Intestinal Pseudo-Obstruction

23

Efstratios Saliakellis, Anna Rybak, and Osvaldo Borrelli

Introduction

The term "pseudo-obstruction" literally denotes the absence of a true mechanical occlusion. Intestinal pseudo-obstruction can be either acute or chronic in nature, reflecting the duration of obstructive symptoms [1, 2]. Chronic intestinal pseudo-obstruction (CIPO) was first described in 1958 by Dudley and colleagues to report a series of 13 patients with symptoms suggestive of intestinal occlusion. These patients underwent exploratory laparotomies, which failed to identify a mechanical cause for their symptomatology [3]. In subsequent years, the existence of this pathological entity in both adults and children was substantiated by a number of other clinicians [4–7].

In 2018, an ESPGHAN-led group of experts introduced the term "pediatric intestinal pseudo-obstruction" (PIPO) in order to distinguish pediatric from adult-onset CIPO. The aforementioned group of experts defined PIPO as a clinical entity "characterized by the chronic inability of the gastrointestinal tract to propel its contents mimicking mechanical obstruction, in the absence of any lesion occluding the gut." The group defined "chronic" as persistence of symptomatology for 2 months from birth or at least 6 months thereafter [8].

The pathophysiologic mechanism of PIPO is represented by abnormal antegrade propulsive activity of the gastrointestinal (GI) tract as a result of processes that affect its neurons, muscles, or interstitial cells of Cajal (ICC) [9]. This functional failure results in a number of clinical symptoms such as abdominal distention with or without abdominal pain, nausea, vomiting, and a reduced inability to tolerate enteral nutrition [10]. These symptoms are, however, nonspecific, and the condition can remain undiagnosed for a long period of time during which patients may undergo multiple diagnostic investigations and often repeated surgical explorations in an effort to identify the cause [10].

Although by definition the small intestine is always involved, any part of the GI tract can be affected in PIPO [1, 2, 8]. Esophageal involvement may lead to dysphagia from impaired peristalsis, in some cases akin to that seen in achalasia [11, 12]. Involvement of the stomach results in poor feed tolerance from gastroparesis suggested by the presence of delayed gastric emptying, while the large bowel by delayed colonic transit and constipation and the anorectum by sphincter dysfunction and defecation disorders [1].

This chapter focuses on various aspects of PIPO and attempts to address areas of controversy by exploring the most recent advances in the overall approach and management of this clinical entity.

Epidemiology

PIPO is a rare disease with scanty epidemiological data and poorly defined incidence and prevalence in both adult and pediatric populations. One of the few initiatives to elucidate its epidemiology suggested that approximately 100 infants are born in the USA every year with PIPO, suggesting an incidence of approximately 1 per 40,000 live births [13, 14].

Adult studies reveal that the disease is more frequent in females [15–17]. In a national survey conducted in Japan, 138 cases of chronic intestinal pseudo-obstruction were identified, with an estimated prevalence of 1.0 and 0.8 cases and incidence of 0.21 and 0.24 cases per 100,000 males and females, respectively [18]. Moreover, a recently published nationwide survey for PIPO in Japan revealed that the prevalence of PIPO, among children younger than 15 years, was 3.7 per one million children. In the aforementioned population, 56.5% of children had developed PIPO during the neonatal period [19].

E. Saliakellis · A. Rybak · O. Borrelli (✉)
Department of Paediatric Gastroenterology, Division of Neurogastroenterology & Motility, Great Ormond Street Hospital for Children, London, UK
e-mail: Osvaldo.Borrelli@gosh.nhs.uk

S. Guandalini, A. Dhawan (eds.), *Textbook of Pediatric Gastroenterology, Hepatology and Nutrition*,
https://doi.org/10.1007/978-3-030-80068-0_23

Undoubtedly, the development of national registries is of paramount importance to delineate more precise epidemiologic characteristics of this orphan clinical entity.

Classification

Classification of PIPO is challenging. Conditions can be classified by whether they primarily affect intestinal nerves (neuropathy), smooth muscle (myopathy), or ICC (mesenchymopathy) and can be further subdivided into primary or secondary, congenital or acquired, mode of inheritance or what part of the GI tract is involved. Where classification is not possible, they are defined as idiopathic. In truth, there is a considerable overlap [1, 2, 8].

In primary PIPO, the disease is usually localized to GI tract, whereas in secondary cases, there is a systemic disorder that affects GI tract motility. It must be noted though that in some cases of primary PIPO extra-GI involvement may also be present, such as the urinary tract (hollow visceral myopathy and megacystis microcolon intestinal hypoperistalsis syndrome), the nervous system (central, peripheral, autonomous), and/or mitochondria (mitochondrial neurogastrointestinal encephalomyopathy, MNGIE) [2, 20–22]. Table 23.1 depicts the classification of PIPO. In children the disease may manifest with symptoms either during the neonatal period (neonatal-onset form) or later (infantile or late-onset form); the majority of PIPO cases are congenital and primary, whereas in adults secondary forms of CIPO (mostly due to systemic disease) are more frequent [8, 23]. Based on histological findings, both primary and secondary PIPO can be further categorized into neuropathies, myopathies, and mesenchymopathies [24–29].

Table 23.1 Classification of Pediatric Intestinal Pseudo-obstruction [8]

Primary PIPO
Sporadic or familial forms of myopathy and/or neuropathy and/or mesenchymopathy that relate to disturbed development, degeneration, or inflammation [7, 20, 28–51]
Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) and other mitochondrial diseases [52–54]
Hirschsprung's disease (e.g., total intestinal aganglionosis)[a] [55–57]
Neuropathy associated with multiple endocrine neoplasia type IIB [58–60]
Secondary PIPO
Conditions affecting GI smooth muscle
Rheumatological conditions (dermatomyositis/polymyositis, scleroderma, systemic lupus erythematosus, Ehlers–Danlos syndrome) [61–72]
Other (Duchenne muscular dystrophy, myotonic dystrophy, amyloidosis, ceroidosis, or alternatively reported as brown bowel syndrome) [73–83]
Pathologies affecting the enteric nervous system (familial dysautonomia, primary dysfunction of the autonomic nervous system, neurofibromatosis, diabetic neuropathy, fetal alcohol syndrome, post-viral-related chronic intestinal pseudo-obstruction, e.g., CMV, EBV, VZV, JC virus) [84–99]
Endocrinological disorders (hypothyroidism, diabetes, hypoparathyroidism, pheochromocytoma) [100–104]
Malrotation or gastroschisis [105–107]
Neuropathy post neonatal necrotizing enterocolitis [108]
Idiopathic (i.e., where forms of PIPO classified as above do not, as yet, have a defined etiopathogenesis)

CMV cytomegalovirus, *EBV* Epstein–Barr virus, *VZV* varicella-zoster virus, *JC* John Cunningham, *GI* gastrointestinal
[a]Needs to be excluded in all cases of PIPO

Etiology and Pathophysiology

The integrity of GI sensorimotor function relies on precise coordination between the autonomic nervous system, enteric nervous system (ENS), ICC, and smooth muscle cells. Any noxious stimulus, irrespective of its origin and etiology, that affects the neuromuscular elements and control of GI tract can lead to impaired peristalsis and the stasis of luminal contents [1]. A variety of disorders and pathophysiological mechanisms can potentially affect the structure or function of the neuromuscular elements of the GI tract and lead to PIPO (Table 23.1) [8]. Neurological (e.g., multiple endocrine neoplasia (MEN) type IIb, familial dysautonomia) and metabolic (e.g., diabetes mellitus) conditions may affect the extrinsic GI nerve supply [23]. Neurotropic viruses may evoke an inflammatory process targeting both the ENS and extrinsic neural pathways [97]. Paraneoplastic syndromes may also exert a destructive effect on the ENS by initiating an inflammatory process that targets the neurons of ganglia located in the submucosal and myenteric plexuses. This is mediated by both a cellular infiltrate and production of circulating antineuronal antibodies [23, 109]. Some pathologies (e.g., muscular dystrophy) may target enteric smooth muscle fibers, whereas others such as dermatomyositis, scleroderma, Ehlers–Danlos syndrome, and radiation enteritis may distort both ENS and gut smooth muscle leading to a mixed neuromyopathic disorder [14, 110, 111]. Finally, although entities such as celiac disease, hypothyroidism, hypoparathyroidism, and pheochromocytoma presumably cause PIPO by affecting the GI neuromuscular integrity, the exact mechanism is not fully understood.

Genetics

Although there has been considerable progress, the elucidation of the genetic basis of PIPO has been rather limited. The majority of PIPO cases are sporadic [8]. Some familial cases of PIPO have been recognized, but there appear to be several patterns of inheritance, perhaps reflective of the great heterogeneity of PIPO conditions. Both autosomal dominant and

recessive modes of inheritance have been described for neuropathic and myopathic types of PIPO [5, 15, 16, 110, 112]. More specifically, rare autosomal dominant mutations in the *SOX10* gene, which encodes a transcription factor important in ENS development, result in a PIPO clinical phenotype along with features such as sensorineural deafness and pigmentary anomalies [113, 114]. Homozygosity on the region 8q23–q24 has been implicated in the pathogenesis of an autosomal recessive form of PIPO characterized by severe GI dysmotility, Barrett's esophagus, and cardiac anomalies [115, 116].

X-linked inheritance (locus Xq28) with recessive transmission has been described in PIPO [17, 117, 118]. Mutations of filamin A *(FLNA)* and L1 cell adhesion molecule *(L1CAM)* genes, which are both located on chromosome Xq28, result in predominantly myopathic and neuropathic forms of PIPO, respectively. Additional involvement of the central nervous system, heart (patent ductus arteriosus), and blood (thrombocytopenia) in both conditions has also been described [118–120].

Mutations in mitochondria are increasingly implicated in PIPO. Mutations in the thymidine phosphorylase gene (*TYMP*, also termed as endothelial cell growth factor-1, *ECGF1*), or in the polymerase-γ gene (*POLG*) result in recessive myopathic forms of PIPO. The former is the cause of MNGIE, whereas the latter leads to a form without encephalopathy. Apart from the GI dysmotility, MNGIE is characterized by severe malnutrition, opthalmoplegia, and leucoencepalopathy on brain MRI [121–123]. Furthermore, mutations in the following genes, *actin G2* [44], *RAD21* [124], and *SGOL1* [125], have been identified in recessive forms of PIPO with an associated syndromic phenotype.

