Chapter 5
Chronic Intestinal Pseudo-Obstruction

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Case Study

A 53-year-old female was referred by her local gastroenterologist for 4 years of progressive gastrointestinal (GI) symptoms. She initially presented to her internist with symptoms of constipation and abdominal bloating. Her internist began an evaluation by ordering a complete blood count (CBC), thyroid-stimulating hormone level (TSH), and colonoscopy – all of which were normal. Based on her symptoms, a normal physical examination, and her normal tests, she was diagnosed with IBS and treated with PEG-3350. She then noted

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increasing episodes of upper abdominal bloating and early satiety. Upper endoscopy including biopsies of the duodenum and stomach was normal. Over the next year, she noted difficulty eating due to postprandial nausea; she lost approximately 15 pounds (10% of the total body weight). Abdominal x-ray revealed dilated loops of small intestine. CT enterography was negative for mechanical obstruction but did demonstrate diffusely dilated loops of small intestine. The patient was diagnosed with chronic intestinal pseudo-obstruction (CIPO).

Objectives

- Discuss the epidemiology, etiology, and pathogenesis of patients with CIPO.
- Outline a stepwise diagnostic approach for patients with suspected CIPO.
- Review treatment strategies for patients with CIPO with an emphasis on optimizing nutritional status (oral, enteral, and parenteral), therapies to improve intestinal motility, and endoscopic and surgical management options.

Epidemiology

Chronic intestinal pseudo-obstruction (CIPO) is a rare and debilitating condition. Patients show severe impairment of gastrointestinal (GI) propulsion leading to symptoms and/or signs suggestive of partial or complete intestinal obstruction in the absence of any mechanical obstruction. Most estimates of the incidence and prevalence of CIPO are from tertiary referral centers. One estimate from a pediatric tertiary care center is that approximately 100 infants are born with CIPO each year in the United States. This figure does not provide a good estimate on prevalence, however, as it does not include

patients who develop CIPO later in life. In a national survey in Japan, the estimated prevalence of CIPO was 0.80 to 1.00 per 100,000, with an incidence of 0.21–0.24 per 100,000 [1]. The mean age at diagnosis was 63.1 years for males and 59.2 for females.

CIPO remains a challenge for most clinicians for several reasons. First, most physicians fail to recognize CIPO patients early due to their limited experience; second, symptoms of CIPO are non-specific. This may lead patients to be subjected to inadequate management including ineffective, and potentially dangerous, surgical procedures. Third, CIPO is an "umbrella term" covering a wide heterogeneous group of patients, i.e., congenital versus acquired/secondary to metabolic/endocrinological, neurological, and paraneoplastic disorders or idiopathic, with no apparent cause underlying the dysmotility. Finally, most CIPO patients show a variable outcome; some patients remain clinically stable over long periods of time, whereas others rapidly decline requiring parenteral nutrition to prevent severe malnutrition and death. These challenges and intrinsic difficulties hinder thorough phenotyping of patients, mechanistic studies, and disease management.

Classification

Several different classification schemes have been used to categorize CIPO patients. The authors prefer to categorize CIPO patients into three broad categories: congenital, acquired/secondary, and idiopathic (Table 5.1). Each of these groups can be further subdivided into three histological categories, neuropathies, myopathies, and mesenchymopathies, although some patients may have coexisting pathological abnormalities. A large proportion of patients are classified under the idiopathic category because no histological abnormality can be identified despite extensive testing.

Table 5.1 Classification of patients with chronic intestinal pseudo-obstruction

Onset	Variant	Typical related conditions
Congenital	CAID syndrome (SGOL 1 mutation)	Associated megacystis-microcolon-intestinal hypoperistalsis syndrome
	ACTG2 gene	Females. Periventricular nodular heterotopia, cardiac complications, thrombocytopenia, Ehlers-Danlos syndrome
	Mutations in *FLNA* and *L1CAM*	MNGIE, MELAS, MERRF
	Mitochondrial diseases (Mutations of TP or ECGF1)	Ehlers-Danlos syndrome
	Small bowel α-actin deficiency	
	Deficient interstitial cells of Cajal	
Acquired	Autoimmune	SLE, systemic sclerosis, dermatomyositis/polymyositis, autoimmune myositis, autoimmune ganglionitis
	Infectious/postinfectious	Chagas' disease, CMV, EBV, VZV, JC virus, Kawasaki disease, post-viral neuropathy
	Endocrine	Diabetes, hypothyroidism, hypoparathyroidism
	Oncology/hematology	Paraneoplastic (anti-Hu antibodies) syndrome small cell lung cancers/carcinoid tumors/malignant thymoma, chemotherapy and/or BM/stem cell transplant, radiation injury, pheochromocytoma
	Muscle disorders	Myotonic dystrophy, Duchenne muscular dystrophy
	Toxins	Fetal alcohol syndrome, alcohol abuse
	Drugs	Diltiazem and nifedipine, clonidine, cyclopentolate/phenylephrine eye drops (neonates), anti-Parkinsonians

