CASE REPORT

Migrating Action Potential Complexes in a Patient with Secretory Diarrhea

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There is growing evidence that disorders of intestinal motility have an important role in the pathogenesis of diarrhea. Vantrappen and Janssens (1) proposed a classification of small intestinal motor disorders based upon abnormalities in slow wave activity or in well-established motility patterns. Many of these motor disorders were associated with diarrhea. With the exception of a disorder characterized by absence of phase 3 of the MMC in patients with bacterial overgrowth (2) and the motor equivalent of the MAPC in a patient with laxative abuse (3), these motility patterns were recorded in experimental animals by means of electromyographic techniques.

Marlett and Code (4) described in dogs with celiac and superior mesenteric ganglionectomy a nonmigrating phase 3 (pseudofront) that was composed of a series of peristaltic contractions and that was uniformly associated with diarrhea. Mathias and coworkers (5–8) induced in rabbit ileum an abnormal myoelectrical pattern, called the migrating action potential complex (MAPC), by intraileal administration of some diarrheogenic bacteria or their toxins and by perfusion of the ileum with castor oil or ricinoleic acid. These bursts of intensive spiking activity led to stripping contractions that progressed distally and emptied the bowel loop. Another electrical pattern, called repetitive

bursts of action potentials (RBAPs), was observed in ileal loops infected with invasive bacteria such as *Shigella dysenteriae, Campylobacter jejuni,* and some strains of *Escherichia coli* (9–11). The RBAPs were either stationary or migrating distally. Caudally migrating short repetitive bursts of spikes, closely resembling RBAPs, were observed by Atchison et al (12, 13) in conscious dogs exposed to laxatives such as castor oil, phenolphthalein and magnesium sulfate. Finally, Code (14) observed occasionally in dogs a series of powerful peristaltic contractions replacing phase 3. These bursts of contractions, called type II peristaltic contractions, progressed to the terminal ileum with a velocity that was slower than that of the individual pacesetter potentials. This pattern also closely resembles RBAPs.

These diarrheogenic electromygraphic patterns are difficult to identify in the human small bowel because of technical problems in recording the electrical activity simultaneously at different sites for a long period of time. We developed a novel technique of recording small intestinal myoelectrical activity in man. This technique was applied in a patient with secretory diarrhea and in 10 healthy volunteers in order to study diarrhea-associated small intestinal motility patterns.

CASE REPORT

A 70-year-old nun presented with watery diarrhea of three months' duration. At the time the diarrhea developed she had been active as a missionary in Dominica for 30 years. A cholecystectomy had been performed 14 years earlier for lithiasis. She had constipation for many years, but denied the intake of laxatives.

At the time the patient was referred to our outpatient clinic, she was passing up to 15 motions per day contain-

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ing mucus but no blood. She had lost 3 kg of weight. Body temperature and other findings on physical examination were normal. Fecal volumes of 410–480 ml/day were measured. Bile acid loss in the stool was 0.44 mmol/24 hr (normal ≤ 1.12 mmol), and fecal fat excretion was less than 2 g/day. Several stool specimens and duodenal aspirations were free of ova, cysts, and parasites. Stool cultures revealed no pathogenic bacteria. Because all investigations for infectious diarrhea were negative, the patient was admitted to the hospital for additional studies. Proctoscopy with biopsy was normal. Colonoscopy revealed the presence of diverticula in the sigmoid colon; transverse and ascending colon and the terminal 15 cm of the ileum were normal.

Other studies including barium examinations of the small bowel, jejunal suction biopsy, ultrasonography of the abdomen, breath tests for bacterial overgrowth, bile acid loss, and lactose maldigestion were all normal. A detailed investigation for endocrinological disorders or a hormone-secreting tumor was performed. Serum T4, free T4, T3, and TSH were normal. Serum gastrin level was 38 pg/ml (normal range 0–100 pg/ml), VIP was 30 pg/ml (normal range 100 pg/ml), motiline was 259 pg/ml (normal range 0–700 pg/ml), somatostatin 10 (normal range 0–100 pg/ml), glucagon 81 pg/ml (normal range 0–250 pg/ml), and PP was 57 pg/ml (normal range 0–400 pg/ml). The serum calcitonin level and urinary excretion of 5-HIAA, cathecholamines, and prostaglandins were normal. Repeated tests for phenolphthalein, sennosides, sulfates,

and bisacodyl in stools were negative. In the course of the hospitalization, the number of stools spontaneously decreased to three to five per day. Total parenteral nutrition for 48 hr resulted in a significant decrease of fecal volume from ±450 to 180 g/day, suggesting a secretory factor in the pathogenesis of the diarrhea. A specific cause of the secretory diarrhea was not found. The patient was discharged from hospital after 20 days in good clinical condition, having only one to two stools per day. She has remained symptom free up to now without any specific therapeutic measures.

