ANNALS OF SURGERY
Vol. 218, No. 6, 761–768

Rectal Wall Contractility in Healthy Subjects and in Patients with Chronic Severe Constipation

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Objective
The aim of this study was to identify differences in rectal wall contractility between healthy volunteers and patients with chronic severe constipation.

Summary Background Data
Whether motor function of the rectum contributes to slow-transit constipation is unknown. Measurements of rectal contractility have been performed traditionally with perfused catheters or microtransducers. The rectal barostat is a new technique that quantifies the volume of air within an infinitely compliant intrarectal bag maintained at constant pressure; decreases in bag volume therefore reflect increases in rectal muscular contractility (tone). Increases in volume reflect decreased contractility.

Methods
Fifteen healthy volunteers (ten women and five men; mean age, 36 years) and eight patients (seven women and one man; mean age, 44 years) were studied. Barostat recordings were made for 1 hour before and after a meal. Randomly, neostigmine (0.5 mg) or glucagon (1 unit) was then given intravenously. After 1 hour, the other medication was given.

Results
The fasting rectal volume was similar in the patient and control groups (113 ± 7 mL *vs.* 103 ± 4 mL, respectively; $p > 0.05$). Compared with controls, constipated patients had a significantly lower reduction in rectal volume after a meal (constipated, 35 ± 8% *vs.* controls, 65 ± 7%; $p < 0.05$) and after neostigmine administration (constipated, 39 ± 6% *vs.* controls, 58 ± 6%; $p < 0.05$). Moreover, constipated patients had a smaller increase in rectal volume after glucagon administration than did controls (28 ± 6% *vs.* 64 ± 18%, respectively; $p < 0.05$.

Conclusions
Changes in rectal wall contractility in response to feeding, a cholinergic agonist, and a smooth muscle relaxant were decreased in constipated patients. These findings suggest that an abnormality of rectal muscular wall contractility is present in constipated patients.

The pathophysiology of chronic constipation is incompletely understood. On the one hand, structural and metabolic causes are easy to identify and to correct. On the other, patients without such disorders who nonetheless are constipated have abnormalities of motor function, such as slow-transit constipation[1] and/or disordered defecation.[2,3] Comprehensive anorectal and colonic physiologic testing dictates appropriate surgical intervention for colonic dysmotility or behavioral modification for disordered defecation.[4–6]

Whether motor dysfunction of the rectum contributes to slow-transit constipation is unknown. Measurements of rectal motor events have been performed traditionally using intraluminal perfused catheters or microtransducers. However, an electronic barostat placed into the stomach,[7] colon,[8] and rectum[9] has demonstrated variations in muscular wall contractility (tone) and contractions not associated with changes in intraluminal pressure.

The barostat was developed to measure changes in gastric intraluminal volume directly, thus quantifying muscular wall contractility (tone) indirectly.[7] The barostat maintains a constant pressure within an infinitely compliant bag such that, when contraction of the viscus occurs, the barostat removes air from the bag, allowing the pressure to remain constant. Alternatively, when the viscus relaxes, air is injected into the balloon. Changes in barostat volume are inversely related to the contractile state of the rectal muscular wall,[9] with rectal wall tone being defined as the resistance of the wall to passive stretch.[9]

The aims of this study were to quantify variations in the contractile state of the rectal wall (tone) using an electromechanical barostat in healthy controls and in patients with profound slow-transit constipation. The hypothesis was that patients with slow-transit constipation might have abnormalities of rectal wall contractility that could be identified and quantified by the barostat.

MATERIALS AND METHODS

Volunteers and Patients

Fifteen healthy volunteers (five men and ten women; mean age, 36 years) without gastrointestinal symptoms and eight patients (seven women and one man; mean age, 44 years) with a history of chronic severe constipation participated in the study after giving informed written consent. Recruitment of the 15 healthy volunteers was by public advertisement. All healthy subjects had a normal bowel habit (varying between three stools/day to three stools/week). All women of childbearing potential required a negative serum pregnancy test 24 hours before participation in the study.