Pathology	
Extrinsic autonomic nervous system	Stroke, encephalitis, calcification of basal ganglia, orthostatic hypotension, diabetes
Enteric nervous system	Hirschsprung's disease, Chagas disease, Von Recklinghausen disease
Mixed enteric neuromyopathy	Paraneoplastic (central nervous system neoplasms, bronchial carcinoid, leimyosarcoma, viral infections
Enteric smooth muscle layer	Systemic sclerosis, dermatomyositis, Ehlers-Danlos, jejunal diverticulosis, amyloidosis, diabetes
Idiopathic	Myotonic dystrophy, progressive systemic sclerosis, degenerative leiomyopathy, intestinal leiomyositis

CMV cytomegalovirus, *EBV* Epstein-Barr virus, *ECGF1* endothelial cell growth factor-1, *FLNA* filamin A gene, *JC virus* John Cunningham virus, *L1CAM* L1 cell adhesion molecule, *MELAS* mitochondrial encephalopathy with lactic acidosis and stroke-like episodes, *MERRF* myoclonus epilepsy associated with ragged-red fibers, *MNGIE* mitochondrial neurogastrointestinal encephalomyopathy, *SLE* systemic lupus erythematosus, *TP* thymidine phosphorylase gene, *VZV* varicella zoster virus

Etiology and Pathophysiology

Pathophysiologically, CIPO patients either have an impairment of the enteric nervous system, the intestinal smooth muscle, or the interstitial cells of Cajal (ICC), individually or in combination. Regardless of the cause, the end result is severe impairment of GI propulsion. These pathophysiologic abnormalities may arise due to another disease (secondary CIPO) or be idiopathic in nature. Approximately half of the cases of CIPO are secondary to neurologic, paraneoplastic, autoimmune, metabolic/endocrine, and infectious diseases [2].

Neuropathies

Neurologic disorders can affect the extrinsic autonomic nerve pathways supplying the gut (e.g., encephalitis, Parkinson's disease, or after a cerebrovascular accident) or the enteric nervous system (ENS) due to either an inflammatory (myenteric ganglionitis) or degenerative process. Degenerative neuropathies (paraneoplastic or immune-mediated) 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. In paraneoplastic syndromes associated with small cell lung cancers, carcinoid tumors, or malignant thymoma, the circulating antineuronal (anti-Hu) antibodies are thought to target both the neurons in the submucosa and myenteric ganglia ENS damaging the enteric reflexes, thereby causing dysmotility. Immune-mediated pseudo-obstruction is seen in systemic sclerosis (SSc), dermatomyositis, and systemic lupus erythematosus. Neurotropic viruses (Herpes viridae, John Cunningham virus) may cause morphologic (i.e., inflammatory) or functional changes of the enteric nervous system and extrinsic neural pathways supplying the gut [3–5].

Congenital forms of neuropathies include genetic neuromuscular denervation or aganglionosis, Hirschsprung's disease, mitochondrial cytopathies such as mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), myoclonus epilepsy associated with ragged-red fibers (MERRF), and syndromes such as Waardenburg-Shah syndrome (deafness and pigmentary abnormalities in association with aganglionic megacolon) associated with mutations in neural crest-derived cells [6].

The interstitial cells of Cajal (ICC) are present within the submucosal, intramuscular, and intermuscular layers of the GI tract and serve as pacemaker cells, generating bioelectric slow-wave potentials leading to enteric smooth muscle contraction. Decreased number of ICCs, along with structural abnormalities, such as loss of processes and damaged intracellular cytoskeleton and organelles, has been reported in children (congenital) and adults (autoimmune diseases like SSc) with CIPO.

Intestinal Myopathies

The muscularis propria of the intestinal tract is normally composed of two layers, external (longitudinal) and internal (circular), oriented perpendicularly. These may be affected in some patients with CIPO. In degenerative leiomyopathy, there is a progressive loss of enteric smooth muscle and replacement with fibrous tissue. Symptoms of CIPO may not develop until adolescence. Patients with smooth muscle involvement may have impaired urinary bladder function. Intestinal leiomyositis, characterized by dense and diffuse lymphocytic infiltration of the muscularis propria, is another rare disease which predominantly affects children, and less than 12 patients have been reported in the world literature. In addition to the aforementioned diseases, secondary myopathies due to bowel ischemia, drug toxicity, radiation injury, and autoimmune disorders (myotonic dystrophy, progressive systemic sclerosis) are also seen [7].