Of note, with the advancement in genetic testing, novel mutations (MYLK, LMOD1, MYL9, MYH11, PDCL3, and ACTG2 variants) were identified and were subsequently related to the etiopathogenesis of megacystis microcolon intestinal hypoperistalsis syndrome [126–132].

Histopathology

In adults, GI histology is reported to be normal in approximately 10% of CIPO cases, while in the experience of the authors, this figure is likely to be higher in children. However, its role in PIPO remains crucial in order to inform prognosis and also guide further investigations for systemic diseases that require specific treatment; therefore, an adequate full-thickness biopsy is recommended whenever surgery is being considered [29]. Recent initiatives are addressing a more standardized and hopefully effective histological approach to diagnosis in GI motility disorders such as PIPO [29, 133, 134].

On the basis of histology, PIPO is classified into neuropathy, myopathy, or mesenchymopathy [29, 135]. However, mixed forms (e.g., neuromyopathy) are also recognized [29].

Neuropathies and myopathies can be further subdivided into inflammatory and degenerative. Inflammatory neuropathies are characterized by an infiltration of T lymphocytes and plasma cells in the myenteric plexuses (myenteric ganglionitis) and neuronal axons (axonopathy) [136–138]. It has been proposed that five or more lymphocytes per ganglion are required for the diagnosis of myenteric ganglionitis [137, 139]. Of note, patients with lymphocytic infiltration of the myenteric plexuses may also develop increased titers of antinuclear antibodies (ANNA-1/anti-Hu, anti-voltage-gated potassium channel or VGKC) [49, 140–142]. These immunologic responses may result in neuronal degeneration and loss by activating apoptotic and autophagic mechanisms [143]. Infiltration of the myenteric ganglia with other cells such as eosinophils and mast cells has been described, but their exact clinicopathological significance is yet to be clarified given limited data [144–146]. All these data support the role of the immune system in the pathogenesis of inflammatory PIPO [135, 147].

Degenerative neuropathies are poorly understood given the limited amount of available data [133, 147–149]. Main histopathologic characteristics of this group include a decrease in the number of intramural neurons along with changes in nerve cell bodies and axons [46, 150]. It has been postulated that apoptotic mechanisms are involved in the degenerative process potentially caused by aberrant calcium signaling, mitochondrial disorders, production of free radicals, and abnormalities in the function of glial cells [151, 152].

Similarly to neuropathies, myopathies are also divided into inflammatory and degenerative. Inflammatory myopathies, also reported by the term "leiomyositis," are characterized by infiltration of T lymphocytes into both the circular and longitudinal enteric muscle layers. This process if not treated appropriately with immunosuppressive agents may lead to a severe clinical picture of PIPO [121, 123].

The histopathologic findings in degenerative myopathies include smooth muscle fiber vacuolization and fibrosis [153]. Diverticula may also be present especially if the longitudinal muscle coat is more affected compared to the circular muscle layer [147, 154].

Novel immunohistochemical techniques, such as smooth muscle markers, namely, smoothelin, smooth muscle myosin heavy chain, and histone deacetylase 8, may reveal histiopathologic subtleties otherwise not detectable with conventional immunostaining and histochemistry methods [29].

Mesenchymopathies are defined by ICC abnormalities (decreased density of ICC network, intracellular abnormalities) and have been demonstrated in patients with chronic intestinal pseudo-obstruction [8, 9, 155]. Although sufficient

data exist regarding their role in the pathogenesis of diabetic gastroparesis, further research is required regarding ICC involvement in the etiopathogenesis of other GI motility disorders [26].

Clinical Picture

In a few cases, the diagnosis of PIPO is suggested in utero by ultrasonographic findings of polyhydramnios, abdominal distention, and megacystis; however, the majority of cases present in the neonatal period or early infancy [9, 10, 156]. The symptomatology varies according to the age at diagnosis and the part of the GI tract, which is primarily affected. Approximately, one-third of children with congenital PIPO (myopathic and neuropathic) have intestinal malrotation [156]. Cardinal signs and symptoms of PIPO include those of obstruction, namely abdominal distention (88%), vomiting (72%, which can be bilious), and constipation (61%). Abdominal pain (44%), failure to thrive (31%), and diarrhea (28%) may also be part of the clinical picture [20, 122].

Dehydration (which can be severe) and malnutrition are often underdiagnosed especially given that weight can be an unreliable measure due to pooling of significant volumes of fluid (third spacing) within distended gut loops. Intraluminal gut content stasis can also lead to small bowel bacterial overgrowth which can further exacerbate symptoms of diarrhea and abdominal distention [62].

PIPO may also manifest with extraintestinal signs and symptoms, such as recurrent urinary tract infections or neurologic abnormalities [155]. Furthermore, patients may complain of symptoms indicative of an underlying disorder that accounts for secondary PIPO (e.g., proximal muscle weakness in dermatomyositis) [10, 156].

The clinical course of PIPO is characterized by exacerbations and remissions, where the former can be precipitated by a number of factors such as surgery, general anesthesia, infections, and emotional stress [8]. In the most severe cases, the natural course of the disease leads to worsening intestinal function and ultimately to intestinal failure [8]. This is especially true in cases where the diagnosis and/or institution of appropriate treatment has been delayed.

Diagnosis

PIPO should be suspected in children with early onset, chronic, recurrent, or continuous signs of intestinal obstruction especially where a surgical cause cannot be established (e.g., repeated "normal" exploratory laparotomies). The diagnosis of PIPO should follow a structured algorithm as proposed by the ESPGHAN-led expert group [2, 156, 157]. Although a detailed history, clinical examination, and laboratory tests may suggest the presence of PIPO, or help elucidate its cause, the ESPGHAN-led expert group proposed that the definitive diagnosis requires at least two out of the four following criteria [158]:

(i) Objective measure of small intestinal neuromuscular involvement (manometry, histopathology, transit studies)
(ii) Recurrent and/or persistently dilated loops of small intestine with air fluid levels
(iii) Genetic and/or metabolic abnormalities definitively associated with PIPO
(iv) Inability to maintain adequate nutrition and/or growth on oral feeding (needing specialized enteral nutrition and/or parenteral nutrition support)

Careful clinical history and physical examination may help in defining the onset, the severity and progression of the disease, and the part of the GI tract primarily affected, and they also provide useful information regarding associations (e.g., family history), potential secondary causes (e.g., medications), and complications (e.g., dehydration). Laboratory tests [e.g., serum electrolytes, thyroid-stimulating hormone (TSH), lactic acid, specific autoantibodies] are useful in cases of secondary PIPO and in order to assess the clinical state of the patients admitted acutely or undergoing a diagnostic protocol.

Imaging

Plain abdominal radiographs may demonstrate a dilated GI tract, with air-fluid levels, whereas contrast GI series can reveal anatomical abnormalities (e.g., malrotation, microcolon) and exclude the presence of gut occlusive lesions (Fig. 23.1a) [159]. It needs to be kept in mind that a water-soluble substance should be used instead of barium in order to prevent flocculation and inspissation of the contrast material.

Novel imaging modalities such as cine MRI have been recently performed with promising results in adult series, but there are no data regarding their applicability and usefulness in pediatrics [160, 161].

Endoscopy

Endoscopy may identify fore- or hindgut mechanical occlusion previously missed on radiology, and it allows duodenal biopsies to exclude mucosal inflammation [9, 162, 163]. Novel techniques (e.g., natural orifice transluminal endoscopic surgery—NOTES) may revolutionize the role of endoscopy in the diagnosis of gut motility disorders by

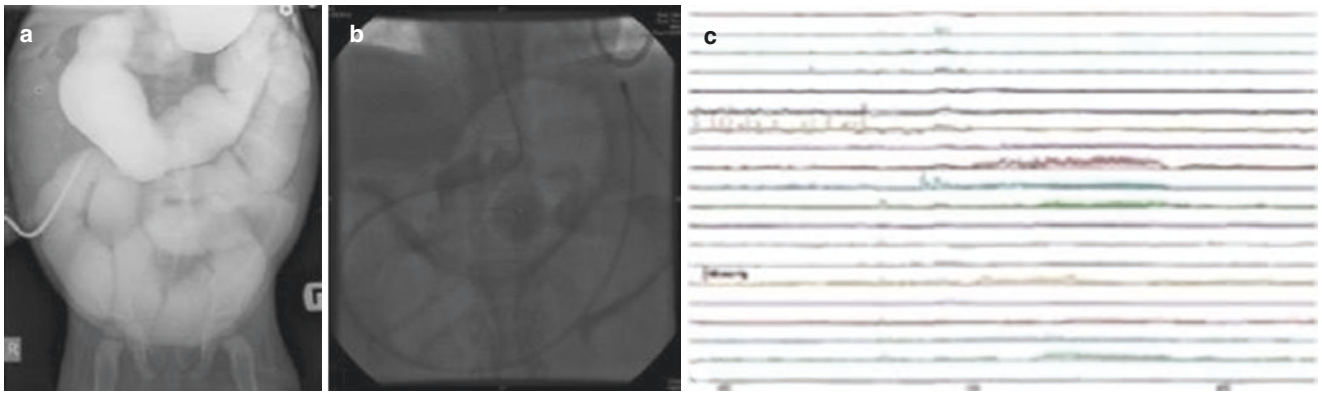

Fig. 23.1 Investigation findings of a 3-year-old boy with a history of recurrent episodes of abdominal distension and vomiting since the neonatal period, and now showing a marked reduction in enteral feed tolerance. (**a**) Contrast follow-through study (administered via gastrostomy) showing filling of grossly dilated small intestinal loops, without any apparent hold up or change in caliber. (**b**) Plain abdominal radiograph taken following placement of antroduodenal manometry catheter into the same patient performed under fluoroscopic guidance. The tip of the catheter has been advanced beyond the duodenojejunal junction to facilitate optimal manometric recording of both the stomach and small intestine. (**c**) Antroduodenal manometry tracing from patient showing the presence of some gastric antral contractions and a migrating motor complex (phase III activity) passing down the small intestine. The amplitude of small intestinal contractile activity is very low (not exceeding 20 mmHg) suggesting a diagnosis of myopathic chronic intestinal pseudo-obstruction

providing the ability of full-thickness biopsy sampling in a safe and minimally invasive way [164].

