# Chronic intestinal pseudo-obstruction: Etiology, clinical manifestations, and diagnosis

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## INTRODUCTION

Pseudo-obstruction is characterized by signs and symptoms of a mechanical obstruction of the small or large bowel in the absence of an anatomic lesion that obstructs the flow of intestinal contents, and the presence of dilation of the bowel on imaging. This topic review will discuss the etiology, clinical manifestations, and diagnosis and treatment of chronic intestinal pseudo-obstruction (CIPO). The management of CIPO, acute colonic pseudo-obstruction, and slow transit constipation/colon inertia are discussed separately. (See "Chronic intestinal pseudo-obstruction: Management" and "Acute colonic pseudo-obstruction (Ogilvie's syndrome)" and "Etiology and evaluation of chronic constipation in adults".)

## EPIDEMIOLOGY

Chronic intestinal pseudo-obstruction (CIPO) is rare, and most estimates of the incidence and prevalence are from tertiary referral centers. In a national survey in Japan, the estimated prevalence of CIPO was 0.80 to 1.00 per 100,000, with an incidence of 0.21 to 0.24 per 100,000 [1]. The mean age at diagnosis was 63.1 years for males and 59.2 for females. The dilatation may involve the small bowel or colon or both, and patients with CIPO affecting either the small bowel or colon may have delayed gastric emptying that may result from involvement of the stomach in the same disease process or that may result from reflex inhibition of gastric function

or increased resistance to flow of food from the stomach as a result of the impaired small bowel transit. There are no large series documenting these features. In one series of seven patients with CIPO, one patient also had evidence of antral hypomotility consistent with a concomitant gastric motor dysfunction typically associated with gastroparesis [2].

## PATHOGENESIS

Chronic intestinal pseudo-obstruction (CIPO) may be due to an underlying neuropathic disorder (involving the enteric nervous system or extrinsic nervous system), a myopathic disorder (involving the smooth muscle), or abnormality in the interstitial cells of Cajal (ICC) [3]. More than one of the elements of the neuromuscular apparatus of the gut may be affected in certain diseases. For example, there is an intrinsic neuropathic phase of scleroderma before the smooth muscle involvement results in myopathy. Similarly, mitochondrial cytopathy first results in neuropathy and eventually myopathy. Moreover, diabetes mellitus affects extrinsic nerves through autonomic neuropathy, and the ICC and amyloidosis cause an extrinsic neuropathy followed by myopathic CIPO. A case series that evaluated 14 parameters in full thickness small intestinal biopsies from 19 patients with CIPO or chronic enteric dysmotility showed heterogeneous functional abnormalities, with the most prevalent abnormality being decreased purinergic neuromuscular transmission, which was detected in 44 percent of jejunal samples [4]. This suggests that the neuromuscular impairment cannot be attributed to a single mechanism.

## ETIOLOGY

Neuropathic, myopathic, or interstitial cells of Cajal (ICC) abnormalities that result in chronic intestinal pseudo-obstruction (CIPO) may be idiopathic in etiology or secondary to another disease. Approximately one-half of the cases of CIPO are secondary to neurologic, paraneoplastic, autoimmune, metabolic/endocrine, or infectious diseases.

**Neurologic** — Neurologic (eg, Parkinson disease and Shy-Drager syndrome) and metabolic disorders (eg, diabetes mellitus) can affect the extrinsic nerve pathways supplying the gut. Degenerative neuropathies may result from several putative pathogenetic mechanisms, including altered calcium signaling, mitochondrial dysfunction, and production of free radicals, leading to degeneration and loss of gut intrinsic neurons [5]. Neuropathic disorders may be complicated by a myopathic stage when the muscle layer is infiltrated, as in primary or secondary amyloidosis.

CIPO has been described in association with radiotherapy and chemotherapy for gynecological cancer [6]. The pathogenesis of CIPO in such patients is likely to be the combined effects of external bean radiation and chemotherapy as evidenced by the presence of damage to the ICC network in six of seven patients evaluated [6].

### Immune-mediated

**Autoimmune disease** — CIPO has been reported in association with scleroderma, dermatomyositis, and systemic lupus erythematosus, all of which can alter the enteric nerves, the smooth muscle cells, and possibly the ICC [7-10]. A small proportion of patients with inflammatory enteric neuropathy have antibodies directed towards neuronal ion channels (voltage-gated potassium channels and neuronal alpha3-AChR) [11]. In one case report, CIPO resulted from the development of antibodies to buserelin, an analogue of gonadotropin-releasing hormone (GNRH), leading to the immune-mediated destruction of myenteric neurons [12]. Case reports have described CIPO in association with lymphocytic infiltration of the myenteric plexus [3,13] or smooth muscle [14,15].

