the transit of chyme through the proximal small intestine in humans is related to the number of propagated PW sequences. However, because of the limitations in temporal resolution of the scintigraphic technique, discrete episodes of flow can
not be related to individual PW sequences. In the jejunum of minipigs, Huge et al. (18) reported that decreased motility index and propagation distance were associated with decreased flow rate and increased transit time. In dogs, Furukawa and Hatano (15) have shown a clear relationship between retrograde small intestinal contractions and intraluminal flow: contractions traveling in an oral direction preceded emesis and transported intestinal contents in a retrograde direction. In humans, simultaneous manometric and videofluoroscopic studies (3, 4) have categorized manometric PW sequences as stationary (mixing), antegrade, or retrograde. However, in these studies (3, 4), only four channels at 3-cm intervals in the proximal half of the duodenum were used.

Duodenal motor activity may influence gastric emptying in a number of ways (7): rapid clearance is thought to facilitate emptying, delayed clearance to impede emptying (28, 31), and duodenogastric reflux returns content to the stomach, also effectively slowing emptying (9). Although net duodenal flow is antegrade, in humans, retrograde flow is also known to occur, particularly in the proximal duodenum, both during the fed (16) and the fasted state (8, 10). Our data, with a predominance of antegrade sequences but a significant proportion of retrograde sequences observed, would support this contention. Although with only one-eighth of the sequences over a 20-min period observed in our study being predominantly (or purely) retrograde, it does not appear likely that postprandial duodenogastric reflux is a major determinant of gastric emptying rate (9) under these conditions, unless it is of high volume. Other duodenal motor patterns associated with slowing of gastric emptying in humans include dilatation and reduction of propagating PWs, leading to delayed duodenal clearance and prolonged tonic occlusion giving high resistance to further gastric outflow (31). Because our study examined pressures but not diameter we cannot entirely clarify this matter, although we recorded an apparently dose-related reduction in PW sequences during ID lipid infusion, which would tend to support the findings of Rao et al. (31). When considering the influence of the duodenum on gastric emptying, it must be remembered that the pylorus lies at the junction of these two organs and acts as a sphincter when nutrient is present in the small intestine. Thus the timing of pyloric opening relative to the sequencing of duodenal motor events is likely to be pivotal in determining whether or not transpyloric flow occurs.

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