Hirschsprung Disease

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Jeffrey R. Avansino and Marc A. Levitt

Hirschsprung disease (HD) results from an abnormal development of the enteric nervous system leading to the absence of ganglion cells in the myenteric and submucosal plexuses of the distal intestine. Aganglionosis is due to a failure of migration of the ganglion cells, which are derived from the neural crest. Gene mutations may be the cause, particularly the Ret proto-oncogene and the endothelin family of genes. HD occurs in one in 5000 live births, resulting in absent peristalsis in the affected bowel and a functional intestinal obstruction. In the majority of cases, the affected segment involves the rectum or recto-sigmoid, but the aganglionosis can extend for varying lengths to involve the entire colon, sometimes the small intestine and rarely the entire length of the large and small bowel.

Hirschsprung disease typically presents as a neonatal bowel obstruction with or without enterocolitis. More benign phenotypes present later with constipation and chronic distension. Failure to thrive is also common in those with a delayed presentation. The newborn has distension, poor feeding, and bilious emesis. Free air with a cecal perforation occasionally is seen. Distal bowel obstruction on plain abdominal X-ray could be Hirschsprung disease but could also be meconium ileus, meconium plug, ileal atresia, ileal stenosis, or one of the number of medical conditions such as hypothyroidism, narcotic overdose, gestational diabetes, and effects of magnesium sulfate.

The cases diagnosed outside the newborn period may show constipation symptoms on breast milk, or dramatic worsening of constipation when transitioning to normal foods. These patients usually have short-segment disease, but rarely total colonic cases can have a delayed diagnosis as well. The most worrisome condition is enterocolitis, which can be life-threatening and is thought to be due to stasis, bacterial overgrowth, and bacterial translocation. It is clear that there is a difference in mucosal immunity in Hirschsprung patients, but this is not well understood. Patients with trisomy 21 are particularly prone to enterocolitis.

Anomalies such as malrotation, genitourinary abnormalities, congenital heart disease, limb abnormalities, cleft lip and palate, hearing loss, cognitive delays and dysmorphic features, and certain syndromes such as trisomy 21, congenital hypoventilation syndrome, Mowat–Wilson, or a neurocristopathy can be associated with Hirschsprung disease.

Diagnosis

With signs and symptoms consistent with Hirschsprung disease and an X-ray showing distal bowel obstruction, the clinician should proceed with a water-soluble contrast enema, which in a majority of cases shows a transition zone (Fig. 62.1). A pathologic confirmation of HD is made with tissue from a suction rectal biopsy. A full-thickness biopsy should be performed in a child over one year of age.

The pathology specimen reveals the absence of ganglion cells and the presence of hypertrophic nerves (>40 μm). The specimen much be taken at least 0.5 cm above the dentate line to avoid the normally aganglionic area of the anal canal. Acetylcholinesterase staining is often used as is calretinin, which is more sensitive. Calretinin is a calcium transporter found on enteric ganglion cells, thus an absence of it suggests HD.

Anorectal manometry can be used in the older child. In the patient with HD, manometry demonstrates a failure to relax the internal sphincter when the rectum is distended. The constipated patient with normal manometry can sometimes avoid an unnecessary rectal biopsy. In the patient following a

J.R. Avansino, MD
Department of Surgery, Seattle Children's Hospital, University of Washington, 4800 Sandpoint Way NE, OA 9.256, Seattle, WA 98004, USA
e-mail: Jeffrey.Avansino@seattlechildrens.org

M.A. Levitt, MD (✉)
Center for Colorectal and Pelvic Reconstruction, Nationwide Children's Hospital, 700 Children's Drive, Columbus, OH 43205, USA

The Ohio State University, Columbus, OH, USA
e-mail: Marc.Levitt@nationwidechildrens.org

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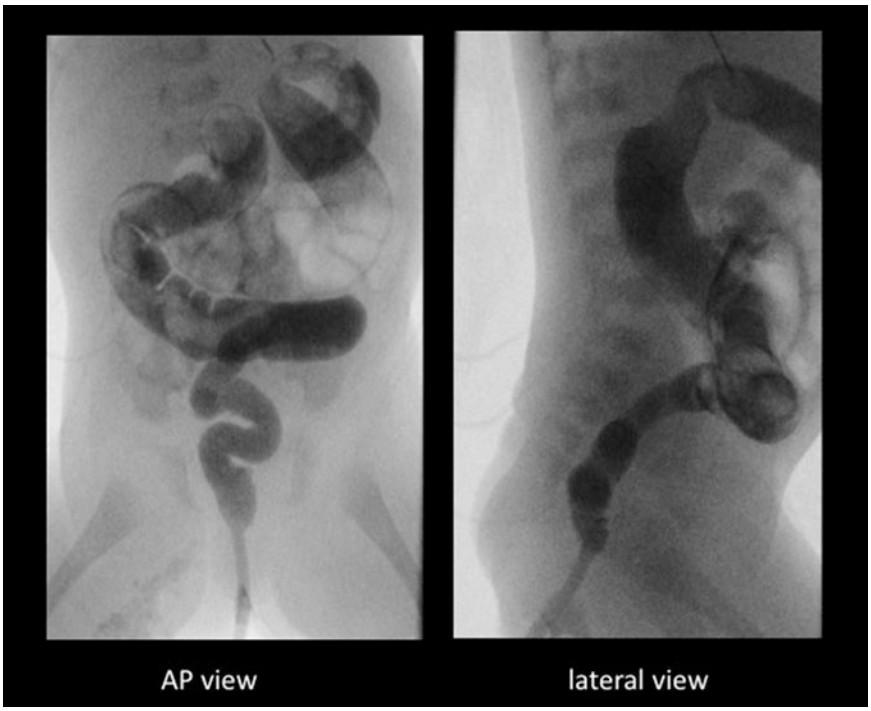

Fig. 62.1 Water-soluble contrast enema (AP and lateral views) demonstrating a transition zone in the recto-sigmoid colon. The lateral view is the most important one to identify a low transition zone. Other findings on the contrast enema that suggest the diagnosis of Hirschsprung disease include a recto-sigmoid index (the ratio of rectal diameter/sigmoid diameter) <1.0, and retention of contrast on a 24-hour post-evacuation film

pull-through who is soiling, anorectal manometry is used to objectively assess the quality of the sphincters.

Treatment

Neonates require intravenous resuscitation and antibiotics, as well as nasogastric decompression. Distension and enterocolitis are treated with colonic irrigations 20 mL/kg every 4–6 h (Fig. 62.2). If the child is extremely ill and not responding to antibiotics and irrigations, an urgent ostomy should be performed. In these very rare cases, we prefer to perform multiple colonic biopsies and an ileostomy. Frozen section analysis for leveling colostomy requires sophisticated pediatric pathologic analysis and surgery performed in the urgent setting often occurs after hours when pediatric pathology is not widely available. An ileostomy is the safest and most reliable diversion, although it will require a third stage surgery (following the 2nd stage pull-through) to close the ileostomy.

