

## Disorders of Colonic Motility in Patients with Diabetes Mellitus

W.M. BATTLE, M.D., JEROME D. COHEN, M.D.  
AND WILLIAM J. SNAPE, Jr., M.D.

*Division of Gastroenterology, Harbor-UCLA Medical Center, Torrance,  
California*

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Motility disturbances of the colon can give significant symptoms in patients with diabetes mellitus. Constipation is a common complaint in these patients. Diarrhea associated with a generalized autonomic neuropathy can be very troublesome.

There is a disturbance in the gastrocolonic response to eating in patients with diabetes mellitus who have constipation. These patients have no postprandial increase in colonic motility. However, their colonic smooth muscle contracts normally to the exogenous administration of neostigmine or metoclopramide.

Stool softeners used in combination with the smooth muscle stimulants (neostigmine or metoclopramide) are helpful in treating constipation in patients with diabetes mellitus. Diarrhea can be treated with loperamide or diphenoxylate. Biofeedback may be useful in treating incontinence associated with diarrhea in these patients.

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Gastrointestinal motility disturbances are common among diabetic patients [1,2,3]. Many patients are free of significant gastrointestinal symptoms, while others develop disabling syndromes. Esophageal motor dysfunction [4,5], gastroparesis [6], and diarrhea [7,8] have been the most frequently reported and studied intestinal manifestations of diabetes mellitus. Despite the presence of significant symptoms related to colonic dysfunction, the literature on the colonic complications of diabetes mellitus is sparse. In this article we review the clinical manifestations, pathogenesis, and approach to treatment of diabetic colonic dysfunction.

The potential colonic complications of diabetes mellitus are listed in Table 1. Constipation has been cited as the most common gastrointestinal complaint of diabetic patients [1,2,3]. The true incidence is difficult to ascertain compared to the normal population, but severe symptoms have been reported in 20 percent of patients with diabetic neuropathy [9]. Profound constipation with massive fecal impaction may occur [1,10]. These patients may develop marked abdominal distention and severe nausea and vomiting associated with electrolyte disturbances. Prolonged fecal impaction may lead to stercoral ulcerations and perforation.

Unexplained chronic diarrhea, with or without steatorrhea, can be a major problem in some diabetic patients. Steatorrhea has generally been attributed to pancreatic insufficiency, celiac disease, or bacterial overgrowth of the small intestine [1,2,3]. In these patients the colon appears to play a secondary or permissive role in

TABLE 1  
Potential Colonic Complications of Diabetes

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Constipation
Fecal impaction
Stercoral ulceration or perforation
Megacolon or megasigmoid
Barium impaction
Volvulus
Diarrhea
Fecal incontinence

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the production of diarrhea. In the absence of steatorrhea, colonic dysfunction may be a primary contributor to diabetic diarrhea.

Gross atonic dilation of the colon simulating organic obstruction has been reported in a diabetic patient with prolonged intractable diarrhea [11]. At autopsy, ulcerations were present in the descending and sigmoid colon. The precise nature of the colonic lesion in this patient could not be identified, but either stercoral ulceration or segmental colitis seemed most likely. This case suggests that diabetic enteropathy should be included in the differential diagnosis of megacolon.

Berenyi and Schwarz described 13 patients with autonomic dysfunction and marked sigmoid dilation [12]. Diabetes mellitus was present in nine patients, while the others suffered from Parkinson's disease or traumatic paraplegia. Diarrhea occurred in the majority of patients, and sigmoid volvulus was a frequent complication. The authors suggested an association between diabetic visceral neuropathy and the megasigmoid syndrome.

Read and associates studied a varied group of patients with fecal incontinence and diarrhea [13]. Diabetes mellitus was felt to be the major contributing factor in 28 percent of their patients. Stool volume, sphincter pressure, and ability to retain rectally infused saline were evaluated. Most diabetic patients had low stool volumes, low sphincter pressures, and an impaired ability to retain saline infused into the rectum. These results suggested weakness of the anal sphincter as the major mechanism responsible for the incontinence. Similarly, Schiller and associates compared diabetics with fecal incontinence to continent diabetics and non-diabetic controls [14]. They found that the onset of incontinence usually coincided with the onset of chronic diarrhea. Moreover, their results confirmed that the mechanism of incontinence in diabetic patients is related to internal anal sphincter dysfunction. Wald demonstrated an absent or weakened external sphincter contraction and a high normal threshold of rectal sensation (30 ml) in diabetic patients with fecal incontinence [15].