Motility Investigations

These studies are performed to assess the GI motility and to define the underlying pathophysiologic process, and these studies form the hallmark of diagnosis in pediatrics. Investigations include GI manometries (esophageal, antroduodenal, colonic, anorectal), GI scintigraphy (e.g., gastric emptying, colonic transit), electrogastrography, and radiopaque markers. The usefulness of novel technologies, such as SmartPill, remains to be determined [165–167].

Although in children with PIPO the involvement of GI may be generalized, the small intestine is always affected; thus, antroduodenal manometry remains the most discerning test, and its optimal placement is pivotal (Fig. 23.1b) [168–170]. Neuropathic cases manifest with uncoordinated contractions, which are of normal amplitude, whereas in myopathic PIPO, motor patterns have normal coordination; however, the amplitude of intestinal contractions is low (Fig. 23.1c) [171, 172]. Additionally, manometry may facilitate the dynamic assessment of potential pharmacotherapeutic options and feeding strategies (e.g., feasibility of oral or enteral feeds) as well as indicate disease prognosis [156, 173, 174].

In the most challenging cases, exploratory surgery (laparotomy or laparoscopic-assisted procedures) may be required to definitively exclude mechanical obstruction from PIPO. One however should bear in mind that surgery may precipitate a pseudo-obstructive episode and may also lead to adhesions formation, which can further complicate future diagnostic or therapeutic procedures. Where possible, investigations and then diagnostic/therapeutic surgery should be performed in timeline sequence and in referral center.

Histopathology along with genetics can also be very useful in establishing or confirming the diagnosis of PIPO, highlighting the underlying pathophysiologic process, thus aiding the overall management.

Differential Diagnosis

PIPO has to be differentiated from mechanical obstruction; the latter is usually characterized by marked abdominal pain (in keeping with the abdominal distention), specific radiologic signs, and manometric patterns [111, 175]. Acute functional obstruction (e.g., postoperative ileus), functional GI disorders (e.g., rumination syndrome), and pediatric condition falsification should be considered and appropriately investigated and managed [9].

Treatment

The therapeutic approach in PIPO is threefold as it aims to (i) preserve growth and development by maintaining adequate caloric intake, (ii) promote GI motility with combined medical and surgical interventions, and (iii) treat disease-related complications or underlying pathologies that cause secondary PIPO. Despite the limited effects of the currently applied therapeutic modalities, refinements and evolution in nutritional, medical, and surgical strategies have considerably

improved the overall management of PIPO [155]. Acute management of episodes of pseudo-obstruction is generally treated conservatively by nil by mouth, intravenous fluid, and drainage of stasis through nasogastric (NG) tube or preformed ostomies. Careful attention to fluid and electrolytes is imperative.

Nutrition

The role of nutrition in PIPO is of paramount significance as it is well known that gut motility improves with optimal nutritional support and declines in the face of under- or malnutrition [176–180]. In the long term, approximately one-third of PIPO patients require either partial or total parenteral nutrition, another third require a degree of intragastric or intra-enteral feeding, whereas the remaining children are able to tolerate sufficient oral nutrition. However, within all of groups, patients able to tolerate feeds may require some dietary modification in order to maintain enteral nutrition and avoid bezoar formation (e.g., bite and dissolvable feeds, restriction diets, hydrolyzed formula).

Although parenteral nutrition is lifesaving, it is associated with significant risk of complications, such as central line infections and liver disease, and therefore maintaining patients on maximally tolerated enteral nutrition is always strongly encouraged [169, 178]. In the more severe PIPO cases, continuous rather than bolus feeds administered via a gastrostomy or jejunostomy may be better tolerated particularly in children with impaired gastric motor function [8, 181–184].

Medications

The therapeutic role of drugs in PIPO patients is mainly limited to the control of intestinal inflammation, suppression of bacterial overgrowth, and promotion of GI motility [185].

Prokinetics (e.g., metoclopramide, domperidone, erythromycin, azithromycin, octreotide, neostigmine, pyridostigmine) usually combined with antiemetics (e.g., promethazine, ondansetron) have been used in an attempt to improve the GI motor function and reduce the severity of nausea and vomiting [186–191]. The use of some of these agents is limited by variable efficacy and unacceptable extraintestinal side effects (e.g., metoclopramide, neostigmine). The best-studied and tested prokinetics, that is, cisapride and tegaserod have been withdrawn from the market due to safety concerns [169, 192]. The need for new prokinetics with increased safety and efficacy has resulted in new products (e.g., prucalopride, aprepitant, ghrelin), but there are limited data of their use in pediatric PIPO, further impacted on by restricted availability and licensing [178, 193, 194].

Undoubtedly, current medical regimens for PIPO are based on limited literature and/or expert opinion (e.g., combined use of octreotide and erythromycin) and are yet to be tested in future in the context of controlled trials [178, 193].

Surgery

Surgery remains a valuable intervention on patients with PIPO as it has a multidimensional role in both the diagnostic (e.g., full thickness biopsies) and therapeutic processes (e.g., insertion of feeding tubes, formation of decompressing ostomies such as gastrostomy, ileostomy) [195, 196].

Indeed, adequate bowel decompression is crucial not only in providing symptomatic relief by reducing the frequency and the severity of pseudo-obstructive episodes but also in limiting further deterioration of the intestinal motor activity secondary to chronic distention, and in enhancing the tolerance of enteral feeding [197]. Long decompression enteral tubes and extensive bowel resections are approaches mainly reported in adult CIPO cohorts but remain untested in terms of practicality, efficacy, and safety in pediatrics [198–201]. Rate of significant surgical complications, such as stoma prolapse, infection, and leakage can be significant.

Novel surgical methods involve implantation of devices providing electrical pacing of the GI neuromusculature, but data in children are scanty and limited [8, 15–17, 144].

Small bowel transplantation remains the only definitive cure. Recent advances in both surgical techniques (e.g., multivisceral transplantation) and immunosuppression strategies have resulted in improved outcomes and survival as reported by centers with the relevant expertise showing a survival rate of 50% at 3 years [13, 25, 31, 202–206].

Natural History and Prognosis

Both pediatric and adult chronic intestinal pseudo-obstructions have a severe clinical course, characterized by repetitive relapses and remissions. Unfortunately, the low index of suspicion among physicians along with lack of well-defined diagnostic criteria and readily available facilities in performing specialized diagnostic tests (e.g., manometry) often accounts for delays in the diagnosis and repetitive unnecessary investigations and surgery [206].

The majority of the patients complain of symptoms, which progressively worsen and impact upon the tolerance of enteral nutrition and increasing reliance on total parenteral nutrition [179, 180]. The latter in conjunction with disease-related adverse events (e.g., central line infections, impairment of the liver function, immunosuppression after small bowel transplantation, surgical procedures) accounts for

high morbidity, poor quality of life, and mortality rates up to 30% [13, 25, 31, 202–206].

Despite recent diagnostic and therapeutic advances, PIPO in children remains a serious, life-threatening disease with significant impact on the well-being not only of patients themselves but also of their families [206].

Summary

PIPO is a debilitating disease with poorly defined etiopathogenesis, which is reflected on the limitations encountered in both the diagnostic process and therapeutic management. Clearly, multinational initiatives are required to raise awareness and evolve current diagnostic modalities and therapeutic options.