Table 1. CONSTIPATED PATIENT CHARACTERISTICS

Characteristic	No. of Patients (n = 8)
Diagnosis	5 STC 1 PFD 2 Combined
Symptom duration (yr)	
Mean ± SD	24.5 ± 12.9
Range	4–40
Stool frequency (no./wk)	
Mean ± SD	1.3 ± 1.0
Range	0.25–3.5
Laxative use	8
Enema use	2
Manual disimpaction	2

STC = slow transit constipation, PFD = pelvic floor dysfunction, Combined = slow transit constipation and pelvic floor dysfunction.

The eight patients with known chronic severe constipation were contacted through the mail for study participation. The characteristics of the patient study group are listed in Table 1. Each patient had previously (on a separate day) undergone proctoscopy and contrast enema to exclude mechanical causes of constipation. Physiologic testing included measurement of colonic transit time, anorectal manometry with measurement of the rectoanal sphincter inhibition response, defecography with calculation of the anorectal angle, scintigraphic rectal emptying, balloon expulsion, and electromyography.[4] The results of these tests are shown in Table 2.

Electromechanical Barostat

The barostat is a sensitive strain gauge linked by an electronic relay to an air-injection system with a 900-mL reservoir capacity (Fig. 1). An operating pressure may be selected between 0 and 15 mmHg. Incremental changes in pressure as low as 0.25 mmHg can be recorded above and below preset values by withdrawing or injecting air, respectively. The maximal air flow rate is 25 mL/sec with a lag time for barostat activation of less than 5 msec. The rectal balloon volume was calculated electronically by using predetermined excursion of the bellows within the reservoir chamber.[7–9]

Using a double-lumen 16-French polyvinyl tube (Salem sump, Argyle, St. Louis, MO), the two lumens are

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Accepted for publication April 21, 1993.

Table 2. PHYSIOLOGIC TESTING RESULTS IN THE CONSTIPATED PATIENTS

Patient No.	CTT (hr)	ARM	RAIR	SE (%)	BE	EMG	ARA	PD (cm)	Diagnosis
1	97	NL	+	72	NL	*	NL	3.3	STC + PFD
2	104	NL	+	42	NL	—	NL	0	STC
3	24	NL	+	64	†	*	‡	0	PFD
4	130	NL	+	84	NL	NL	NL	2.1	STC
5	122	NL	+	75	NL	NL	NL	3.8	STC
6	133	NL	+	49	NL	NL	NL	2.8	STC
7	124	NL	+	70	NL	*	NL	0.6	STC + PFD
8	75	NL	+	70	NL	—	NL	1.1	STC

CTT = colon transit time (NL = 35 hr[4]), NL = normal, ARM = anal rectal manometry, RAIR = rectal-anal inhibition response, SE = scintigraphic expulsion test (NL >65%[4]), BE = balloon expulsion test, EMG = electromyography of the external anal sphincter, ARA = anorectal angle, PD = perineal descent during defecation (normally >1 cm[4]).
* Paradoxical increase in external anal sphincter motor activity with straining.
† Patient required 521 g of weight before expelling balloon (NL 0–300 g).
‡ Anorectal angles during rest, squeeze, and defecation were 94°, 84°, and 95°, respectively.

connected to the barostat strain gauge and air-injection system, respectively. An ultrathin polyurethane bag (Mobile Chemical, Pittsford, NY) is hermetically sealed on the distal end of the tube. The bag has a maximal potential diameter of 12 cm and a length of 15 cm; the maximal capacity exceeded 900 mL. A soft flexible 16-gauge rubber catheter is placed into the barostat balloon to enable passage through the anal canal and into the rectum. Calibration at room air within the range of inflation volumes using 30-mL increments of air reaching a volume of 1100 mL demonstrated that the pressure in the bag remained at zero. After insertion, the barostat withdraws air to maintain a constant pressure within the bag when the rectum contracts; conversely, when the rectum relaxes, air is injected into the bag.

