

*Alimentary tract and pancreas*

# Chronic idiopathic intestinal pseudo-obstruction: clinical and intestinal manometric findings

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**SUMMARY** We report the clinical and intestinal manometric findings in a group of 42 patients with chronic idiopathic intestinal pseudo-obstruction evaluated at the Mayo Clinic. The main clinical manifestations in these patients were nausea and vomiting (83%), abdominal pain (74%), distension (57%), constipation (36%), diarrhoea (29%), and urinary symptoms (17%). These symptoms preceded surgery in all patients. Air fluid levels or distended bowel loops occurred in 57% and a dilated bladder or urinary excretory pathway in 17%. All patients showed intestinal manometric abnormalities none of which are seen in healthy individuals: (a) aberrant configuration or propagation of interdigestive motor complexes in 25 patients; (b) bursts (>2 min duration) of non-propagated phasic pressure activity in fasting and/or fed state in 30 patients; (c) sustained incoordinated fasting pressure activity in 15 patients; and (d) inability of an ingested meal to convert fasting into fed pattern in 28 patients. We conclude that qualitative analysis of intestinal manometry provides evidence of gut dysmotility in patients with the clinical syndrome of chronic intestinal pseudo-obstruction. These abnormalities of motility can help to establish the correct diagnosis.

Chronic intestinal pseudo-obstruction is a disorder of gut motility that may result from a number of different underlying conditions.<sup>1</sup> Most commonly, it is idiopathic, and it occurs in isolation, affecting either neural or muscular elements<sup>2,3</sup> of the gut wall. Up to the present time the disorder has constituted a difficult clinical problem not only because of the inadequacy of treatment but also because the diagnosis has predominantly been one of exclusion. Thus treatment often entails therapeutic trial with a gut prokinetic agent or selective surgical resections in patients with disease apparently localised to one region of the gut.<sup>4</sup> The diagnosis of chronic idiopathic intestinal pseudo-obstruction (CIIP) has rested largely on compatible symptoms of subacute small bowel obstruction, and exclusion of mechanical obstruction either on endoscopic or radiologic examination, or at laparotomy. In recent years, a more functional approach to the diagnosis has been forthcoming with reports of the usefulness of oesophageal and anorectal

manometry.<sup>2,3</sup> Such evidence, however, does not directly examine the small bowel itself, which often shows radiological signs of involvement.<sup>1,2</sup> Two reports have documented myo- or electrical activity in the small bowel in a few patients.<sup>5-6</sup> There has not been, however, a systematic study of intestinal motility patterns in CIIP. Our aim was to reassess the clinical presentation of a large number of these patients and to determine whether intestinal manometry can provide evidence of gut dysmotility in this disorder.

## Methods

### PATIENTS

Forty two consecutive patients with CIIP were studied. These were patients who presented with chronic, recurrent abdominal pain associated with episodic nausea, vomiting, and abdominal distension resembling partial intestinal obstruction<sup>1-3</sup> (Table 1). Their age range was 5-76 years; there were 28 women and 14 men. Mechanical obstruction was excluded in all by contrast radiology and in 33 by laparotomy. Other exclusion criteria were: (1) the presence of associated systemic disease that may produce a picture of chronic intestinal pseudo-

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Received for publication 28 April 1986

Table 1 Clinical features in 42 patients with chronic idiopathic intestinal pseudo-obstruction

Group	n	Age range	M	F	Abdominal pain	N/V	Dist/bloat	Constipation	Diarrhoea	Urinary tract involvement
No surgery	9	21-52	2	7	5	9	4	5	4	2
Laparotomy	12	5-76	5	7	9	8	8	4	5	0
Gastric surgery	10	21-61	2	8	8	9	5	3	1	2
Small bowel resection	7	19-58	5	2	7	6	6	2	0	2
Colectomy	4	27-68	3	1	3	4	2	1	2	1

N=nausea; V=vomiting; dist=distension; bloat=bloating.

obstruction, such as hypothyroidism or systemic sclerosis; (2) evidence of visceral autonomic neuropathy (excluded by sweat test, vasomotor reflex testing, and fractionated catecholamines when clinically indicated;<sup>7</sup> and (3) evidence on full thickness biopsy of an infiltrative – that is, amyloidosis – or scleroderma or degenerative disorder of the small intestinal muscle resulting in ‘myopathic’ pseudo-obstruction.