Mesenchymopathies

More than one element of the neuromuscular apparatus of the gastrointestinal tract may be affected by various disease processes. For example, in SSc, immune-mediated destruction of the enteric nerves occurs before smooth muscle involvement. Similarly, mitochondrial cytopathy may result in neuropathy and subsequently myopathy. In diabetes mellitus, the extrinsic autonomic nerves and the ICCs are affected, whereas amyloidosis may cause an extrinsic neuropathy followed by myopathy.

Symptoms

Symptoms of CIPO vary from patient to patient based on the location and the extent of the GI tract involved. Symptoms may be acute, recurrent, or chronic. Abdominal pain and distension are reported by most (80%) patients. Nausea and vomiting occur in 75% and 40–50% of cases with documented gastroparesis (e.g., confirmed with a 4-h solid-phase gastric emptying scan). Esophageal dysmotility has been reported in approximately 70% of patients, while constipation occurs in 40%, and diarrhea (rarely steatorrhea) occurs in about 20–30% of cases (Table 5.2) [8, 9]. Diarrhea may be related to small intestinal bacterial overgrowth (SIBO) due to intestinal stasis and usually results in malabsorption and nutritional deficiencies in most patients. Although predominantly chronic in nature, these symptoms worsen during acute sub-occlusive episodes characterized by the abrupt onset of intense, cramping abdominal pain, distention, nausea, and vomiting. Intestinal volvulus must be excluded during an acute episode.

Patients may also have symptoms due to the underlying disorder (e.g., dysphagia due to esophageal involvement in CIPO related to SSc, proximal muscle weakness in patients with polymyositis/dermatomyositis, and bladder dysfunction in neuropathic and myopathic CIPO). Urinary bladder dys-

Table 5.2 Symptoms reported by patients with chronic intestinal pseudo-obstruction

Symptom	Reported frequency [8, 20]
Abdominal pain	58–80%
Abdominal distension	75–80%
Nausea	49–75%
Vomiting	40–50%
Heartburn/regurgitation	~50%
Dysphagia	70%
Early satiety	~40%
Constipation	40–50%
Diarrhea	20–30%

function (with or without megacystis and megaureter) often coexists with CIPO, more commonly detectable in children with an underlying myopathic derangement of the GI tract. Finally, CIPO patients may develop depression and/or other psychological disorders as a consequence of the disabling nature of this condition and the frustrating ineffectiveness of most prokinetic drugs.

Diagnosis

As yet, no single diagnostic test or pathognomonic finding indicative of CIPO has been identified. Thus, a stepwise diagnostic approach is recommended, aimed at ruling out mechanical obstruction, identifying underlying diseases, and understanding the pathophysiological features.

A thorough history and physical examination must be performed first. This should cover the patient's current medical conditions (autoimmune, connective tissue disorders), prior surgeries (the presence of adhesions, diverticula), family history (GI malignancies, similar constellation of symptoms), medication use, and any previous diagnostic tests performed

in the evaluation of their symptoms. Warning signs, such as unintentional weight loss (more than 10% of the ideal body weight), hematemesis, and hematochezia, or signs of complete obstruction if present, warrant a more urgent workup and possible early surgical intervention.

To diagnose CIPO, patients should have symptoms for at least 6 months. The initial evaluation should aim at differentiating the patient with pseudo-obstruction from those with mechanical obstruction (Fig. 5.1). All patients should have a plain X-ray of the abdomen; air-fluid levels and dilated bowel loops with the patient in upright position are mandatory to suspect CIPO. In current clinical practice, dedicated enterography by computerized tomography (CT) or magnetic resonance imaging (MRI) is preferred as it more accurately demonstrates air-fluid levels, helps rule out mechanical causes as well as intestinal wall adhesions, and allows for transit time examination (Fig. 5.2). Cine MRI is an emerging, non-invasive, radiation-free technique to assess GI motility in CIPO patients. Fuyuki and colleagues studied 33 patients using cine MRI and demonstrated that the mean luminal diameter and contraction ratio in the CIPO group differed significantly from healthy volunteers [10]. Further validation of this method is necessary. Upper endoscopy and colonoscopy should be performed to help exclude mechanical occlusions and collect routine mucosal biopsies to exclude rare instances in which celiac disease or eosinophilic gastroenteropathy may be associated with dysmotility.

