Relationships between spatial patterns of colonic pressure and individual movements of content

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Departments of 1Medicine, 3Gastroenterology, and 2Nuclear Medicine, Royal Adelaide Hospital, University of Adelaide, Adelaide 5000; and 4Department of Gastroenterology, St. George Hospital, University of New South Wales, Sydney 2217, Australia

Cook, Ian J., Yoshiyuki Furukawa, Voula Panagopoulos, Peter J. Collins, and John Dent. Relationships between spatial patterns of colonic pressure and individual movements of content. Am. J. Physiol. Gastrointest. Liver Physiol. 278: G329–G341, 2000.—The aim of this study was to examine the relationship between colonic pressure waves and movement of content. In 11 healthy subjects, pressures were recorded at 10-cm intervals from cecum to rectum for 32 h. In six subjects, transit was simultaneously measured for 8 h after direct cecal instillation of 1.5 mCi of $^{99m}$Tc sulfur colloid. Thirty-two percent of isotope movements were related to nonpropagating activity and twenty-eight percent to propagating sequences. The extent of isotope movement related to propagating sequences (25.1 ± 2.1 cm) was greater than that due to nonpropagating activity (12.8 ± 0.7 cm; P = 0.0001). Propagating sequences originated significantly more frequently (P = 0.004) and propagated further (P = 0.0006) in the proximal compared with the distal colon. Only 36% of propagating sequences were propulsive of content, and compared with nonpropulsive sequences, these propagated further (41 ± 6 vs. 27 ± 2 cm; P < 0.05) and had a higher probability of originating proximally (P = 0.0003), a higher pressure wave amplitude (50 ± 5 vs. 34 ± 4 mmHg; P = 0.0001), and slower velocity (2.2 ± 0.3 vs. 3.6 ± 0.47 cm/s; P = 0.02). We conclude that most movements of colonic content are related to pressure waves. There is marked regional variation in the prevalence, velocity, and extent of propagation of propagating pressure wave sequences, which are an important mechanism for transporting content over long distances. The effectiveness of transport by a propagating sequence is influenced by its site of origin, amplitude, and velocity.

colon; manometry; motility; scintiscanning; transit

DISORDERS OF TRANSIT AND DEFECATION logically have their basis in abnormal colonic propulsive forces. There are fundamental gaps in our understanding of the colonic motor patterns that are responsible for colonic propulsion. Mass movements have long been recognized to move colonic content over large distances (10, 16, 17), and high-amplitude propagating pressure waves have been found to be associated with defecation (2, 3, 15). Mass movements and defecation, however, are infrequent, occurring only once or twice daily, whereas cecal filling and most discrete movements of colonic content are slow and occur in a stepwise fashion over short distances (29, 31, 32).

Earlier studies relating colonic pressure and flow were largely indirect. Qualitative differences exist between rectosigmoid motility indexes in patients with diarrhea compared with those with constipation (5, 8). Electromyographic recordings from the human and canine colon have shown an inverse correlation of averaged flow rates of a nonabsorbable marker with the frequency of bursts of electromyographic activity that extended over relatively long distances (5, 34).

The introduction of colonic scintigraphy permitted appreciation of regional variations in movement and relative dwell times of colonic content (6, 21, 23, 31). A few studies have subsequently combined colonic scintigraphy with manometry (4, 15, 27). This approach, by following the progress of the geometric center of the isotope column, demonstrated regional differences in mean motility indexes that might favor isotope movement between regions (4, 27) but did not have sufficient temporal resolution to identify specific motor patterns responsible for episodic colonic flow. Herbst and colleagues (15) used a similar approach and were able to record colonic pressures and quantify regional colonic emptying before and after defecation. However, there are no published data relating, on a minute-by-minute basis, the relationship between spatial patterning of colonic pressures and discrete movement of content along the unstimulated, healthy human colon (19, 20).

The aim of this study was to make prolonged, simultaneous multipoint pressure recordings and scintigraphic measurements from the entire colon to correlate pressure with discrete movements of colonic content. The specific aims were to quantify colonic motor patterns along the entire length of the healthy colon, to determine whether pressure patterns are responsible for individual movements of colonic content and, if so, which types of pressure waves are propulsive, and to examine which variables, if any, correlate with effective propulsion of content in particular regions.

METHODS

Subjects

We studied 14 healthy male volunteers (mean age 23.2 ± 1.0 yr, range 18–33 yr), who had no history of gastrointestinal

complaints and who had normal bowel habits defined as having between two bowel actions daily and one bowel action every two days. None had had previous abdominal surgery other than appendectomy. None was taking laxatives or other medications. Observations on the influence of sleep stage on colonic motility were reported previously in this same study population (9). Written informed consent was obtained from participants, and the study was approved by the Ethics Committee of the Royal Adelaide Hospital.

