Published in final edited form as:
Semin Pediatr Surg. 2012 November ; 21(4): 328–335. doi:10.1053/j.sempedsurg.2012.07.007.

Hirschsprung-Associated Enterocolitis: Prevention and Therapy

Philip K. Frykman, MD, PhD, FACS, FAAP and **Scott S. Short, MD**

Abstract

Hirschsprung-associated enterocolitis (HAEC) remains the greatest cause of morbidity and mortality in children with Hirschsprung disease. This chapter details the various approaches used to treat and prevent this disease process. This includes prevention of complications such as stricture formation, prophylaxis with rectal washouts and identification of high risk individuals. The chapter also details approaches to diagnose HAEC as well as to exclude other etiologies.

Keywords

Hirschsprung disease; enterocolitis; Trisomy-21; aganglionosis; rectal stricture

Introduction

Hirschsprung-associated enterocolitis (HAEC) was first recognized in the late nineteenth century by Härald Hirschsprung who included it in his hallmark description of congenital megacolon.(1) HAEC is a condition of intestinal inflammation characterized clinically by fever, abdominal distention, diarrhea and sepsis.(2) Hirschsprung also noted key pathologic findings of HAEC at autopsy; including crypt abscesses, mucosal ulceration, and transmural necrosis.(3) Today HAEC is the leading cause of morbidity and is responsible for half of deaths associated with Hirschsprung disease (HD).(4) Despite many proposed etiologies, the biological mechanisms underlying HAEC are poorly understood.

This paper focuses on early identification of high-risk patients and reviews the evidence supporting preventative strategies to reduce the likelihood of patients developing HAEC. It also reviews diagnostic criteria for HAEC and current pre-surgical and post-surgical management approaches. In addition, we also describe a strategy to work up post-surgical patients with chronic or recurrent HAEC and discuss the management options to treat each underlying cause.

Early Diagnosis

Recognition

One of the keys to prevention of HAEC is early diagnosis of HD in the perinatal period. Hirschsprung disease occurs in approximately 1 in 5000 live births(5) and should be considered in infants who fail to pass meconium in the first 24 hours of life.(6) Failure to

Corresponding Author: Philip K. Frykman, MD, PhD, Division of Pediatric Surgery, 8635 W. Third St. Suite 665 W, Los Angeles, CA 90048 Philip.Frykman@cshs.org.

recognize HD in the early perinatal period places children at greater risk of HAEC(7), with HAEC complicating 18% to as many as 50% of these children in the pre-operative period.(8) One study showed that the incidence of HAEC was 24% for infants diagnosed with HD after the first week of life compared to 11% if diagnosed within the first week.(9) Further supporting this finding, another study found a greater delay in passage of meconium (53 hrs. vs. 44 hrs.) and a much more significant delay in HD diagnosis (16.6 vs. 4.6 days) in children who developed HAEC.(10) Paradoxically, children who are diagnosed with HD outside the neonatal period may actually be resistant to the development of HAEC.(11) Decreased rates of HAEC in this group of children may be secondary to improved mucosal defenses(12) or may represent a different disease phenotype. It is important to note that not all studies have found association between increased incidence of HAEC and delayed diagnosis of HD. (13)

Conversely, establishing a diagnosis of HAEC can be challenging prior to the diagnosis of HD being made. Hirschsprung-associated enterocolitis can be the presenting symptom in some HD patients, and may not be immediately recognized due to the relative rarity of HD.(14) These factors may potentially lead to a delay in diagnosis. Hence, evaluating physicians and surgeons should keep HAEC in mind as a potential diagnosis, especially when assessing a newborn with possible necrotizing enterocolitis or distal bowel obstruction with loose stools.