Once stable, surgery can be done semi-electively. While waiting for surgery, most children can be fed breast milk or an elemental formula, while continuing with rectal irrigations. Our preference is to perform surgery in the newborn period. In the older child with a very dilated colon, a period of irrigations is helpful before proceeding with surgery. Sometimes, in such a case, an ileostomy is required as a first step. A definitive pull-through procedure can be done months later. A repeat contrast enema at that time might more clearly show a transition zone.

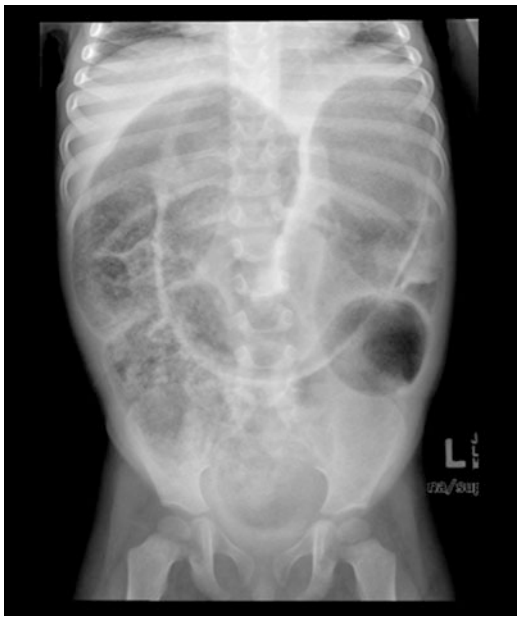

Fig. 62.2 Abdominal radiography showing colonic distension in a patient with enterocolitis. (Reprinted from Levitt MA, Dickie B, Peña A. Levitt MA, Dickie B, Peña A. Evaluation and treatment of the patient with Hirschsprung disease who is not doing well after a pull-through procedure. Semin Pediatr Surg. 2010 May;19(2):146-53, with permission from Elsevier.)

The goals of surgical management for Hirschsprung disease are to remove the aganglionic bowel, pull-through ganglionated bowel, and preserve the anal canal and sphincter mechanism. Orvar Swenson described the first operation in

1948. Since that time the surgical management has evolved to include Swenson's full-thickness recto-sigmoid dissection, Soave's endorectal dissection, and creation of the Duhamel partially aganglionic rectorectal pouch (Fig. 62.3). Rehbein's operation, essentially a low anterior resection, more commonly done in the past in Europe, is becoming increasingly rare. These definitive procedures were often preceded by a diverting colostomy due to the high incidence of complications seen with the initial experience. Dr. Henry So in the Philippines first did a primary pull-through with no stoma, and this was related to his desire to avoid creating a stoma, fearing parents would not care for the child given the significant social stigma associated with a colostomy.

Despite the trend to avoid stomas, it is important to remember that a stoma may still be indicated for children with severe enterocolitis, perforation, malnutrition, or massively dilated proximal bowel. A staged approach should also be used in situations where there are inadequate pathology services to reliably identify the transition zone on frozen section from the operating room. Modifications to the procedures have included the transanal approach (de la Torre and Langer) with or without laparoscopy (Georgeson). Currently,

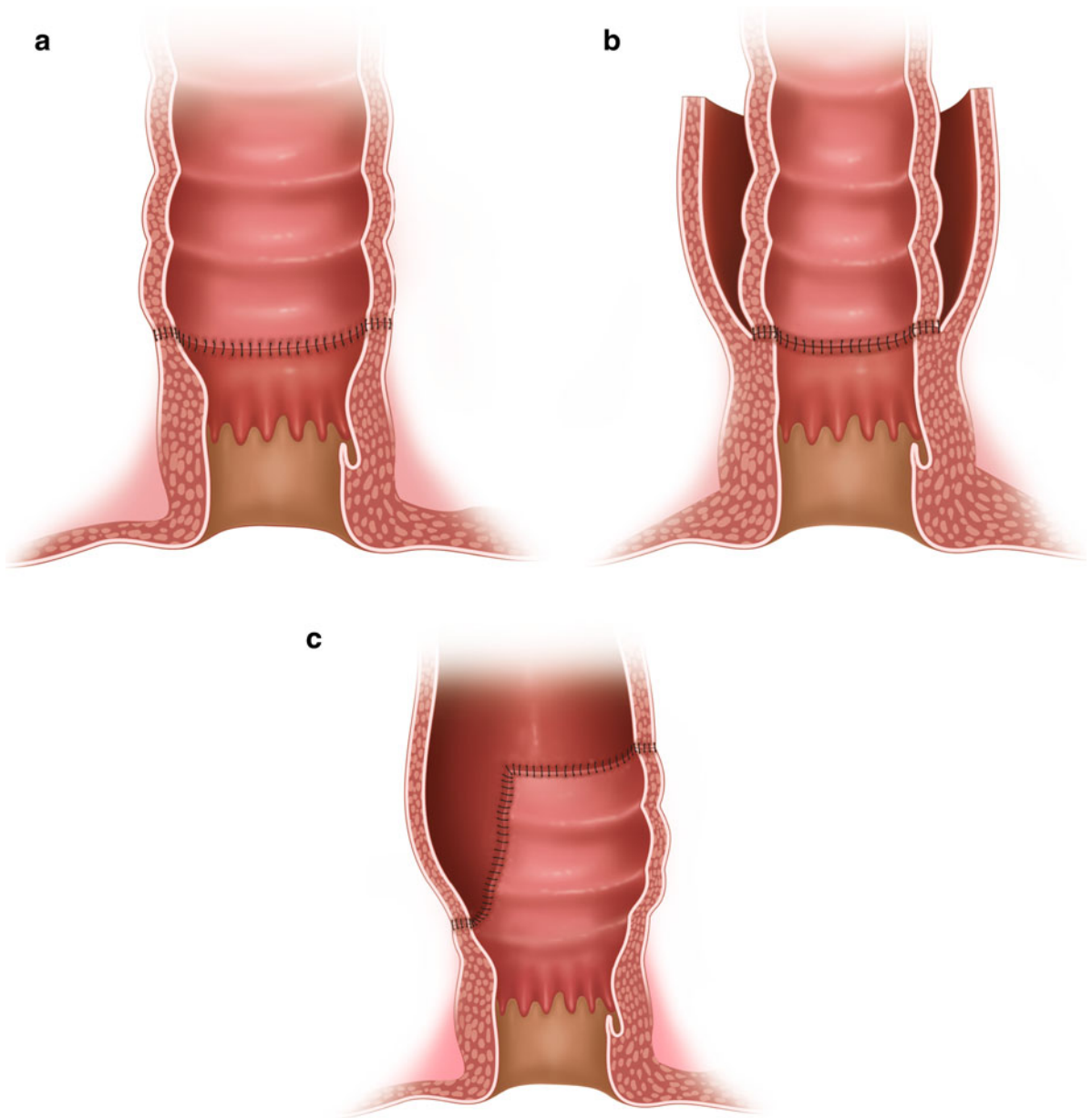

Fig. 62.3 (**a**) Swenson's full-thickness recto-sigmoid dissection. (**b**) Soave's endorectal dissection. (**c**) Rectorectal pouch (Duhamel)

there is no compelling evidence that any technique is best and all are acceptable options in the hands of a well-trained and experienced surgeon. Long-term outcomes studies comparing the various approaches are lacking.