Study Protocol

Between 2:00 PM and 4:00 PM the day before the study, subjects ingested 4 liters of a standard colonic lavage solution (Golytely; Golytely Products, Melbourne, Australia). The next day at around 8:00 AM, subjects underwent colonoscopy while self-administering Entonox (50% nitrous oxide-50% oxygen mix) by inhalation as required for discomfort. No other medication was administered to subjects. A flexible, Teflon-coated 400-cm guide wire (diameter 0.038 in.; WA Cook) was passed through the colonoscope, and the tip was positioned in the cecum under direct vision as described previously (12). The manometry catheter was passed over the guide wire, and the catheter tip position in the cecum was confirmed fluoroscopically. Fluoroscopy exposure time was 30–60 s, and the maximum whole body effective radiation dose equivalent was 0.8–1.6 mSv. Colonic pressures were recorded continuously for 32 h until 5:00 PM the following day. Subjects ate standard meals (breakfast: 300 kcal, 15% protein, 34% fat, 51% carbohydrate; lunch and dinner: 1,000 kcal, 24% protein, 43% fat, 33% carbohydrate) at 8:00 AM, 12:00 PM, and 7:00 PM (12). Subjects sat in bed during waking hours with the bed head at a fixed 45° and lay flat during sleep. Subjects were asked to press an event marker, and to note the time in a diary, at the onset of any sensations including an urge to defecate, an urge to pass flatus or the passage of flatus, or any other sensations that they perceived within the abdomen.

On the second study day, colonic transit was monitored scintigraphically in six subjects for 8 h simultaneously with continued manometry. At 8:00 AM on the second day, 60 MBq (4 µCi) of 99mTc sulfur colloid in 10 ml of saline was instilled into the cecum in these six subjects via the manometry catheter. Isotope images were then recorded continuously until 5:00 PM at a rate of 15 s/frame by scintillation camera (Pho-gamma III, Nuclear, Chicago, IL) with a low-energy collimator, peaked for 140 keV (technetium-99m). The camera was linked to a dedicated computer (PC 386s, Compaq) for later retrieval and analysis (Polygraf software, Synectics Medical). Scintigraphic images were continuously fused with manometric side holes. In addition to tracings on paper, manometric signals from channels 1–5, 7, 9, and 11 were simultaneously processed by separate preamplifiers, digitized on-line (PC polygram, Synectics Medical), and stored on computer (PC 386s, Compaq) for later retrieval and analysis (Polygraf software, Synectics Medical).

Data Analysis

Definitions and classification of colonic pressure patterns. Two major pressure patterns were readily discernible from colonic pressure recordings. The most prevalent pattern was phasic on tonic variations in pressure of variable conformation, duration, and amplitude. This pattern was associated neither morphologically nor temporally with pressure patterns recorded in adjacent side holes, and was termed non-propagating activity (see Other definitions). The other recognizable pattern consisted of an array of predominantly monophasic pressure waves among which there was a temporal association consistent with the phenomenon of propagation (propagating sequence; defined below).

Analysis was accomplished both visually and, where necessary, with computer assistance. The initial screening process involved 1) determination of regional baselines to which pressures within individual channels were referenced, 2) identification of artifacts and strain patterns (see Other definitions), and 3) identification of candidate propagating sequences, which were flagged and later subjected to closer scrutiny. The later examination of the candidate propagating sequence involved two steps: 1) examination of individual pressure changes within each channel to define individual pressure waves and 2) consideration of the temporal relationships among pressure waves in adjacent channels; if the criteria for propagation were met, the sequence of waves was classified as a propagating sequence.

The baseline for each channel was established from segments of the trace when the subject was supine by visual inspection of a horizontal cursor on screen that was adjusted to identify the minimum end-expiratory pressure for the 24-h recording period. All subsequent pressure measurements within each channel were referenced to each channel-specific baseline. Adjustments to the baseline were made where appropriate at times when the subject altered body posture, such as assuming the supine posture at night, by adding or subtracting the pressure change induced acutely by the change in posture. For example, just before sleep, subjects’ posture changed from a 45° head-up angle to the supine posture, resulting in a variable fall in baseline in each side hole depending on the height of each side hole relative to the external pressure transducers. The acute fall in baseline at this moment was noted and was later added to all subsequent pressure values obtained while the subjects lay supine to correct for this systematic postural offset at night.
First, each pressure change in each channel within the candidate propagating sequences was examined. A pressure wave was defined as a predominantly monophasic pressure change with a discernable onset, peak, and offset, which had an onset to peak amplitude $>5$ mmHg and which did not have the features of pressure increases generated by artifact, straining, or respiratory oscillations (see Other definitions). The timing of pressure wave onsets (see Other definitions) was then determined. The temporal relationships among pressure waves in adjacent channels were then considered to determine whether the combination of pressure waves would meet the criteria for propagation based on the following velocity criteria. A propagating sequence was defined as an array of three or more pressure waves recorded from adjacent recording sites in which the conduction velocity between wave onsets within that sequence lay between 0.2 and 12 cm/s. If these criteria for propagation were met, the individual pressure waves within a propagating sequence were then called propagating pressure waves. If the conduction velocity among two or more pressure waves within a candidate sequence exceeded 12 cm/s, these particular pressure waves were called synchronous pressure waves and the distal extent of the propagating sequence was deemed to be the point at which propagation velocity equaled 12 cm/s and synchrony began. Pressure waves identified in nonad- jacent side holes could be deemed to be associated with each other if the two waves were separated by not more than one intervening channel and if the above velocity criteria were met. If more than two recording sites were skipped, each potential sequence above and below the skipped region was considered individually according to the above criteria and could potentially be classified as two separate propagating sequences, one sequence, or no sequences.

Propagating sequences were qualified as antegrade or retrograde according to the direction of propagation. Propagating sequences were further subclassified as high-amplitude propagating sequences if the amplitude of one or more of the component propagating pressure waves in the propagating sequence was $>90$ mmHg (12). This value was chosen because it represents mean propagating pressure wave amplitude plus 2 standard deviations for midcolonic propagating pressure waves.