Motility Studies. The electrical activity of the jejunum was recorded by means of a novel recording technique. The probe consisted of a polyvinyl tube with an outer diameter of 6 mm and a length of 300 cm. A small latex balloon that could be filled with mercury or air was attached to the tip of the probe. The tube was introduced via the mouth and could easily be passed through the pylorus and distal duodenum under fluoroscopic control. After the tip of the probe had passed the angle of Treitz, the mercury was removed from the balloon and the probe was allowed to move freely down the intestine. Eight bipolar electrodes were arranged along the tube. The electrodes were built in the rim of a series of suction holes, 10 cm apart. The two discrete conductive surfaces of the electrodes were located at the two poles of the oval suction orifices, which measured 3 and 4 mm (Figure 1). The conductive surfaces consisted of silver powder dispersed in a mixture of tetrahydrofuran and polyvinyl
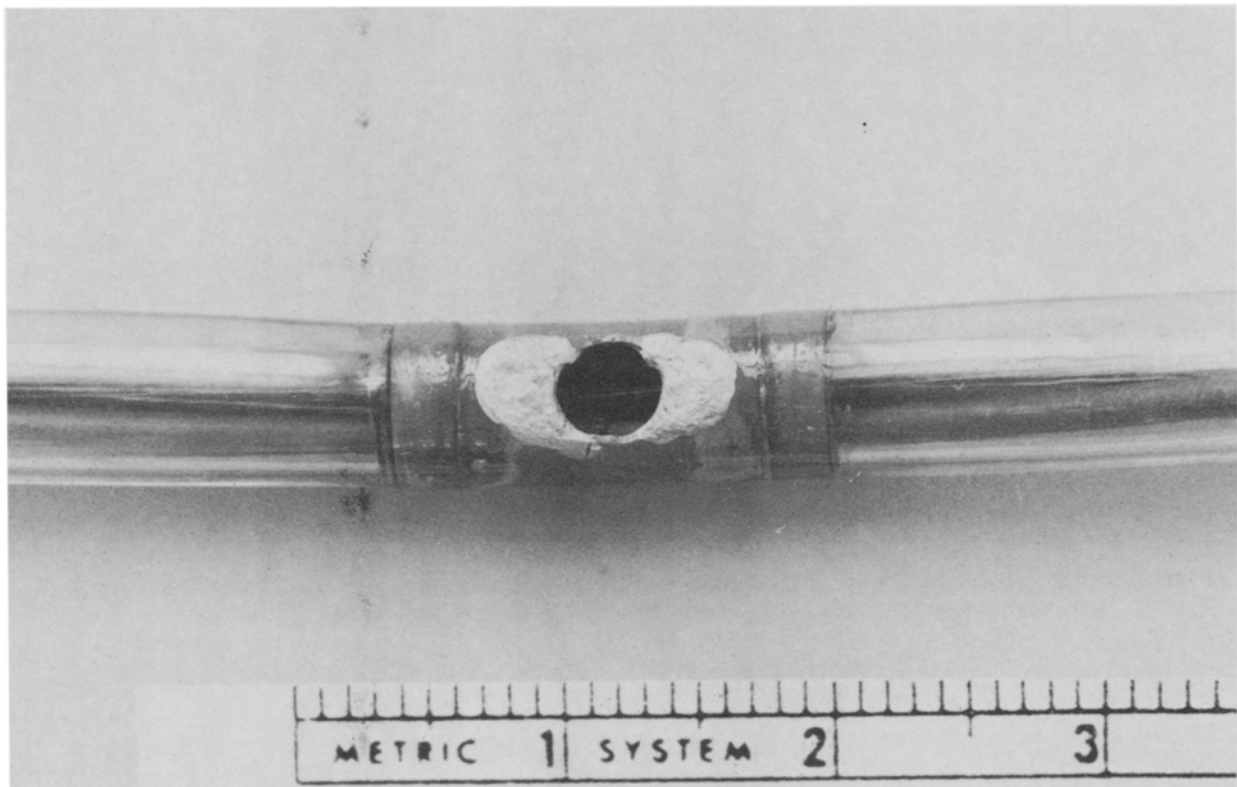