Diabetes mellitus is one of the four endocrine disorders considered to be secondary causes of the chronic intestinal pseudo-obstruction syndrome [16]. The other disorders are myxedema, hypoparathyroidism, and pheochromocytoma.

Significant colonic dysfunction generally occurs in the setting of diabetic neuropathy, as is true of motor abnormalities elsewhere in the gastrointestinal tract. Widespread involvement of the autonomic nervous system may occur, and many of these patients will demonstrate orthostatic hypotension, impotence, neurogenic bladder, anhidrosis, or vasomotor instability [17]. Vascular responses to the Valsalva maneuver and sustained handgrip have been proposed as a practical objective assessment of the integrity of the autonomic nervous system in diabetic patients [18].

No specific predisposing factors have been identified for colonic dysfunction in diabetes mellitus. Analysis of the clinical profile of the patients in our study of diabetic constipation failed to reveal a correlation between duration of disease or total daily insulin dose and severity of symptoms. However, patients with an early age of onset of clinical diabetes, regardless of duration, tended to have the worst symptoms [17].

There are no pathognomonic radiographic findings on barium enema for diabetes mellitus. A dilated ahaustral colon, similar to that associated with laxative abuse, may occur in some patients. Significant symptoms may be present, however, in the absence of radiographic abnormalities. In other disorders associated with a hypomotile colonic state, such as scleroderma, severe barium impaction has occurred [20]. This should be kept in mind when barium studies are performed on diabetic patients with severe colonic hypomotility. Thorough cleansing maneuvers should be performed post-examination.

### PATHOGENESIS

#### *General*

The movement of material through the colon is controlled by the contractile pattern of the colonic smooth muscle [21]. Studies in the cat showed that colonic segmental contractile activity propagates toward the cecum, allowing complete absorption of electrolytes and water in the ascending colon [22]. Thus, segmental contractions in the colon act as a functional brake of the flow of intraluminal contents. This gives the colonic mucosa time to fully absorb water and electrolytes still present in the intraluminal contents.

Colonic motility is controlled by the inherent rhythmicity of the colonic smooth muscle. Continuous cyclical depolarization of the smooth muscle membrane is called slow-wave activity. Spike potentials are superimposed on the slow waves and they initiate the contractile process. Spike potentials occur at one phase of the slow-wave cycle. Thus, the frequency of the slow waves determines the contractile frequency of the colonic smooth muscle. Any disease process which alters either the slow-wave pattern or the spike response to physiologic stimuli will alter the pattern of contraction and thus the flow of luminal contents.

### CONSTIPATION IN PATIENTS WITH DIABETES MELLITUS

In patients with diabetes mellitus whose major complaint is constipation, the colonic slow-wave pattern is similar to the one present in healthy controls [17]. In healthy controls, slow waves predominantly occur at a frequency of 6 cycles/minute. The slow wave frequency in patients with diabetes mellitus is also 6 cycles/minute. Thus, if the colon responds to physiologic or pharmacologic stimuli, the contractile pattern should be similar to that of healthy subjects.

When fasting, spike activity is minimal in both healthy subjects and patients with diabetes mellitus. In healthy subjects, spike activity increases rapidly after eating a meal. In healthy subjects, spike activity superimposed on slow waves increases during the first ten minutes postprandially and remains elevated for thirty minutes after eating. The pre-administration of an anticholinergic drug inhibits the postprandial increase in spike activity. Either oral or intravenous administration of an anticholinergic drug will inhibit colonic spike and contractile activity. Thus, the postprandial gastrocolonic response appears to be mediated through the cholinergic nervous system.

Constipation is one of the major problems in chronic insulin-requiring diabetics. In these patients the gastrocolonic response to eating is disturbed. After a 1,000-calorie meal, diabetic patients with constipation have no increase in colonic spike activity. In those patients with normal bowel habit, the postprandial spike response is similar to that of healthy controls. These data suggest that the gastrocolonic response to a meal is abnormal in diabetic patients.