Other definitions. Nonpropagating activity was defined as a phasic on tonic pressure change of magnitude $>5$ mmHg above regional baseline, with duration of $>15$ s, which incorporated two or more pressure peaks and which bore no temporal or morphological relationship to pressure profiles in adjacent channels. Respiratory oscillations were defined as sinusoidal pressure oscillations, identical in at least four channels, with a frequency of 8–12 cpm or which were consistent with the respiratory rate of the subject at the time of the study. The term artifact was used to describe recorded signals from extracorporeal mechanical or electrical events that were not detected by a side hole (e.g., catheter movement, equipment adjustments). Strain pattern was used to describe a change in pressure detected at multiple intraluminal recording sites that arose from extraluminal mechanical influences generated by the subject (e.g., cough, body movement, strain). A strain pattern was distinct from passive alterations in pressure secondary to alterations in body position or posture (see description of baseline) and was defined as a pressure wave with rapid upstroke, which was identical in shape and which was registered simultaneously across all recording channels. Pressure wave onset was defined as the onset of the major pressure upstroke of a pressure change considered not to be artifactual or respiratory in nature.

Measurments. The colon was divided into 12 anatomic regions by assigning region 1 to the cecum, region 6 to the splenic flexure, and region 12 to the rectum. Each recording side hole was then allocated to its closest anatomic region. The entire 24-h recording period was divided into twenty-four 1-h epochs. The 1-h before and the 3 h after lunch on day 2 (test meal) were divided further into twelve 15-min epochs to provide greater temporal resolution of any meal response. We then quantified each of the pressure variables defined above for each region, for each time epoch, in each subject before calculating time- and region-specific group mean values for statistical analysis.

The number of propagating sequences per hour and the extent of propagation of each sequence were first determined. Each propagating sequence was then assigned to its region of origin to determine any regional variations in the frequency with which these events were activated. The point of termination of each propagating sequence was noted to measure the extent of propagation of each sequence. Next, within each propagating sequence, and for each colonic region, we determined the frequency, amplitude, and propagation velocity of each of the component propagating pressure waves. These variables were further subclassified according to physiological state such as fasting, fed, awake, and asleep. The amount of nonpropagating activity was measured by determining the proportion of time occupied by it in each region and for each time epoch.

The area under the pressure curve (AUC) was used as an overall measure of motor activity and as an approximate index of nonpropagating activity because this was by far the most prevalent pressure pattern seen. The AUC for each 1-h epoch was calculated by computer from the eight digitized channels for the entire 24-h period, yielding sufficient data values for meaningful comparisons among regions and diurnal changes in 10 of the 12 colonic recording sites. The AUC was also measured for each of the twelve 15-min epochs in the periprandial period to assess the meal response.

Scintigraphic frames were aligned to a fixed region of interest (ROI) of the colon, which was drawn with the aid of a joystick, using an interactive computer program. The analysis of scintigraphic images was first done without reference to the manometry tracings. The isotopic images were replayed in real time and examined visually frame by frame at variable speed with the aid of a joystick. The times of onset and termination of discrete isotope movements, corresponding scintigraphic frame numbers, colonic region, and direction and extent of all isotope movements were noted and later transcribed onto the manometric tracing. The extent of movement of content was calculated from the distance traveled by the “tail” of the segment of isotope. If doubt arose as to whether a net isotope shift was apparent visually, ROIs were then drawn to encompass the adjacent recording sites and isotope counts were calculated for the two regions by the camera’s computer. Isotope movement to or from a region was deemed to be present if the counts in the ROI varied by $3S D$ (99% confidence interval) from the ROI counts in the preceding image (where the SD of counts follows a Poisson distribution in which SD = square root of counts in the ROI). By directly correlating each isotope movement with the manometric tracing, we could determine whether a specific isotope movement was associated with one of the pressure patterns defined above.

In the second stage of this analysis, we examined for possible relationships between each propagating sequence and isotope movement. We selected for analysis only those sequences that were seen to occur within colonic regions that contained isotope at the time of occurrence of that propagat-
ing sequence. We then examined frame by frame all the isotope images within the time period that encompassed each propagating sequence. Each propagating sequence was then defined as propulsive or nonpropulsive according to whether or not it was temporally associated with isotopic motion. A propagating sequence was defined as propulsive if net movement of isotopic activity was observed to occur in the direction of propagation of the propagating sequence and if the movement of the tail of the isotope column was seen to occur no more than two frames (30 s) before the onset and ≤ 30 s after the onset of the propagating pressure wave upstroke at the site of commencement of the observed isotope movement.

The region of origin of each propagating sequence as well as the amplitude, wave onset timing, and conduction velocity of all its component propagating pressure waves were compared between propulsive and nonpropulsive sequences to define how these variables relate to the phenomenon of colonic propulsion by a propagating sequence.

Statistical Analysis

Inferences regarding the possible influence of colonic region on propagating sequence frequency, amplitude, and velocity were tested using a single-factor repeated-measures ANOVA (Statview, Abacus Concepts, Berkeley, CA). A paired t-test was used in instances in which pooled mean values from the proximal colon were compared with those from the distal colon. Measures of the meal response (propagating sequence frequency, percent time occupied by nonpropagating activity, and AUC) for the first and second postprandial hours were compared with mean fasting values averaged over the 1 h before the meal using a paired t-test and, where appropriate, a Bonferroni correction factor for multiple comparisons. Inferences regarding possible differences in subject mean propagating pressure wave amplitude and velocity were tested between propulsive and nonpropulsive sequences using an unpaired t-test. Comparisons among proportions of propulsive and nonpropulsive propagating sequences and regions of origin were made using a χ² statistic. All data are presented as means ± SE unless otherwise stated.