**Paraneoplastic** — CIPO has been reported in association with small cell lung cancers or carcinoid tumors and malignant thymoma [16,17] or prostate cancer [18]. These patients often have antineuronal nuclear (anti-Hu) antibodies [19]. The antibody is postulated to be directed toward an epitope that is shared between the neuronal elements within the enteric nervous system and the underlying malignancy [20]. Paraneoplastic syndromes may evoke an inflammatory/immune infiltrate targeting neurons located in both submucosal and myenteric ganglia of the enteric nervous system (ENS) [21]; the cellular infiltrate along with circulating antineuronal antibodies is thought to damage the enteric reflexes, thereby contributing to paraneoplastic dysmotility. (See "Overview of paraneoplastic syndromes of the nervous system" and "Paraneoplastic syndromes affecting spinal cord, peripheral nerve, and muscle", section on 'Autonomic neuropathy'.)

**Infectious** — Viruses may cause morphologic (ie, inflammatory) or functional changes of the ENS and extrinsic neural pathways supplying the gut and are detectable in a subset of patients with CIPO. Chagas disease caused by infection with the protozoan parasite *Trypanosoma cruzi* is the most common infectious cause of CIPO. A potential role of a chronic JC virus (of the Polyoma virus family) infection has been suggested in observational studies [22,23]. (See "Chagas disease: Epidemiology, screening, and prevention", section on 'Geographic distribution' and "Overview and virology of JC polyomavirus, BK polyomavirus, and other polyomavirus infections".)

**Genetic** — Although most cases of CIPO are sporadic, familial cases have been described, suggesting an underlying genetic basis [24]. Specific examples include [25]:

- Dominant mutations in the smooth muscle actin gene, *ACTG2*, account for 44 to 50 percent of familial CIPO. *ACTG2* (actin, gamma2) disorders result in different phenotypes: megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS), prune-belly syndrome, or CIPO [26-29]. A pathogenic variant in *ACTG2* has been reported in association with visceral myopathy, CIPO, intestinal malrotation, hypertrophic pyloric stenosis, and choledochal cyst [30]. Similar phenotypes of visceral myopathy have been reported in association with variants in *ACTA2* and *MYH11* [28,31].

- Mitochondrial myopathies associated with CIPO, including mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), myoclonus epilepsy associated with ragged-red fibers (MERRF), and familial mitochondrial neurogastrointestinal encephalomyopathy due to pathogenic variants in the *TYMP* gene (also called *ECGF1*) that encodes thymidine phosphorylase [32].

- Transcription factor SOX10 on chromosome 22 (22p12). De novo *Sox 10* genetic variant (defined as c.895delC) has been associated with CIPO presenting in infancy in association with Waardenburg syndrome type IV, which is characterized by pigmentary abnormalities and deafness, but without Hirschsprung's disease [33].

- Waardenburg-Shah syndrome (deafness and pigmentary abnormalities in association with aganglionic megacolon), in which mutations in neural crest-derived cells have been identified in some kindreds with CIPO [34].

- Alpers-Huttenlocher syndrome (AHS) caused by pathogenic variants in DNA polymerase gamma gene (*POLG*) on chromosome 21 (21q17) [35].

- X-linked inherited CIPO can result from pathogenic variants in filamin A gene (*FLNA*) and L1 cell adhesion molecule (*L1CAM*)). Loss-of-function mutations in *FLNA* cause an X-linked dominant disorder with multiple organ involvement [36-38]. Affected females present with periventricular nodular heterotopia in the brain, cardiovascular complications, thrombocytopenia, and Ehlers-Danlos syndrome [39].

- Mutations in *RAD21* that disrupt the ability of its product to regulate genes such as *RUNX1* and *APOB* have been associated with CIPO [40]. *RAD21* is an essential gene that encodes a DNA double-strand break repair protein that is evolutionarily conserved and is essential for proper chromosome segregation, post-replicative DNA repair, and prevention of inappropriate recombination between repetitive regions [41].

- Upregulation of the RNA-binding protein for multiple splicing 2 (*RBPMS2*) has been reported in patients with CIPO [42]. This protein is expressed strongly during the early stage of visceral smooth muscle cell (SMC) development and quickly downregulated in differentiated and mature SMCs. Sustained expression of *RBPMS2* inhibits the expression of markers of SMC differentiation by inhibiting bone morphogenetic protein activity and stimulates SMC proliferation.

- Ehlers-Danlos syndrome due to small bowel alpha-actin deficiency [43].