References

1. Gabbard SL, Lacy BE. Chronic intestinal pseudo-obstruction. Nutr Clin Pract. 2013;28:307–16. https://doi.org/10.1177/0884533613485904.
2. Rudolph CD, Hyman PE, Altschuler SM, et al. Diagnosis and treatment of chronic intestinal pseudo-obstruction in children: report of consensus workshop. J Pediatr Gastroenterol Nutr. 1997;24:102–12. http://www.ncbi.nlm.nih.gov/pubmed/9093995
3. Dudley HA, Sinclair IS, Mc LI, et al. Intestinal pseudo-obstruction. J R Coll Surg Edinb. 1958;3:206–17. http://www.ncbi.nlm.nih.gov/pubmed/13514744
4. Naish JM, Capper WM, Brown NJ. Intestinal pseudoobstruction with steatorrhoea. Gut. 1960;1:62–6. http://www.ncbi.nlm.nih.gov/pubmed/14425851
5. Stephens FO. Syndrome of Intestinal Pseudo-obstruction. Br Med J. 1962;1:1248–1238 2. http://www.ncbi.nlm.nih.gov/pubmed/20789407
6. Byrne WJ, Cipel L, Euler AR, et al. Chronic idiopathic intestinal pseudo-obstruction syndrome in children–clinical characteristics and prognosis. J Pediatr. 1977;90:585–9. http://www.ncbi.nlm.nih.gov/pubmed/839371
7. Schuffler MD, Pope CE 2nd. Studies of idiopathic intestinal pseudoobstruction. II. Hereditary hollow visceral myopathy: family studies. Gastroenterology. 1977;73:339–44. http://www.ncbi.nlm.nih.gov/pubmed/873135
8. Thapar N, Saliakellis E, Benninga MA, et al. Paediatric intestinal pseudo-obstruction: evidence and consensus-based recommendations from an ESPGHAN-Led Expert Group. J Pediatr Gastroenterol Nutr. 2018;66:991–1019. https://doi.org/10.1097/MPG.0000000000001982.
9. Hyman P, Thapar N. Gastrointestinal Motility and Functional Disorders in Children. In: Faure C, di Lorenzo C, Thapar N, editors. Pediatric Neurogastroenterology. Springer Inc; 2013. p. 257–70.
10. Thapar N. Clinical picture of intestinal pseudo-obstruction syndrome. J Pediatr Gastroenterol Nutr. 2011;53 Suppl 2:S58–9. http://www.ncbi.nlm.nih.gov/pubmed/22235480
11. Amiot A, Joly F, Cazals-Hatem D, et al. Prognostic yield of esophageal manometry in chronic intestinal pseudo-obstruction: a retrospective cohort of 116 adult patients. Neurogastroenterol Motil. 2012;24:1008–e542. https://doi.org/10.1111/j.1365-2982.2012.01973.x.
12. Kocoshis SA, Goldschmidt ML, Nathan JD, et al. Esophageal dysmotility: an intrinsic feature of megacystis, microcolon, hypoperistalsis syndrome (MMIHS). J Pediatr Surg. 2019;54:1303–7. https://doi.org/10.1016/j.jpedsurg.2018.08.051.
13. Vargas JH, Sachs P, Ament ME. Chronic intestinal pseudo-obstruction syndrome in pediatrics. Results of a national survey by members of the North American Society of Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr. 1988;7:323–32. http://www.ncbi.nlm.nih.gov/pubmed/3290417
14. di Lorenzo C. Pseudo-obstruction: current approaches. Gastroenterology. 1999;116:980–7. http://www.ncbi.nlm.nih.gov/pubmed/10092321
15. Stanghellini V, Cogliandro RF, de Giorgio R, et al. Natural history of chronic idiopathic intestinal pseudo-obstruction in adults: a single center study. Clin Gastroenterol Hepatol. 2005;3:449–58. http://www.ncbi.nlm.nih.gov/pubmed/15880314
16. Amiot A, Joly F, Alves A, et al. Long-term outcome of chronic intestinal pseudo-obstruction adult patients requiring home parenteral nutrition. Am J Gastroenterol. 2009;104:1262–70. https://doi.org/10.1038/ajg.2009.58.
17. Lindberg G, Iwarzon M, Tornblom H. Clinical features and long-term survival in chronic intestinal pseudo-obstruction and enteric dysmotility. Scand J Gastroenterol. 2009;44:692–9. https://doi.org/10.1080/00365520902839642.
18. Iida H, Ohkubo H, Inamori M, et al. Epidemiology and clinical experience of chronic intestinal pseudo-obstruction in Japan: a nationwide epidemiologic survey. J Epidemiol. 2013;23:288–94. http://www.ncbi.nlm.nih.gov/pubmed/23831693
19. Muto M, Matsufuji H, Tomomasa T, et al. Pediatric chronic intestinal pseudo-obstruction is a rare, serious, and intractable disease: a report of a nationwide survey in Japan. J Pediatr Surg Int. 2014;49:1799–803.
20. Mc Laughlin D, Puri P. Familial megacystis microcolon intestinal hypoperistalsis syndrome: a systematic review. Pediatr Surg Int. 2013;29:947–51. https://doi.org/10.1007/s00383-013-3357-x.
21. Blondon H, Polivka M, Joly F, et al. Digestive smooth muscle mitochondrial myopathy in patients with mitochondrial-neurogastro-intestinal encephalomyopathy (MNGIE). Gastroenterol Clin Biol. 2005;29:773–8. http://www.ncbi.nlm.nih.gov/pubmed/16294144
22. Hugar LA, Chaudhry R, Fuller TW, et al. Urologic phenotype and patterns of care in patients with megacystis microcolon intestinal hypoperistalsis syndrome presenting to a major pediatric transplantation center. Urology. 2018;119:127–32. https://doi.org/10.1016/j.urology.2018.05.002.
23. de Giorgio R, Cogliandro RF, Barbara G, et al. Chronic intestinal pseudo-obstruction: clinical features, diagnosis, and therapy. Gastroenterol Clin N Am. 2011;40:787–807. https://doi.org/10.1016/j.gtc.2011.09.005.
24. Mousa H, Hyman PE, Cocjin J, et al. Long-term outcome of congenital intestinal pseudoobstruction. Dig Dis Sci. 2002;47:2298–305. http://www.ncbi.nlm.nih.gov/pubmed/12395903
25. Heneyke S, Smith VV, Spitz L, et al. Chronic intestinal pseudo-obstruction: treatment and long term follow up of 44 patients. Arch Dis Child. 1999;81:21–7. http://www.ncbi.nlm.nih.gov/pubmed/10373127
26. Streutker CJ, Huizinga JD, Campbell F, et al. Loss of CD117 (c-kit)- and CD34-positive ICC and associated CD34-positive fibroblasts defines a subpopulation of chronic intestinal pseudo-obstruction. Am J Surg Pathol. 2003;27:228–35. http://www.ncbi.nlm.nih.gov/pubmed/12548170
27. Jain D, Moussa K, Tandon M, et al. Role of interstitial cells of Cajal in motility disorders of the bowel. Am J Gastroenterol. 2003;98:618–24. http://www.ncbi.nlm.nih.gov/pubmed/12650797

28. Struijs MC, Diamond IR, Pencharz PB, et al. Absence of the interstitial cells of Cajal in a child with chronic pseudoobstruction. J Pediatr Surg. 2008;43:e25–9. https://doi.org/10.1016/j.jpedsurg.2008.09.017.
29. Knowles CH, de Giorgio R, Kapur RP, et al. The London Classification of gastrointestinal neuromuscular pathology: report on behalf of the Gastro 2009 International Working Group. Gut. 2010;59:882–7. https://doi.org/10.1136/gut.2009.200444. 59/7/882 [pii].
30. Puri P, Shinkai M. Megacystis microcolon intestinal hypoperistalsis syndrome. Semin Pediatr Surg. 2005;14:58–63. S1055858604000824 [pii].
31. Schuffler MD, Pagon RA, Schwartz R, et al. Visceral myopathy of the gastrointestinal and genitourinary tracts in infants. Gastroenterology. 1988;94:892–8. http://www.ncbi.nlm.nih.gov/pubmed/3345889
32. Martin JE, Benson M, Swash M, et al. Myofibroblasts in hollow visceral myopathy: the origin of gastrointestinal fibrosis? Gut. 1993;34:999–1001. http://www.ncbi.nlm.nih.gov/pubmed/8344591
33. Jayachandar J, Frank JL, Jonas MM. Isolated intestinal myopathy resembling progressive systemic sclerosis in a child. Gastroenterology. 1988;95:1114–8. http://www.ncbi.nlm.nih.gov/pubmed/3410225
34. Lowsky R, Davidson G, Wolman S, et al. Familial visceral myopathy associated with a mitochondrial myopathy. Gut. 1993;34:279–83. http://www.ncbi.nlm.nih.gov/pubmed/8432486
35. Schuffler MD, Lowe MC, Bill AH. Studies of idiopathic intestinal pseudoobstruction. I. Hereditary hollow visceral myopathy: clinical and pathological studies. Gastroenterology. 1977;73:327–38. http://www.ncbi.nlm.nih.gov/pubmed/873134
36. Jones SC, Dixon MF, Lintott DJ, et al. Familial visceral myopathy. A family with involvement of four generations. Dig Dis Sci. 1992;37:464–9. http://www.ncbi.nlm.nih.gov/pubmed/1735371
37. Threlkeld AB, Miller NR, Golnik KC, et al. Ophthalmic involvement in myo-neuro-gastrointestinal encephalopathy syndrome. Am J Ophthalmol. 1992;114:322–8. http://www.ncbi.nlm.nih.gov/pubmed/1524123
38. Li V, Hostein J, Romero NB, et al. Chronic intestinal pseudoobstruction with myopathy and ophthalmoplegia. A muscular biochemical study of a mitochondrial disorder. Dig Dis Sci. 1992;37:456–63. http://www.ncbi.nlm.nih.gov/pubmed/1735370
39. Ahlfors F, Linander H, Lindstrom M, et al. Familial intestinal degenerative neuropathy associated with chronic intestinal pseudo-obstruction. Neurogastroenterol Motil. 2011;23:347–55, e159. https://doi.org/10.1111/j.1365-2982.2010.01638.x.
40. Roper EC, Gibson A, McAlindon ME, et al. Familial visceral neuropathy: a defined entity? Am J Med Genet A. 2005;137A:249–54. https://doi.org/10.1002/ajmg.a.30880.
41. Niwamoto H, Okamoto E, Toyosaka A, et al. Sporadic visceral neuropathy. Surg Today. 1995;25:763–70. http://www.ncbi.nlm.nih.gov/pubmed/8555692
42. Low PA. Autonomic neuropathies. Curr Opin Neurol. 1994;7:402–6. http://www.ncbi.nlm.nih.gov/pubmed/7804460
43. Camilleri M, Balm RK, Low PA. Autonomic dysfunction in patients with chronic intestinal pseudo-obstruction. Clin Auton Res. 1993;3:95–100. http://www.ncbi.nlm.nih.gov/pubmed/8324379
44. Lehtonen HJ, Sipponen T, Tojkander S, et al. Segregation of a missense variant in enteric smooth muscle actin gamma-2 with autosomal dominant familial visceral myopathy. Gastroenterology. 2012;143:1482–1491 e3. https://doi.org/10.1053/j.gastro.2012.08.045.
45. Cho YH, Park JH, Park do Y, et al. Segmental transposition of ileal muscle layers: a rare cause of myopathic pseudoobstruction in a newborn. J Pediatr Surg. 2011;46:e1–3. https://doi.org/10.1016/j.jpedsurg.2010.09.014.
46. Dewit S, de Hertogh G, Geboes K, et al. Chronic intestinal pseudo-obstruction caused by an intestinal inflammatory myopathy: case report and review of the literature. Neurogastroenterol Motil. 2008;20:343–8. https://doi.org/10.1111/j.1365-2982.2007.01033.x.
47. Feldstein AE, Miller SM, El-Youssef M, et al. Chronic intestinal pseudoobstruction associated with altered interstitial cells of cajal networks. J Pediatr Gastroenterol Nutr. 2003;36:492–7. http://www.ncbi.nlm.nih.gov/pubmed/12658043
48. Yamataka A, Ohshiro K, Kobayashi H, et al. Abnormal distribution of intestinal pacemaker (C-KIT-positive) cells in an infant with chronic idiopathic intestinal pseudoobstruction. J Pediatr Surg. 1998;33:859–62. http://www.ncbi.nlm.nih.gov/pubmed/9660215
49. Schappi MG, Smith VV, Milla PJ, et al. Eosinophilic myenteric ganglionitis is associated with functional intestinal obstruction. Gut. 2003;52:752–5.
50. Haas S, Bindl L, Fischer HP. Autoimmune enteric leiomyositis: a rare cause of chronic intestinal pseudo-obstruction with specific morphological features. Hum Pathol. 2005;36:576–80. https://doi.org/10.1016/j.humpath.2005.01.005.
51. Ruuska TH, Karikoski R, Smith VV, et al. Acquired myopathic intestinal pseudo-obstruction may be due to autoimmune enteric leiomyositis. Gastroenterology. 2002;122:1133–9. http://www.ncbi.nlm.nih.gov/pubmed/11910363
52. Garone C, Tadesse S, Hirano M. Clinical and genetic spectrum of mitochondrial neurogastrointestinal encephalomyopathy. Brain. 2011;134:3326–32. https://doi.org/10.1093/brain/awr245.
53. Perez-Atayde AR. Diagnosis of mitochondrial neurogastrointestinal encephalopathy disease in gastrointestinal biopsies. Hum Pathol. 2013;44:1440–6. https://doi.org/10.1016/j.humpath.2012.12.005.
54. Nishino I, Spinazzola A, Papadimitriou A, et al. Mitochondrial neurogastrointestinal encephalomyopathy: an autosomal recessive disorder due to thymidine phosphorylase mutations. Ann Neurol. 2000;47:792–800. http://www.ncbi.nlm.nih.gov/pubmed/10852545
55. Puri P, Gosemann JH. Variants of Hirschsprung disease. Semin Pediatr Surg. 2012;21:310–8. https://doi.org/10.1053/j.sempedsurg.2012.07.005.
56. Wu TT, Tsai TW, Chang H, et al. Polymorphisms of the RET gene in Hirschsprung disease, anorectal malformation and intestinal pseudo-obstruction in Taiwan. J Formos Med Assoc. 2010;109:32–8. http://www.ncbi.nlm.nih.gov/pubmed/20123584
57. Qualman SJ, Murray R. Aganglionosis and related disorders. Hum Pathol. 1994;25:1141–9. http://www.ncbi.nlm.nih.gov/pubmed/7959658
58. Qualia CM, Brown MR, Ryan CK, et al. Oral mucosal neuromas leading to the diagnosis of multiple endocrine neoplasia type 2B in a child with intestinal pseudo-obstruction. Gastroenterol Hepatol (N Y). 2007;3:208–11. http://www.ncbi.nlm.nih.gov/pubmed/21960833
59. Erdogan MF, Gulec B, Gursoy A, et al. Multiple endocrine neoplasia 2B presenting with pseudo-Hirschsprung's disease. J Natl Med Assoc. 2006;98:783–6. http://www.ncbi.nlm.nih.gov/pubmed/16749656
60. Grobmyer SR, Guillem JG, O'Riordain DS, et al. Colonic manifestations of multiple endocrine neoplasia type 2B: report of four cases. Dis Colon Rectum. 1999;42:1216–9. http://www.ncbi.nlm.nih.gov/pubmed/10496565
61. Ohkubo H, Iida H, Takahashi H, et al. An epidemiologic survey of chronic intestinal pseudo-obstruction and evaluation of the newly proposed diagnostic criteria. Digestion. 2012;86:12–9. https://doi.org/10.1159/000337528.