RESULTS

Of the 14 subjects, the manometry catheter tip lay in the cecum in 11 and in the middle ascending colon in 3 subjects. During the subsequent adaptation and recording period, the catheter was expelled in two subjects, 5 and 14 h after placement. The catheter tip migrated distally a distance of up to 20 cm in another three subjects. Hence, data are only presented for the remaining 11 subjects in whom the catheter tip remained in an acceptable position for the entire study: at the hepatic flexure (2), middle ascending colon (2), or cecum (7 subjects). In 6 of these 11 subjects, combined scintigraphic transit and manometry was measured on the second day. The only selection criterion for these six subjects was that the catheter tip lay in the cecum (for isotope instillation) on the morning of the second day.

AUC and Nonpropagating Activity

The regional values for AUC averaged over the entire 24-h period in all subjects are shown in Table 1. There was a significant, steady increase in AUC paralleling distance of the recording side hole from the cecum (P = 0.02). There was a significant increase in AUC in response to the 1,000-kcal test meal (lunch, day 2) for the first (P = 0.01) and the second (P = 0.004) postprandial hours, but the magnitude of this meal response was not regionally dependent. Nonpropagating activity demonstrated a similar regional variation in that the proportion of time occupied by nonpropagating activity was significantly greater in the distal colon compared with the proximal colon (P = 0.004) (Table 1). Periods of occurrence of nonpropagating pressure activity ranged from 15 to 670 s (mean 86 ± 25 s).

Propagating Sequences

Propagating sequences showed antegrade migration in all 11 subjects and retrograde migration in 9 subjects. Antegrade propagating sequences occurred with a mean frequency of 1.9 ± 0.1/h (range 0–11.8/h). Retrograde propagating sequences were almost exclusively confined to the proximal colon, were less frequent (0.5 ± 0.1/h, range 0–15/h), and propagated over shorter distances than antegrade propagating sequences (Table 1). Antegrade propagating sequences ceased to propagate in one of three ways: 1) terminating (72%), 2) transforming into synchronous pressure waves with amplitude and pattern that differed in adjacent distal sites (9%), and 3) transforming into synchronous pressure waves of identical morphology across several recording sites (19%). The frequency of occurrence of index propagating pressure waves (site of origin of propagating sequence) showed a significant negative correlation (P = 0.004) with distance from the cecum (Fig. 1), that is, propagating sequences originated significantly more frequently in the proximal compared with the distal colon. The extent of antegrade propagating sequences was also significantly greater for those sequences originating in the proximal compared with the distal colon (P = 0.0006) (Table 1, Fig. 1). For example, the mean extent of antegrade propagating sequences originating in the cecum was just over double that of those originating in the descending colon. Because only 4.1% of all propagating sequences actually reached the rectum, this regional difference in extent of propagating sequence could not be accounted for by proximity of the more distal recording sites to the rectum.

The mean peak amplitude of antegrade propagating pressure waves for all colonic regions (41.8 ± 2.3 mmHg; range 5–169 mmHg) was significantly greater than that of retrograde propagating pressure waves (19.7 ± 1.1 mmHg; range 4–70 mmHg) (P = 0.0001; Table 1). There was a trend for the mean amplitude of antegrade propagating pressure waves to progressively decline with distance from the cecum and for the mean amplitude of retrograde propagating pressure waves to diminish with proximity to the cecum. However, these trends were not statistically significant (Table 1). The propagation velocity of antegrade propagating pressure waves showed a strong positive correlation with distance of the wave from the cecum (P = 0.001), with propagation velocity of individual propagating pres-
From 0 to 40 per subject per day with a group meaning sequences varied widely among subjects, ranging sequences. The frequency of high-amplitude propagating sequences comprised 24.6% of a total of 455 propagating sequences were observed in 8 of 11 subjects, and the mean frequency of propagating sequences was not influenced significantly by the meal.

Frequency of propagating sequences was not influenced significantly by the meal.

Waking, high-amplitude propagating sequences occurred in only 3 of 11 subjects. Thus most propagating sequences that occurred in the postwaking period were of lesser amplitude.

**Table 1. Regional variations in parameters of propagating sequences, propagating pressure waves, nonpropagating activity, and AUC**