- Lysosomal storage disease or Fabry disease (due to X-linked deficiency in lysosomal alpha-Gal A) may be associated with CIPO [44]; colonic dysmotility has been associated with glycolipid deposition in plexuses and ganglia [44]. These genetic mutations may require investigation of tissue samples by exome sequencing, as was reported for *ACTG2* mutation [45], or systematic histopathologic examination of tissue [46]. In one study that included 115 patients with apparently idiopathic CIPO, disturbances in smooth muscle alpha-actin expression in intestinal smooth muscle were demonstrated histopathologically in 24 percent [47].

- A localized form of genetic neuromuscular denervation or aganglionosis, Hirschsprung disease, is associated with secondary dilatation proximal to the affected segment. (See "Congenital aganglionic megacolon (Hirschsprung disease)" and "Mitochondrial myopathies: Clinical features and diagnosis", section on 'MELAS'.)

## CLINICAL MANIFESTATIONS

**Clinical features** — Abdominal pain, bloating, and distension are the most common clinical features of chronic intestinal pseudo-obstruction (CIPO). In one series that included 59 patients, symptoms included abdominal distension (75 percent), abdominal pain (58 percent), nausea (49 percent), constipation (48 percent), heartburn/regurgitation (46 percent), fullness (44 percent), epigastric pain/burning (34 percent), early satiety (37 percent), and vomiting (36 percent) [48,49]. These symptoms may be acute, recurrent, or chronic.

Acute episodes are characterized by abrupt onset of intense, cramping pain, abdominal distention, nausea, and vomiting. After the acute episode, patients may be asymptomatic or, more often, continue to experience symptoms due to delayed transit in the proximal (eg, anorexia, early satiety, nausea and vomiting) and/or distal (constipation) gastrointestinal tract. Patients may have diarrhea due to small bowel bacterial overgrowth. Weight loss results from impaired intestinal transit, malabsorption due to bacterial overgrowth, and inadequate intake

due to exacerbation of symptoms with food ingestion. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis".)

Patients may also have symptoms due to an underlying disorder (eg, dysphagia related to Chagas disease, proximal muscle weakness leading to difficulty climbing stairs in patients with polymyositis/dermatomyositis, bladder dysfunction in neuropathic and myopathic CIPO). (See "Manifestations of multiple sclerosis in adults" and "Clinical manifestations and diagnosis of systemic sclerosis (scleroderma) in adults" and "Clinical manifestations of hypothyroidism" and "Clinical manifestations of hypocalcemia" and "Clinical presentation and diagnosis of pheochromocytoma" and "Screening for diabetic polyneuropathy" and "Chronic Chagas cardiomyopathy: Clinical manifestations and diagnosis" and "Congenital aganglionic megacolon (Hirschsprung disease)".)

**Physical examination** — The main physical findings are abdominal distention, abdominal tenderness on palpation (localized to the epigastric and periumbilical regions or, more commonly, over the whole abdomen), and a succussion splash, which would be typically present if there is either gastric involvement or impairment of gastric emptying secondary to the delay in intestinal transit. (See "Gastric outlet obstruction in adults", section on 'Physical examination'.)

## DIAGNOSTIC APPROACH

**Clinical suspicion** — Chronic intestinal pseudo-obstruction (CIPO) should be suspected in patients with long-standing abdominal pain, bloating, and visible distension of at least three months' duration. Confirmation of the diagnosis requires exclusion of mechanical obstruction and other causes of dysmotility by performing imaging studies, endoscopy, and scintigraphy to assess motility.

**Laboratory studies** — Laboratory studies are not routinely necessary in the evaluation of patients with CIPO but may be warranted in patients with significant vomiting, diarrhea, or malnutrition. A complete blood count and comprehensive metabolic panel may reveal hypokalemia and metabolic acidosis in patients with severe diarrhea. Hypokalemia and metabolic alkalosis may be present if there is prominent vomiting. Patients may also have hypoalbuminemia due to malnutrition. Rarely, serum vitamin B12 levels are low due to small intestinal bacterial overgrowth. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis", section on 'Laboratory findings'.)

### Evaluation to rule out obstruction

**Imaging** — Radiographic evaluation should be performed to exclude an organic cause of obstruction. In patients with CIPO, computed tomographic (CT)/magnetic resonance (MR) enterography may demonstrate dilated loops [50]. MR angiography should be considered in patients with evidence of obstruction when congenital or acquired vascular abnormalities are suspected based on enterography.

Cine MR imaging may be used to assess small bowel motility in patients with CIPO by quantitative analysis of luminal diameter, however, further studies are needed to validate these results [51,52].

Radiographic testing does not usually provide an etiologic diagnosis of CIPO. An exception is systemic sclerosis affecting the small intestine, which is characterized by dilated segments, edema, and abnormal texture and motility of the valvulae conniventes ( image 1). (See "Gastrointestinal manifestations of systemic sclerosis (scleroderma)".)