Identification of high-risk Hirschsprung patients

While any patient with HD is theoretically at risk for developing HAEC, there appear to be a number of factors that contribute to increased risk of HAEC development. These include family history, Trisomy-21, long-segment disease, and prior episodes of HAEC. HD is heritable with 2.8% to 12% of patients with a family history of HD(15-18) and development of HAEC may also be influenced by heritable factors. Engum et al. demonstrated a 35% incidence of HAEC in patients with a family history of HD compared to a 16% incidence among those without a family history of HD.(19) Similarly, HD and Trisomy-21 have a known association with 2.9 to 8.2% of HD patients also having Trisomy-21.(4, 20-22) Children with Down's syndrome and HD are at significantly higher risk of developing HAEC with an incidence as high as 50%.(6, 23) An incidence of HAEC as high as 48% has been identified in in HD patients with Trisomy-21 compared to a 25% incidence in those without Trisomy 21.(24, 25) Similar risk of HAEC may exist in patients who concomitantly have intestinal neuronal dysplasia and trisomy 21(26). While most studies support the association of HAEC and HD-Trisomy 21, not all studies found this associated risk. Haricharan reported that Trisomy 21 may be protective against HAEC with a hazard ratio of 0.1 ($p=0.09$) amongst a cohort of 52 patients(11).

Long-segment disease, that is aganglionosis proximal to the splenic flexure, may confer increased risk of HAEC due to dysmotility of the residual segment leading to stasis of luminal contents. In 1995, Elhalaby showed significantly higher rates of HAEC in patients with long-segment disease compared to those with short-aganglionic segment disease, 49% vs. 31%, respectively.(27) Similar data from Reding et al. report a 56% incidence of HAEC in the pre-operative period among children with long-segment disease compared to a 16% incidence among children with short-segment disease ($p<0.01$).(28) More recent data from Lacher et al. showed a lower overall incidence of HAEC, but demonstrated continued increase in prevalence of HAEC in the long-segment cohort (17.6% vs. 11.4%) in both the pre- or post-operative periods.

Other Factors

Most authors believe that some children have a predisposition toward development of HAEC, and that one episode of HAEC may increase risk of future HAEC regardless of therapy. (2, 10) Reding and colleagues reported twelve cases of pre-operative HAEC, four of which redeveloped HAEC in the post-operative period.(28) A retrospective study of 168 patients with HD found that 57 patients developed 119 episodes of HAEC. Twenty-one children (37%) developed HAEC pre-operatively with eight recurring in the post-operative period. The remaining 36 children (63%) developed only post-surgical HAEC.(29) Other authors have suggested that HAEC may be associated with female gender(30) and while increased incidence of HAEC has been reported in girls (42% vs. 30%, $p = 0.16$), the observation did not reach significance.(29)

Preoperative Prevention

Prophylactic Interventions

For prophylactic prevention of HAEC, some have advocated for routine rectal washouts or diverting enterostomy in select populations. Due to an immature immune system, young infants are thought to be at higher risk of HAEC and therefore require frequent assessment. Hence, this group may benefit from routine rectal washout which reduces fecal stasis and bacterial load, thereby limiting colonic distension.(8) Routine washouts should be performed, especially if there are anticipated delays in surgical management. While certainly not needed in most cases, diversion should be considered for those HD patients with severe congenital heart disease, due to their compromised physiology and impaired tolerance to insult.(4)

Probiotics

Probiotics have been used to prevent colitis in a number of pediatric conditions and may be beneficial in the prevention of HAEC. Use of *Lactobacillus*, *Bifidobacterium*, *Saccharomyces*, and *Streptococcus sp.* have been reported in children. These organisms have been evaluated for treatment of infectious diarrhea, antibiotic associated diarrhea, atopic dermatitis, necrotizing enterocolitis, *Helicobacter pylori* infection, Crohn's disease, and ulcerative colitis.(31-33) Shen et al. reported markedly decreased *Lactobacillus sp.* and *Bifidobacteria sp.* in children with HAEC.(34) Proponents suggest that replacement of these commensal strains may restore bacterial equilibria and thereby play a preventive role against HAEC. Further, Herek proposed that probiotic therapy with *Saccharomyces boulardii* may be beneficial against HAEC associated with *C. difficile* due to its ability to stimulate secretion of IgA and its production of an a protease that inactivates *C. diff.* endotoxin, however currently this remains speculative.(35) To date we are not aware of published studies that have evaluated probiotics as preventive therapy in HAEC.