<table>
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<th>Region</th>
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<td>PS frequency, sequence·subject(^{-1})-day(^{-1})</td>
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<tr>
<td>Antegrade†</td>
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<td>7.64</td>
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<tr>
<td>Postprandial (0–60 min)</td>
<td>14.4</td>
<td>102</td>
<td>236</td>
<td>284</td>
<td>400</td>
<td>370</td>
<td>690</td>
<td>545</td>
<td>617</td>
<td>573</td>
<td>56.5</td>
<td>10.4</td>
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<tr>
<td>±9.5</td>
<td>±75.7</td>
<td>±142</td>
<td>±113</td>
<td>±265</td>
<td>±230</td>
<td>±286</td>
<td>±333</td>
<td>±378</td>
<td>±296</td>
<td>±48.2</td>
<td>±10.4</td>
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<tr>
<td>Postprandial (60–120 min)</td>
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<td>161</td>
<td>349</td>
<td>335</td>
<td>323</td>
<td>612</td>
<td>607</td>
<td>805</td>
<td>619</td>
<td>109</td>
<td>19.1</td>
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<tr>
<td>±65</td>
<td>±83.7</td>
<td>±124</td>
<td>±256</td>
<td>±163</td>
<td>±230</td>
<td>±326</td>
<td>±350</td>
<td>±347</td>
<td>±33.5</td>
<td>±19.1</td>
<td></td>
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<tr>
<td>AUC* mmHg·s·h(^{-1})</td>
<td>346</td>
<td>335</td>
<td>478</td>
<td>519</td>
<td>485</td>
<td>524</td>
<td>635</td>
<td>452</td>
<td>587</td>
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<td>651</td>
<td>5</td>
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<tr>
<td>±22</td>
<td>±36</td>
<td>±61</td>
<td>±69</td>
<td>±68</td>
<td>±121</td>
<td>±131</td>
<td>±144</td>
<td>±91</td>
<td>±110</td>
<td></td>
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</table>

Values are means ± SE; for propagating sequence (PS) frequency and extent propagated, data depict mean no. of PS originating at region specified and mean distance propagated. Region 1, cecum; region 12, rectum; PPW, propagating pressure wave within PS; AUC, area under curve. Statistical significance of region effect: *P < 0.05; †P < 0.01; ‡P < 0.001. §Insufficient data (computer acquisition limited to 8 channels).

Pressure waves increasing steadily from the cecum to the proximal descending colon (Table 1, Fig. 2). The test meal was associated with an increase in propagating sequences in only 3 of 11 subjects, and the mean frequency of propagating sequences was not influenced significantly by the meal.

High-Amplitude Propagating Sequences

During the 24-h analysis period, 112 high-amplitude propagating sequences were observed in 8 of 11 subjects and comprised 24.6% of a total of 455 propagating sequences. The frequency of high-amplitude propagating sequences varied widely among subjects, ranging from 0 to 40 per subject per day with a group mean frequency of 0.425 ± 0.193 per subject per hour. None propagated retrogradely. The site of origin of high-amplitude propagating sequences had the same regional distribution as that of propagating sequences overall, with 86 of 112 (77%) high-amplitude propagating sequences originating proximal to the hepatic flexure. Neither mean extent (46 ± 5.7 cm; range 20–90 cm) nor propagation velocity of high-amplitude propagating sequences differed significantly from these measures for the other propagating sequences. High-amplitude propagating sequences were rare at night, with a total of 13 of these events occurring during sleep in only 3 of 11 subjects. In the 2 h after morning waking, high-amplitude propagating sequences occurred in only 3 of 11 subjects. Thus most propagating sequences that occurred in the postwaking period were of lesser amplitude.

Discrete Isotope Movements

Eight hours after cecal instillation in the six individual subjects in whom isotope movement was monitored, the position of the head of the isotope column was at the splenic flexure (3 subjects), distal descending colon (2 subjects), and rectum (1 subject). In all, 123 discrete isotope movements were identified. Of these, 34 (28%) were associated with propagating sequences and 39 (32%) with nonpropagating activity, whereas 50 (40%) isotope movements had no discernible associated pressure event.

Movements of isotope in association with a propagating sequence were at times quite striking, as such isotope movements were sometimes seen to extend over half the length of the colon (Fig. 3). None of the six subjects experienced an urge to defecate in association with any isotope movements, even those in which propagating sequences were associated with movements of isotope that exceeded one-half the colonic length. The amplitude of propagating pressure waves...
related to these major movements was often <40 mmHg (Fig. 3). The minimum propagating pressure wave amplitudes seen to be associated with movement of isotope were 8 (ascending), 16 (transverse), 14 (descending), and 30 (sigmoid) mmHg.

There were instances where the isotope tail ceased to progress despite the continued presence of propagating pressure waves at and distal to the point at which the tail of the isotope column "escaped" or failed to progress. In some such instances, the lumen at and adjacent to the side hole registering the pressure wave at the point of isotope escape could be seen to be filled with isotope, strongly suggesting loss of lumen occlusion at that particular side hole (Fig. 3).

The mean distance of isotope movement that was linked to propagating sequences (25.1 ± 2.1 cm) was significantly greater than the isotope movement associated with nonpropagating activity (12.8 ± 0.7 cm; \( P = 0.0001 \)) and those movements that could not be attributed to an identifiable pressure pattern (13.5 ± 0.6 cm; \( P = 0.0001 \)). Nonpropagating pressure activity was sometimes associated with a small antegrade movement followed by a retrograde movement (Fig. 4).

Propagating Sequences: Possible Determinants of Propulsion

The manometric tracing revealed a total of 191 propagating sequences (antegrade and retrograde) in the six subjects over the 8 h of scintigraphic recording (Table 2). We were unable to determine whether 61 (32%) of propagating sequences were correlated with movement of luminal content because the isotope had not reached the region of the colon in which pressure sequences occurred. Of the remaining 130 propagating sequences, only 47 (36%) were seen to be propulsive. Thirty-two of these forty-seven propagating sequences propelled isotope over the full distance of the propagating sequence (complete transport); the distance of isotope transport was less than the distance of sequence propagation in the remaining fifteen sequences. In the case of incomplete transport, escape generally occurred between the proximal transverse and proximal descending colon (Fig. 2). Hence, of the sequences for which it was possible to monitor movement of luminal content, only 31% of antegrade propagating sequences and 10% of retrograde sequences were propulsive for the entire extent of the propagating sequence and 64% of propagating sequences caused no discernible propulsion of content (Table 2).