**Endoscopy** — Upper endoscopy and colonoscopy should be performed to rule out an intraluminal or extraluminal cause of obstruction and to identify the location of the obstruction (upper [gastrojejunal] or lower [ileocolonic] gastrointestinal tract). Upper gastrointestinal endoscopy is useful to exclude an aorto-mesenteric artery compression syndrome, which may be difficult to differentiate on imaging from CIPO due to the impact of severe dysmotility on this segment of the small intestine (ie, sustained uncoordinated contractions in the distal duodenum). The duodenal mucosa should be biopsied to exclude celiac disease.

**Assessment of intestinal motility** — In patients in whom CIPO is suspected and there is no evidence of an intraluminal or extraluminal cause of obstruction on imaging and by endoscopy, the presence of a motility disorder should be confirmed with scintigraphy.

- **Scintigraphy** — Scintigraphy is the method of choice in the evaluation of gastric, small bowel, and colon transit. While interpreting scintigraphy results, it is important to note that delayed colonic transit may cause delayed small bowel transit. Therefore, it is important to consider gastrointestinal transit in all three main regions (stomach, small bowel, and colon) before concluding that delayed small bowel transit defines small intestinal dysmotility.

  Normal small bowel transit time can vary depending on the methods used. Using resin pellets mixed with a meal, small bowel transit time in healthy individuals reportedly ranged from 151 to 290 minutes [53]. Using the liquid phase of a mixed solid–liquid meal, small bowel transit time ranged from 72 to 392 minutes in healthy individuals [54].

A useful clue to clinically significant small intestinal disease is the finding of delayed gastric emptying [2,55]. Thus, when small bowel and colonic transit are delayed and gastric emptying is normal, the main focus of treatment should be normalization of colonic motor function and treatment of constipation, rather than attempting to normalize the small bowel transit alone. Novel approaches using fewer scans have been devised to simplify the evaluation of bowel transit using scintigraphy [53,56,57]. However, there is a wide range of normality (essentially 0 to 100 percent in a sample of 319 healthy volunteers) in the surrogate endpoint of small bowel transit commonly used in scintigraphic studies that is the percent colonic filling at six hours. Therefore, small bowel transit measurement may require more scans to have sufficient specificity to diagnose intestinal motility disorder and in these situations, careful assessment of gastric and colonic transit is also key.

- **Wireless motility capsule** — Small bowel transit in suspected chronic intestinal dysmotility can also be measured by wireless motility capsule, which assesses small bowel transit time by a sharp increase in pH on entry into the duodenum and by a fall in pH at the ileocecal junction [58]. Evaluation of intestinal motility using endoluminal image analysis acquired by capsule has also been developed [59]. However, further validation of these techniques is needed before they can be routinely used to assess motility. (See "Overview of gastrointestinal motility testing" and "Etiology and evaluation of chronic constipation in adults", section on 'Wireless motility capsule'.)

**Diagnosis** — The diagnosis of chronic intestinal pseudo-obstruction (CIPO) is based on the presence of long-standing symptoms of mechanical obstruction in the absence of an anatomic cause on radiologic examination and endoscopy, and evidence of impaired motility.

**Differential diagnosis** — Patients with chronic intestinal dysmotility and slow transit constipation/colon inertia can have similar symptoms to patients with CIPO, but these conditions are not associated with dilatation on imaging ( table 1).

CIPO can be distinguished from mechanical obstruction and other acute functional causes of obstruction (eg, postoperative ileus and acute pseudo-obstruction) based on the time course, location of dilation, symptom progression, and findings on imaging ( table 2). The differentiation of CIPO (encompassing heterogeneous conditions leading to severe, end-stage gut motor failure and defined clinically and radiologically by evidence of abnormal small bowel motility and episodic or chronic signs mimicking mechanical obstruction) from enteric dysmotility (defined as demonstrable abnormal small bowel motor activity but without any features mimicking mechanical obstruction) is relevant since CIPO is more likely to require long-term home parenteral nutrition [60].

## IDENTIFYING THE UNDERLYING ETIOLOGY

Once the diagnosis of chronic intestinal pseudo-obstruction (CIPO) is established, the underlying etiology should be determined.

**History** — Patient may provide a history of culprit medications (including anticholinergic antidepressants, calcium channel blockers, and the alpha-2 adrenergic agonists such as clonidine, or cancer immunotherapy with immune checkpoint inhibitors [61]) or a family history of relatives with a similar clinical presentation (eg, mitochondrial neurogastrointestinal encephalopathy [MNGIE], familial amyloidosis) [62].