Fig 1. Suction electrode with two conductive surfaces located at the two poles of the oval orifice.
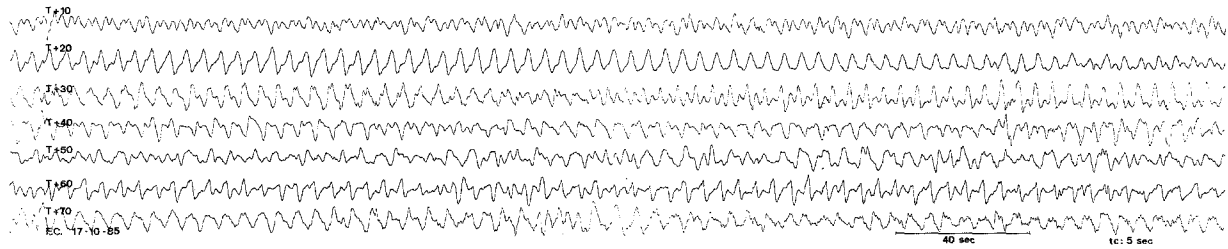
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Fig 2. Continuously recorded slow waves in the jejunum of a normal subject during phase 1 and early phase 2 of the MMC.

chloride and were connected to the exterior with fine insulated copper wires (diameter 100 μm), lying in the lumen of the tube. The strand of 16 copper wires was shielded by polyvinyl tubing (outer diameter 1.2 mm). The electrode wires were fixed to a connector box.

Each pair of electrodes was connected to two different Siemens Fet preamplifiers (amplification: ×10). The time constant of one amplifier was set at 0.03 sec, that of the other was set at 5 sec. The signals were amplified by two eight-channel Siemens-Elema Mingographs 82 with universal amplifiers (type 854) and modifiable external electrical time constant. The time constant was kept at 0.002 sec for spike recording and 5 sec for the recording of slow waves. In this way the electrical activity picked up by each electrode was displayed in two different recordings: one well suited for slow wave activity (Figure 2), the other for spike activity (Figure 3). During recording both the patient and the probe were grounded. To obtain uninterrupted detection of slow waves and spikes, a negative pressure of 25–50 cm water was applied on the proximal end of the probe. The intraluminal electromyographic technique used in this study is well tolerated and can routinely be applied in both volunteers and patients. The probe, which is relatively simple to construct, provides uninterrupted recording of slow waves and spikes at eight or more sites along the small intestine. The recordings provide no major difficulties of interpretation.

RESULTS

In the patient, recordings were made during the period of diarrhea and were repeated after regression of the symptoms. The study started after an overnight fast of 12 hr. The tube was positioned in such a way that the proximal electrode was located at the angle of Treitz and the eighth electrode 70 cm more distally. Recordings were made for periods of

150 min. During phase 2 of the interdigestive myoelectric complex, strong propagated spike bursts occurred at irregular intervals (Figure 4). The amplitude of these bursts was significantly higher than that of the preceding and following spike bursts of phase 2. The strong spike bursts nearly completely obliterated the pacesetter potentials on which they were superimposed. They extended over one to two cycles, lasting for 5.27 ± 0.54 sec (mean ± SEM), and migrated aborally over a distance of 36 ± 11.4 cm (mean ± SEM) with a propagation velocity of 2.84 ± 0.25 (mean ± SEM) cm/sec (Figure 5).

Continuous recordings of slow waves and spikes were obtained in 10 healthy subjects, covering a total of 44 hr. In this control group 38 activity fronts were recorded. Only one MAPC was detected in the 44-hr period. The strong spike burst lasted for 4.5 sec and propagated distally over a distance of 40 cm with a propagation velocity of 2.2 cm/sec.

DISCUSSION

A characteristic electromyographic motility pattern was recorded in a patient with secretory diarrhea of unknown origin. The pattern was identified as a migrating action potential complex, a myoelectric motility pattern first described in isolated and ligated loops of rabbit ileum (5). The motor equivalent of the MAPC has been reported by Mathias et al (3) in a patient with surreptitious laxative abuse. Very recently J. Kellow and S.
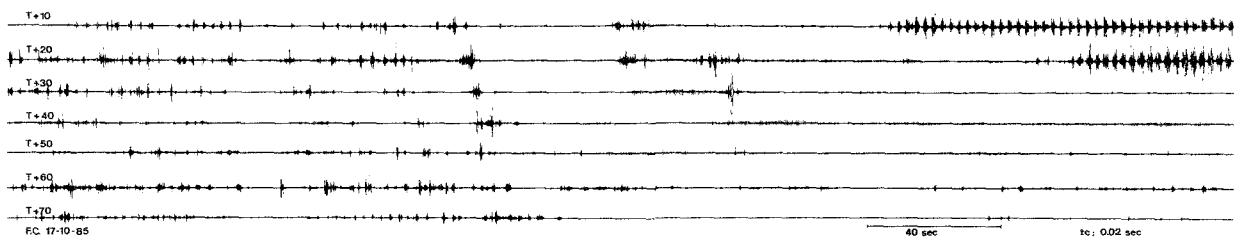