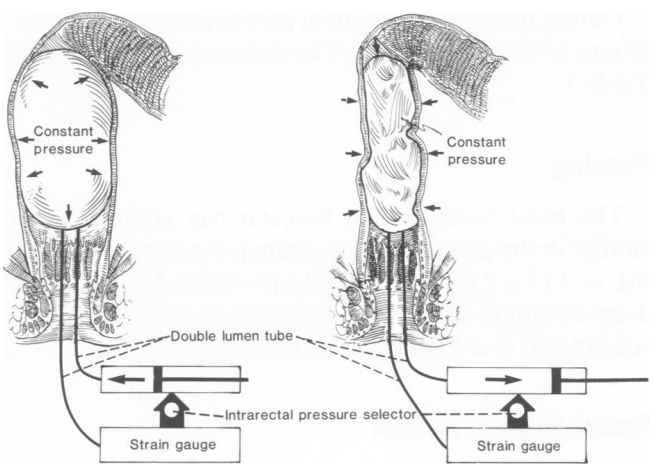

Figure 1. Diagram of the barostat assembly. The device maintains a constant pressure within the intrarectal balloon. The system injects air when the rectum relaxes (left) and aspirates air when the rectum contracts. Reprinted with permission from Bell AM et al.[9]

After insertion of the bag into the rectum, pressure and volume recordings are obtained on a six-channel strip chart recorder (Honeywell, Denver, CO). The channels are simultaneously analyzed on a AST 286 microcomputer (AST Research, Irvine, CA) at a frequency of 4 Hz using ASYST software and a 16-channel analog-to-digital conversion board (DAS-16G, Metrabyte, Taunton, MA).

Perfused Manometry Assembly

Simultaneous manometric recordings were obtained with a triple-lumen tube assembly with an outer diameter of 2.5 mm. Each lumen was perfused at a rate of 0.1 mL/min with distilled water using a pneumohydraulic perfusion.[10] Each lumen opened as a side hole 5-cm apart with the most distal lumen at the catheter tip.

Conduct of the Study

This study was approved by the Mayo Institutional Review Board, and all participants signed informed con-

Table 3. EFFECT OF FEEDING, NEOSTIGMINE, AND GLUCAGON ON BAROSTAT RECORDINGS

	Intrarectal Volume		
Group	Fed (% decrease)	Neostigmine (% decrease)	Glucagon (% increase)
Controls	65 ± 7	58 ± 6	64 ± 18
Constipated	35 ± 8*	39 ± 6*	28 ± 6*

Values are mean ± SEM.
* $p < 0.05$.

sent. Participants presented to the Clinical Research Center after a 12-hour fast. The rectum was evacuated with a phosphate enema (American Hospital Supply, McGaw Park, IL). After 1 hour, the study was commenced.

With the patient in the left lateral decubitus position, the lubricated and tightly folded barostat bag was introduced through the anus. Black markings on the external aspect of the device permitted recognition of catheter migration and rapid correction. In addition, the manometric catheter assembly was positioned inside the rectum alongside the barostat bag such that side holes rested at 5, 10, and 15 cm from the anal verge.

The studies were conducted in the prone position in a 20° Trendelenburg position to reduce the gravitational effects of the abdominal organs. A pneumograph belt positioned around the lower chest recorded respiratory activity. Disturbances of rectal motility from unnecessary movements (*i.e.*, coughing or restlessness) were continuously monitored by an investigator.

The barostat bag was initially inflated to a pressure of 20 mmHg to facilitate unfolding of the bag and then deflated. The bag was then again inflated with air in 1-mmHg increments until a minimum distending pressure (MDP) was identified. This was determined as the pressure at which respiratory variations were clearly noted from the barostat volume recording or, if respiratory excursions were not evident, the pressure at which the bag volume reached 25 mL. Subsequently, all studies were performed at a barostat pressure of 2 mmHg above the MDP.

Calibration of the device was done while the patient performed a vigorous Valsalva maneuver three times. The rise in intra-abdominal pressure emptied the intrarectal bag and facilitated determining the baseline volume at the operating pressure. This allowed for compensation of the residual gas in the reservoir tank and connecting tubing.

For a period of 1 hour, a fasting recording was obtained. A solid–liquid meal of 750 kcal (53% fat, 35% carbohydrate, and 12% protein) was then ingested. No change in position was permitted during the meal. Postprandial recording was then performed for 1 hour in all individuals. The recordings were then interrupted briefly to permit subjects to change position or void. After a 30-minute period to allow stabilization of the recordings and in random order, an intravenous bolus of either neostigmine (0.5 mg) or glucagon (1 unit) was given. The other agent was then administered 1 hour later.