Patients may also have signs of an underlying collagen vascular or neuromuscular disease (eg, proximal muscle weakness may indicate polymyositis/dermatomyositis; classic skin abnormalities associated with scleroderma; ptosis, ophthalmoplegia, peripheral polyneuropathy, and sensorineural hearing loss in MNGIE). (See "Clinical manifestations of dermatomyositis and polymyositis in adults" and "Clinical manifestations and diagnosis of systemic sclerosis (scleroderma) in adults" and "Manifestations of multiple sclerosis in adults".)

**Laboratory testing** — Laboratory examination can identify secondary causes of CIPO related to potentially curable diseases. The following tests should therefore be performed in all patients with CIPO:

- Celiac serologies.
- Thyrotropin (TSH).
- Serologic testing for herpes simplex virus (HSV), cytomegalovirus (CMV), and Epstein-Barr virus (EBV).
- Markers of inflammation including erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP).
- Auto-antibodies (specific antibodies to glutamic acid decarboxylase, voltage-gated calcium channels [P/Q subtype], nicotinic acetylcholine receptors, and voltage-gated potassium channels) to identify an association of an immune-mediated process [63].
- Antineuronal antibodies (ANNA-1/anti-Hu) in patients with suspected paraneoplastic syndrome [64].
- In patients with suspected MNGIE, lactic acid (at rest and during exercise), thymidine phosphorylase levels in the buffy coat, nucleotide concentrations, and genetic analysis

should be performed. (See "Mitochondrial myopathies: Clinical features and diagnosis", section on 'Evaluation and diagnosis'.)

**Additional testing in selected patients** — If the etiology is evident based on the clinical history and initial laboratory testing, no further investigation is necessary.

- **Manometry** – Manometry plays a supportive role in determining if the underlying etiology is a myopathic or neuropathic disorder but lacks specificity.

  - **Technique** – Manometry is performed by placement of a multilumen tube through the nose or mouth into the small intestine. Positioning of the tube is facilitated by endoscopy or a steerable catheter system to place a guidewire through the stomach and duodenum and into the jejunum. Perfusion of the lumens or solid state transducers placed along the tube allows measurement of the pressure profile of the stomach and small intestine. These profiles are measured over several hours during fasting and after standard meals.

  - **Interpretation** – Myopathic disorders are typically associated with low amplitude contractions, whereas in neuropathic disorders, the amplitude of contractions is typically normal, but the organization of the contractile response is abnormal ( image 2). A mechanical obstruction of the intestine typically shows simultaneous, prolonged contractions at the level of the small intestine [65]. Of note, esophageal manometry may show ineffective peristalsis in approximately one-half the patients with CIPO [66].

- **Autonomic testing** — Autonomic testing is useful in patients with evidence of neuropathic dysmotility on manometry but without a known underlying neurologic disorder. Several common neurologic disorders can affect gastrointestinal motility by altering the parasympathetic or sympathetic supply to the gut ( figure 1). These include [62]:

  - Brainstem tumors or strokes
  - Diabetes mellitus
  - Spinal cord injury
  - Multiple sclerosis
  - Parkinson disease
  - Autonomic system degeneration

  Tests of autonomic function can differentiate a preganglionic or central lesion from a peripheral neuropathy associated with autonomic dysfunction ( table 3) [67]. Brain and

spinal cord magnetic resonance imaging (MRI) is essential in patients in whom a central lesion is suggested from the history or the results of autonomic testing. A peripheral neuropathy requires further screening for a toxic, metabolic, or paraneoplastic process (eg, lead poisoning, porphyria, or lung cancer, respectively).

- **Full-thickness intestinal biopsy** – Full thickness biopsies should be considered in patients with severe dysmotility of unknown etiology. We perform a full thickness biopsy to diagnose the underlying etiology in the following groups of patients:

  - Undergoing abdominal surgery for any reason, especially in those with intractable symptoms.
  - Poor postsurgical outcomes.
  - Permanent catheter for enteral or parenteral nutrition.

  Histologic findings may help differentiate myopathic, neuropathic, or other disorders. Histopathologic techniques also allow for detection of subtle abnormalities in the enteric nervous system and underlying deficiencies in specific neuropeptides and neurotransmitters, thereby providing information for diagnosis, prognosis, and management [3,9,68,69].

  - Histologic findings on full-thickness specimens have been found to correlate with manometric findings [70-72]. In case reports, decreased numbers of myenteric and submucosal neurons with increased interganglionic distance correlated with the severity of symptoms and clinical manifestations of deranged intestinal motility [73].

  - MNGIE has been reported to be associated with altered interstitial cells of Cajal (ICC) [74].

  - Reports of inflammatory cell infiltration of the myenteric plexus (including eosinophilic or lymphocytic ganglionitis in several reports) [75-78] or muscle have been described in the literature; however, it is unclear whether antiinflammatory therapy is efficacious in reversing the inflammation, and it is still unclear whether the presence of inflammatory infiltration represents cause or effect of CIPO [71,79,80].