Full thickness biopsies of the stomach, small bowel or colon were evaluated in 15 patients. None of the biopsies showed evidence of smooth muscle infiltration or degeneration. Evaluation of myenteric plexus ganglion cells by light microscopy of sections stained with haematoxylin and eosin (H & E) revealed abnormalities in three cases. These abnormalities were: a lymphoid cell infiltration of the myenteric plexus in one, and clustering of nuclei and scanty cytoplasm or degenerative changes in ganglion cells in the two others. Although no histological abnormalities were noted in the other patients, an apparently normal appearance of myenteric plexus on H & E staining does not exclude neuropathy.

#### INTESTINAL MANOMETRY

Intestinal manometry was carried out after an overnight fast with an 8-lumen perfusion tube (external diameter 6 mm) that was introduced along a fluoroscopically placed guidewire. Each catheter was perfused with distilled water *via* a pneumohydraulic pump (perfusion rate 0.5 ml/min; perfusion pressure 14 psi) and attached to a strain gauge transducer (Gould Statham Instrument, Model P23, Hato Rey, Puerto Rico). One side opening was made in each catheter. These openings were at the tip of the tube and 10, 20, 30, 40, 50, 51, and 52 cm from the tip. The latter three openings were positioned fluoroscopically across the pylorus or, in patients with previous gastric surgery, across the gastroenteric anastomosis. Gastrointestinal pressure activity was recorded continuously in each patient for three hours before (fasting period) and two

hours after ingestion of a mixed solid-liquid meal (fed period). The meal consisted of chicken, potato, tapioca pudding (511 calories total) and 190 ml water. Details of the manometric technique have been published<sup>7-9</sup> and an example of normal fasting and postprandial gastrointestinal manometry is demonstrated in Figure 1.

Analysis of intestinal manometric tracings was performed visually. Abnormalities were identified by comparison with a large pool of similar manometric studies done in healthy volunteers and reported in previous publications from our laboratory.<sup>7-11</sup> Only patterns of pressure activity that were not observed in healthy individuals were categorised as abnormal (see Results). As a sizable fraction of our patients with the chronic pseudo-obstruction syndrome had previous gastric surgery, antral motility was not quantified.

#### Results

##### CLINICAL FEATURES (Table 1)

The distribution of abdominal symptoms in our patient population was as follows. Nausea and vomiting were present in 83%, abdominal pain in 74%, distension or bloating in 57%, constipation in 36%, and diarrhoea in 29% of patients. Thirty three of the 42 patients had undergone at least one previous abdominal exploratory or resective surgery: 12 laparotomy alone, 10 gastric surgery (vagotomy in all, partial resection in eight), seven segmental small bowel resection, and four colectomy with ileoproctostomy. In all patients, symptoms preceded the surgical procedure and their severity and course were unaltered by the surgical intervention. The barium small bowel radiograph or plain abdominal film was abnormal (fluid levels, distended loops) in 57%. Evidence of urinary tract involvement was evidenced in 17% by dilation of ureter, pelvis or calyces on excretory urography or abnormality in bladder function (increased residual volume, detrusor dysfunction).