Data Analysis

Only slow volume changes[9] (changes in intraluminal bag volume occurring over 2 minutes or more) and not rapid volume waves[9] (changes in bag volume lasting longer than one respiratory cycle but < 2 minutes) were analyzed in this study.

The recordings were visually inspected initially for individual patterns of slow volume changes. The data were then transferred to the mainframe computer for digital analysis. Analysis of the summary values of the mean baseline bag volume for fasting *versus* fed states (before and after pharmacologic perturbation) and comparisons of the mean percentages of increase or decrease in pressures between interventions were made with the paired Student's t test.

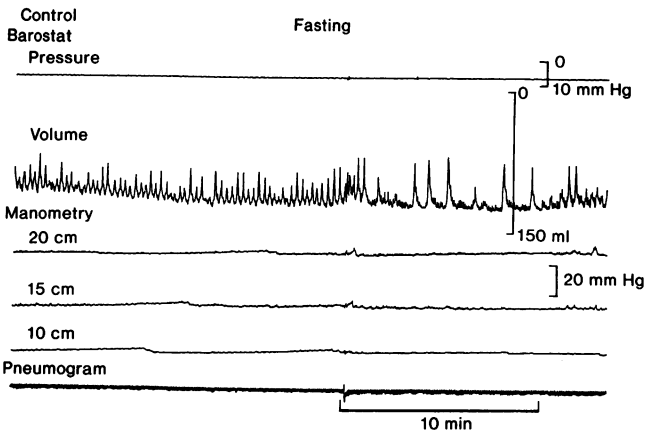

Figure 2. Simultaneous barostat pressure and volume, perfused manometry, and respiratory recordings in a control subject during fasting. The pressure within the barostat bag is constant while the volume increases very slowly (slow volume change). There are multiple rapid volume waves present, each of which represents a decrease in bag volume (*i.e.*, an increase in rectal wall tone). The manometric recording remains quiet.

RESULTS

During this study, no patient perceived inflation or deflation of the barostat bag. The data are summarized in Table 3.

Fasting

The basal fasting rectal barostat bag volumes were similar in the controls and constipated patients (103 ± 4 mL *vs.* 113 ± 7 mL, respectively; $p > 0.05$). Figures 2 and 3 are examples of a fasting recording in a single control subject and in a constipated patient, respectively.

Responses to a Meal

After the meal, controls experienced significantly more reduction in rectal volume than did constipated patients (65 ± 7% *vs.* 35 ± 8%, respectively; $p < 0.05$). Figure 4 demonstrates the prompt response to a meal in

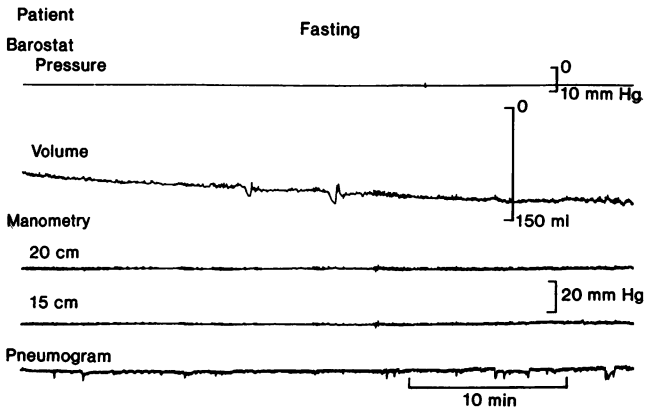

Figure 3. Concomitant barostat pressure and volume, perfused manometry, and respiratory recordings in a constipated patient during fasting. Pressure in the barostat is unchanged while the volume increases very slowly. The manometric recording shows no phasic activity.