If imaging studies and endoscopy raise suspicion for CIPO and exclude mechanical (either intraluminal or extraluminal) obstruction, it is important to investigate potential underlying diseases and secondary causes of CIPO. Routine laboratory tests including a complete blood count, metabolic panel, hemoglobin A1C, and thyroid-stimulating hormone should be obtained. Appropriate laboratory tests and diagnostic studies should be considered to evaluate and then treat potential secondary causes of pseudo-obstruction including systemic autoimmune rheumatic diseases, autonomic neuropathies, endocrinopathies, viral etiologies, and malignancies/paraneoplastic processes.

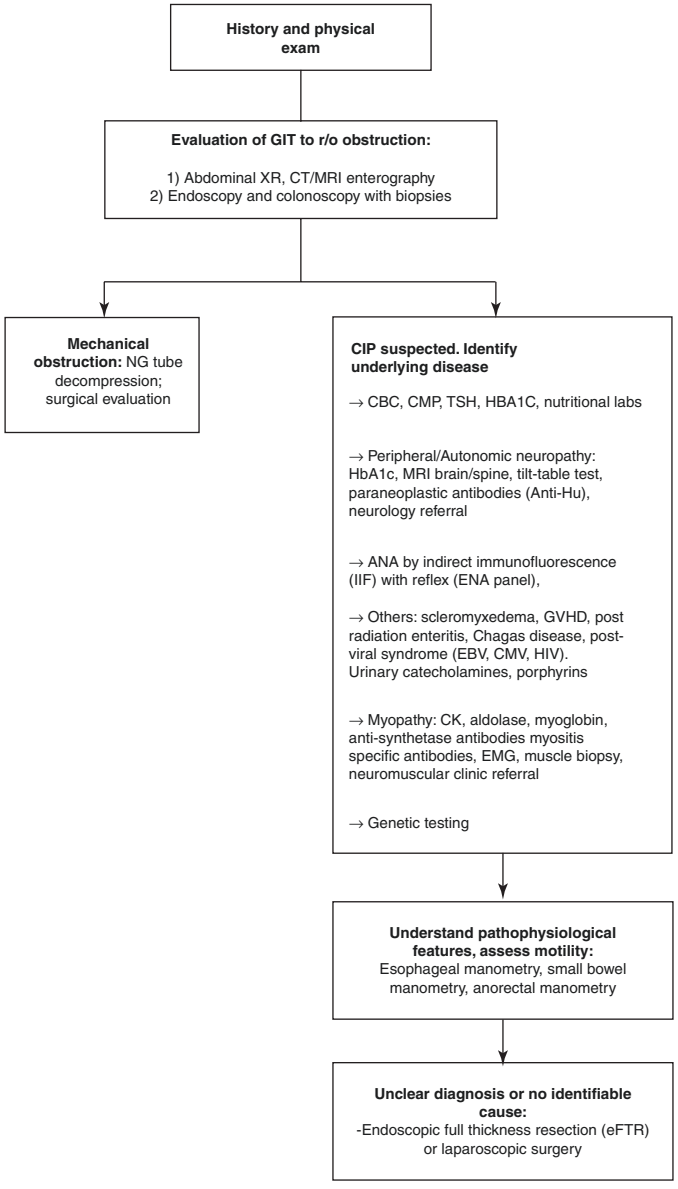

FIGURE 5.1 Diagnostic algorithm for evaluation of patients with suspected chronic intestinal pseudo-obstruction