Previous studies in patients with diabetes mellitus have suggested that there are motor disturbances throughout the gastrointestinal tract which are secondary to a dysfunction of the autonomic nervous system. In the esophagus there is a diminished velocity of esophageal peristalsis in the presence of a normal contractile response of the lower esophageal sphincter to edrophonium [4]. Histologic abnormalities of the parasympathetic nerve fibers and the myenteric ganglia in patients with diabetes mellitus have been implicated as the cause of reduced gastric acid secretion and delayed gastric emptying [23]. Small intestinal motility studies in diabetic patients with diarrhea have shown a decreased response to intestinal distention but a normal response to the administration of catecholamines or cholinergic drugs [7]. Sympathetic ganglia and the interneuronal pathways are degenerated in diabetic patients [24]. These ganglia are important for the integration of impulses in the various parts of the colon and may play an important role in the disordered control of gastrointestinal motility in patients with diabetes mellitus.

Dysfunction of colonic motility in diabetic patients may be primarily due to an abnormality in the autonomic neural control. The cholinergic nervous system appears to be disturbed in diabetic patients whose major complaint is constipation, since the gastrocolonic response is abnormal [17].

Previous studies have shown that the colonic smooth muscle is capable of being stimulated in diabetic patients with constipation. Administration of a parasympathomimetic drug, such as neostigmine or metoclopramide, can increase colonic spike activity and colonic contractile activity [17]. Thus the smooth muscle appears normally responsive in patients with diabetes mellitus despite the lack of a gastrocolonic response.

The motor defect in patients with insulin-requiring diabetes mellitus and constipation may be at several levels. The defect in the neuroreceptors in the mucosa of the upper gastrointestinal tract may cause abnormalities in the gastrocolonic response. Blocking neuroreceptors with procaine has abolished the gastrocolonic motor response [25]. Thus it is important to have intact mucosal receptors upon which the dietary components can act. There also may be a defect in the long arc gastrointestinal reflex. There are defects in the prevertebral and paravertebral sympathetic ganglia important to the control of colonic function, as previously described [7]. Furthermore, there are abnormalities in autonomic nerve conduction which may be important in the control of the gastrocolonic response. Further studies are needed to evaluate these hypotheses.

Attempts to correlate the degree of peripheral neuropathy with the severity of motor abnormalities in various segments of the gastrointestinal tract have been variable [4,5,17,19]. We found no correlation between peripheral nerve conduction velocities and postprandial colonic myoelectric and motor activity in diabetic patients with varying degrees of constipation. Similarly, we found no correlation between gastric emptying of a liquid meal and colonic motility or between peripheral nerve conduction velocity and gastric emptying [17]. This suggests that patchy involvement of the autonomic nervous system occurs and may explain the variable manifestations of diabetic enteropathy in an individual patient.

## DIARRHEA IN PATIENTS WITH DIABETES MELLITUS

Diarrhea is a much less common problem in patients with diabetes mellitus. In a recent survey only 22 percent of diabetic outpatients complained of diarrhea (loose stools or frequency). The episodes of diarrhea were mostly acute and intermittent [3].

Certain chronic disorders which can cause increased stool volume (weight greater than 200 g/day) are seen with increased frequency in diabetics. These conditions are celiac sprue (gluten-sensitive enteropathy), pancreatic insufficiency, and bacterial overgrowth of the small intestine [3]. These conditions, plus other causes of non-diabetic diarrhea, must be excluded before a diagnosis of idiopathic diabetic diarrhea can be made.

The cause of idiopathic diabetic diarrhea is not known but multiple factors may be responsible for the pathogenesis [3]. Colonic motility has not been measured in diabetic patients with diarrhea, but colon dilation may occur in patients with nocturnal diarrhea associated with diabetes mellitus [11].

Fecal incontinence is often associated with chronic diarrhea in diabetic patients [14] and is a common but often unmentioned episodic problem in diabetics without diarrhea [3]. The cause of fecal incontinence appears to be related to weakened contractions of the internal anal sphincter [14].

Disordered small intestinal motility may be the major cause of the diarrhea in diabetic patients. Degeneration of the interneuronal pathways controlling small intestinal smooth muscle function may cause the decreased tone and increased amplitude of phasic small intestinal contractions [7,26]. The myenteric plexus appears functional, since there was no hypersensitivity to methacholine.

The information currently available suggests that both diarrhea and constipation in patients with diabetes mellitus are due to autonomic neural dysfunction. When neural control of the colon is disrupted, constipation results. When neural control of the small intestine is disrupted, diarrhea may be the result.

## TREATMENT

Management of the symptoms relating to diabetic colonic dysfunction has not yet been extensively evaluated. We have developed a regimen based on general measures and the results of the limited pathophysiologic studies performed to date. Our approach is outlined in Table 2.