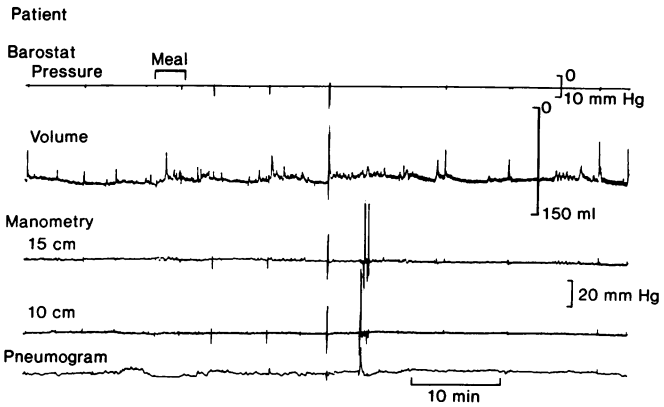

Figure 5. In a constipated patient, the response to a meal with a reduction of barostat volume is less dramatic than in controls. No phasic activity is identified in the manometric recordings.

one volunteer; the volume within the barostat bag decreased to zero over 20 minutes with little concomitant phasic activity recorded manometrically. By contrast, Figure 5 depicts the response to a meal in a constipated subject; the volume within the bag did not change.

Response to Neostigmine

The decrease in mean rectal volume (increased resistance to stretch and increasing tone) in controls after neostigmine administration was 58 ± 6% compared with 39 ± 6% in constipated subjects ($p < 0.05$). Figure 6 illustrates progressive reduction in barostat volume with increased phasic activity in the manometric ports in response to neostigmine in a volunteer. Figure 7 illustrates little or no response by a constipated patient. Two control subjects and one constipated patient noted increased salivation after neostigmine administration.

Response to Glucagon

The mean percent increase in rectal volume (decreased resistance to passive stretch and decreased tone) after intravenous glucagon administration was fully 64 ± 18% in controls; it was only 28 ± 6% in constipated patients ($p < 0.05$). One control patient had nausea after glucagon administration. An example of the rapid increase in intrabag volume and the concomitant reduction in the frequency of rapid volume waves and manometrically recorded phasic activity in a normal subject is depicted in Figure 8. By contrast, Figure 9 demonstrates that the effect of glucagon appeared to be blunted in constipated patients.

DISCUSSION

Although anorectal manometry has characterized contractile activity within the rectum,[10–12] no obvious correlation has been documented between such contrac-

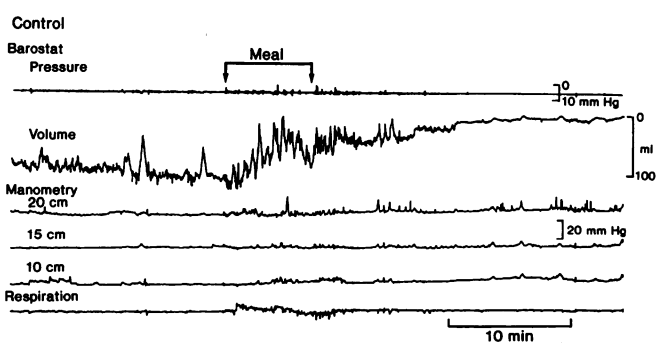

Figure 4. In response to a meal in a control subject, the barostat volume declines progressively. This continues until the volume is zero. Minor phasic pressure activity in the manometric recordings is evident at the onset of the meal.

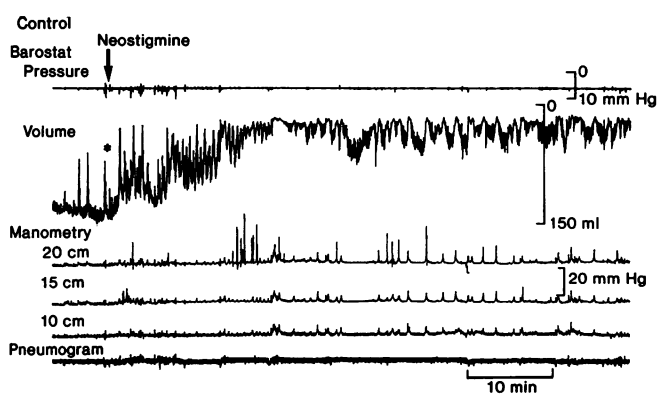

Figure 6. The administration of neostigmine in a control subject causes rapid volume waves, progressive reduction in bag volume (slow volume waves), and an increase in phasic activity recorded manometrically.