There were striking differences in the regional distributions of propulsive and nonpropulsive propagating sequences related to nonpropagating activity (12.8 ± 0.32).246 on June 25, 2017 http://ajpgi.physiology.org/ Downloaded from http://ajpgi.physiology.org/
sequences. There was a highly statistically significant regional influence on the proportions of propulsive and nonpropulsive propagating sequences originating at each colonic site ($P = 0.0003, \chi^2$; Fig. 5). For example, 86% of propagating sequences originating in the ceco-ascending colon were propulsive whereas only 30% of propagating sequences originating at or distal to the hepatic flexure (region 3) were propulsive of content.

Fig. 3. Pressure tracing and corresponding scintiscans showing clear correlation between a propagating sequence and a discrete (asymptomatic) movement of isotope from cecum to sigmoid colon in one movement. Vertical arrows linked with individual scintiscan images correspond to time along horizontal axis at which acquisition of particular scintigraphic frame was completed. Each small arrowhead indicates location of manometric side hole from which corresponding pressure trace was recorded. In proximal and midcolon (channels 2, 3, 4 from top) there is a close temporal relationship between movement of isotope and onset of propagating pressure wave upstroke. When pressure wave reaches splenic flexure, however, entire descending colon is seen to expand to accommodate isotope, consistent with loss of lumen occlusion at this region. Pressure waves in channels 5 and 6 do not appear to correspond to lumen occluding contractions. Note also that propagating pressure wave amplitudes in channels 3 and 4 are only 30 and 39 mmHg, respectively, yet motor pattern is clearly propulsive.

Fig. 4. Scintiscans and corresponding pressure traces from left colon showing to-and-fro motion of isotope over a short segment of colon in response to nonpropagating pressure activity. From 1st ($t = 0$) to 2nd ($t = 30$ s) scintiscans there is a small net movement of isotope from proximal to middle descending colon. From 4th ($t = 90$ s) to 5th ($t = 120$ s) scintiscans there is a small retrograde isotope shift from middle descending colon to splenic flexure.
Although propagating pressure wave amplitude overall was not regionally dependent (see Propagating Sequences), mean propagating pressure wave amplitudes within propulsive propagating sequences were significantly greater than those within nonpropulsive propagating sequences \( (P = 0.0001) \) (Fig. 6A). This difference was more marked in the proximal colon than it was in the distal colon. The extent of propagation by propulsive propagating sequences was significantly greater (41 ± 6 cm) than that of nonpropulsive propagating sequences (27 ± 2 cm) \( (P < 0.05) \). Mean propagating pressure wave conduction velocities within propulsive propagating sequences were significantly slower than those within nonpropulsive propagating sequences \( (P = 0.02; \text{Fig. 6B}) \). Comparison of mean pressure wave velocity with likelihood of propulsion yields a highly significant negative linear correlation \( (r = 0.89; R^2 = 0.78; P = 0.007) \).

Of the 15 antegrade propagating sequences that demonstrated incomplete transport, 11 had a conduction velocity that exceeded our upper limit of normal in the region of the colon where isotope escape was seen to occur (Figs. 2 and 7). In two of these instances the propagating pressure waves transformed into synchronous pressure waves in the vicinity of the region of isotope escape (Fig. 8).

Correlation of Sensations With Motor Events

Sensations reported by some of the 11 subjects included passage of flatus, urge to pass flatus, “rumbling,” or a sense of “air movement” in the abdomen. None of the study population defecated or reported an urge to do so. Subjects commonly reported the passage of flatus in the early morning, and these events were sometimes associated (sensation recorded within 1 min of onset of propagating sequence) with propagating sequences or with low-amplitude synchronous pressure waves.

Table 2. Relationship between PSs and isotope movement in 6 subjects

<table>
<thead>
<tr>
<th></th>
<th>Antegrade PSs</th>
<th>Retrograde PSs</th>
<th>All PSs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonpropulsive PSs</td>
<td>48 (53.3%)</td>
<td>35 (89.7%)</td>
<td>83 (63.8%)</td>
</tr>
<tr>
<td>Propulsive PSs</td>
<td>43 (47.7%)</td>
<td>4 (10.2%)</td>
<td>47 (36.2%)</td>
</tr>
<tr>
<td>Complete transport</td>
<td>28 (31.1%)</td>
<td>4 (10.2%)</td>
<td>32 (24.6%)</td>
</tr>
<tr>
<td>Incomplete transport</td>
<td>15 (16.6%)</td>
<td>0 (0)</td>
<td>15 (11.5%)</td>
</tr>
<tr>
<td>PSs in regions occupied by isotope</td>
<td>91</td>
<td>39</td>
<td>130</td>
</tr>
<tr>
<td>PSs in regions not occupied by isotope</td>
<td>44</td>
<td>17</td>
<td>61</td>
</tr>
<tr>
<td>Total PSs</td>
<td>135</td>
<td>56</td>
<td>191</td>
</tr>
</tbody>
</table>

Values are no. of PS recorded over 8 h; nos. in parentheses indicate % of PSs recorded in region occupied by isotope.
waves usually recorded across three or more distal pressure channels. These two patterns were the only motor patterns that we could confidently associate with sensations. The number of episodes of sensations reported varied widely among subjects, ranging from 7 to 37. The correlation of sensation reports with an unequivocal pressure phenomenon ranged among subjects from 6 of 31 (19%) to 7 of 8 (88%) sensations. The proportion of sensation episodes related to propagating sequences ranged among different subjects from 9 to 46%, whereas the proportion related to propagating sequences with amplitudes ≥90 mmHg ranged from 0 to 36%.