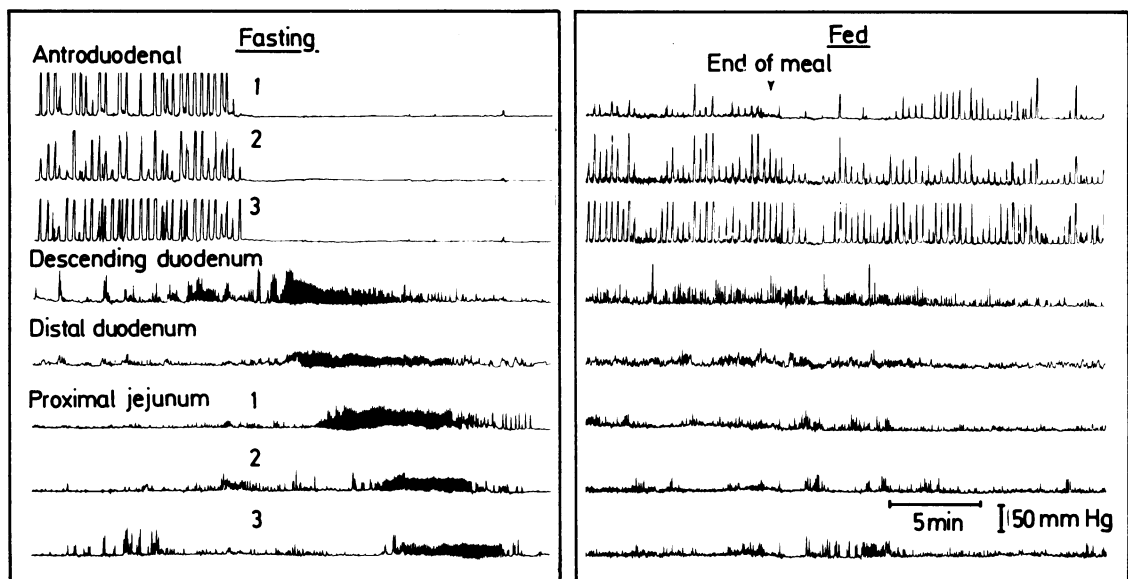


Fig. 1 Normal fasting and fed upper gut motility in a healthy individual. Note the normal antral component and propagation of the interdigestive motor complex in the fasting state, and the irregular but persistent phasic pressure activity that characterises the fed state.

#### MANOMETRIC ABNORMALITIES

##### *Types of manometric abnormalities*

In our group 42 patients, the following four major patterns of intestinal manometric abnormality were detected:

(a) aberrant propagation and/or configuration (Fig. 2) of interdigestive migrating motor complexes or MMC. Two major abnormalities are comprised in this category. One, absence of propagation of phase III activity (either simultaneous or retrograde) over at least a 30 cm segment of small bowel (Fig. 2). Two, marked tonic (>30 mm Hg amplitude, >3 min duration) rises of baseline pressure during propagation of the activity front through one or more levels of the small bowel assessed. Note that the absence of MMC during the three hour fasting period does not qualify as abnormal as an MMC may not be recorded during a three hour fasting observation period, even in healthy volunteers (unpublished observations). (b) Bursts of non-propagated phasic pressure activity in the fasting (Fig. 3) and fed states. Bursts were defined as periods of at least two minutes duration with continuous high amplitude (>20 mm Hg) and high frequency (10–12/min) phasic pressure activity that were not propagated and not followed by motor quiescence (in contrast to typical phase III activity of the MMC). These bursts could sometimes be associated with tonic rise of baseline pressure as

noted in pattern (a) (see above). (c) Sustained (for over 30 min) and intense phasic pressure activity that occurred in a segment of intestine while normal or reduced activity were noted simultaneously at other levels of the intestine (Fig. 4). This pattern of activity was similar to the burst activity of pattern (b) except that it was much more prolonged and segmental in localisation. (d) Inability of the ingested meal to change fasting intestinal activity into a fed pattern (Fig. 5). This was characterised by a repetition of the same abnormal fasting pattern (either a, b or c) during the two hour period after ingestion of the full meal, or by complete absence of the irregular but uniform pressure activity that characterises the normal fed pattern.

None of these four abnormalities have been previously observed in normal individuals, as reported in previous publications from this laboratory.<sup>7–11</sup>

#### PREVALENCE OF MANOMETRIC ABNORMALITIES

Abnormalities in the configuration and/or propagation of interdigestive motor complexes (abnormal pattern (a) were present in 25 patients (60%). Three patients with abnormal complexes exhibited normal appearing activity fronts at other times during the fasting observation period.

Bursts of non-propagated phasic pressure activity (abnormal pattern (b)) were present in the fasting