Fig 3. Continuously recorded spiking activity in the jejunum of a normal subject at the end of phase 2 and the start of phase 3 of MMC.
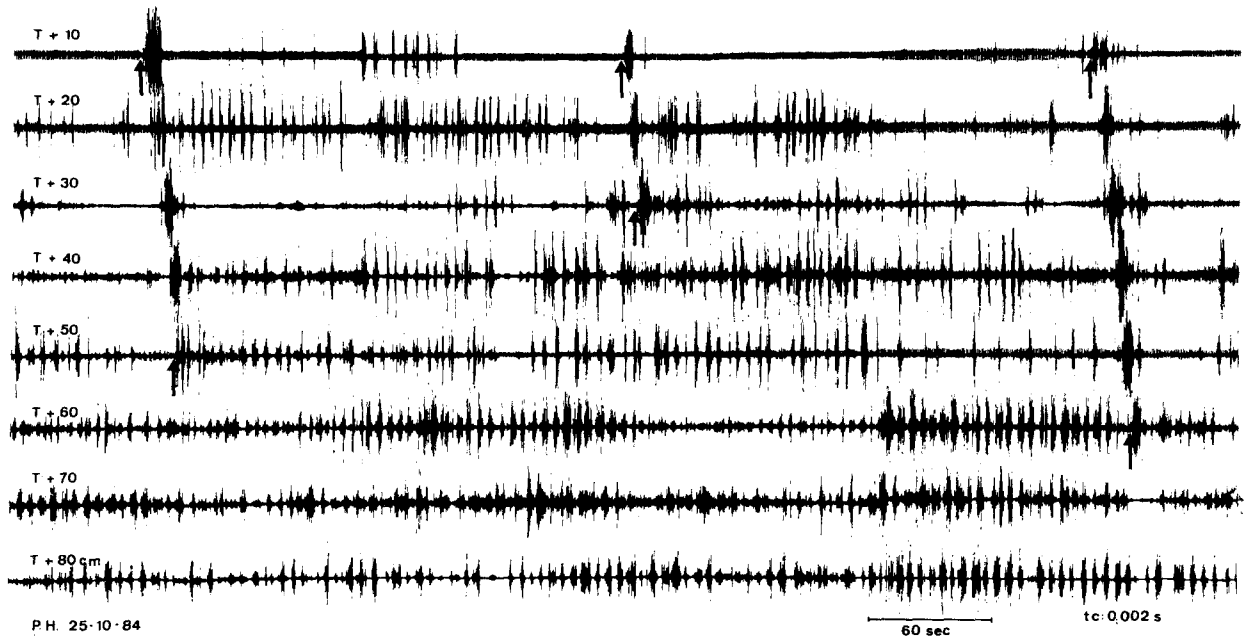
Fig 4. A 9-min segment of the recording of the myoelectrical activity obtained from the jejunum of a 70-year-old female with secretory diarrhea. The electrodes are located 10, 20, 30, 40, 50, 60, 70, and 80 cm below the ligament of Treitz. In addition to the phase 2 activity of the MMC, three bursts of intensive spike activity (arrows) that are migrating in an aboral direction over a distance of, respectively, 40, 20, and 50 cm are seen.

Phillips (15) reported monophasic high-pressure waves extending over 12–48 sec and propagating rapidly (0.6–1.93 cm/sec) throughout long jejunal segments in patients with a still unidentified infectious diarrhea. These manometric complexes, however, have not yet been identified as the motor equivalent of MAPC activity. The MAPC has been identified as a diarrheogenic pattern.