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Bowel obstruction".)

## SUMMARY AND RECOMMENDATIONS

- **Definition** – Chronic intestinal pseudo-obstruction (CIPO) is a rare syndrome that is characterized by signs and symptoms of a mechanical obstruction of the small or large bowel in the absence of an anatomic lesion that obstructs the flow of intestinal contents, and the presence of dilation of the bowel on imaging. (See 'Epidemiology' above.)

- **Etiology** – CIPO may be due to an underlying neuropathic disorder (involving the enteric nervous system or extrinsic nervous system), a myopathic disorder (involving the smooth muscle), or abnormality in the interstitial cells of Cajal (ICC). Neuropathic, myopathic, or ICC abnormalities that result in CIPO may be idiopathic in etiology or secondary to another disease. Approximately one-half of the cases of CIPO are secondary to neurologic, paraneoplastic, autoimmune, metabolic/endocrine, and infectious diseases. (See 'Etiology' above.)

- **Clinical features** – Abdominal pain and distension are the most common clinical features. Patients may have diarrhea due to small bowel bacterial overgrowth. Nausea, vomiting, and weight loss are predominant symptoms in patients with CIPO involving the proximal gastrointestinal tract. Other features include anorexia, alternating bowel habits, and urinary symptoms. These symptoms may be acute, recurrent, or chronic. (See 'Clinical manifestations' above.)

- **Diagnosis** – CIPO should be suspected in patients with long-standing abdominal pain, bloating, and visible distension of at least three months' duration. The diagnosis of CIPO is based on all of the following:

  - The presence of long-standing symptoms of obstruction.
  - Absence of an anatomic cause of obstruction on upper endoscopy and colonoscopy and/or radiologic examination (computed tomographic/magnetic resonance enterography).
  - Confirmation of impaired motility with scintigraphy. (See 'Diagnostic approach' above.)

- **Identifying the underlying etiology** – All patients should undergo laboratory testing to identify secondary causes of CIPO.

  In patients with abnormal transit on scintigraphy and in whom there is a known underlying disease, no further investigation is necessary and appropriate therapy can be initiated. In patients with abnormal transit on scintigraphy and no known underlying disease, manometry should be performed.

Autonomic testing is useful in patients with evidence of a neuropathic disorder on manometry but without a known underlying neurologic disorder. (See 'Identifying the underlying etiology' above.)



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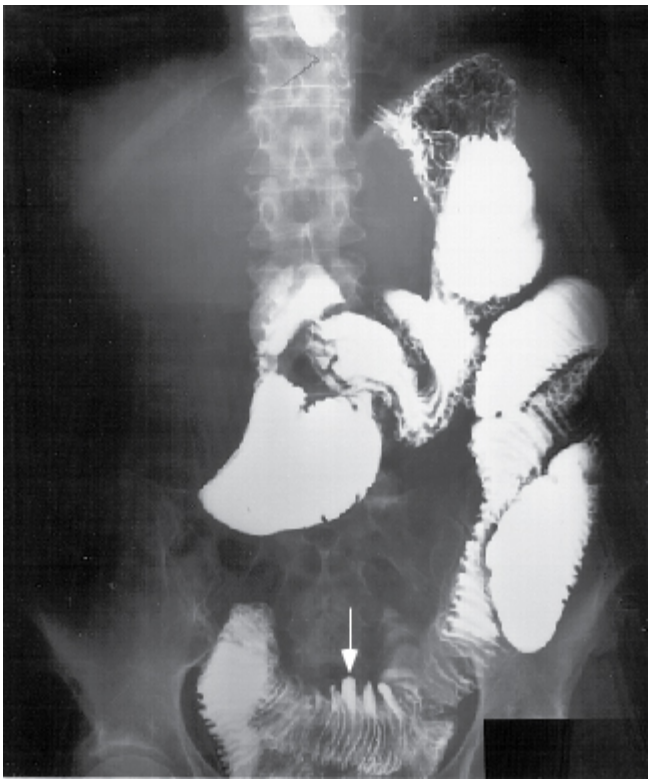
Topic 2639 Version 23.0

## GRAPHICS

### Intestinal pseudo-obstruction in scleroderma



Barium radiograph in a patient with small bowel scleroderma and pseudo-obstruction syndrome reveals a dilated post-bulbar duodenum (megaduodenum) and jejunum, with infiltrated valvulae conniventes (arrow) in the lower jejunal loop.