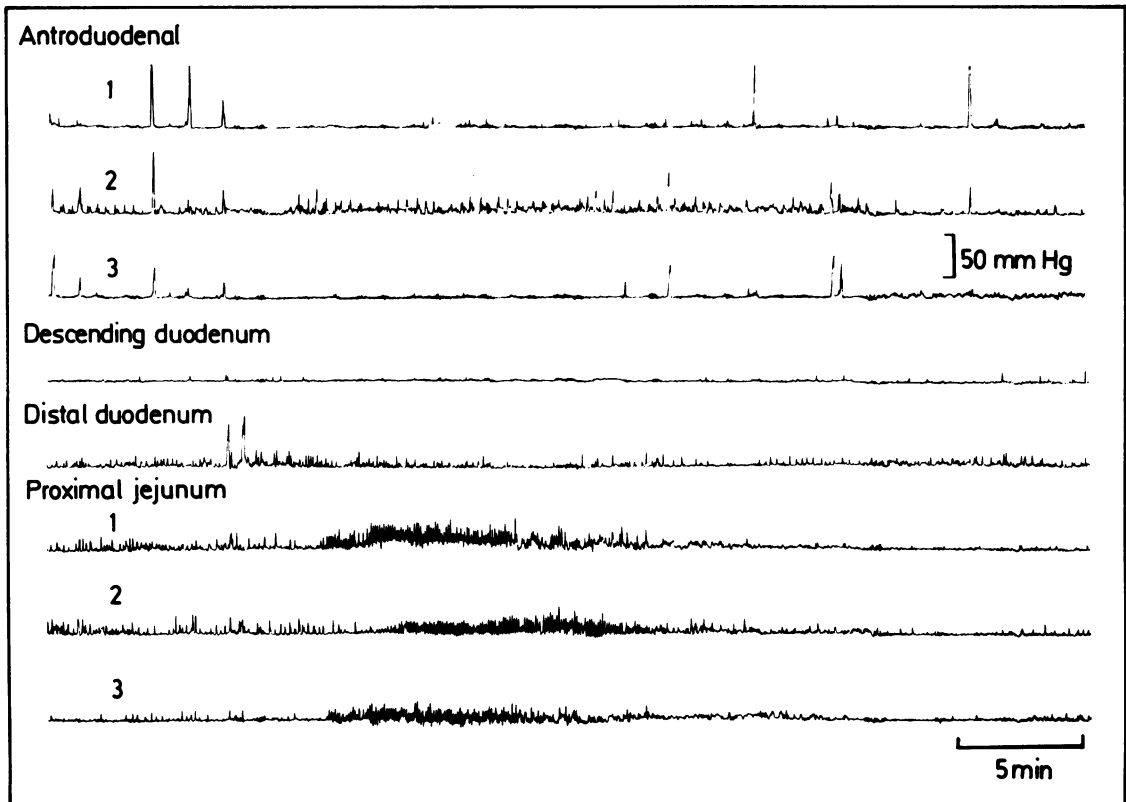


Fig. 2 Abnormal propagation of interdigestive motor complex in a patient with chronic idiopathic intestinal pseudo-obstruction. Note the presence of simultaneous phase III activity in the proximal jejunum and the persistence of antroduodenal pressure activity after this complex.

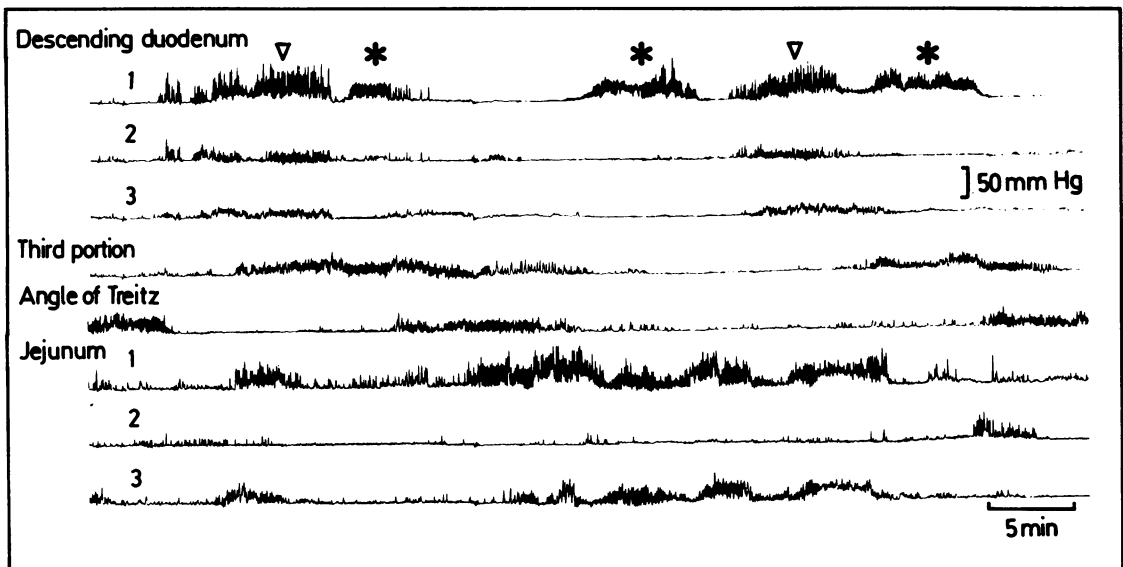


Fig. 3 Bursts of propagated (↓) and non-propagated (\*) pressure activity in the intestine in a patient with chronic idiopathic intestinal pseudo-obstruction. Non-propagated bursts are of greater than two minutes' duration.