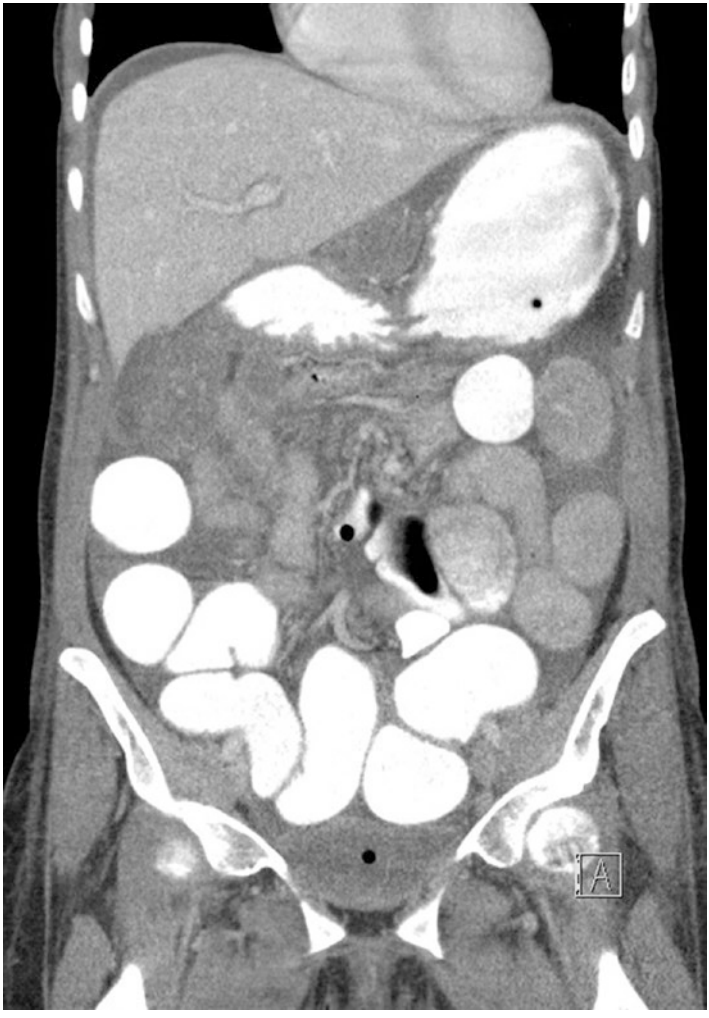

FIGURE 5.2 Computerized tomography (coronal view) image demonstrating air-fluid levels and dilated small bowel loops in patient with chronic intestinal pseudo-obstruction

Esophageal and/or small bowel manometry may provide pathophysiologic information on the mechanisms underlying dysmotility in CIPO patients (e.g., neuropathic vs myopathic patterns). Although this does not affect management, the evidence of a propulsive pattern (i.e., migrating motor complexes) predicts successful adaptation to jejunal feeding in children. Esophageal manometry may predict survival, inability to maintain adequate oral feeding, and parenteral nutrition requirement. Anorectal manometry is indicated in patients with intractable constipation and marked colonic distension to exclude Hirschsprung's disease. A manometric assessment of the entire GI tract is also essential prior to intestinal transplantation as it may provide clues about the outcome of isolated versus multivisceral transplantation in carefully selected patients.

The availability of minimally invasive procedures such as laparoscopic and endoscopic surgery have refueled interest in histopathological analysis of full-thickness intestinal biopsies [9]. These samples may demonstrate smooth muscle atrophy in the primary myopathic processes, neuropathic degeneration in the primary neuropathic disorders, and various findings for the secondary causes of CIP, including fibrosis in primary systemic sclerosis or evidence of amyloid or lymphoma. Recently, Valli and colleagues used endoscopic, full-thickness resection (eFTR) in four CIPO patients with suspected neuromuscular gut disorders. Large colonic full-thickness tissue samples obtained helped identify neuromuscular changes in all four patients with no adverse events suggesting that eFTR may be used as a safe and minimally invasive technique for obtaining biopsies [11].

Treatment

CIPO remains a challenge to treat. Once the diagnosis is made, therapy should focus on (1) avoidance of unnecessary surgery, (2) maintenance of adequate nutritional status including fluid and mineral balances, (3) improvement of

intestinal propulsion, and (4) minimization of symptoms such as nausea, vomiting, bloating, and pain. Additionally, the underlying etiology (i.e., SSc) should be aggressively treated.

Nutrition Assessment

Nutritional evaluation should begin with anthropometric measures alongside a thorough dietary history, including oral intake and diet restrictions. Laboratory testing to evaluate the severity of the illness may include serum albumin, prealbumin, lymphocyte count, and C-reactive protein. Because of poor intake or absorption, it is also reasonable to measure calcium, iron, vitamin B12, folate, and fat-soluble vitamins. Thiamine and nicotinamide deficiencies have been reported in severe cases of SIBO; clinicians should be aware of these possible deficiencies and test as appropriate. Patients should undergo a formal nutrition evaluation by a registered dietician with experience in treating patients with CIPO [5].

Oral Diet

In patients with adequate intestinal absorption, maximization of oral intake is preferred as it has been found to be an independent predictor of survival [12]. Patients should be encouraged to take small, frequent meals (5–6 per day), with an emphasis on liquid calories and protein, while avoiding meals with high fat, high residue (delaying gastric emptying), and high lactose/fructose (evoking bloating/discomfort). Nutritional deficiencies also need to be corrected particularly fat-soluble vitamins (A, D, E, and K) as well as B12 and folate if bacterial overgrowth is present. Elemental feeding and dietary supplements with medium-chain fatty acids may also be used in combination when the aforementioned dietary changes are not successful [5, 13].