Diagnosis

Clinical Diagnosis

Bill and Chapman described HAEC as a clinical syndrome of abdominal distension, pain, explosive watery diarrhea, fever, and prostration.(36) Elhalaby et al, characterized the incidence of presenting symptoms in children with HAEC: abdominal distension in 99% of cases, explosive diarrhea in 82%, vomiting in 61%, fever in 40%, lethargy, in 32%, rectal bleeding in 6%, and shock in 6%.(29) In addition to these "classic" diagnostic criteria many patients will present with less specific symptoms such as loose stool or perianal excoriation. (2) Due to lack of clearly defined diagnostic criteria for HAEC, the reported incidence of HAEC has wide variation in the literature. As an attempt to standardize the diagnostic criteria for HAEC, Pastor(2) developed and validated a scoring system using a Delphi

analysis to gain consensus from a panel of experts. The HAEC scoring system serves as a standardized and reproducible outcome measure for future studies, rather than an aid to clinicians for establishing a diagnosis of HAEC.

Diagnostic Imaging

Diagnostic imaging for HAEC consists mostly of plain abdominal radiographs. Several radiographic findings are associated with HAEC and were included in the recent Delphi analysis.(2) These include the “cutoff” sign in the rectosigmoid colon with absent distal air, dilated loops of bowel, air fluid levels, pneumatosis intestinalis, “sawtooth” appearance with irregular intestinal lining, and even free intraabdominal air from intestinal perforation proximal to an aganglionic segment. While these findings may aid in the diagnosis of HAEC in an appropriate clinical setting, taken in isolation they are highly nonspecific. Elhalaby(29) reviewed clinical-radiologic correlations and found colonic dilatation on plain radiography to have a sensitivity (90%) but low specificity (24%). Use of barium enema was found to be of little clinical use, and could be dangerous should the child develop a perforation. Others have suggested adjunctive use of ultrasound which may identify peritoneal ascites or internal septations that are suggestive of peritonitis or intestinal inflammation.(14) In one unusual case, Sheth et al. reported the diagnosis of HAEC in a 3 month-old infant using computed tomography (CT).(37) However, the routine use of CT is not recommended due to increased radiation exposure and addition of little value to the diagnosis or treatment of HAEC.(38)

Other Diagnostic Modalities

When the diagnosis of HAEC may be unclear in a clinically stable patient, other procedures such as colonoscopy or capsule endoscopy have been described to evaluate for HAEC.(39) If HD is complicated by pseudoemembranous colitis secondary to *C. difficile*, endoscopy may show typical plaque-like lesions(40). Endoscopic evaluation should be approached with caution and it is relatively contraindicated to perform endoscopy in the setting of suspected moderate to severe HAEC due to risk of intestinal perforation. (41)

Therapy

Acute Presentation

Children presenting with a suspected diagnosis of HAEC require broad-spectrum antibiotics and intravenous (IV) fluid resuscitation. At our institution we provide a 20 ml/kg bolus of isotonic fluids followed by continued fluid replacement at one and one half times the maintenance rate. Children who appear ill are immediately started on ampicillin, gentamicin and metronidazole and require close hemodynamic monitoring. Patients presenting with severe HAEC and sepsis will need admission to the intensive care unit, aggressive fluid resuscitation and in some severe cases require vasopressors and ventilatory support.(37) Other less ill children are started on metronidazole alone to empirically treat for anaerobes, including *C. difficile*, an organism that can be associated with HAEC.(42) Rectal washouts with warm saline should be instituted as soon as possible. Most authors recommend use of a “large bore” rubber catheter (depending on the size of the child) and saline washouts at 10 to 20 ml/kg.(8, 43) Washouts may be performed two to four times daily, and cutting additional holes in the catheter will assist with instillation and drainage(44, 45). On initial presentation, we perform washouts until the effluent is clear and then continue twice daily until symptoms resolve. Alternate methods have been described, including a continuous irrigation method. (46) Regardless of approach chosen, it is critically important to distinguish these “rectal washouts” from retention enemata, in which fluid is instilled and retained. Retention of a large volume of fluid can cause further bowel distention leading to increased risk of perforation.