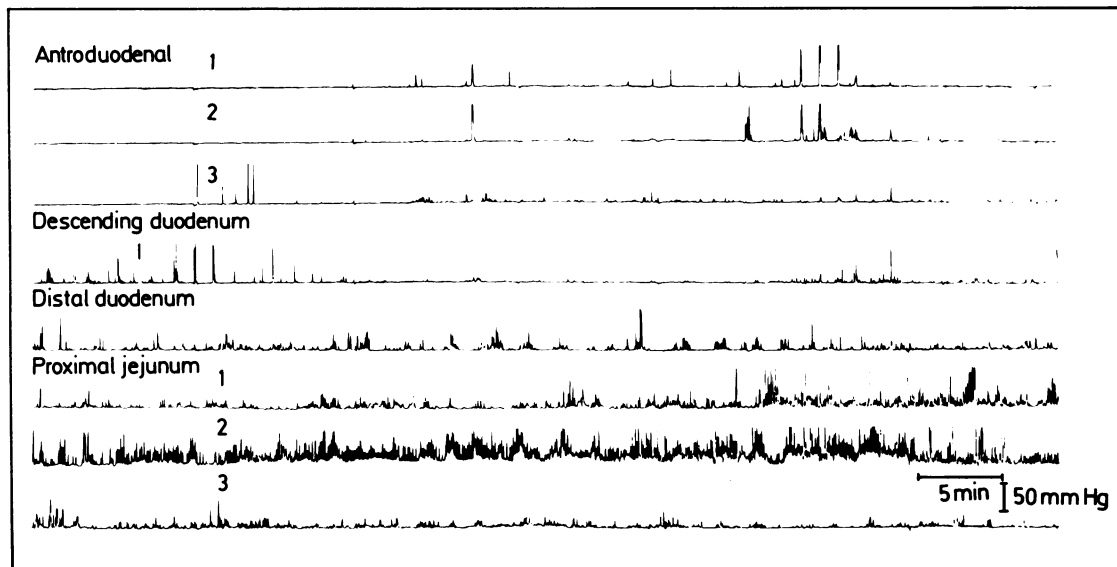


Fig. 4 Sustained incoordinated fasting phasic and tonic pressure activity in the intestine in a patient with chronic idiopathic intestinal pseudo-obstruction. The intense fasting activity observed at the level of the jejunum appears incoordinated with adjacent segments of the intestine.

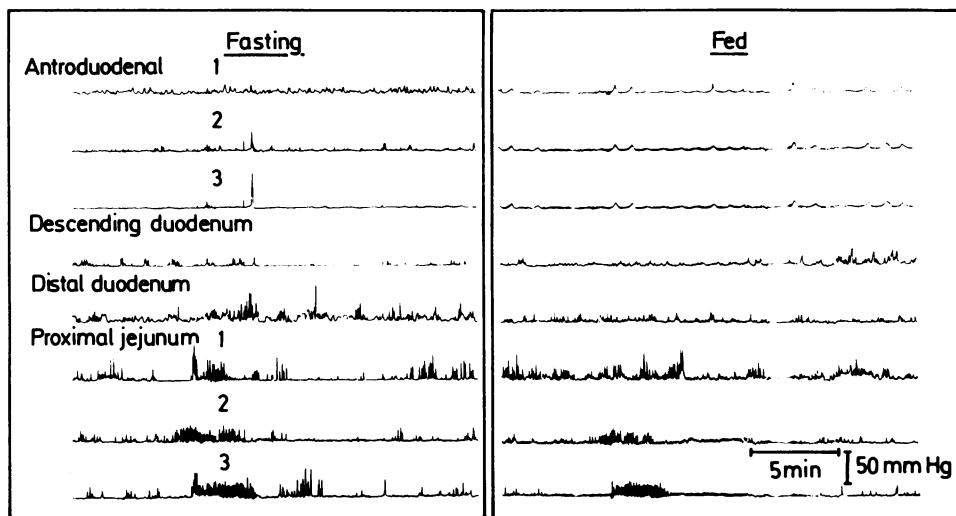


Fig. 5 Similarity of manometric tracing obtained during fasting and postprandially. Note the inability of the meal to induce the postprandial irregular but persistent phasic pressure response. In contrast with Figure 1, the fed state shows a non-propagated burst of activity that is virtually identical to that seen in fasting record.

state in 30 patients (71%) and in the fed state in eight patients (19%). The median number of fasting bursts was 3.5 and in the fed state 2. Sustained incoordinated pressure activity (abnormal pattern c) was detected in the fasting studies of 16 patients. The appearance of the tracing in the postprandial

period was unaltered from the abnormal fasting pattern in 28 patients (abnormal pattern d).