The Swenson procedure is the only operation that leaves behind essentially no aganglionic bowel (except for the 1 cm preserved adjacent to the dentate line). The Soave procedure leaves behind the outer rectal wall but this cuff has been created shorter and shorter over the years to the point where only a 1 cm cuff is now recommended for this technique, sometimes referred to as a "Soaveson." The Duhamel and Rehbein intentionally leave behind aganglionic bowel, connected to ganglionated bowel. These techniques were developed due to complications occurring with the Swenson, which were likely due to an extensive rectal dissection that was too wide. We prefer the Swenson technique performing a full-thickness dissection in the avascular plane.

Leveling biopsies are performed via a laparoscopic or umbilical approach, although in certain cases when the transition is clearly in the rectum or mid-sigmoid, a transanal-only approach can be used. In both approaches, the bowel is inspected and findings correlated with the preoperative contrast enema. A biopsy is taken above the suspected area of aganglionosis, full-thickness or seromuscular. Seromuscular biopsies prevent spillage; however, biopsies taken at this level can provide false reassurance that one is outside the transition zone as hypoganglionosis and hypertrophic nerves could still be present in the submucosal layer despite seeing ganglion cells in the seromuscular layer. We request that our pathologist measure the size of the nerves, as nerves greater than 40 μm are considered hypertrophic. Due to an irregular distribution of ganglion cells in a transition zone, hypoganglionosis may exist at the same level of a biopsy demonstrating an adequate distribution of ganglion cells. Transition zone length is variable, which is why assessment of the nerve size is so valuable. In addition, transition zones have been described to measure anywhere from 1 to 10 cm so it is recommended to perform an anastomosis some distance (3–10 cm) above the biopsy site to ensure one is out of the transition zone. In patients with total colon aganglionosis, the appendix is an inadequate specimen to evaluate the transition zone, as even in normal children it might be aganglionic.

In the umbilical approach, an infra-umbilical incision is made and the fascia split vertically being mindful of the bladder. A Hegar dilator is passed through the anus to allow identification of the rectum and sigmoid. The bowel is exteriorized and inspected, and the biopsy is taken and sent for frozen section. In the laparoscopic approach, the biopsy can be performed using laparoscopic endoshears or an endoloop. Alternatively, the segment can be identified laparoscopically and the biopsy performed at the umbilicus with the colon exteriorized. Once the level has been confirmed, mobilization of the recto-sigmoid colon can be performed; ideally it is mobilized as far distally as possible to minimize the amount of transanal dissection required. This is preferable to the potential over-stretching of the sphincters during a transanal-only approach.

Transanal Dissection

The transanal dissection can be done in the prone or lithotomy position. If a laparoscopic biopsy and mobilization is performed, the dissection is performed in the lithotomy position; otherwise we prefer the prone position if a transanal-only approach is being utilized. We begin our dissection by placing a lone-star retractor (Cooper Surgical) at the ano-cutaneous junction. We identify the dentate line and replace the hooks in the rectal mucosa to protect the dentate line (Fig. 62.4). Next, we place a series of retraction sutures and make a full-thickness circumferential incision 1.0 cm above the dentate line and continue the dissection on the rectal wall dividing vessels as they enter the rectum. This is a readily identifiable areolar plane. If doing a transanal-only technique, the anterior rectum frees up more easily than the posterior rectum. One can then enter the peritoneum, pull out the sigmoid, send a biopsy, and then continue with the posterior dissection. This makes for an efficient procedure, with minimal delay waiting for the biopsy result. A two-layered anastomosis is then performed suturing the seromuscular layer of the pull-through segment to the musculature of the anal canal, followed by a separate mucosal layer. It is important to reposition the hooks at the ano-cutaneous junction prior to doing the mucosal anastomosis. While doing the anastomosis, the proximal margin of the resected specimen is sent for confirmation of adequate distribution and quality of ganglion cells and nerves.

In the Soave procedure, the mucosa is separated from the underlying muscle for a distance of a few centimeters before transitioning to a full-thickness dissection. The operation then proceeds as described above for the Swenson. The retained muscular cuff is split posteriorly to prevent obstruction.

Pure Transanal Pull-Through

The pure transanal pull-through was first described by de la Torre and Langer. This procedure is reserved for biopsy-proven HD in patients with a clear transition zone in the recto-sigmoid region on the contrast enema. Whether to determine the level of transition first with a biopsy or start transanally is a point of controversy. Proponents of a preliminary biopsy point to the inaccuracy of the contrast enema in predicting the level of aganglionosis. Approximately 8 % of children with an apparent recto-sigmoid transition zone on contrast study turn out to have a more proximal patho-