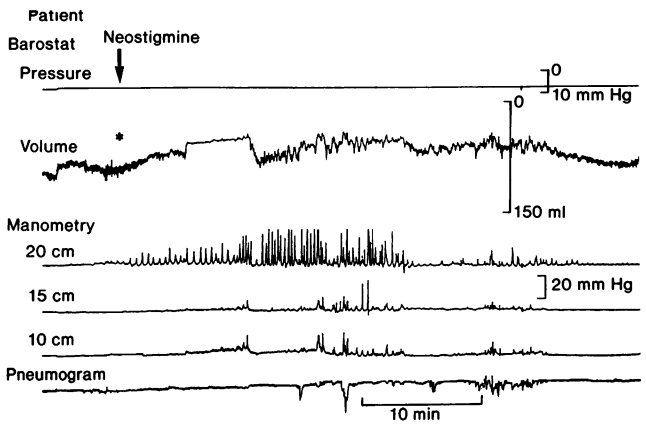

Figure 7. Neostigmine injection in a constipated patient causes a less pronounced reduction in barostat bag volume with fewer rapid volume changes. Phasic activity recorded manometrically is increased.

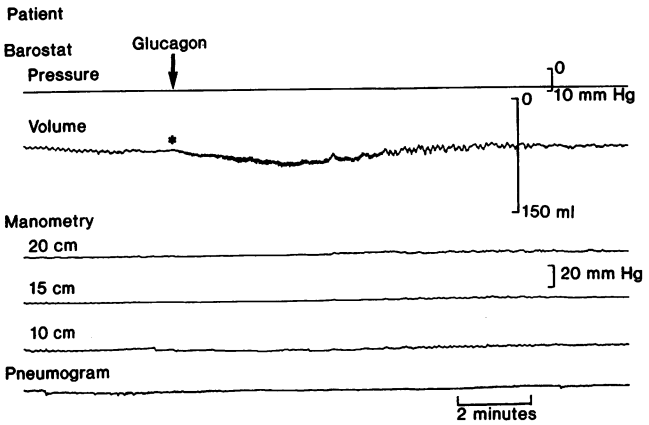

Figure 9. In the constipated patient, glucagon causes a slow increase in intrabag volume lasting 6 minutes after its administration. The manometric recordings are unaltered.

tions and the function of the rectum. The primary role of the rectum is to store its contents at low intraluminal pressure; its role during defecation, whether it is active or passive, is completely unclear. Storage at low pressure is facilitated by the viscoelastic properties of the rectal muscular wall,[2] which can be measured easily, but statically, by plotting the slope of the change in volume over the change in pressure.[13,14] Recently, we measured these changes dynamically[9] using an electronic barostat, developed earlier,[7] that was adapted to study rectal motor activity. We found that the rectal barostat recorded changes in intraluminal volume in response to feeding, neostigmine (a stimulator of smooth muscle contraction), and glucagon (a drug that relaxes smooth muscle). These changes likely represented changes in rectal wall contractility (resistance to stretch and tone). These changes were not manifested manometrically. We further hypothesized that disturbed function of the rectum and colon may be mediated by changes in the contractility of the rectal wall that would be quantified by the barostat.

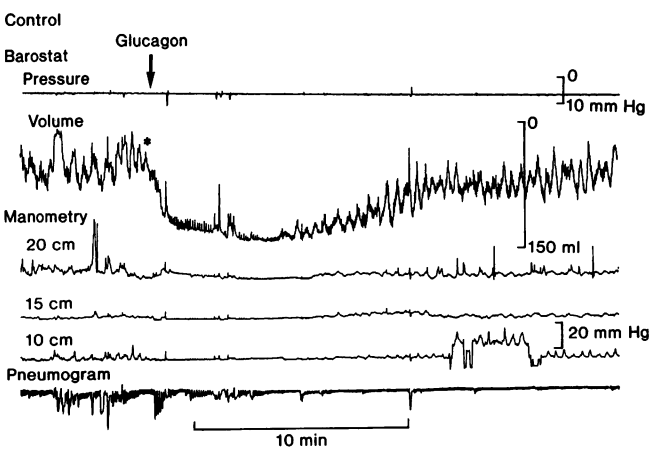

Figure 8. After glucagon administration in a control subject, the barostat bag volume increases while the phasic pressure activity is abolished for 6 minutes. Likewise, the phasic activity recorded manometrically is diminished for a similar period.