62. Kleckner FS. Dermatomyositis and its manifestations in the gastrointestinal tract. Am J Gastroenterol. 1970;53:141–6.
63. Laskin BL, Choyke P, Keenan GF, et al. Novel gastrointestinal tract manifestations in juvenile dermatomyositis. J Pediatr. 1999;135:371–4. S0022-3476(99)70137-X [pii].
64. Sjogren RW. Gastrointestinal features of scleroderma. Curr Opin Rheumatol. 1996;8:569–75. http://www.ncbi.nlm.nih.gov/pubmed/9018461
65. Perlemuter G, Cacoub P, Wechsler B, et al. Chronic intestinal pseudo-obstruction secondary to connective tissue diseases. Gastroenterol Clin Biol. 2001;25:251–8. http://www.ncbi.nlm.nih.gov/pubmed/11395671
66. Adachi Y, Yabana T, Kohri T, et al. A case of chronic idiopathic intestinal pseudo-obstruction with Sjogren's syndrome. Nihon Shokakibyo Gakkai Zasshi. 1990;87:1223–7. http://www.ncbi.nlm.nih.gov/pubmed/2117087
67. Khairullah S, Jasmin R, Yahya F, et al. Chronic intestinal pseudo-obstruction: a rare first manifestation of systemic lupus erythematosus. Lupus. 2013;22:957–60. https://doi.org/10.1177/0961203313492873.
68. Kansal A, Jain A, Thenozhi S, et al. Intestinal pseudo-obstruction associated with biliary tract dilatation in a patient with systemic lupus erythematosus. Lupus. 2013;22:87–91. https://doi.org/10.1177/0961203312464091.
69. Zhang J, Fang M, Wang Y, et al. Intestinal pseudo-obstruction syndrome in systemic lupus erythematosus. Lupus. 2011;20:1324–8. https://doi.org/10.1177/0961203311405702.
70. Yamazaki-Nakashimada MA, Rodriguez-Jurado R, Ortega-Salgado A, et al. Intestinal pseudoobstruction associated with eosinophilic enteritis as the initial presentation of systemic lupus erythematosus in children. J Pediatr Gastroenterol Nutr. 2009;48:482–6. http://www.ncbi.nlm.nih.gov/pubmed/19330936
71. Pelizzo G, Villanacci V, Salemme M, et al. Intestinal pseudo-obstruction due to small bowel alpha-actin deficiency in a child with Ehlers-Danlos syndrome. Tech Coloproctol. 2013; https://doi.org/10.1007/s10151-013-1057-0.
72. Sato T, Ito H, Miyazaki S, et al. Megacystis and megacolon in an infant with Ehlers-Danlos syndrome. Acta Paediatr Jpn. 1993;35:358–60.
73. Camelo AL, Awad RA, Madrazo A, et al. Esophageal motility disorders in Mexican patients with Duchenne's muscular dystrophy. Acta Gastroenterol Latinoam. 1997;27:119–22. http://www.ncbi.nlm.nih.gov/pubmed/9339236
74. Bensen ES, Jaffe KM, Tarr PI. Acute gastric dilatation in Duchenne muscular dystrophy: a case report and review of the literature. Arch Phys Med Rehabil. 1996;77:512–4. http://www.ncbi.nlm.nih.gov/pubmed/8629931
75. Garcia Aroca J, Sanz N, Alonso JL, et al. Intestinal pseudo-obstruction secondary to systemic neuropathies and myopathies. Cir Pediatr. 1994;7:115–20. http://www.ncbi.nlm.nih.gov/pubmed/7999513
76. Leon SH, Schuffler MD, Kettler M, et al. Chronic intestinal pseudoobstruction as a complication of Duchenne's muscular dystrophy. Gastroenterology. 1986;90:455–9. http://www.ncbi.nlm.nih.gov/pubmed/3753595
77. Kim YJ, Kim HS, Park SY, et al. Intestinal amyloidosis with intractable diarrhea and intestinal pseudo-obstruction. Korean J Gastroenterol. 2012;60:172–6. http://www.ncbi.nlm.nih.gov/pubmed/23018539
78. Liapis K, Michelis FV, Delimpasi S, et al. Intestinal pseudo-obstruction associated with amyloidosis. Amyloid. 2011;18:76–8. https://doi.org/10.3109/13506129.2010.548085.
79. Illescas Megias V, Marquez Moreno AJ. Intestinal pseudo-obstruction in Steinert myotonic dystrophy: a clinical-radiological description of 2 cases. Radiologia. 2013;55:88–90. https://doi.org/10.1016/j.rx.2011.07.003.
80. Bruinenberg JF, Rieu PN, Gabreels FM, et al. Intestinal pseudo-obstruction syndrome in a child with myotonic dystrophy. Acta Paediatr. 1996;85:121–3. http://www.ncbi.nlm.nih.gov/pubmed/8834995
81. Boller M, Fiocchi C, Brown CH. Pseudoobstruction in ceroidosis. AJR Am J Roentgenol. 1976;127:277–9. https://doi.org/10.2214/ajr.127.2.277.
82. Michaely HJ, Daroca PJ, Plavsic BM. Brown bowel syndrome--an unusual etiology of pseudo-obstruction of the small intestine. Rofo. 2003;175:1143–4. https://doi.org/10.1055/s-2003-40913.
83. Pelizzo G, Calcaterra V, Villanacci V, et al. Myotonic dystrophy type 1 and pseudo-obstruction in a child with smooth muscle α-actin deficiency and eosinophilic myenteric plexitis. Turkish J Gastroenterol. 2018;29:226–9. https://doi.org/10.5152/tjg.2018.17582.
84. Assor P, Negreanu L, Picon L, et al. Slowly regressing acute pandysautonomia associated with esophageal achalasia: a case report. Gastroenterol Clin Biol. 2008;32:46–50. https://doi.org/10.1016/j.gcb.2007.12.013.
85. Palao S, Corral I, Vera R, et al. Progressive dysautonomia as initial manifestation of anti-Hu antibody-related syndrome. Neurologia. 2007;22:899–902. http://www.ncbi.nlm.nih.gov/pubmed/18040905
86. Besnard M, Faure C, Fromont-Hankard G, et al. Intestinal pseudo-obstruction and acute pandysautonomia associated with Epstein-Barr virus infection. Am J Gastroenterol. 2000;95:280–4. https://doi.org/10.1111/j.1572-0241.2000.01709.x.
87. Taguchi T, Ikeda K, Shono T, et al. Autonomic innervation of the intestine from a baby with megacystis microcolon intestinal hypoperistalsis syndrome: I. Immunohistochemical study. J Pediatr Surg. 1989;24:1264–6. http://www.ncbi.nlm.nih.gov/pubmed/2593057
88. Yamanaka Y, Sakakibara R, Asahina M, et al. Chronic intestinal pseudo-obstruction as the initial feature of pure autonomic failure. J Neurol Neurosurg Psychiatry. 2006;77:800. https://doi.org/10.1136/jnnp.2005.079905.
89. Sinha SK, Kochhar R, Rana S, et al. Intestinal pseudo-obstruction due to neurofibromatosis responding to cisapride. Indian J Gastroenterol. 2000;19:83–4. http://www.ncbi.nlm.nih.gov/pubmed/10812823
90. Hanemann CO, Hayward C, Hilton DA. Neurofibromatosis type 1 with involvement of the enteric nerves. J Neurol Neurosurg Psychiatry. 2007;78:1163–4. https://doi.org/10.1136/jnnp.2007.120451.
91. Aoki Y, Hosaka S, Kiyosawa K. Intestinal pseudo-obstruction in a diabetic man: role of the mitochondrial A3243G mutation. Ann Intern Med. 2002;137:703–4. http://www.ncbi.nlm.nih.gov/pubmed/12379086
92. Reid B, DiLorenzo C, Travis L, et al. Diabetic gastroparesis due to postprandial antral hypomotility in childhood. Pediatrics. 1992;90:43–6.
93. Hendriks G, McPartland J, El-Matary W. Gastrointestinal presentation and outcome of perinatal cytomegalovirus infection. BMJ Case Rep. 2013;2013 https://doi.org/10.1136/bcr-2012-007671.
94. Ategbo S, Turck D, Gottrand F, et al. Chronic intestinal pseudo-obstruction associated with cytomegalovirus infection in an infant. J Pediatr Gastroenterol Nutr. 1996;23:457–60. http://www.ncbi.nlm.nih.gov/pubmed/8956187
95. Precupanu CM, Girodet J, Mariani P, et al. Pseudo-bowel obstruction due to varicella zoster virus infection after autologous stem cell transplantation. Am J Hematol. 2009;84:127–8. https://doi.org/10.1002/ajh.21309.
96. Tanida E, Izumi M, Abe T, et al. Disseminated varicella-zoster virus infection complicated with severe abdominal pain and colonic pseudo-obstruction. Nihon Shokakibyo Gakkai