**DISCUSSION**

This study shows that the majority of discrete movements of colonic content are associated with measurable pressure events, both propagating and nonpropagating. It demonstrates a preponderance of nonpropagating pressure events in the distal colon and a marked regional variation in the quantity, manometric characteristics, and propulsiveness of propagating sequences. Two-thirds of propagating sequences are nonpropulsive of content, and one-third of the remainder are only partially propulsive. Compared with the distal colon, the proximal colon displays more frequent propagating sequences, a greater proportion of which are propulsive in nature. Factors that are associated with propulsiveness of a propagating sequence include proximity of site of origin to the cecum, lower propagation velocity, and higher amplitude.

Advances in our understanding of the relationship between pressure and flow of colonic content are important to a better understanding of disorders of stooling habit. The strength of the present study lies in the level of temporal resolution with which we were able to identify individual movements of colonic content. This enabled us to determine with a level of precision whether a temporal relationship existed between such movements and defined pressure patterns. We were able to attribute the phenomenon of propulsion to a subset of propagating sequences by virtue of a close temporal relationship between discrete isotope movements and the onset of component propagating pressure waves within a propagating sequence. The certainty of this association is inevitably greatest when propagation of pressure waves parallels motion over longer distances. Coupled with the relative infrequency of both isotope motion and propagating sequences, it is with a high degree of certainty that we can link these phenomena causatively.

![Fig. 7. Example of incomplete isotope transport. In this instance propagating sequence is seen to transport a large amount of isotope from ascending colon to descending colon. At level of proximal descending colon, pressure wave is seen to accelerate and "overrun" tail of isotope column (between channels 6 and 7 from top). As a result, some of the isotope column continues to fill distal descending colon but a large portion of it is left behind in proximal descending colon. Vertical arrows linked with individual scintiscan images correspond to times on manometry traces at which acquisition of particular scintigraphic frame was completed; small arrowheads indicate locations of manometric side holes that correspond to attached pressure trace.](image-url)
The marked regional variation in the frequency, extent of propagation, and conduction velocity of propagating sequences in general, as well as the observation that propagating sequences are responsible for discrete movements of content over greater distances than nonpropagating activity, predicts that the proximal colon would be more consistently and frequently propulsive than the distal colon. Our direct scintigraphic observation of movements of colonic content supports this because 86% of sequences originating in the cecum-to-ascending colon were propulsive, compared with only 30% of sequences originating distal to the ascending colon. All of the determinants of propulsion by a propagating sequence remain unknown. However, we can say from the data obtained in this study that region does influence propulsive qualities, that a number of potentially relevant propagating sequence variables show marked regional variation, and that both low conduction velocity and high amplitude of propagating sequences are important for propulsion.

The overall functional consequence of these findings is that the propagating sequence is a relatively inefficient propulsive mechanism much of the time and the relative effectiveness of this particular propulsive mechanism progressively diminishes toward the distal colon. The majority (64%) of propagating sequences were not propulsive of isotope and roughly one-third of propulsive propagating sequences were only partially so. The likelihood of failure of propulsion was greatest in the middle and distal colon. If we accept that the functions of the ascending and transverse colon are storage, mixing, and absorption (7, 14, 23, 31), then the high proportion of nonpropulsive sequences and the relative rarity of effective propulsion beyond the splenic flexure are consistent with these functions. Our observations are very similar to those of a previous radiological study that noted that the majority of migratory contractions originated proximal to the splenic flexure and most terminated between the middle transverse and descending colon (37). Additionally, we have shown that the likelihood of propulsion is also low in sequences that do propagate to the distal colon. In other words, this combination of characteristics means that the majority of propagating sequences do not pose a challenge to continence. In contrast, the propagating sequences that are associated with defecation probably

Fig. 8. Pressure traces and corresponding scintiscans showing isotope movement ahead of a propagating sequence resulting in effective propulsion through proximal colon but failure of propulsion with isotope escape in proximal descending colon. In this example, propagating sequence terminates and transforms into an array of synchronous pressure waves between proximal descending (channel 6 from top) and sigmoid colon (channel 8). This corresponds to segmentation of isotope column in descending colon and incomplete transport at this site.
demonstrate the property of propulsion in the proximal and in the distal colon, as suggested by scintigraphic monitoring during defecation (25). Although possible, it is unlikely that failure of detection of isotope movement in areas of overlapping colon (flexures and sigmoid) accounts for significant numbers of these nonpropulsive propagating sequences. If this were a significant technical limitation, these anatomic areas would be expected to show high rates of focal nonpropulsive sequences rather than the observed steady decline across the colon.