Role for Diversion

Immediate diversion should be strongly considered for all patients presenting with sepsis and severe HAEC, especially in newborns when this is the initial presentation. Although recently there is a trend toward managing stable neonates who have been treated for HAEC with a single stage procedure without creation of an enterostomy. Nonetheless, risk factors such as delayed presentation, co-morbid conditions, presence of HAEC, or multiple risk factors for HAEC in the pre-operative period warrant consideration of diversion when determining operative strategy. It has been suggested that stable children with delayed presentation of HD and HAEC may benefit from prolonged decompression with rectal irrigations and delayed pull-through to allow the bowel to resume a more normal caliber. A 2011 survey of pediatric surgeons in the U.K. and Ireland found that 19 of 34 would change to a staged operation in the setting of HAEC and 7 of 34 would do so in the setting of Down's syndrome.(47) It is important to note that diversion will virtually always improve a patient's condition, but may not resolve HAEC in all cases.(48)

Post-Operative Prevention

Anal Dilations and Nitrates

In one study, Gao and colleagues reported routine anal dilations for a period of three months following transanal pull-through procedure to prevent stricture. They found post-operative development of HAEC in only 2/34 (6%) patients(49) which is significantly lower than most published series. However, more recent data has questioned the need for daily dilation. A study by Temple et al. found daily dilation by family members to have similar efficacy to weekly dilations by medical staff with similar rates of HAEC, 18% and 12%, respectively(50) A separate study showed that weekly dilations by medical staff diminish negative psychological and social effects that families experience from routine anal dilations.(51) Since many pediatric surgeons do not routinely perform anal dilatations after primary or staged pull-through operations, the value of routine anal dilatation as a potential means of HAEC prevention is uncertain at best.

Others have explored a less invasive method to relax the internal anal sphincter termed "chemical sphicterotomy" with use topical isorbide dinitrate or nitroglycerin applied to the anal canal. Topical nitrates serve as exogenous nitric oxide "donors" which are known to relax the smooth muscle of the anal sphincter. Tiryaki et al. treated a series of six children and demonstrated resolution of obstructive symptoms and recurrent episodes of HAEC.(52) These authors advocate for the routine use of topical nitrates as a preventative measure against post-pull-through HAEC.

Prophylactic Washouts

In addition to pre-operative prevention, rectal washout is also effective for prevention of postoperative HAEC. Irrigations are performed with 10 to 20 ml/kg aliquots one to two times daily. Marty and colleagues reported decreased incidence (7.5% vs. 35.8%) and severity of HAEC in children receiving scheduled rectal washouts. Irrigations were started 1 to 2 weeks post-operatively and continued twice daily for three months, then once daily for three months.(53) Similar results were found in a Spanish study of 37 children with HD.(45)

Antibiotics & Antimicrobials

Antibiotics are a mainstay of therapy for HAEC. Clinical suspicion of HAEC should prompt early antibiotic administration to prevent advancement of disease (55). In addition to bacterial overgrowth, it is thought that alterations in bacterial composition (54) and certain pathogens (*C. diff., Candida sp.*, *Rotavirus*) may increase risk of HAEC.(55, 56) To avoid morbidity from septicemia it is not only imperative to recognize HAEC, but also to institute

appropriate antimicrobial therapy. Metronidazole is the most commonly used agent for treatment of both simple and complicated disease, and should be instituted even if patients are manifesting mild symptoms (55). Alternatively, one may empirically use metronidazole and norfloxacin for antibiotic therapy as described by Rintala and Lindahl(57). Stool cultures should be sent to identify causal organisms and also to rule out other infectious etiologies (such as, *Shigella*). Significant *Candidal* infections should be treated with antifungals such as fluconazole. Interestingly microbial genomics offer a potentially powerful tool to evaluate the intestinal microbiota and may provide insight into pathogenesis of HAEC. One study analyzed changes in stool bacterial composition of a single patient with multiple episodes of HAEC and multiple courses of antibiotics. The authors suggest that application of this approach to additional patients may help guide antibiotic therapy in the future.(54)