Zasshi. 2013;110:839–45. http://www.ncbi.nlm.nih.gov/pubmed/23648540
97. de Giorgio R, Ricciardiello L, Naponelli V, et al. Chronic intestinal pseudo-obstruction related to viral infections. Transplant Proc. 2010;42:9–14. https://doi.org/10.1016/j.transproceed.2009.12.014.
98. Selgrad M, de Giorgio R, Fini L, et al. JC virus infects the enteric glia of patients with chronic idiopathic intestinal pseudo-obstruction. Gut. 2009;58:25–32. https://doi.org/10.1136/gut.2008.152512.
99. Uc A, Vasiliauskas E, Piccoli DA, et al. Chronic intestinal pseudoobstruction associated with fetal alcohol syndrome. Dig Dis Sci. 1997;42:1163–7. http://www.ncbi.nlm.nih.gov/pubmed/9201078
100. Abboud B, Sayegh R, Medlej R, et al. A rare manifestation of hypothyroidism: intestinal obstruction. Report of 2 cases and review of the literature. J Med Liban. 1999;47:364–6. http://www.ncbi.nlm.nih.gov/pubmed/10758712
101. Bassotti G, Pagliacci MC, Nicoletti I, et al. Intestinal pseudoobstruction secondary to hypothyroidism. Importance of small bowel manometry. J Clin Gastroenterol. 1992;14:56–8. http://www.ncbi.nlm.nih.gov/pubmed/1556409
102. Siegrist D, Teuscher AU, Ruchti C. Intestinal paralysis in long-term diabetes mellitus. Praxis (Bern 1994). 1998;87:769–72. http://www.ncbi.nlm.nih.gov/pubmed/9654991
103. Camilleri M, Parkman HP, Shafi MA, et al. Clinical guideline: management of gastroparesis. Am J Gastroenterol. 2013;108:18–37; quiz 38. ajg2012373 [pii]. https://doi.org/10.1038/ajg.2012.373.
104. Wu HW, Liou WP, Chou CC, et al. Pheochromocytoma presented as intestinal pseudo-obstruction and hyperamylasemia. Am J Emerg Med. 2008;26:971 e1–4. https://doi.org/10.1016/j.ajem.2008.01.052.
105. Singh G, Hershman MJ, Loft DE, et al. Partial malrotation associated with pseudo-obstruction of the small bowel. Br J Clin Pract. 1993;47:274–5. http://www.ncbi.nlm.nih.gov/pubmed/8292481
106. Devane SP, Coombes R, Smith VV, et al. Persistent gastrointestinal symptoms after correction of malrotation. Arch Dis Child. 1992;67:218–21. http://www.ncbi.nlm.nih.gov/pubmed/1543383
107. Bagwell CE, Filler RM, Cutz E, et al. Neonatal intestinal pseudoobstruction. J Pediatr Surg. 1984;19:732–9. http://www.ncbi.nlm.nih.gov/pubmed/6440967
108. Vanderwinden JM, Dassonville M, van der Veken E, et al. Post-necrotising enterocolitis pseudo-obstruction treated with Cisapride. Z Kinderchir. 1990;45:282–5. https://doi.org/10.1055/s-2008-1042601.
109. Koike H, Sobue G. Paraneoplastic neuropathy. Handb Clin Neurol. 2013;115:713–26. https://doi.org/10.1016/B978-0-444-52902-2.00041-2.
110. Stanghellini V, Corinaldesi R, Barbara L. Pseudo-obstruction syndromes. Baillieres Clin Gastroenterol. 1988;2:225–54. http://www.ncbi.nlm.nih.gov/pubmed/3289641
111. Stanghellini V, Cogliandro RF, de Giorgio R, et al. Chronic intestinal pseudo-obstruction: manifestations, natural history and management. Neurogastroenterol Motil. 2007;19:440–52. https://doi.org/10.1111/j.1365-2982.2007.00902.x.
112. Stanghellini V, Camilleri M, Malagelada JR. Chronic idiopathic intestinal pseudo-obstruction: clinical and intestinal manometric findings. Gut. 1987;28:5–12. http://www.ncbi.nlm.nih.gov/pubmed/3817584
113. Pingault V, Guiochon-Mantel A, Bondurand N, et al. Peripheral neuropathy with hypomyelination, chronic intestinal pseudo-obstruction and deafness: a developmental "neural crest syndrome" related to a SOX10 mutation. Ann Neurol. 2000;48:671–6. http://www.ncbi.nlm.nih.gov/pubmed/11026454
114. Pingault V, Girard M, Bondurand N, et al. SOX10 mutations in chronic intestinal pseudo-obstruction suggest a complex physiopathological mechanism. Hum Genet. 2002;111:198–206. https://doi.org/10.1007/s00439-002-0765-8.
115. Mungan Z, Akyuz F, Bugra Z, et al. Familial visceral myopathy with pseudo-obstruction, megaduodenum, Barrett's esophagus, and cardiac abnormalities. Am J Gastroenterol. 2003;98:2556–60. https://doi.org/10.1111/j.1572-0241.2003.08707.x.
116. Deglincerti A, de Giorgio R, Cefle K, et al. A novel locus for syndromic chronic idiopathic intestinal pseudo-obstruction maps to chromosome 8q23-q24. Eur J Hum Genet. 2007;15:889–97. https://doi.org/10.1038/sj.ejhg.5201844.
117. Auricchio A, Brancolini V, Casari G, et al. The locus for a novel syndromic form of neuronal intestinal pseudoobstruction maps to Xq28. Am J Hum Genet. 1996;58:743–8. http://www.ncbi.nlm.nih.gov/pubmed/8644737
118. Clayton-Smith J, Walters S, Hobson E, et al. Xq28 duplication presenting with intestinal and bladder dysfunction and a distinctive facial appearance. Eur J Hum Genet. 2009;17:434–43. https://doi.org/10.1038/ejhg.2008.192.
119. Gargiulo A, Auricchio R, Barone MV, et al. Filamin A is mutated in X-linked chronic idiopathic intestinal pseudo-obstruction with central nervous system involvement. Am J Hum Genet. 2007;80:751–8. https://doi.org/10.1086/513321.
120. Kapur RP, Robertson SP, Hannibal MC, et al. Diffuse abnormal layering of small intestinal smooth muscle is present in patients with FLNA mutations and x-linked intestinal pseudo-obstruction. Am J Surg Pathol. 2010;34:1528–43. https://doi.org/10.1097/PAS.0b013e3181f0ae47.
121. Bardosi A, Creutzfeldt W, DiMauro S, et al. Myo-, neuro-, gastrointestinal encephalopathy (MNGIE syndrome) due to partial deficiency of cytochrome-c-oxidase. A new mitochondrial multisystem disorder. Acta Neuropathol. 1987;74:248–58.
122. Nishino I, Spinazzola A, Hirano M. Thymidine phosphorylase gene mutations in MNGIE, a human mitochondrial disorder. Science. 1999;283:689–92.
123. Giordano C, Sebastiani M, de Giorgio R, et al. Gastrointestinal dysmotility in mitochondrial neurogastrointestinal encephalomyopathy is caused by mitochondrial DNA depletion. Am J Pathol. 2008;173:1120–8. https://doi.org/10.2353/ajpath.2008.080252.
124. Bonora E, Bianco F, Cordeddu L, et al. Mutations in RAD21 disrupt regulation of apob in patients with chronic intestinal pseudo-obstruction. Gastroenterology. 2015;148 https://doi.org/10.1053/j.gastro.2014.12.034.
125. Chetaille P, Preuss C, Burkhard S, et al. Mutations in SGOL1 cause a novel cohesinopathy affecting heart and gut rhythm. Nat Genet. 2014;46 https://doi.org/10.1038/ng.3113.
126. Wang Q, Zhang J, Wang H, et al. Compound heterozygous variants in MYH11 underlie autosomal recessive megacystis-microcolon-intestinal hypoperistalsis syndrome in a Chinese family. J Hum Genet. 2019; https://doi.org/10.1038/s10038-019-0651-z.
127. Ravenscroft G, Pannell S, O'Grady G, et al. Variants in ACTG2 underlie a substantial number of Australasian patients with primary chronic intestinal pseudo-obstruction. Neurogastroenterol Motil. 2018; https://doi.org/10.1111/nmo.13371.
128. Billon C, Molin A, Poirsier C, et al. Fetal megacystis-microcolon: genetic mutational spectrum and identification of PDCL3 as a novel candidate gene. Clin Genet. 2020; https://doi.org/10.1111/cge.13801.
129. Moreno CA, Sobreira N, Pugh E, et al. Homozygous deletion in MYL9 expands the molecular basis of megacystis-microcolon-intestinal hypoperistalsis syndrome. Eur J Hum Genet. 2018; https://doi.org/10.1038/s41431-017-0055-5.
130. Halim D, Brosens E, Muller F, et al. Loss-of-function variants in MYLK cause recessive megacystis microcolon intestinal hypoperistalsis syndrome. Am J Hum Genet. 2017; https://doi.org/10.1016/j.ajhg.2017.05.011.