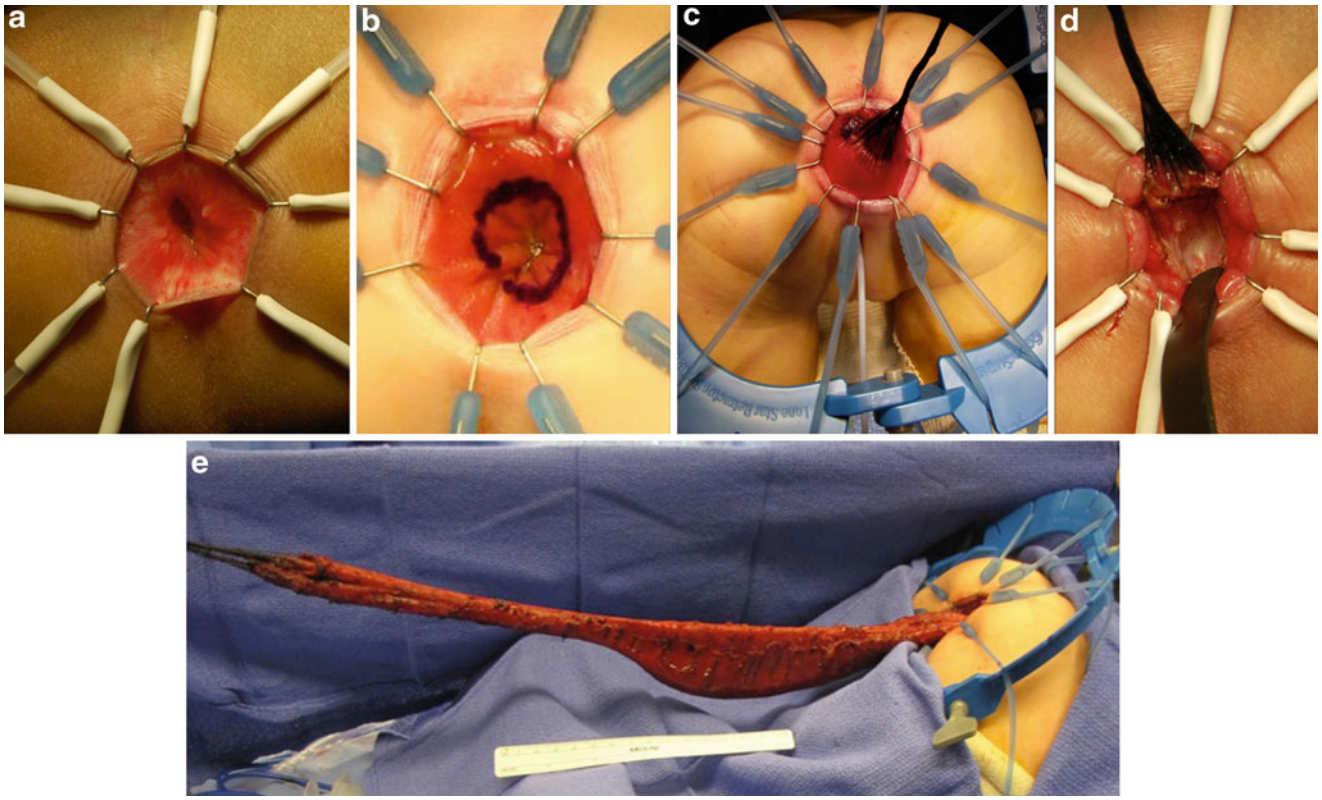

Fig. 62.4 Transanal Swenson. (**a**) The dentate line. (**b**) Line 1 cm above the dentate line where dissection into full-thickness Swenson plane begins. Note the dentate line is protected by placing the lone-star hooks into the rectal mucosa. (**c**) Circumferential silk sutures are placed to provide traction. (**d**) The areolar Swenson plane. (**e**) The fully mobilized segment, by transanal technique in prone position

logical transition zone at operation. This is particularly important for the surgeon who prefers a different operation for long-segment disease than for recto-sigmoid disease (an ileal-Duhamel procedure for total colonic HD), in which case it would be best to have avoided a transanal dissection.

The transanal approach has a low complication rate, requires minimal analgesia, is associated with early feeding and discharge and can be done by any pediatric surgeon, including those without laparoscopic availability. The key technical issue is to avoid over-stretching from retraction during the rectal dissection. For the Swenson approach, finding the perfect full-thickness plane is key to a comfortable dissection.

Long-Segment Hirschsprung Disease

Aganglionosis extending proximal to the sigmoid will require additional colonic mobilization. Disease extending to the proximal sigmoid often requires ligation of the inferior mesenteric artery near its base to adequately mobilize the sigmoid colon. It is vital to identify the "Y" of the mesenteric vessel, ligate the stem of the "Y" and then once ligated, the top part of the "Y" extends and lengthens the pull-through, with a nicely preserved arcade (Fig. 62.5). Aganglionosis ending in the left colon requires mobilization of the splenic flexure and division of the left colic artery with careful preservation of the sigmoid arcade. Aganglionosis at the hepatic flexure provides an interesting dilemma of whether to bring the colon down the right or left colic gutter. Our preference is to bring the colon down the right gutter by dividing the blood supply at the middle colic artery, mobilizing the hepatic flexure and right colon, and detaching the small bowel mesentery from the retroperitoneum (Fig. 62.6). The right colic artery usually must be ligated to gain adequate length with distal perfusion dependent on preservation of the ileocolic arcade to the right colon.

Total Colonic Hirschsprung Disease

Total colonic aganglionosis occurs in about 5–10 % of patients with HD, and usually involves part of the distal ileum. In rare cases, most or all of the small bowel is also involved. Contrast enema typically shows a shortened, relatively narrow colon, often with a transition zone in the small bowel. The rectal biopsy shows absence of ganglion cells, but in many cases there are no hypertrophic nerves or abnormalities of acetylcholinesterase staining and frozen section of these cases is particularly challenging. Once the level of

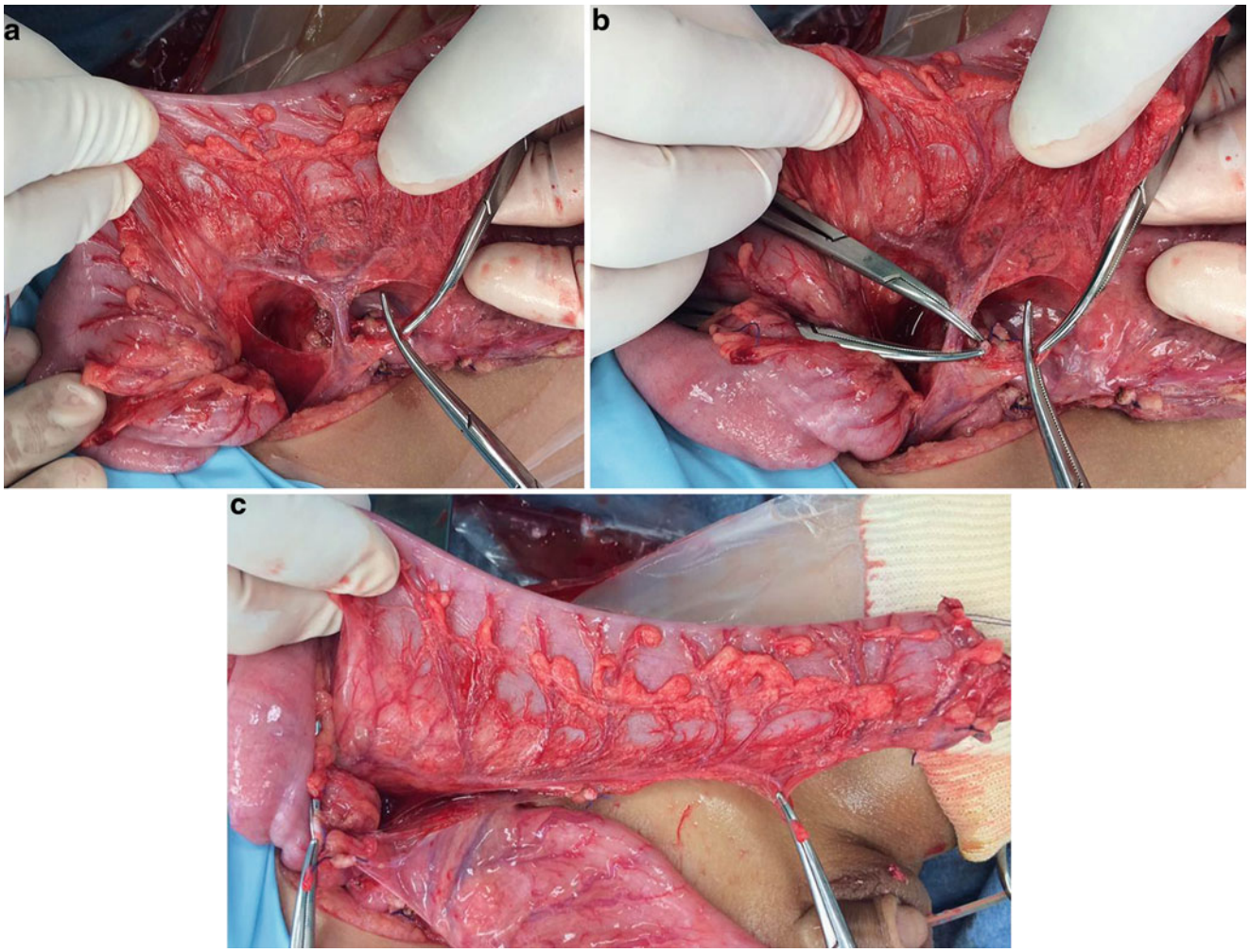

Fig. 62.5 Mobilization of colon with division of mesentery. (**a**) Arcade of the colon showing the "Y" of the vessel. (**b**) Division of the mesenteric vessel. (**c**) Straightening of the "Y" to gain additional length on the colon