Enteral Nutrition Considerations

In cases of inadequate oral intake, enteral nutrition with a standard, non-elemental formula should be the next consideration [14]. Enteral nutrition starting with a slow infusion and continuous feeding or cyclical feeding (e.g., overnight) is preferred to large bolus feedings, especially if the feeding tube is distal to the pylorus. Before the placement of a permanent feeding tube, it is mandatory that a trial of nasogastric or nasojejunal feeding be performed using an enteral formula at the predetermined goal rate. If tolerated without significant discomfort, permanent enteral access may be placed.

Patients should be assessed for delayed gastric emptying, and if present, and there is objective evidence of malnutrition, a feeding tube should be placed distal to the pylorus. Antroduodenal manometry can help predict those who will tolerate enteral feeding; a study in children found that jejunal tube feeds were tolerated in all patients with an MMC on antroduodenal manometry compared to 33% of those without.

Parenteral Nutrition Considerations

In the most severe cases, total parenteral nutrition is required to maintain nutritional support and an adequate level of hydration once aforementioned therapies have failed. If patients are dependent on parenteral nutrition (PN) exclusively, they should receive approximately 25 kcal/kg/d, and lipids should supply approximately 30% of total parenteral calories with 1.0–1.5 g/kg/d protein and dextrose providing the remainder of required calories [5, 13].

Use of PN is not without risk, with a recent retrospective analysis of 51 patients receiving PN for an average of 8.3 years found 180 episodes of catheter-related sepsis, nine episodes of acute pancreatitis (two-thirds due to metabolic condition, one-third due to gallstones), five cases of D-lactic acidosis encephalopathy, and four patients with progression

to cirrhosis; one death was directly related to a PN complication (catheter-related sepsis) in this population. Overall survival was 75% at 10 years compared with 48% at 5 years that had previously been reported [14]. As previously noted, oral intake is a major independent factor associated with better survival; thus, patients receiving PN should be encouraged to maximize oral intake as tolerated while receiving PN.

Medications and Other Therapies

Medications are often the first treatment attempted to try to ameliorate symptoms and improve nutritional intake. The various classes of medications used include (1) prokinetic agents to improve GI motility, (2) antiemetics, (3) pain medications, and (4) antibiotics to treat SIBO (Table 5.3). Regardless of the underlying process, all patients with CIPO have disordered GI tract motility, and so prokinetic agents remain one of the mainstays of treatment. Few investigational studies have been available to demonstrate their efficacy. In practice, the association of different prokinetic drugs and/or their rotation may be a strategy useful to increase therapeutic efficacy while minimizing tachyphylaxis and side effects. Similarly, antiemetics are used with variable efficacy and should be individualized based on the clinical presentation.

The most common symptom, however, is abdominal pain. Unfortunately, many patients with CIPO eventually require opiates for pain control. Few medications have demonstrated benefit for pain in CIPO. Non-opiate pain modulators such as tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, and GABA analogues may be employed while monitoring for significant side effects such as constipation or drowsiness. Tramadol, a μ-opioid receptor agonist, can also be used and may be less constipating than opiates. If opiates are used, careful attention should be paid to antimotility effects, as well as the development of tolerance. Transdermal buprenorphine has been studied in children with idiopathic

TABLE 5.3 Medications that have been used for chronic intestinal pseudo-obstruction

Medication	Comments
Prokinetics	
Erythromycin	Off-label use, macrolide antibiotic with motilin agonist properties Efficacy at a dose of 1.5–2 g/day in adults, or 3–5 mg/kg/day in children. Accelerates gastric emptying and symptom relief. Tachyphylaxis is common
Metoclopramide	Available in the United States. Exerts prokinetic effects via type 2 dopamine receptor antagonism. Mainly used for acute episodes. Chronic use increases risk for severe extrapyramidal side effects
Cisapride	Taken off the US market in 1999 due to cardiac arrhythmia issues and drug interactions, available by FDA compassionate use
Domperidone	Available in the United States through FDA IND Dopamine agonist but does not pass the blood-brain barrier May be useful for gastroparesis, effective for nausea QTc prolongation or arrhythmia may occur
Tegaserod	Taken off the US market in 2007 for concerns of increased cardiac issues, not available in the United States except by FDA compassionate use

(continued)

TABLE 5.3 (continued)