There are likely to be many other factors that influence propulsion such as fecal viscosity, colonic wall characteristics such as tone and colonic capacitance, and shear forces with content (18, 31, 35, 36). Movements of colonic content are a result of an interplay among all these and other as yet unknown factors. For example, it is not clear why 64% of all propagating sequences observed in this study were nonpropulsive whereas many propagating sequences of comparable amplitude, velocity, and region of origin were propulsive. It is noteworthy, for example, that propagating pressure waves with an amplitude <20 mmHg can be propulsive in some propagating sequences but not in others. Although group mean differences in amplitude are evident between propulsive and nonpropulsive propagating sequences, the part played by low propagating pressure wave amplitude in loss of propulsion appears to diminish distally. For example, the group differences in propagating pressure wave amplitude between propulsive and nonpropulsive propagating sequences are more apparent proximally. Furthermore, the association between partial failure of propulsion by propagating sequences and low amplitude is less impressive than its association with high velocity in the distal colon. Although high conduction velocity or synchronicity seem to be strongly associated with isotope escape, there must also be additional factors to account for the one-third of propulsive propagating sequences that demonstrate partial failure of propulsion en route. It might be argued that the wide variability in propagation velocities observed could account for inappropriate classification of potentially unrelated pressure waves as propagating sequences and thereby account for the relatively high proportion of these sequences that were nonpropulsive of content. We think this is most unlikely because propagating sequences with velocities as low as 0.2 cm/s and as high as 12 cm/s were clearly seen to propagate long distances, at times in complete isolation from the potential confounder of adjacent repetitive phasic activity, and the reproducible acceleration of pressure waves as they propagate distally is the main determinant of the overall variance in velocity. Although region-specific mean velocities did vary widely from 0.95 ± 0.13 cm/s in the proximal colon to 7.58 ± 2.49 cm/s in the distal colon, it can be seen clearly that this variation is region dependent and that the variation within any particular region is no greater than that reported by others (24).

Our findings may not necessarily be extrapolated to the movement of solid or semisolid fecal material, because we used a liquid isotope marker in these studies. However, the marker was instilled into the cecum, itself a liquid milieu, and the subsequent mixing and handling of the marker by the colon should have rendered it a consistency similar to that of the native fecal matter in any particular region. Our subjects were necessarily semirecumbent throughout the study, and prolonged immobility may have influenced the quantity of motor patterns. Studies were performed after bowel preparation. However, the effect of bowel preparation on the fundamental patterns of propagating sequences may not be great (24), and the correlative studies with isotope transit commenced 40 h after bowel preparation. Although this should have given sufficient time for substantial natural colonic filling (22, 26, 31), unrecognized effects on stool consistency, volume, and bacterial composition cannot be ruled out. At the low perfusion rate used the catheter delivered a total of 2,592 ml of water throughout the colon per 24 h. This volume is well within the normal absorptive capacity of the healthy colon, which, in response to a slow, constant fluid infusion of this type, can accommodate a net absorption of water of 5–6 l/day (9, 28). Furthermore, cecal fluid infusion rates greater than that of the present study have been shown not to influence proximal colonic transit of either liquids or solids (30). These data therefore suggest that any effect of the perfusate, if present, would be minimal.

The present study failed to identify a responsible pressure wave in association with 40% of isotope movements. As some of these movements were over short distances only, it is possible that the 10-cm inter-side hole distance used in our manometry catheter might be too great to capture all motor events confined to shorter segments of colon. This issue could be resolved by adoption of more closely spaced side holes. It is also possible that subtle pressure gradients between adjacent regions or other forces are operative that are capable of effecting transport but that are undetectable by intraluminal manometry. By our definitions, isotope movements that were not attributable to a defined pressure event were occurring in a region in which the pressure change was <5 mmHg above baseline. Within this low pressure range it would be difficult to be certain that real pressure differences, distinct from any baseline changes, could be reliably discerned to attribute movements to subtle changes in pressure gradient between adjacent regions. It is also possible that segmental colonic shortening, perhaps facilitated by haustra, may be associated with fecal movement and cause much lower changes in intraluminal pressure than those associated with radial contractions of the colonic wall (13). We were not able to detect segmental shortening scintigraphically in the present study. Nevertheless, these arguments do not detract from the observations on the functional significance of the large number of pressure waves that were detected by our manometric technique, which did detect pressure waves responsible for movement of isotope over greater distances. All subjects in the present study were young, healthy males. Although subsequent studies in males...
and females with normal bowel habits have not demonstrated significant gender differences (1), the findings of the present study are not necessarily applicable to the aged or to females.

Previous scintigraphic (29) or combined scintigraphic and manometric studies (4, 15, 27) examined discrete movements of colonic content. Picon et al. (29) studied both left and right colonic transit using a dual-isotope technique. They found a meal-stimulated net outflow from the ceco-ascending colon but not from the rectosigmoid and speculated that the paucity of antegrade flow in the rectosigmoid may relate to the relative predominance of nonpropagating activity in the rectosigmoid.

The present study confirms the relative preponderance of nonpropagating activity and paucity of propagating activity in the rectosigmoid. In the rectosigmoid, the paucity of antegrade flow as originally postulated by Connell (8). This view is supported by combined scintigraphic and manometric studies of the left colon showing that the gradient in averaged postprandial motility indexes between descending and transverse colonic regions correlates with net retrograde isotope movement between these regions (4, 27).

Retrograde movement of proximal colonic content has been long recognized in the human (10, 11, 33). In the present study, retrograde propagating sequences were largely confined to the proximal colon and were far less prevalent than antegrade propagating sequences. Only 10% of retrograde propagating sequences were associated with isotopic movements, usually over short distances, and nonpropagating activity was also capable of causing small retrograde movements.

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