Constipation is the most common symptom of diabetic colonic dysfunction. A simple increase in dietary fiber may reduce intestinal transit time. Some high-fiber

TABLE 2  
Treatment of Colonic Dysfunction in Diabetes

	Constipation	Diarrhea
General	<ul style="list-style-type: none"> <li>High-fiber diet</li> <li>Psyllium</li> <li>Lactulose<sup>a</sup></li> <li>Stool softeners, Enemas</li> </ul>	<ul style="list-style-type: none"> <li>Diphenoxylate with atropine</li> <li>Loperamide</li> <li>Biofeedback (fecal incontinence)</li> </ul>
Severe Symptoms	<ul style="list-style-type: none"> <li>Bethanecol</li> <li>Pyridostigmine</li> <li>Metoclopramide</li> </ul>	

<sup>a</sup>Large doses may elevate the blood sugar.

foods may lead to increased gas production. Therefore, the quantity of fiber in the diet should be increased gradually to avoid excessive flatulence and bloating. There is recent evidence that fiber improves glucose tolerance and reduces insulin requirements. Thus patients should be cautioned that the need for insulin or oral hypoglycemic agents may be decreased [27]. Supplement with a hydrophillic mucilloid psyllium preparation is a practical method of increasing stool bulk.

Lactulose has recently been proposed for use in chronic constipation. This non-absorbing carbohydrate is degraded by the colonic bacteria to low molecular weight fatty acids which act as osmotically active particles. The acid pH and increased osmotic activity stimulate colonic propulsive activity. The commercial preparation of lactulose syrup (Chronulac) contains small quantities of galactose, lactose, and other sugars. Therefore, it should be used with caution in diabetics. We have found small quantities (10 cc by mouth, twice a day) of lactulose useful in some patients and have observed no appreciable effect on blood sugar.

Periodic usage of stool softeners, mineral oil, or enemas may be needed to prevent fecal impaction. Patients should be counseled against chronic laxative usage, particularly the anthraquinone group (senna, cascara, aloes) [28]. These substances may produce progressive toxic damage to the intrinsic nerve plexuses of the colon, thus aggravating an already existing autonomic neuropathy of the gastrointestinal tract.

A small group of patients with advanced diabetic enteropathy may develop severe constipation or obstipation that is unresponsive to the above measures. These patients may benefit from a pharmacologic trial of drugs which stimulate the colonic smooth muscle. Cholinergic agents such as bethanechol (cholinergic agonist) or pyridostigmine (cholinesterase inhibitor) can be tried. Recently metoclopramide (Reglan) has been approved for treatment of diabetic gastroparesis, and we have observed an improvement in severe constipation during treatment of diabetic gastropathy [17]. This clinical observation is consistent with the cholinergic-like stimulatory effect of metoclopramide on colonic smooth muscle [17]. Metoclopramide also suppresses the chemoreceptor trigger zone of the vomiting pathway and is, therefore, a powerful antimetic [29].

In some diabetic patients with colonic dysfunction, diarrhea, with or without incontinence, may be the predominant manifestation. Several studies have demonstrated the efficacy of both loperamide and diphenoxylate with atropine in the treatment of chronic diarrhea [30]. Temporary or intermittent therapy using these agents has been very helpful among our diabetic population.

Two recent studies evaluated biofeedback conditioning for fecal incontinence related to various medical disorders [15,31]. A small number of diabetic patients were among those studied. Patients were taught to develop reflex transient contraction of the external sphincter in response to rectal distention. Ability to sense rectal distention was a major prerequisite for successful conditioning. Cerulli and associates found a poor response in the one diabetic patient they evaluated [31]. Most of the patients in their poor-response group were felt to have lesions involving the afferent nerve pathways with loss of sensation. Wald studied five insulin-dependent diabetics with peripheral neuropathy and fecal incontinence [15]. Three patients improved dramatically with biofeedback conditioning, suggesting that this may be a valuable therapeutic modality in some diabetic patients with fecal incontinence.