Medication	Comments
Octreotide	Long-acting somatostatin analogue. Used at a dose of 50 mcg SQ every evening. Reported beneficial in scleroderma patients with CIPO and has also been studied with erythromycin May improve enteral nutrition tolerance, better studied in children
Leuprolide	Gonadotropin-releasing hormone analogue shown to decrease symptoms in patients with irritable bowel syndrome and CIPO – no large trials
Prucalopride	Highly selective 5-hydroxytryptamine 4 ($5\text{-}HT_4$) receptor agonist, not available in the United States Enhances motility through stomach, small bowel, and colon Studied in a small, randomized, placebo-controlled, single-center study
Lubiprostone, linaclotide	Stimulates ClCN-2 channels and intestinal guanylate cyclase receptors, respectively. Used to treat chronic constipation and irritable bowel syndrome with constipation Not systematically studied in CIPO

Antiemetics

Antihistamines (diphenhydramine, promethazine) Anticholinergics (scopolamine) Phenothiazines (prochlorperazine, promethezine) Butyrophenones (haloperidol, droperidol) Dopaminergic antagonists (metaclopramide, domperidone) Serotonin receptor antagonist (ondansetron, granistron) Miscellaneous (ginger, trimethobenzamide, lorazapem, dronabinol)	No single agent is particularly suited for the treatment of nausea and vomiting in CIPO. Rather, each patient needs to be assessed individually to determine current medication use, previous trials of antiemetics, adverse reactions, and financial status

(continued)

Table 5.3 (continued)

Medication	Comments
Antibiotics Rifaximin Amoxicillin and clavulanic acid Gentamicin Cephalosporin and metronidazole Tetracycline	Aimed at treating small intestinal bacterial overgrowth (see Chap. 20) Non-absorbable antibiotics, such as rifaximin, can be administered, although broad-spectrum antibiotics, such as amoxicillin and clavulanic acid, gentamicin, and metronidazole, often with antifungal compounds (e.g., nystatin or fluconazole), can be used for 1–2 week cycles alternated with antibiotic-free periods. Recently, amoxicillin-clavulanate has been demonstrated to accelerate intestinal transit in children, thus representing an interesting therapeutic option combining antibiotic and prokinetic effects
Pain control	Non-narcotic pain modulators, tricyclic antidepressants, selective serotonin reuptake inhibitors, and GABA analogues, used with caution because of their significant side effects – constipation and/or drowsiness Tramadol. In patients with chronic and unsustainable visceral pain, careful use of opiates paying attention to their known antimotility effects Transdermal buprenorphine
Fecal transplant	In the United States, an IND is required for use other than treatment of severe or recurrent *C. difficile* infection Small open-label study from China showed some reduction in symptoms and increased tolerance of enteral nutrition via nasojejunal tube

CIPO, with three of four children reporting adequate pain relief and none requiring further dose increases [11]. Other μ-opioid receptor antagonists (methylnaltrexone, naloxegol, naldemedine) have not been prospectively studied in CIPO.

Often patients will require rotating antibiotics to treat SIBO to help relieve symptoms of diarrhea and bloating and improve the nutritional status. No controlled trials have been performed to determine which antibiotics are best, but many clinicians recommend a rotating schedule of different antibiotics every month for 7–10 days over a 5- to 6-month cycle (please see Chap. 20 for specific information regarding treatment regimens).

Fecal Transplant

Fecal transplant is an intriguing potential treatment option for CIPO. A small open-label study from China prospectively studied nine adult patients for 8 weeks after receiving fecal transplant from volunteer donors via nasojejunal tube (NJT) daily for 6 days after 3 days of daily NJT administration of 500 mg of liquid vancomycin. This reportedly resulted in significant reduction in symptoms and increased tolerance of enteral nutrition via NJT [7]. However, based on this one study, there are many more questions that need to be answered.

GI Decompression

As bowel distension is commonly associated with pain and other symptoms in CIPO patients, intestinal segment decompression therapy represents one of the key aspects in CIPO management. No pharmacological therapies to date have been shown to achieve effective, non-invasive decompression in CIPO. Decompression may be attempted using conventional methods such as intermittent nasogastric suction, rectal tubes/colonoscopic decompression, or via surgical proce-

dures, such as feeding/venting gastrojejunostomies/jejunostomies (or other intestinal "ostomies"). Ohkuba and colleagues assessed the efficacy and safety of percutaneous endoscopic gastrojejunostomy (PEG-J) decompression therapy in seven CIPO patients. A significant decrease in the number of days without abdominal symptoms was observed in six out of the seven patients, along with the improvement in malnutrition and wasting [15]. Surgically placed gastrostomy tubes have been shown to decrease hospital admissions (0.2 admissions per patient year) from baseline before tube placement (1.2 admissions per patient year) [16].