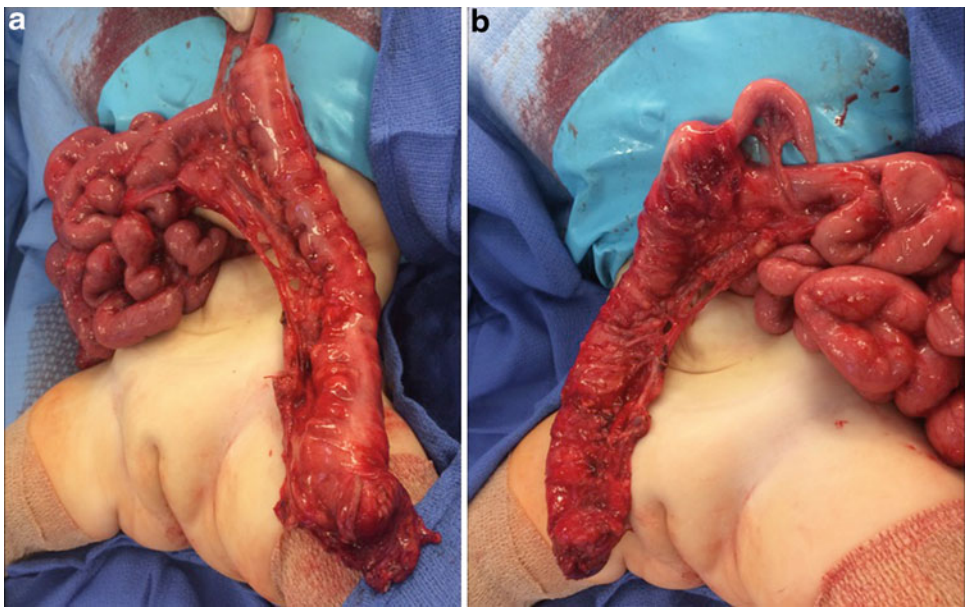

Fig. 62.6 Options for a hepatic flexure pull-through, down the right or the left pelvis. (**a**) Pull-through down left side into pelvis. (**b**) Pull-through down right side into pelvis

aganglionosis has been identified, a stoma is created and a definitive reconstructive procedure performed at 6–12 months of age. We recommend repair after the stools have thickened and the child is demonstrating adequate growth and nutrition. Skin care to avoid perineal rash has dramatically improved in recent years and thus the pull-through can be done earlier than previously recommended. Parents need to be taught how to do rectal irrigations as the incidence of enterocolitis is highest in this patient group and prophylactic irrigations after pull-through are very helpful. This timing for a pull-though needs to be balanced with the advantage of waiting until the child can sit on a toilet and is toilet trained for urine, which dramatically reduces the perineal rash that occurs with an earlier in life pull-through. Although primary pull-through without ileostomy for total colonic disease has been reported, we strongly urge against this practice as frozen section can be misleading and permanent section and immunostaining are required for definitive diagnosis and level.

Reconstruction for total colonic HD traditionally included an ileal Duhamel, or a longer patch (Martin) or a J-pouch. Our preference is a straight ileoanal, but many centers prefer a Duhamel approach. If this method is chosen, we recommend a relatively short colonic segment below the peritoneal reflection. Although the colon patch procedures theoretically result in decreased stool output due to better water absorption, the aganglionic colon tends to gradually dilate, for reasons that are poorly understood. As the Duhamel pouch dilates, stasis ensues and some of these patients develop severe enterocolitis requiring removal of the pouch. We believe the issue is not the stasis induced by the Duhamel but rather the inability of the ganglionic bowel to work well and overcome stasis. Why some ganglionated bowel works poorly is a mystery, but probably relates to the wide phenotypic expression of HD. The J-pouch procedure is the same as that done commonly for children and adults with ulcerative colitis and familial polyposis syndrome. And like the Duhamel risks inducing stasis.

Postoperative Care

Following surgery, the child is fed when bowel function has commenced and the abdomen is not distended. The anastomosis should be calibrated with a dilator four weeks after surgery. We recommend daily dilations if any narrowing is detected (Table 62.1) and calibration daily for the postoperative infant to help stimulate stooling for several months. Children with a late diagnosis typically do not require dilations with the two-layered anastomosis. Protection of the buttocks with a barrier cream is mandatory, since at least 50 % of children will have frequent stools postoperatively and are prone to perineal skin breakdown. These products have improved dramatically, which may allow for earlier pull-through in patients with total colon disease. Fortunately, this is a problem that tends to resolve over time.

Table 62.1 Dilator size by age

Dilator size by age (mm)	
Newborn	11/12
1 year old	14/15
2–5 year old	15
>5 year old	16

Post Pull-Through Problems

We categorize patients with long-term problems following surgery for HD into: (1) fecal incontinence with soiling and (2) obstructive symptoms and recurrent enterocolitis (Fig. 62.7). Sometimes an individual child may have a combination of problems. These complications are more common than previously recognized and it is incumbent upon the surgeon to follow these children closely and determine whether an anatomic or pathologic problem is present.

The initial evaluation begins with a thorough history asking about constipation, enterocolitis, abdominal distension, failure to thrive, laxative and enema use. It is also imperative to know the type of operation performed and have the original pathology reviewed if possible. We perform a contrast enema in all patients, examining the post pull-through anatomy. An examination under anesthesia is also performed to evaluate the following: (1) integrity of the anal canal/dentate line, (2) presence of a stricture, (3) status of the sphincters, (4) presence of a large rectal (Duhamel) pouch, and (5) presence of an obstructive Soave cuff. We perform a full-thickness biopsy to assess for aganglionosis or transition zone bowel and obtain anal manometry to analyze the sphincter function.

Fecal Incontinence

We define fecal continence as having voluntary bowel movements without soiling or need for enemas. Patients with HD are born with a normal continence mechanism (normal sphincter function and anal canal sensation) and should not experience fecal incontinence after surgical management. Disruption of the anal sphincter, anal canal, or colonic motility may result in soiling. Pseudo-incontinence occurs when the continence mechanism is intact but the child continues to soil. This is usually due to severe constipation and is treatable with the right medical regimen, usually laxative treatment. Uncommonly, pseudo-incontinence is secondary to a hypermotile colon.