Different mechanisms, including "hypermotility," "hypomotility," increased permeability of the intestinal mucosa, hypersecretion, and malabsorption, alone or in association with each other, may play a role in the pathogenesis of diarrhea. Although the contribution of motility to accelerated transit and diarrhea is largely unknown, it seems logical to assume that an increase in the number of stripping peristaltic contractions, progressing over long segments of small bowel during the interdigestive and digestive phases, will result in an accelerated transit and in an increase in the volume of intestinal contents flowing into the colon, which may favor diarrhea.

A number of myoelectric patterns that are known to be associated with diarrhea have been observed in animals (1, 14). The role of MAPC activity in the pathogenesis of diarrhea is controversial. Intestinal fluid accumulation primarily caused by hypersecre-

tion could stimulate secondary peristalsis. However, Mathias et al (5) showed that cholera enterotoxin stimulates myoelectrical activity and results in propulsive ring contractions in the rabbit ileum that were independent of fluid accumulation in the lumen. This altered myoelectric activity, called migrating action potential complexes, is predominantly induced by noninvasive bacteria such as *Vibrio cholerae* and enterotoxigenic *Escherichia coli* and their heat-labile toxins, including choleragenoid, the 5-beta subunits of choleragen (6, 16), and by exposure of the small intestine to castor oil or ricinoleic acid (11). Although these agents are known to enhance intestinal secretion, the studies of Sinar et al (16), Burrows and Merritt (17) and Schanbacker et al (18) suggest that, in addition to the secretory state, a motility component has a role in the production of these infectious or laxative-induced diarrheas. The observation of Sinar et al that choleragenoid induced MAPC activity without stimulating adenylate cyclase and fluid output indicates that, although secretion and motility may occur at the same time, each process is occurring by different "second messengers" (16, 19). In animals with diarrhea following infection with viral enteropathogens and parasites, a disruption of the normal myoelectrical activity was observed, sug-
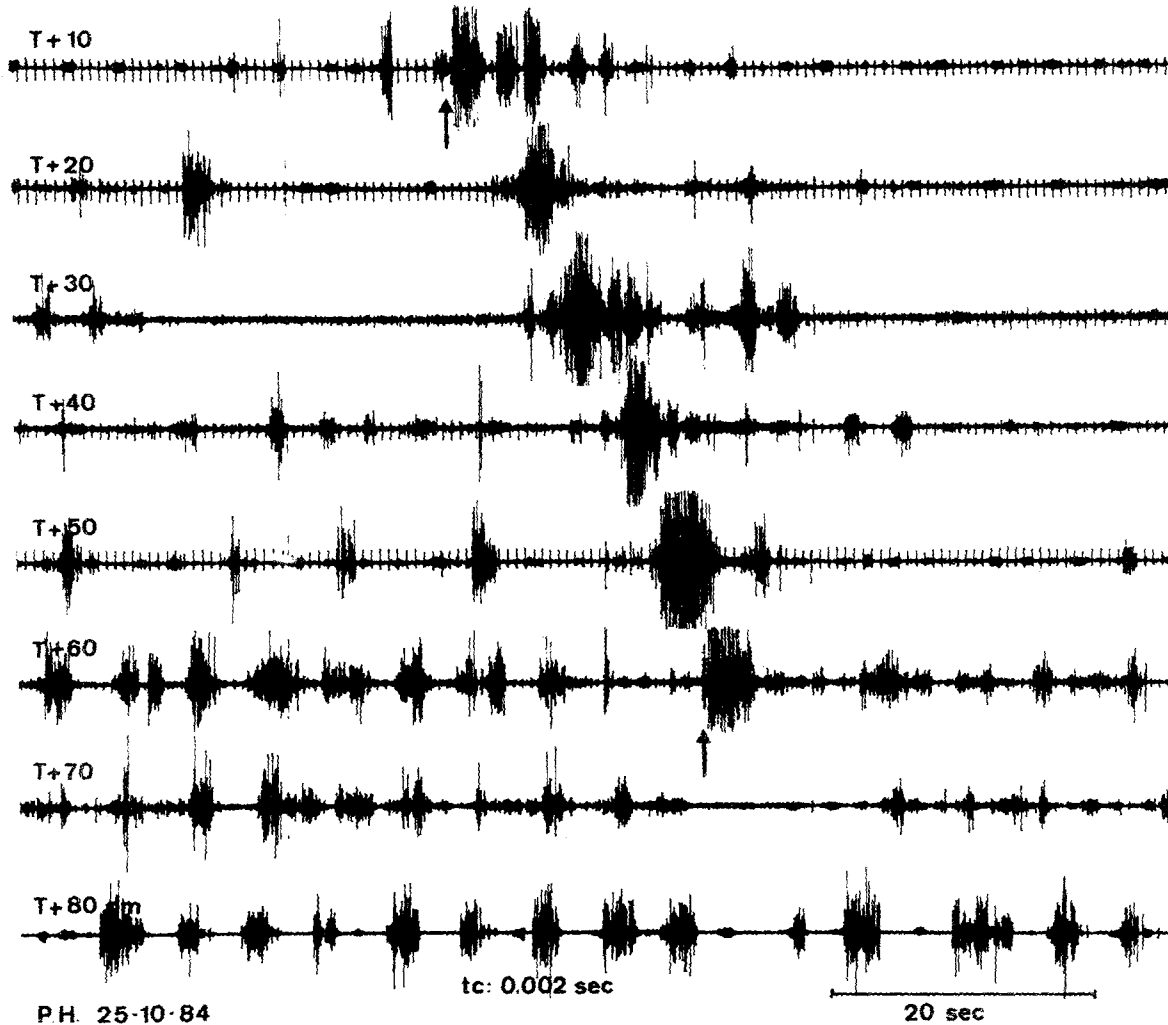
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Fig 5. An intrajejunally recorded migrating action-potential complex (MAPC) in a patient with watery diarrhea after an 8-hr fasting period. The intense spike activity was recorded sequentially over six electrodes located between 10 and 60 cm below the ligament of Treitz. Duration of the complex was 5.5 ± 0.51 sec (mean ± SEM). Mean propagation velocity of MAPC was 2.78 cm/sec.