If the use of venting procedures does not provide adequate relief, then subtotal enterectomy has been performed for palliation. This may be in addition to long-term PN and/or in preparation to an intestinal transplant. In general, attempts should be made to avoid surgery when possible given the high postoperative morbidity (58.2%) and mortality rates (7.9%) and frequent CIPO-related reoperations (44% at 1 year, 66% at 5 years) as demonstrated by Sabbagh et al. in their analysis of 63 patients who underwent surgery for CIPO [17]. Surgery also has a high rate of stoma prolapse along with considerable risk of dehydration due to enteric fluid losses [17, 18].

Small Intestinal Transplantation

Intestinal transplantation has been increasingly used for the management of intestinal failure and irreversible TPN complications secondary to CIPO, accounting for about 9% of the transplants performed and can be a life-saving procedure with good long-term survival for selected patients. The severity of bowel disease and liver status dictates the type of the transplant, isolated small bowel, or multivisceral transplantation. Recent United Network for Organ Sharing data in children demonstrated 1- and 5-year survival rates for patients transplanted for functional disorders of 75% and 57%, respectively; these rates are comparable to the overall survival rates for intestinal transplant [19]. Infectious and opportunistic complications are seen at similar rates between patients with

CIPO and those with other indications for transplant. Early referral to specialized tertiary centers is critical, allowing for timely intervention and ultimately a better outcome.

Case Study Follow-Up

A 4-h solid-phase gastric emptying scan revealed 95% gastric emptying at 4 h (normal). Esophageal manometry revealed ineffective esophageal motility but no evidence of a myopathic process affecting the smooth muscle of the esophagus; it was presumed that her CIPO was secondary to a neuropathic etiology. A nonabsorbable antibiotic was used to empirically treat for presumed small intestine bacterial overgrowth, which improved bloating by approximately 50%. Because of continued symptoms, octreotide 50 mcg was administered subcutaneously each night, which further helped symptoms. The patient was seen by a dietician and started on liquid nutrition supplementation, which allowed her to regain 5 pounds. While the patient has continued episodes of bloating/distention, her quality of life has improved significantly with the above therapies.

Clinical Pearls

- CIPO is a rare and debilitating GI motility disorder, characterized by clinical symptoms of either continuous or intermittent of bowel obstruction (abdominal pain, abdominal distension, nausea, and vomiting) in the absence of mechanical obstruction.
- The diagnostic workup should include imaging, manometry studies, and, occasionally, full-thickness bowel biopsies alongside workup to determine secondary causes.
- Treatment goals should include optimizing the nutritional status, avoiding surgery, and preventing or delaying the development of intestinal failure.

Self-Test

Question 1. A patient with chronic abdominal bloating and distention is found to have severely dilated loops of small bowel visualized on enterography. She has undergone exploratory laparotomy, without evidence of mechanical obstruction. Which of the following tests is not indicated in identifying the cause of the patient's presentation?

A. TSH
B. Fasting glucose
C. Fasting gastrin level
D. ANA

Question 2. A patient with known chronic intestinal pseudo-obstruction (CIPO) presents with chronic abdominal bloating and weight loss of 10 pounds (7.5% of total body weight). Which of the following therapies has been shown to improve bloating in patients with CIP?

A. Simethicone 80 mg PO TID
B. Octreotide 50 mcg subcutaneous QHS
C. Omeprazole 40 mg PO BID
D. Polyethylene glycol 3350 1 capful PO BID

Question 3. A 45-year-old female with known chronic intestinal pseudo-obstruction (CIPO) presents with recurrent episodes of vomiting, leading to hospitalization. Which of the following therapies has been shown to reduce hospitalization in patients with CIPO?

A. Venting gastrostomy tube
B. Cisapride 20 mg PO TID
C. Metoclopramide 10 mg PO ACHS
D. Pyloroplasty

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Essential Reading

El-Chammas K, Sood MR. Chronic intestinal pseudo-obstruction. Clin Colon Rectal Surg. 2018;31(2):99–107. This article provides a detailed overview of the classification and pathophysiology of CIPO

Di Nardo G, Karunaratne TB, Frediani S, De Giorgio R. Chronic intestinal pseudo-obstruction: Progress in management? Neurogastroenterol Motil. 2017;29 This article provides a comprehensive overview on the advances in management for CIPO

Kirby DF, Raheem SA, Corrigan ML. Nutritional interventions in chronic intestinal Pseudoobstruction. Gastroenterol Clin N Am. 2018;47:209–18. This article provides an authoritative overview on the treatment, particularly nutritional interventions for CIPO patients