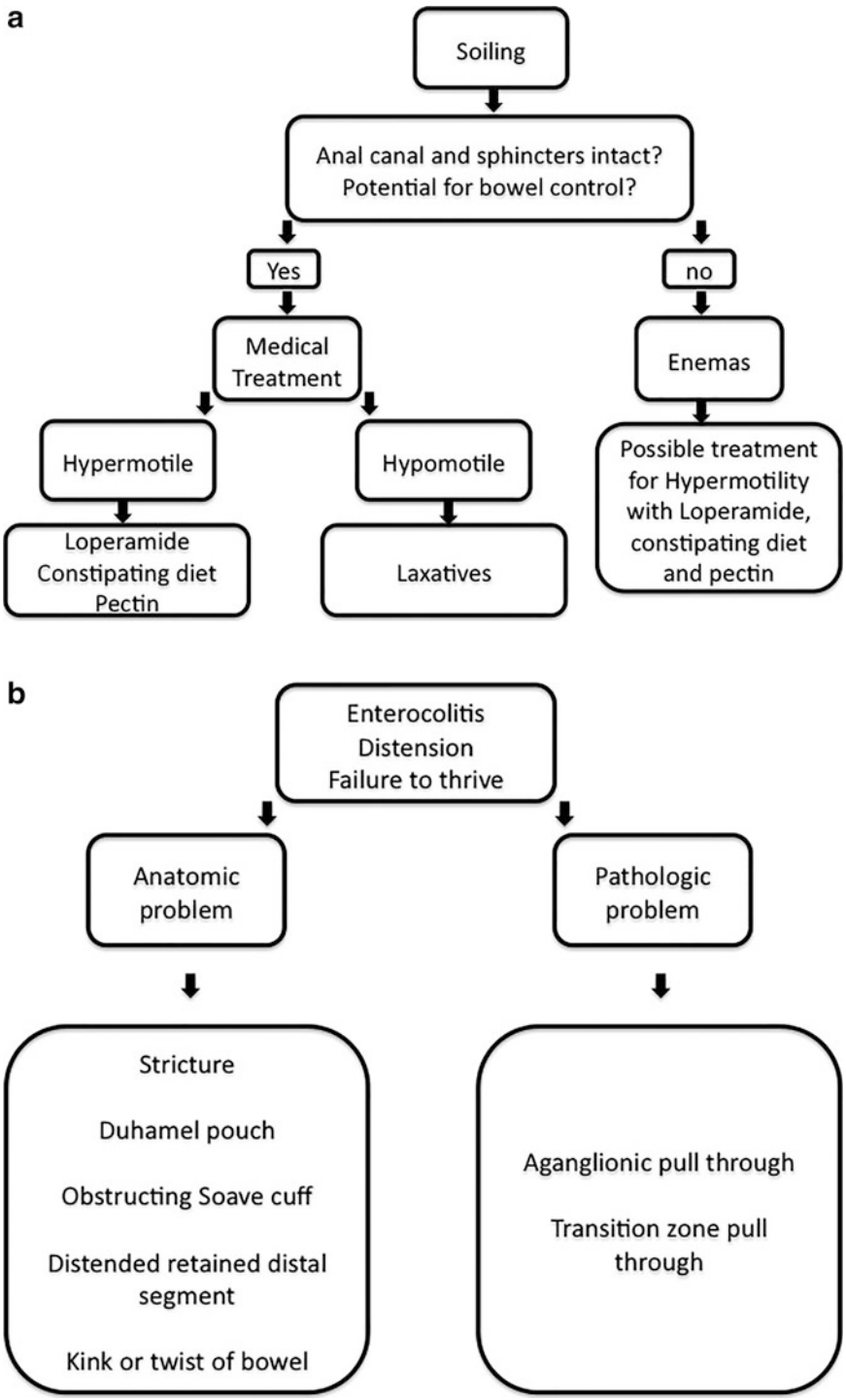

Fig. 62.7 Algorithm for care of the post pull-through problem patient. (**a**) Post pull-through patient with soiling. (**b**) Post pull-through patient with recurrent enterocolitis

It is important to differentiate between fecal incontinence and pseudo-incontinence. This can be determined during the exam under anesthesia. A patulous anus signifies damage to the anal sphincter muscle complex. Disruption of the dentate line, from a dissection that was started too low, results in diminished anal canal sensation. These findings may suggest irreversible incontinence requiring treatment with an enema program to achieve social continence.

Children with an intact sphincter mechanism and intact dentate line should be able to have voluntary bowel movements. Those with a dilated colon on contrast enema are considered to be hypomotile and can be managed with a daily senna-based (stimulant) laxative program. The dose of the laxative is titrated during a week-long laxative trial so the child has one to two large bowel movements per day, no accidents, and an abdominal radiograph showing a distal

colon devoid of stool. Addition of water-soluble fiber to produce bulk makes the laxative more effective and avoids loose stools. Success with this program confirms the diagnosis of pseudo-incontinence. Patients failing this regimen can be managed with large-volume saline enemas (400–600 mL) with a colonic stimulant such as glycerine added to the solution. This allows the child to experience social continence. Children who achieve success with enemas and have an intact sphincter mechanism can trial a laxative program every 6–12 months, as they now know what it is like to be clean after enemas.

Children with contrast enemas demonstrating a non-dilated colon and fecal incontinence may be hypermotile. Although hypomotility is more common after a pull-through for HD, hypermotility happens and is treated differently. As a result, we recommend slowing the colon using a combination of a constipating diet, water-soluble fiber, and antimotility agents (loperamide and diphenoxylate/atropine). In patients unable to have a voluntary bowel movement, we add a daily low volume enema (200–300 mL) to clean the distal colon and slow the colon transit.

Obstructive Symptoms and Recurrent Enterocolitis

Abdominal distention and enterocolitis can be due to either pathologic or anatomic problems. Enterocolitis may be present both before and after surgical correction of the disease and can be very severe, even life-threatening. Although the clinical features of enterocolitis are generally agreed upon (fever, abdominal distention, diarrhea), a precise definition has not been developed and as a result there is a varied reported incidence. The treatment of postoperative enterocolitis involves nasogastric drainage, intravenous fluids, broad-spectrum antibiotics, and decompression of the rectum and colon using rectal irrigations. The goal of rectal irrigations is to wash the colon using aliquots of 10–20 mL of saline at a time. Using a large bore catheter (20–24 Fr), up to 1–2 L of saline can be used; however, a child should not retain more than 20 mL/kg. Irrigations can be administered one to three times per day depending on disease severity. It is extremely important that the family is taught to administer the irrigations and has the needed supplies. We will also send the family home with a prescription for oral metronidazole. We instruct families to begin irrigations and start oral metronidazole at the first sign of enterocolitis, and urgent early return to the hospital if the symptoms worsen. In rare cases where patients are resistant to irrigations and antibiotics, a diverting ileostomy or colostomy may need to be created while an anatomic or pathologic cause is sought.

In patients with recurrent abdominal distension or enterocolitis, a systematic workup is needed to determine the etiology. We begin by requesting the pathology from the original resection and ask our pathologist to determine if the proximal margin has a normal distribution of ganglion cells and normal sized nerves (<40 μm). If the pathology is not available or the proximal margin is consistent with aganglionosis or a transition zone, we perform a full-thickness biopsy. Absent or abnormal distribution of ganglion cells or the presence of hypertrophic nerves with ganglion cells present in the setting of recurrent obstruction and enterocolitis requires surgical revision of the pull-through segment.