131. Halim D, Wilson MP, Oliver D, et al. Loss of LMOD1 impairs smooth muscle cytocontractility and causes megacystis microcolon intestinal hypoperistalsis syndrome in humans and mice. Proc Natl Acad Sci U S A. 2017;114:E2739–47. https://doi.org/10.1073/pnas.1620507114.
132. Gamboa HE, Sood M. Pediatric intestinal pseudo-obstruction in the era of genetic sequencing. Curr Gastroenterol Rep. 2019;21:70. https://doi.org/10.1007/s11894-019-0737-y.
133. de Giorgio R, Camilleri M. Human enteric neuropathies: morphology and molecular pathology. Neurogastroenterol Motil. 2004;16:515–31. https://doi.org/10.1111/j.1365-2982.2004.00538.x.
134. de Giorgio R, Sarnelli G, Corinaldesi R, et al. Advances in our understanding of the pathology of chronic intestinal pseudo-obstruction. Gut. 2004;53:1549–52. https://doi.org/10.1136/gut.2004.043968.
135. de Giorgio R, Guerrini S, Barbara G, et al. Inflammatory neuropathies of the enteric nervous system. Gastroenterology. 2004;126:1872–83. http://www.ncbi.nlm.nih.gov/pubmed/15188182
136. de Giorgio R, Bovara M, Barbara G, et al. Anti-HuD-induced neuronal apoptosis underlying paraneoplastic gut dysmotility. Gastroenterology. 2003;125:70–9. S0016508503006644 [pii].
137. Hubball A, Martin JE, Lang B, et al. The role of humoral autoimmunity in gastrointestinal neuromuscular diseases. Prog Neurobiol. 2009;87:10–20. https://doi.org/10.1016/j.pneurobio.2008.09.011.
138. Hubball AW, Lang B, Souza MA, et al. Voltage-gated potassium channel (K(v) 1) autoantibodies in patients with chagasic gut dysmotility and distribution of K(v) 1 channels in human enteric neuromusculature (autoantibodies in GI dysmotility). Neurogastroenterol Motil. 2012;24:719–28, e344. https://doi.org/10.1111/j.1365-2982.2012.01924.x.
139. de Giorgio R, Barbara G, Stanghellini V, et al. Clinical and morphofunctional features of idiopathic myenteric ganglionitis underlying severe intestinal motor dysfunction: a study of three cases. Am J Gastroenterol. 2002;97:2454–9. https://doi.org/10.1111/j.1572-0241.2002.06002.x.
140. Murch S. Allergy and intestinal dysmotility--evidence of genuine causal linkage? Curr Opin Gastroenterol. 2006;22:664–8. https://doi.org/10.1097/01.mog.0000245546.18279.7e. 00001574-200611000-00014 [pii].
141. Bassotti G, Villanacci V. Mast cells in intestinal motility disorders: please also look beyond IBS. Dig Dis Sci. 2012;57:2475–6; author reply 2476. https://doi.org/10.1007/s10620-012-2303-4.
142. Bassotti G, Villanacci V, Nascimbeni R, et al. Increase of colonic mast cells in obstructed defecation and their relationship with enteric glia. Dig Dis Sci. 2012;57:65–71. https://doi.org/10.1007/s10620-011-1848-y.
143. di Nardo G, Blandizzi C, Volta U, et al. Review article: molecular, pathological and therapeutic features of human enteric neuropathies. Aliment Pharmacol Ther. 2008;28:25–42. https://doi.org/10.1111/j.1365-2036.2008.03707.x.
144. Mann SD, Debinski HS, Kamm MA. Clinical characteristics of chronic idiopathic intestinal pseudo-obstruction in adults. Gut. 1997;41:675–81. http://www.ncbi.nlm.nih.gov/pubmed/9414977
145. Lindberg G, Tornblom H, Iwarzon M, et al. Full-thickness biopsy findings in chronic intestinal pseudo-obstruction and enteric dysmotility. Gut. 2009;58:1084–90. https://doi.org/10.1136/gut.2008.148296.
146. Knowles CH, Silk DB, Darzi A, et al. Deranged smooth muscle alpha-actin as a biomarker of intestinal pseudo-obstruction: a controlled multinational case series. Gut. 2004;53:1583–9. https://doi.org/10.1136/gut.2003.037275.
147. Knowles CH, de Giorgio R, Kapur RP, et al. Gastrointestinal neuromuscular pathology: guidelines for histological techniques and reporting on behalf of the Gastro 2009 International Working Group. Acta Neuropathol. 2009;118:271–301. https://doi.org/10.1007/s00401-009-0527-y.
148. Bassotti G, Villanacci V, Antonelli E, et al. Enteric glial cells: new players in gastrointestinal motility? Lab Investig. 2007;87:628–32. https://doi.org/10.1038/labinvest.3700564.
149. Bassotti G, Villanacci V. Can "functional" constipation be considered as a form of enteric neuro-gliopathy? Glia. 2011;59:345–50. https://doi.org/10.1002/glia.21115.
150. Oton E, Moreira V, Redondo C, et al. Chronic intestinal pseudo-obstruction due to lymphocytic leiomyositis: is there a place for immunomodulatory therapy? Gut. 2005;54:1343–4. https://doi.org/10.1136/gut.2005.071811.
151. Smith JA, Hauser SC, Madara JL. Hollow visceral myopathy: a light- and electron-microscopic study. Am J Surg Pathol. 1982;6:269–75.
152. Schuffler MD. Chronic intestinal pseudo-obstruction syndromes. Med Clin North Am. 1981;65:1331–58. http://www.ncbi.nlm.nih.gov/pubmed/6799718
153. Wedel T, van Eys GJ, Waltregny D, et al. Novel smooth muscle markers reveal abnormalities of the intestinal musculature in severe colorectal motility disorders. Neurogastroenterol Motil. 2006;18:526–38. https://doi.org/10.1111/j.1365--2982.2006.00781.x. NMO781 [pii].
154. Farrugia G. Interstitial cells of Cajal in health and disease. Neurogastroenterol Motil. 2008;20 Suppl 1:54–63. https://doi.org/10.1111/j.1365-2982.2008.01109.x. NMO1109 [pii].
155. Chronic HP. Intestinal Pseudo-obstruction. In: Wyllie R, Hyams J, Kay M, editors. Pediatric gastrointestinal and liver disease. Philadelphia: Elsevier; 2011. p. 505–11.
156. Chronic FC. Intestinal Pseudo-obstruction syndrome. In: Walker WA, Goulet O, Kleinman RE, et al., editors. Pediatric gastrointestinal disease. Ontario: BC Decker; 2004. p. 1044–54.
157. Camilleri M. Intestinal dysmotility: does the X-ray resolve the real dilemma? J Pediatr Gastroenterol Nutr. 1997;24:100–1.
158. Ohkubo H, Kessoku T, Fuyuki A, et al. Assessment of small bowel motility in patients with chronic intestinal pseudo-obstruction using cine-MRI. Am J Gastroenterol. 2013;108:1130–9. https://doi.org/10.1038/ajg.2013.57.
159. Yakan S, Caliskan C, Kaplan H, et al. Superior mesenteric artery syndrome: a rare cause of intestinal obstruction. Diagnosis and surgical management. Indian J Surg. 2013;75:106–10. https://doi.org/10.1007/s12262-012-0423-x. 423 [pii].
160. Sumiyama K, Gostout CJ. Clinical applications of submucosal endoscopy. Curr Opin Gastroenterol. 2011;27:412–7. https://doi.org/10.1097/MOG.0b013e328349cf8e. 00001574-201109000-00003 [pii].
161. Klibansky D, Rothstein RI. Robotics in endoscopy. Curr Opin Gastroenterol. 2012;28:477–82. https://doi.org/10.1097/MOG.0b013e328356ac5e. 00001574-201209000-00010 [pii].
162. Belkind-Gerson J, Tran K, di Lorenzo C. Novel techniques to study colonic motor function in children. Curr Gastroenterol Rep. 2013;15:335. https://doi.org/10.1007/s11894-013-0335-3.
163. Green AD, Belkind-Gerson J, Surjanhata BC, et al. Wireless motility capsule test in children with upper gastrointestinal symptoms. J Pediatr. 2013;162:1181–7. https://doi.org/10.1016/j.jpeds.2012.11.040.
164. Cucchiara S, Borrelli O, Salvia G, et al. A normal gastrointestinal motility excludes chronic intestinal pseudoobstruction in children. Dig Dis Sci. 2000;45:258–64. http://www.ncbi.nlm.nih.gov/pubmed/10711435
165. Boige N, Faure C, Cargill G, et al. Manometrical evaluation in visceral neuropathies in children. J Pediatr Gastroenterol Nutr. 1994;19:71–7. http://www.ncbi.nlm.nih.gov/pubmed/7965481
166. Hyman PE, SV MD, Napolitano J, et al. Antroduodenal motility in children with chronic intestinal pseudo-obstruction. J Pediatr. 1988;112:899–905. http://www.ncbi.nlm.nih.gov/pubmed/3373394