DISTRIBUTION OF THE MANOMETRIC ABNORMALITIES

The distribution of the four types of the intestinal

Table 2 Intestinal manometric features in 42 patients with chronic idiopathic intestinal pseudo-obstruction

Group	n	Manometric bursts recorded						Patients with sustained uncoordinated activity (n)		Patients with intestinal fed pattern (n)		
		Patients with normal MMC (n)		Patients with abnormal MMC (n)		Patients with no MMC (n)		Fasting	Fed	Norm	Abn	Absent
		MMC (n)	MMC (n)	MMC (n)	Max <sup>m</sup>	Median	Max <sup>m</sup>					
No surgery	9	0	8	1	30	8	5	3	4	4	2	
Laparotomy	12	1	7	4	5	3-5	1	1	1	4	6	
Gastric surgery	10	2	5	3	11	3	1	1	5	3	2	
Small bowel resection	7	3	2	2	13	4-5	5	2-5	2	2	3	
Colectomy	4	0	3	1	7	5	5	2-5	2	1	1	

MMC=migrating motor complex. Norm=normal, Abn=abnormal.

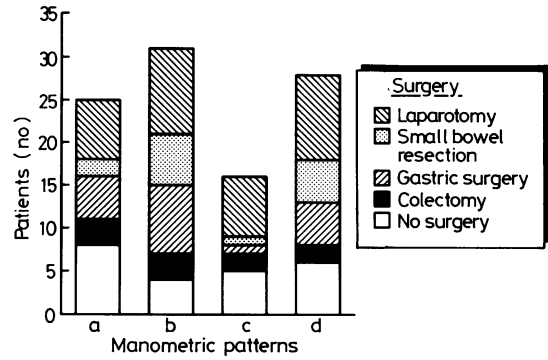


Fig. 6 Distribution of abnormal intestinal manometric pattern in the different subgroups of patients with chronic idiopathic intestinal pseudo-obstruction. Note the similar prevalence of each pattern in the five groups.

manometric abnormalities in each patient subgroup is summarised in Table 2 and Figure 6. All patients had at least one such abnormality, and 86% had at least two abnormal manometric features. Four abnormal intestinal manometric patterns were detected in 12 patients, three in 17 patients, two in seven patients and one in six patients. There was no apparent relationship between the manometric pattern(s) observed and the type or severity of a patient's symptoms.

**Discussion**

The clinical features of our patients are similar to those reported in previous publications which documented the clinical manifestations of patients with chronic intestinal pseudo-obstruction of diverse aetiology.<sup>2,3</sup> Thus, nausea, vomiting, distension, bloating, and abdominal pain (each present in approximately 70% of patients) constituted the predominant symptoms. A sizeable proportion of our study group also had alteration in bowel movements. Symptoms referable to the urinary tract and evidence of bladder dilatation or ureteropelvic-alyectasis were present in 17% of our patients, which is comparable with the 14% incidence in patients with the 'megaduodenum' variant of pseudo-obstruction.<sup>2,3</sup> Similarly, plain or contrast abdominal radiography revealed dilated small bowel loops in almost two-thirds of our group, confirming the experience of Schuffler *et al.*<sup>2,3</sup>

This study shows that patients with chronic idiopathic intestinal pseudo-obstruction have gastrointestinal motor abnormalities that can be documented manometrically. Previous studies have usually evaluated regions of the gastrointestinal