In this study, we detected profound differences in the contractile state of the rectal muscular wall between controls and patients with severe constipation. These changes were not demonstrable by conventional manometric recordings.

The most striking difference was the relative paucity in rectal motor events of any type in patients with constipation; although baseline fasting rectal volumes were similar, the magnitude of changes in intraluminal volume in response to a meal, to neostigmine, or to glucagon was significantly less in the constipated patients compared with controls. It appeared as if responses to perturbations were "blunted," such that the rectal wall of the constipated patients could not be stimulated to increase or decrease its tone.

This lack of response may contribute to the problem of constipation. In healthy subjects, the rectal wall increases its tone in response to a meal.[9] If stool is then emptied into the rectum from the more proximal colon when the rectum is in a state of increased tone, then a greater incremental pressure increase occurs, heightening sensation and providing a prompt urge to evacuate. In our constipated patients, however, the rectal muscular wall did not respond to a meal by increasing its tone. The sensation of rectal filling would then be less intense in these patients, and a prompt call to evacuate stool would never be appreciated. This would favor retention of content and constipation.

These results support and extend those of others who used manometric techniques to study rectal motility. One group studied distal sigmoid and rectal pressures af-

ter a meal and neostigmine administration in patients with constipation and diarrhea.[15] They identified no postprandial increase in motor activity in the constipated patients. More recently, others described impaired postprandial rectosigmoid motor function in patients with severe constipation.[16] By contrast, it was found that the early postprandial response of the sigmoid colon in constipated patients was reduced in 16% of patients, normal in 68% of patients, and increased in 16% of patients.[11]

In an animal model, neostigmine initiates high-amplitude propagating contractions in the colon and induces defecation.[12] Colonic smooth muscle contraction is stimulated by neostigmine and blocked by atropine.[17] A defect in cholinergic activity of the colon has been implicated in patients with severe constipation. Injury to the sacral parasympathetic supply to the left colon and rectum causes constipation.[18,19] Reduced cholinergic nerve activity of colonic taenia in response to electrical field activity has also been demonstrated with idiopathic constipation.[20] Our results demonstrated that neostigmine did elicit increased rectal wall tone in healthy subjects and in patients with constipation. However, the degree of the neostigmine response was reduced significantly in the constipated patients. Thus, the reduced rectal tone in the constipated patients may explain their inability to expel stool. Whether a neurohormonal disorder of the rectum exists or prolonged laxative and enema use in constipated patients contributes to this altered response is unclear. Furthermore, because only one patient had pelvic floor dysfunction, differences in rectal tone between patients with slow-transit constipation and pelvic floor dysfunction were not sought.

Glucagon decreased rectal tone in healthy controls, but the magnitude of the response was less in constipated patients. Such impaired distensibility implies the rectum may be unable to function as an effective storage receptacle in constipated patients. Constipated patients are commonly able to retain large rectal volumes without developing a sense of fecal urgency. It is possible that the rectum in constipated patients is unable to relax appropriately in response to glucagon. Thus, because of constraints on the muscle length–tension characteristics, reduced rectal wall stretch may prevent effective propulsion of feces. Interestingly, previous work has shown that initiation of defecation by rectal distension is unlikely to be influenced by glucagon; rather, glucagon reduces resting anal pressure without initiating the rectoanal inhibitory reflex.[21]

Explanations for impaired relaxation and contraction in the rectum of constipated patients are not readily evident. Receptive relaxation of the rectum is under the control of the pelvic nerves.[22] Injury to these nerves in constipated patients has not been demonstrated conclusively. Impaired rectal sensation is also seen with myenteric nerve degeneration in the anorectum from long-term use of laxatives, anticholinergics, or phenothiazines. Furthermore, the role of gastrointestinal hormones in mediating rectal tone remains unclear.

In conclusion, the electronic barostat used in our studies represents a new approach to evaluating the motor characteristics of the rectum in constipated patients. Changes in rectal wall contractility were measured during fasting, after feeding, and after administration of agents that promoted smooth muscle contraction and relaxation. Patients with chronic severe constipation exhibited abnormal rectal contractility during these perturbations compared with healthy volunteers. The pathophysiology of chronic constipation may be related to the contractile state (tone) of the rectal muscle wall and not to phasic contractile activity alone.

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