Anatomic problems from the original operation can cause an obstruction that leads to stasis and enterocolitis. Three anatomic problems that can occur regardless of the initial procedure include stricture (typically at the anastomosis), retained dilated segment, or a twist or a kink of the pull-through segment (Fig. 62.8). Additionally, an obstruction can be related to mechanical issues specific to the type of pull-through. The muscular cuff of a Soave procedure can cause an obstruction if it is too long or not adequately split. The result is a constricting fibrotic ring and an outlet obstruction. Furthermore, a previously split cuff may scar down or roll up to cause an obstruction. The presence of an obstructing muscular cuff can be seen on contrast enema. (Fig. 62.9) and palpated during an examination under anesthesia.

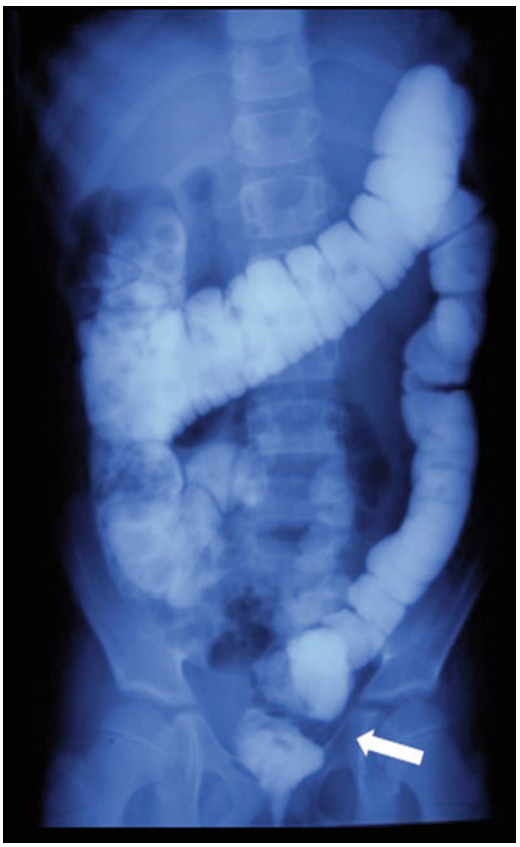

Fig. 62.8 Contrast enema demonstrating a twist of the distal pull-through segment (*white arrow*)

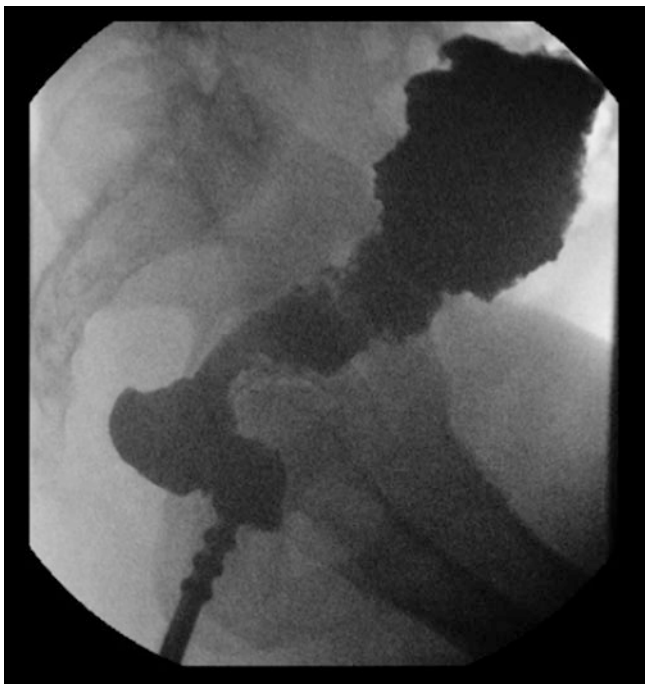

Fig. 62.9 Contrast enema demonstrating an obstructing Soave muscular cuff. (Reprinted from Levitt MA, Dickie B, Peña A. Levitt MA, Dickie B, Peña A. Evaluation and treatment of the patient with Hirschsprung disease who is not doing well after a pull-through procedure. Semin Pediatr Surg. 2010 May;19(2):146-53, with permission from Elsevier.)

Historically, a long muscular cuff was left with the Soave procedure; however, more recently the trend has been to leave only a few centimeters, which should reduce the incidence of cuff problems.

The Duhamel procedure was designed to create a pouch using a portion of aganglionic rectum in an effort to slow colonic transit and create a reservoir for stool. This is commonly used in children with total colonic HD but is the preferred technique of many surgeons for every pull-through. Inadequate emptying of the pouch can result in a "megarectum" that leads to stasis and enterocolitis (Fig. 62.10).

Functional and mechanical obstructions in post pull-through patients are frequently managed with a redo operation. It is our contention that until the distal pull-through has no anatomic or pathologic obstruction, evaluation or treatment of dysmotility problems is unhelpful. The clinician must seek to find the cause of the distal obstruction.

Once identified, we perform a redo transanal pull-through using a Swenson technique with the addition of laparotomy or laparoscopy as necessary. If the rectum is surrounded by dense scar, a posterior sagittal approach may sometimes be necessary for mobilization. There are many patients with persistent obstructive symptoms who are being followed, waiting for improvement. We believe such patients require an evaluation searching for an anatomic or pathologic cause and redo the pull-through if necessary.

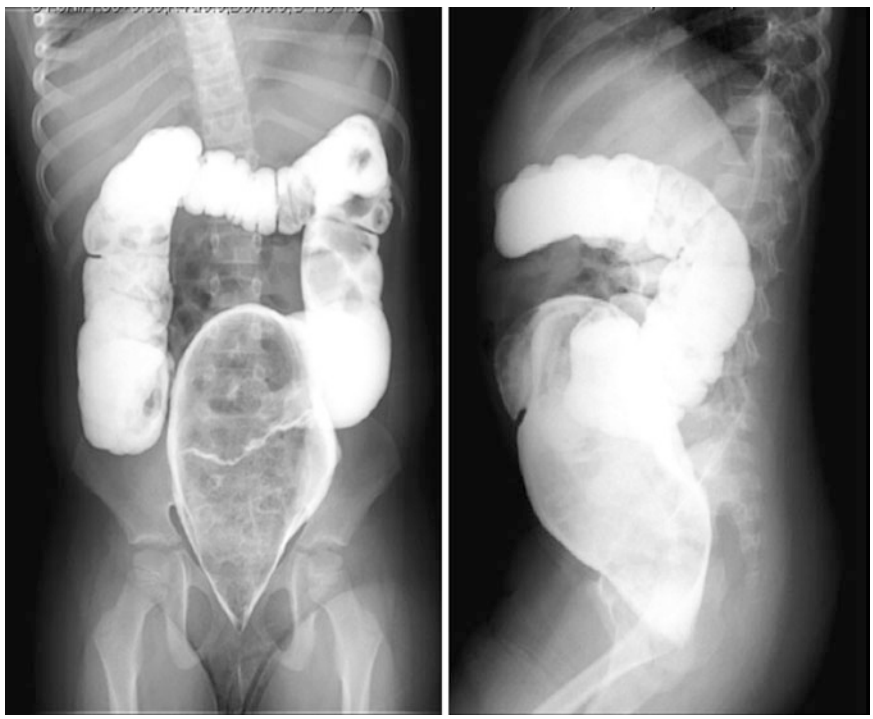

Fig. 62.10 Contrast enema demonstrating a "megarectum" in a patient after a Duhamel procedure. (Reprinted from Levitt MA, Dickie B, Peña A. Levitt MA, Dickie B, Peña A. Evaluation and treatment of the patient with Hirschsprung disease who is not doing well after a pull-through procedure. Semin Pediatr Surg. 2010 May;19(2):146-53, with permission from Elsevier.)