## REFERENCES

1. Katz LA, Spiro HM: Gastrointestinal manifestations of diabetes. *New Eng J Med* 275:1350-1361, 1966

2. Scarpello JHB, Sladen GE: Progress report: Diabetes and the Gut. *Gut* 19:1153-1162, 1978
3. Feldman M, Schiller LR: Disorders of gastrointestinal motility associated with diabetes mellitus. *Ann Int Med* 98:373-384, 1983
4. Hollis JB, Castell DO, Braddim RL: Esophageal function in diabetes mellitus and its relation to peripheral neuropathy. *Gastroenterology* 73:1098-1102, 1977
5. Russell COH, Gannan R, Coatsworth J, et al: Relationship among esophageal dysfunction, diabetic gastroenteropathy, and peripheral neuropathy. *Dig Dis Sci* 28:289-293, 1983
6. Fox S, Behar J: Pathogenesis of diabetic gastroparesis: a pharmacologic study. *Gastroenterology* 78:757-763, 1980
7. Whalen GE, Soergel KH, Geenen JE: Diabetic diarrhea. *Gastroenterology* 56:1021-1032, 1969
8. Goldstein F, Wirts CW, Kowlessar OD: Diabetic diarrhea and steatorrhea: microbiologic and clinical observations. *Ann Int Med* 72:215-218, 1970
9. Rundles RW: Diabetic neuropathy: general review with report of 125 cases. *Medicine (Baltimore)* 24:111-160, 1945
10. Finlay JM: Gastrointestinal complications of diabetes. In *On the Nature and Treatment of Diabetes*. Edited by BS Leibel, GA Wrenshall. The Hague, Netherlands, Moulton & Co, 1965, p 805
11. Paley RG, Mitchell W, Watkinson G: Terminal colonic dilation following intractable diarrhea in a diabetic. *Gastroenterology* 41:401-407, 1961
12. Berenyi MR, Schwarz GS: Megacigmoid syndrome in diabetes and neurologic disease. *Am J Gastro* 47:311-320, 1967
13. Read NW, Harford WV, Schmulen AC, et al: A clinical study of patients with fecal incontinence and diarrhea. *Gastroenterology* 76:747-756, 1979
14. Schiller LR, Santa Ana CA, Schmulen AC, et al: Pathogenesis of fecal incontinence in diabetes mellitus: evidence for internal-anal-sphincter dysfunction. *New Eng J Med* 307:1666-1671, 1983
15. Wald A: Biofeedback therapy for fecal incontinence. *Ann Int Med* 95:146-149, 1981
16. Faulk DL, Anuras S, Christensen J: Chronic intestinal pseudo-obstruction. *Gastroenterology* 74:922-931, 1978
17. Battle WM, Snape WJ Jr, Alavi A, et al: Colonic dysfunction in diabetes mellitus. *Gastroenterology* 79:1217-1221, 1980
18. Ewing DJ, Campbell IW, Burt AA, et al: Vascular reflexes in diabetic autonomic neuropathy. *Lancet* ii:1354-1356, 1973
19. Scarpello JHB, Baber DC, Hague RV, et al: Gastric emptying of solid meals in diabetics. *Br Med J* 2:671-673, 1976
20. Thompson MA Jr, Summers R: Barium impaction as a complication of gastrointestinal scleroderma. *JAMA* 235:1715-1717, 1976
21. Bortoff A: Intestinal motility. *New Eng J Med* 280:1335-1337, 1969
22. Christensen J: Myoelectric control of the cat colon. *Gastroenterology* 68:601-609, 1975
23. Feldman M, Corbett DB, Ronsey EJ, et al: Abnormal gastric function in longstanding insulin-dependent diabetic patients. *Gastroenterology* 77:12-17, 1979
24. Low PA, Walsh HC, Huang CY, et al: The sympathetic nervous system in diabetic neuropathy. A clinical and pathological study. *Brain* 98:341-356, 1975
25. Sun EA, Snape WJ Jr, Cohen S, et al: The role of opiate receptors and cholinergic neurons in the gastrocolonic response. *Gastroenterology*, in press
26. McNally EF, Reinhard AE, Schwartz PE: Small bowel motility in diabetes. *Am J Dig Dis* 14:163-169, 1969
27. Miranda PM, Horwitz DL: High fiber diets in the treatment of diabetes mellitus. *Ann Int Med* 88:482-486, 1978
28. Smith B: Effect of irritant purgatives on the myenteric plexus in man and the mouse. *Gut* 9:139-143, 1968
29. Schulze-Delrieu K: Drug therapy: metoclopramide. *New Eng J Med* 305:28-32, 1981
30. Palmer KR, Corbett CL, Holdsworth CD: Double-blind crossover study comparing loperamide codeine and diphenoxylate in the treatment of chronic diarrhea. *Gastroenterology* 79:1272-1275, 1980
31. Cerulli MA, Nikoomeh P, Schuster MM: Progress in biofeedback conditioning for fecal incontinence. *Gastroenterology* 76:742-746, 1979