167. Tomomasa T, Itoh Z, Koizumi T, et al. Manometric study on the intestinal motility in a case of megacystis-microcolon-intestinal hypoperistalsis syndrome. J Pediatr Gastroenterol Nutr. 1985;4:307–10.
168. Hyman PE, di Lorenzo C, McAdams L, et al. Predicting the clinical response to cisapride in children with chronic intestinal pseudo-obstruction. Am J Gastroenterol. 1993;88:832–6. http://www.ncbi.nlm.nih.gov/pubmed/8503375
169. di Lorenzo C, Lucanto C, Flores AF, et al. Effect of sequential erythromycin and octreotide on antroduodenal manometry. J Pediatr Gastroenterol Nutr. 1999;29:293–6. http://www.ncbi.nlm.nih.gov/pubmed/10467994
170. Fell JM, Smith VV, Milla PJ. Infantile chronic idiopathic intestinal pseudo-obstruction: the role of small intestinal manometry as a diagnostic tool and prognostic indicator. Gut. 1996;39:306–11. http://www.ncbi.nlm.nih.gov/pubmed/8977348
171. Summers RW, Anuras S, Green J. Jejunal manometry patterns in health, partial intestinal obstruction, and pseudoobstruction. Gastroenterology. 1983;85:1290–300. http://www.ncbi.nlm.nih.gov/pubmed/6688790
172. Camilleri M. Jejunal manometry in distal subacute mechanical obstruction: significance of prolonged simultaneous contractions. Gut. 1989;30:468–75.
173. Hyman PE, Bursch B, Beck D, et al. Discriminating pediatric condition falsification from chronic intestinal pseudo-obstruction in toddlers. Child Maltreat. 2002;7:132–7. http://www.ncbi.nlm.nih.gov/pubmed/12020069
174. Hyman PE, Bursch B, Sood M, et al. Visceral pain-associated disability syndrome: a descriptive analysis. J Pediatr Gastroenterol Nutr. 2002;35:663–8.
175. Lyford G, Foxx-Orenstein A. Chronic intestinal pseudoobstruction. Curr Treat Options Gastroenterol. 2004;7:317–25. http://www.ncbi.nlm.nih.gov/pubmed/15238207
176. di Lorenzo C, Flores AF, Buie T, et al. Intestinal motility and jejunal feeding in children with chronic intestinal pseudo-obstruction. Gastroenterology. 1995;108:1379–85. http://www.ncbi.nlm.nih.gov/pubmed/7729629
177. Gariepy CE, Mousa H. Clinical management of motility disorders in children. Semin Pediatr Surg. 2009;18:224–38. https://doi.org/10.1053/j.sempedsurg.2009.07.004.
178. di Lorenzo C, Youssef NN. Diagnosis and management of intestinal motility disorders. Semin Pediatr Surg. 2010;19:50–8. https://doi.org/10.1053/j.sempedsurg.2009.11.006.
179. Çağan Appak Y, Baran M, Öztan MO, et al. Assessment and outcome of pediatric intestinal pseudo-obstruction: a tertiary-care-center experience from Turkey. Turkish J Gastroenterol. 2019;30:357–63. https://doi.org/10.5152/tjg.2019.18287.
180. Diamanti A, Fusaro F, Caldaro T, et al. Pediatric intestinal pseudo-obstruction: impact of neonatal and later onset on clinical and nutritional outcomes. J Pediatr Gastroenterol Nutr. 2019;69:212–7. https://doi.org/10.1097/MPG.0000000000002373.
181. Longo WE, Vernava AM 3rd. Prokinetic agents for lower gastrointestinal motility disorders. Dis Colon Rectum. 1993;36:696–708. http://www.ncbi.nlm.nih.gov/pubmed/8348856
182. Chini P, Toskes PP, Waseem S, et al. Effect of azithromycin on small bowel motility in patients with gastrointestinal dysmotility. Scand J Gastroenterol. 2012;47:422–7. https://doi.org/10.3109/00365521.2012.654402.
183. Sorhaug S, Steinshamn SL, Waldum HL. Octreotide treatment for paraneoplastic intestinal pseudo-obstruction complicating SCLC. Lung Cancer. 2005;48:137–40. https://doi.org/10.1016/j.lungcan.2004.09.008.
184. Lee JW, Bang KW, Jang PS, et al. Neostigmine for the treatment of acute colonic pseudo-obstruction (ACPO) in pediatric hematologic malignancies. Korean J Hematol. 2010;45:62–5. https://doi.org/10.5045/kjh.2010.45.1.62.
185. Tack J, Camilleri M, Chang L, et al. Systematic review: cardiovascular safety profile of 5-HT(4) agonists developed for gastrointestinal disorders. Aliment Pharmacol Ther. 2012;35:745–67. https://doi.org/10.1111/j.1365-2036.2012.05011.x.
186. Winter HS, di Lorenzo C, Benninga MA, et al. Oral prucalopride in children with functional constipation. J Pediatr Gastroenterol Nutr. 2013;57:197–203. https://doi.org/10.1097/MPG.0b013e318292f9ea.
187. Chong K, Dhatariya K. A case of severe, refractory diabetic gastroparesis managed by prolonged use of aprepitant. Nat Rev Endocrinol. 2009;5:285–8. https://doi.org/10.1038/nrendo.2009.50. nrendo.2009.50 [pii].
188. Tack J, Depoortere I, Bisschops R, et al. Influence of ghrelin on gastric emptying and meal-related symptoms in idiopathic gastroparesis. Aliment Pharmacol Ther. 2005;22:847–53. https://doi.org/10.1111/j.1365-2036.2005.02658.x. APT2658 [pii].
189. Hashizume N, Yagi M, Ushijima K, et al. Pharmacotherapy for pediatric chronic intestinal pseudo-obstruction: Nationwide survey in Japan. Pediatr Int. 2017;59:467–72. https://doi.org/10.1111/ped.13201.
190. Choudhury A, Rahyead A, Kammermeier J, et al. The use of pyridostigmine in a child with chronic intestinal pseudo-obstruction. Pediatrics. 2018;141:S404–7. https://doi.org/10.1542/peds.2017-0007.
191. Lee H, Park S, Oh J-T, et al. Oral pyridostigmine-responsive visceral myopathy with ACTG2 mutations: a case series. J Pediatr Gastroenterol Nutr. 2019;68:e16–7. https://doi.org/10.1097/MPG.0000000000002183.
192. Verne GN, Eaker EY, Hardy E, et al. Effect of octreotide and erythromycin on idiopathic and scleroderma-associated intestinal pseudoobstruction. Dig Dis Sci. 1995;40:1892–901. http://www.ncbi.nlm.nih.gov/pubmed/7555439
193. Pakarinen MP, Kurvinen A, Koivusalo AI, et al. Surgical treatment and outcomes of severe pediatric intestinal motility disorders requiring parenteral nutrition. J Pediatr Surg. 2013;48:333–8. https://doi.org/10.1016/j.jpedsurg.2012.11.010.
194. Michaud L, Guimber D, Carpentier B, et al. Gastrostomy as a decompression technique in children with chronic gastrointestinal obstruction. J Pediatr Gastroenterol Nutr. 2001;32:82–5. http://www.ncbi.nlm.nih.gov/pubmed/11176331
195. Lapointe R. Chronic idiopathic intestinal pseudo-obstruction treated by near total small bowel resection: a 20-year experience. J Gastrointest Surg. 2010;14:1937–42. https://doi.org/10.1007/s11605-010-1295-7.
196. Nunokawa T, Yokogawa N, Ohtsuka H, et al. Transgastric long tube placement following percutaneous endoscopic gastrostomy for severe chronic intestinal pseudo-obstruction related to systemic sclerosis. Mod Rheumatol. 2013; https://doi.org/10.3109/14397595.2013.844385.
197. Teich S, Mousa HM, Punati J, et al. Efficacy of permanent gastric electrical stimulation for the treatment of gastroparesis and functional dyspepsia in children and adolescents. J Pediatr Surg. 2013;48:178–83. https://doi.org/10.1016/j.jpedsurg.2012.10.038. S0022-3468(12)00814-7 [pii].
198. D'Antiga L, Goulet O. Intestinal failure in children: the European view. J Pediatr Gastroenterol Nutr. 2013;56:118–26. https://doi.org/10.1097/MPG.0b013e318268a9e3.
199. Goulet O, Lacaille F, Colomb V, et al. Intestinal transplantation in children: Paris experience. Transplant Proc. 2002;34:1887–8. http://www.ncbi.nlm.nih.gov/pubmed/12176615
200. Loinaz C, Rodriguez MM, Kato T, et al. Intestinal and multivisceral transplantation in children with severe gastrointesti-

nal dysmotility. J Pediatr Surg. 2005;40:1598–604. https://doi.org/10.1016/j.jpedsurg.2005.06.002.
201. Millar AJ, Gupte G, Sharif K. Intestinal transplantation for motility disorders. Semin Pediatr Surg. 2009;18:258–62. https://doi.org/10.1053/j.sempedsurg.2009.07.007.
202. Iwarzon M, Gardulf A, Lindberg G. Functional status, health-related quality of life and symptom severity in patients with chronic intestinal pseudo-obstruction and enteric dysmotility. Scand J Gastroenterol. 2009;44:700–7. https://doi.org/10.1080/00365520902840806.
203. Faure C, Goulet O, Ategbo S, et al. Chronic intestinal pseudoobstruction syndrome: clinical analysis, outcome, and prognosis in 105 children. French-Speaking Group of Pediatric Gastroenterology. Dig Dis Sci. 1999;44:953–9. http://www.ncbi.nlm.nih.gov/pubmed/10235603
204. Krishnamurthy S, Heng Y, Schuffler MD. Chronic intestinal pseudo-obstruction in infants and children caused by diverse abnormalities of the myenteric plexus. Gastroenterology. 1993;104:1398–408. http://www.ncbi.nlm.nih.gov/pubmed/7683295
205. Granata C, Puri P. Megacystis-microcolon-intestinal hypoperistalsis syndrome. J Pediatr Gastroenterol Nutr. 1997;25:12–9.
206. Schwankovsky L, Mousa H, Rowhani A, et al. Quality of life outcomes in congenital chronic intestinal pseudo-obstruction. Dig Dis Sci. 2002;47:1965–8. http://www.ncbi.nlm.nih.gov/pubmed/12353838