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*Courtesy of Michael Camilleri, MD.*

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Graphic 65344 Version 4.0

## Gastrointestinal motility disorders

| Region | With dilatation | Without dilatation |
|---|---|---|
| Esophagus | Achalasia with mega-esophagus | Achalasia |
| Stomach | Acute gastric dilatation | Gastroparesis |
| Small bowel | Pseudo-obstruction | Chronic intestinal dysmotility |
| Colon | Megacolon/pseudo-obstruction | Slow transit constipation/colonic inertia |

Graphic 73822 Version 1.0

## Main differences between mechanical versus functional intestinal obstruction

| | Mechanical obstruction | POI | AIPO/ACPO | CIPO |
|---|---|---|---|---|
| **Luminal obstruction** | Yes | No | No | No |
| **Motility** | Initially ↑ then ↓ proximal to obstruction | ↓ | ↓/uncoordinated | ↓/uncoordinated |
| **Dilatation** | Yes (proximal to obstruction) | No | Yes | Yes |
| **GI involvement** | Proximal to obstruction | Mainly small bowel | Mainly colon | Pan-enteric |
| **Radiology** | Typical "cut-off" point; presence of air-fluid levels | "Cut-off point" occasionally present; air-fluid levels usually absent | "Cut-off point" occasionally present; air-fluid levels sometimes detected | "Cut-off point" occasionally present; air-fluid levels detectable |
| **Course** | Acute | Acute | Acute | Chronic |
| **Progression** | Rapidly evolving toward total obstruction | Self-limiting, slowly improving | May respond to medical treatment; major complication may occur | Variable, generally self-limiting |
| **Treatment** | Surgery | Supportive measures | Medical treatment (neostigmine); decompressive endoscopy or surgery in unresponsive cases | Variable; EN, TPN/HPN often needed |

↑: increased; ↓: decreased; AIPO/ACPO: acute intestinal pseudo-obstruction/acute colonic pseudo-obstruction; CIPO: chronic intestinal pseudo-obstruction; EN: enteral nutrition; GI: gastrointestinal; POI: postoperative ileus; TPN/HPN: total/home parenteral nutrition.

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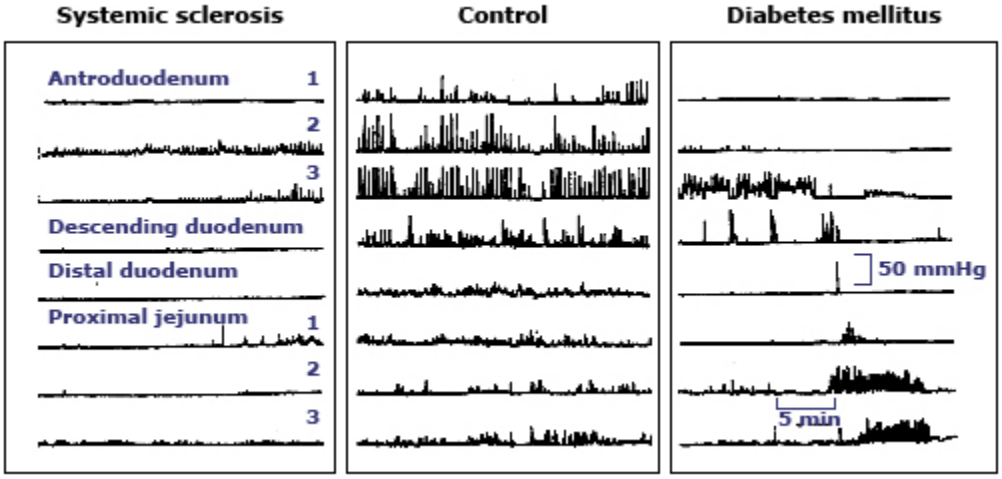
Graphic 84010 Version 2.0

## Manometry of the stomach and small intestine differentiates neuropathic and myopathic disorders




Postprandial gastrointestinal motility in a patient with systemic sclerosis (myopathic disorder, left panel) is characterized by low amplitude contractions at all levels compared with controls. By comparison, a neuropathic disorder such as diabetes mellitus (right panel) is characterized by normal contraction amplitude, but abnormal organization of the contractile response. Specifically, there is a lack of distal antral contractions, pyloric tonic, and phasic pressure activity, and persistence of migrating motor complex-like activity postprandially (proximal jejunum rows 2 and 3) despite the ingestion of a solid-liquid meal.