gesting that motility may contribute to the pathogenesis of infectious diarrhea as well (17, 18).

In patients presenting with spontaneous diarrhea or in volunteers with artificially induced diarrhea, abnormal myoelectrical patterns have not been described. With the development of our novel and simple recording technique, it has become possible to study small intestinal electrical activity in hu-

TABLE 1. PARAMETERS OF SLOW WAVE (SW) AND MIGRATING ACTION POTENTIAL COMPLEX (MAPC)

	Rabbit ileum, live vibrio cholerae [Mathias et al. (5)]	Patient with secretory diarrhea
SW duration (sec)	±4	±5.1
SW propagation velocity (cm/sec)	1.12 (mean, SEM not communicated)	±2
MAPC propagation velocity (cm/sec)	0.85 ± 0.07 (mean ± SEM)	2.84 ± 0.25 (mean ± SEM)
Number of MAPC (per hour)	7.12 ± 3.12 (mean ± SEM)	4 (mean)
Duration of MAPC (sec)	2.5–10 (mean ± SEM not communicated)	5.27 ± 0.54 (mean ± SEM)
Distance of migration of MAPC (cm)	≥2.5 (mean ± SEM not communicated)	36 ± 11.4 (mean ± SEM)

mans. The identification of a characteristic motility pattern in a patient with secretory diarrhea may contribute to the difficult investigation of the role of motility in the pathogenesis of diarrhea in man.

The propagated spike bursts observed in our patient with secretory diarrhea are identical to the MAPCs described by Mathias and coworkers in the rabbit ileum exposed to live *Vibrio cholerae* (Table 1). According to this investigator, the presence of MAPC activity would suggest an infectious cause or surreptitious laxative abuse (3, 8, 11). Similar to the MAPC in experimental animals, the propagated spike bursts recorded in our patient constitute a highly organized and striking pattern that occurs irregularly with widely varying time intervals. It extends over more than one slow wave and migrates distally over long bowel segments, the propagation velocity being that of the slow waves. This motility pattern is very rare in fasted normal volunteers.

The significance of MAPC activity in patients with diarrhea has to be determined. In our patient with secretory diarrhea of unknown origin, the abnormal motility pattern was no longer observed after regression of the symptoms, suggesting an association of this propulsive motility pattern with diarrhea.

SUMMARY

A 70-year-old woman with secretory diarrhea was studied with a novel technique of recording small intestinal myoelectrical activity which allowed us to obtain long, uninterrupted records of slow waves and spikes at eight or more different intestinal levels simultaneously. Typical migrating action potential complexes (MAPCs) were observed, consisting of spike bursts that extended over more than one slow wave and migrated distally at the same propagation velocity as the slow waves. This motility pattern occurred frequently during the period the patient presented with secretory diarrhea and disappeared with the disappearance of the diarrhea. It was observed only once in a series of 10 normal control subjects. This is the first report on MAPC activity in man and on the association of this myoelectrical pattern with secretory diarrhea in man.

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