Internal Sphincter Achalasia

Internal sphincter achalasia refers to the lack of a normal recto-anal inhibitory reflex that is present in all children with Hirschsprung disease but in some significantly impairs normal defecation after definitive pull-through. This is a diagnosis of exclusion, after ruling out mechanical obstruction, aganglionosis, and dysmotility. The diagnosis is confirmed with anal manometry. Since this problem tends to resolve on its own in most children, we prefer the use of intrasphincteric botulinum toxin (6 units/kg, max 100 units, 25 units given in each quadrant of the anal canal). In many cases, repeated injection of botulinum toxin, application of nitroglycerine paste or topical nifedipine is necessary while waiting for resolution of the problem. Because of the spontaneous resolution of this problem as children grow and become more effective at defecating and coordinating sphincter relaxation, we believe internal sphincterotomy or myectomy should be avoided, as it could lead to permanent fecal incontinence.

Near-Total Intestinal Aganglionosis

Intestinal failure and the need for total parenteral nutrition from birth is present in total intestinal aganglionosis and is associated with a very high risk of mortality from liver failure. The extent of aganglionosis should be established at the time of the first laparotomy and a stoma brought out at the most distal point that has normally innervated bowel. The practice of bringing out a more distal stoma risks chronic intestinal obstruction and bacterial overgrowth. Long-term total parenteral nutrition and a gastrostomy for trophic feeding are usually required.

Surgical options for such patients include tapering, imbrication, or bowel lengthening procedures such as the Bianchi or serial transverse enteroplasty (STEP) particularly to enhance absorptive capacity. For children with ongoing liver failure, small bowel or combined small bowel-liver transplantation might offer the only chance for survival. Patch procedures of the left and right colon (Martin and Kimura) are no longer done as they cause too much stasis in their attempt to slow motility and increase absorption.

Conditions that Mimic Hirschsprung Disease

There are a number of conditions that resemble Hirschsprung disease in presentation and clinical course but are not characterized by the absence of ganglion cells on rectal biopsy. *Intestinal neuronal dysplasia* (IND) in its usual form consists of dysplasia of the submucosal plexus with thickened nerve fibers and giant ganglion cells, increased acetylcholinesterase staining and ectopic ganglion cells in the lamina propria. However, this condition is often described in a patient with Hirschsprung disease that has been previously operated on and therefore may indicate that the original pull-through was performed in the transition zone.

Hypoganglionosis is even less common and is characterized by sparse, small ganglion cells, usually in the distal bowel. There can also be abnormalities in acetylcholinesterase distribution. A similar condition might occur in a premature infant and thus the concept of "immature ganglion cells" has been described. This is usually self-limited and should not be treated surgically, except sometimes a temporary ileostomy is required.

Almost all children with HD lack the recto-anal inhibitory reflex. However, there are some children with ganglion cells present on rectal biopsy who also lack the inhibitory reflex and develop similar obstructive symptoms, although usually these patients develop constipation and impaction rather than enterocolitis. This condition has been termed *internal sphincter achalasia* or *ultra-short segment HD* (although we prefer to save the latter term for children with a documented aganglionic segment of less than 3–4 cm).

These children should be initially managed with a bowel management regimen. If this is unsuccessful, some surgeons advocate anal sphincter myectomy. We prefer temporary sphincter-relaxing measures such as botulinum toxin or nitroglycerine paste and strongly recommend against a sphincter myectomy as it can cause permanent fecal incontinence. The symptoms normally improve significantly over time in most of these children as they learn to better coordinate sphincter relaxation with defecation, so minimal intervention is recommended.

Future Considerations

Hirschsprung disease has a widely variable phenotype even in families with the same apparent genetic mutation. The incidence and severity of Hirschsprung-associated enterocolitis is also variable. Further genetic investigation is necessary to aid with prognosis, as patients with long-segment disease tend to have worse outcomes. A universally agreed upon definition of enterocolitis is needed in order to ensure that this outcome measure is reported similarly. Finally, long-term functional outcome and quality of life studies are needed to accurately assess the burden of this disease.

Editor's Comment

Radiographic identification of the transition zone in Hirschsprung disease needs to be regarded with caution. The contrast enema will identify what appears to be an obvious transition zone in the majority of cases, but the concordance between radiology and pathology is in the range of 50–90 % and perhaps as low as 30 % for long-segment disease. This should be recognized, particularly when planning a one-stage transanal pull-through.

The absence of calretinin staining suggests HD. However, claretinin staining can be misleading in ultra-short-segment disease (2–3 cm aganglionic segment) as mucosal nerves that stain positive for calretinin can extend into the proximal 1–2 cm of aganglionic bowel. This must be considered in rectal biopsies in which ganglion cells are not observed and calretinin staining is positive. In this scenario, more than four nerves >30 μm thick/×200 field or more than two nerves >40 μm thick/×200 field confirms the diagnosis of HD.

A common belief is that HD is rare in premature infants, though this has been disproved in large population-based studies. Many premature infants have an abnormal stooling pattern due to poor GI motility, which often results in a delayed diagnosis. Clinical features (failure to pass meconium, bilious emesis) are the same but contrast enema fails to demonstrate a transition zone in a higher percentage of premature babies with HD even though the distribution of the level of aganglionosis is similar to term infants.

Approximately one-third of patients will experience enterocolitis following surgery. This is less common after about two years. Trisomy 21, poor nutrition and anastomotic stricture are risk factors. Routine rectal saline irrigations beginning 3–4 weeks postoperatively and continuing for 1–3 months seem to decrease the occurrence of enterocolitis, especially in infants at higher risk.

Parents need to be told that any operation for HD is essentially palliative, not curative in the traditional sense. Patients should expect to be able to stool voluntarily with less difficulty and have a lower risk of enterocolitis but many will still have some degree of constipation and all patients should be followed closely for many years after surgery. Most will have some degree of intestinal dysmotility or sphincter dysfunction despite a technically excellent operation. Constipation is managed with diet modification but often requires a structured bowel management program. The need for a stimulant laxative is not uncommon and routine long-term follow-up is critical to avoid the morbidity associated with severe constipation such as megarectum and overflow pseudo-incontinence.

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