*Manometry in intestinal pseudo-obstruction.*

tract other than the small bowel, which appears on clinical and radiologic criteria to bear the brunt of this disease.<sup>2,3</sup> Two studies have addressed the question of functional diagnosis of small bowel disease by directly studying the small intestine. Sullivan *et al*<sup>5</sup> reported abnormalities in spike frequency and in the response of the small bowel to distension and to pharmacologic stimulation by neostigmine and secretin. Summers *et al*<sup>6</sup> evaluated three patients with pseudo-obstruction and suggested that manometric features in these patients were not specific and would not differentiate pseudo-obstruction from mechanical obstruction. Two of the three patients reported,<sup>6</sup> however, had muscle degeneration and replacement fibrosis. Manometrically they showed low amplitude phasic waves which are more reminiscent of a myopathic or infiltrative process than the intense, incoordinated, pressure activity we observed in our patients. Kumar and Wingate<sup>12</sup> recently have reported small bowel motor abnormalities in patients with the irritable bowel syndrome. It is conceivable that irritable bowel syndrome and CIIP are related conditions but the issue cannot be settled without direct comparative studies using the same method.

The manometric abnormalities detected in patients with chronic idiopathic intestinal pseudo-obstruction resemble those observed in diseases affecting the extrinsic nerve supply to the gut. Thus abnormalities in configuration and propagation of interdigestive motor complexes also occur in gut autonomic neuropathies<sup>7,9,13</sup> and central nervous system lesions, such as brain stem tumours<sup>14</sup> or infarcts (unpublished observation). Non-propagated, incoordinated bursts of pressure activity often associated with tonic rises of baseline pressure and lasting at least two minutes are also found in extrinsic, probably sympathetic, denervation of the gut.<sup>7,9</sup> Vagotomy may shorten, but does not abolish, the fed pattern after a meal.<sup>15-17</sup> Furthermore, there was no relationship between vagotomy and any of the particular manometric patterns described. Thus, we believe that previous vagotomy does not contribute to the abnormalities reported or interfere with the ability to make a manometric diagnosis. Furthermore, the manometric abnormalities in the cohort of patients reported in this paper differ markedly from the clustered contractions in minute intervals indicative of mechanical obstruction,<sup>6</sup> and the low amplitude but organised contractions seen in pseudo-obstruction associated with visceral myopathy or infiltration of the intestinal wall.<sup>18</sup>

The absence of an animal model for diffuse intrinsic plexus disease has hampered further experimental evaluation of the pathophysiology of this condition. The piebald lethal mouse model for

localised distal colonic aganglionosis or Hirschsprung's disease was shown to have delayed gastric and small bowel transit.<sup>19</sup> These delays, however, were considered secondary to distal colonic obstruction.<sup>19</sup> As we have shown impaired gastric emptying of solids and small bowel transit of solids and liquids in chronic intestinal pseudo-obstruction,<sup>20</sup> the abnormal intestinal manometric features described in the present study are likely to be functionally important.

Our group of patients shows the clinical heterogeneity in the initial presentation of chronic idiopathic intestinal pseudo-obstruction. Some patients presented with gastric stasis whereas others exhibited constipation necessitating local surgery; however, the majority eventually manifested features of subacute small bowel obstruction leading to repeated laparotomies to attempt relieving the obstructive episodes. These observations also imply that resection of an apparently localised disease of the gut<sup>4,21,22</sup> may not be as promising a therapy as was originally thought. Thus, at a later stage in the disease, other regions of the gut may also be affected. In this context, a gastrointestinal manometry study may be useful to assess the small bowel when the clinical presentation is with constipation or gastric stasis. Proof of a generalised gastrointestinal dysmotility should alert the clinician not to carry out local surgery such as antrectomy or colectomy. The former operation is deleterious to the emptying of solids from the stomach when small bowel involvement later becomes the dominant dysmotility. Colectomy renders management of fluid and electrolyte homeostasis more difficult in those patients who eventually suffer from small bowel disease or resection.

Intestinal manometry also has a potentially useful role to confirm the clinical diagnosis of CIIP. If adequate radiologic examination excludes mechanical obstruction, a positive manometric test showing diffuse and multifocal disturbances in intestinal motility strongly suggests the diagnosis of CIIP. Further studies, however, should be undertaken to determine the specificity and predictability of this new diagnostic modality in a broader clinical setting.

This study was supported in part by Grants AM 26428 and AM 34988 from the National Institutes of Health. This paper was presented in part at the Plenary Session of the annual meeting of the American Gastroenterological Association, New York 1985 and appears in abstract form in *Gastroenterology* (1985) 88, 1596. We wish to thank Mr Craig Reeves for technical assistance, our colleagues in the Gastroenterology Division for referring patients, and Ms Velda Woyczik for typing and preparing this manuscript.

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