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*Adapted from: Camilleri M. Medical treatment of chronic intestinal pseudo-obstruction. Pract Gastroenterol 1991; 15:10.*

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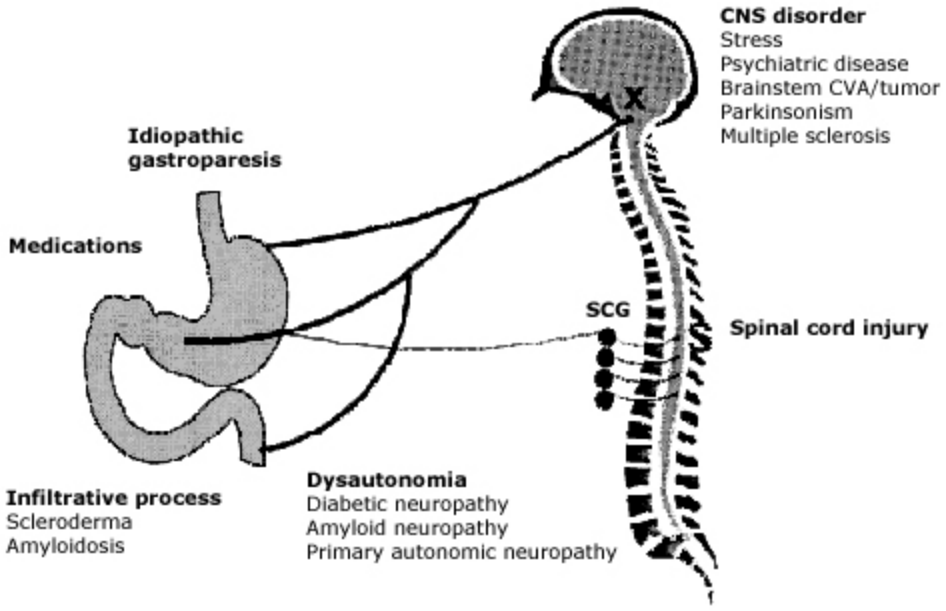
Graphic 51540 Version 6.0

## Neuromuscular disorders impairing gastric motor function




Several common neurologic disorders can affect gastrointestinal motility by altering the parasympathetic or sympathetic supply to the gut.

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X: vagal nuceli; CNS: central nervous system; CVA: cerebrovascular accident; SCG: sympathetic chain ganglia.

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Graphic 52708 Version 5.0

## Commonly performed tests of autonomic function

| Test | Principle | Nerves assessed |
|---|---|---|
| Sweat test | Heat stimulates thermoregulatory center | Central sympathetic adrenergic and peripheral sympathetic cholinergic |
| BP lying, standing | Postural BP control by adrenergic nerves | Sympathetic adrenergic |
| RR interval with deep breathing | Vagal reflux bradycardia | Cardiac vagus |
| Plasma pancreatic polypeptide response to modified sham feeding | Sham feeding stimulates vagal center and efferents | Efferent vagus to abdomen |

Graphic 82750 Version 2.0

## Contributor Disclosures

**Michael Camilleri, MD** Equity Ownership/Stock Options: Bilayer Therapeutics [Bile acids in constipation]; Dignify Therapeutics [Spinal cord injury]; Enterin [Constipation in Parkinson disease]; Thelium Therapeutics [Epithelial barrier function]. Patent Holder: 13C-mannitol for permeability measurement [Intestinal diseases]; Capsule for colonic transit by scintigraphy [Colonic motility disorders, including constipation and diarrhea]; Obesity-metabolomics to identify different phenotypes [Obesity subgroups]. Grant/Research/Clinical Trial Support: Allergan [Bile acid malabsorption]; NGM Biopharmaceuticals [Bile acid diarrhea; bile acid malabsorption]; Vanda [Gastroparesis]. Consultant/Advisory Boards: Aclipse Therapeutics [Gastroparesis]; Aditum Bio [Gastroparesis, IBS, IBD]; AEON Pharma [Gastroparesis]; Arena [Visceral pain in GI disorders]; BioKier [Obesity, diabetes]; Coloplast [Colonic motility disorders]; Colospan [Device to measure colon pressure]; Cosmo Pharmaceuticals [Bile acid diarrhea]; Fauna Bio [Intestinal mucosal barrier]; GlaxoSmithKline [Chronic idiopathic constipation]; Invea Therapeutics [IBS-D]; InveniAI [GI motility disorders]; Ironwood [IBS, gastroparesis, bile acid diarrhea]; Kallyope [Obesity, GI function and appetite control]; Novome [GI motility diseases and role of bile acids]; Pfizer [Intestinal epithelial biology and "leaky gut"]; Protagonist Therapeutics [IBS-diarrhea]; QED Therapeutics [Diarrhea]; Sunovion Pharmaceuticals [Gastric functions, satiation, incretins and glycemic control]; Takeda [Gastroparesis screening tool]; VIPUN Medical [Gastric monitoring system]; Virios [HSV-1 and pain in GI diseases]; Zealand Biopharma [Gastroparesis, IBS-D]. All of the relevant financial relationships listed have been mitigated. **Lawrence S Friedman, MD** Other Financial Interest: Elsevier [Gastroenterology]; McGraw-Hill [Gastroenterology]; Wiley [Gastroenterology]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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