As previously mentioned, for complicated or advanced cases of HAEC we implement broad spectrum antibiotic therapy (ampicillin, gentamicin and metronidazole). Those patients found to have *C. diff.* in the setting of severe HAEC may benefit from addition of oral or rectal vancomycin.(58) Overall, studies comparing antimicrobial agents or regimens for the treatment of HAEC are lacking.

Recurrent or Refractory HAEC

Much has been written regarding the management of challenging Hirschsprung patients with “recurrent”, “chronic”, “chronic recurrent” or “refractory” HAEC. Not surprisingly, the number of episodes, or duration of symptoms that constitutes each term is not agreed upon among authors, thus making it difficult to compare studies and their results. Despite this lack of consensus, most authors describe patients who have failed antibiotic/washout regimens and “medical” therapy constituting multiple courses of antibiotics, and possibly trials of cromoglycate with continued recurrence of HAEC. For the purposes of this paper, these terms may be used interchangeably, unless otherwise stated.

Identifying Underlying Causes

When post-pull-through patients present with recurrent HAEC, the pediatric surgeon must diligently employ a strategy to evaluate these patients for potential anatomic and pathologic causes, and then have a rational approach to treat each cause.(43, 59-61) A first step is to obtain a detailed history of enterocolitis, abdominal distention, failure to thrive, including dilatations, washouts, laxatives or anti-motility medications. It is also helpful to review operative reports of the pull-through operation and pathology specimens from the original operation, if available. A physical exam should be performed specifically focused on presence of an anastomotic stricture. Water soluble contrast enema is necessary to evaluate the anatomy of the pull-through with attention given to the presence of stricture, massively enlarged post-Duhamel pouch, obstructing Soave cuff, dilated retained aganglionic segment, and kink or twist of the pull-through segment. Next, an anorectal examination under anesthesia should be performed to carefully evaluate the anal canal, and rectal biopsies taken to evaluate for ganglion cells and the presence of nerve trunk hypertrophy. Suction rectal biopsies are reported to be adequate to provide sufficient tissue in children three years and younger. It is recommended older children undergo full-thickness open biopsy. The primary goal is to evaluate for a retained aganglionic segment, aganglionic or transition zone pull-through, all of which can lead to obstructive symptoms, fecal stasis and enterocolitis. Intestinal neuronal dysplasia has also been reported by multiple authors in the pull-through segment of patients with recurrent enterocolitis (59, 60, 62), however these findings have been questioned by others suggesting that many of these may be the transition zone.(43) Anorectal manometry can be helpful as an adjunctive diagnostic test in selected patients in whom either an anatomic or pathologic abnormality has not been identified, or in patients

with suspected internal anal sphincter achalasia or colonic dysmotility. Most authors have not found value in its routine use for work up of patients with recurrent HAEC.

Approaches to manage patients with recurrent post-pull-through HAEC

For patients presenting with anastomotic strictures, most authors recommend a trial of dilatations. If dilatations are unsuccessful in achieving clinical response, then re-do pull-through is recommended. One group advocates re-do pull-through operations for retained aganglionic segment, aganglionic or transition zone pull-through, stricture, dilated Duhamel pouches and obstructing Soave cuff. Their preferred strategy is a transanal Swenson approach with selective use of either laparoscopy or laparotomy. (43) In patients with a rectum frozen in scar this group uses the posterior sagittal approach. Other authors have reported managing anastomotic stricture and Soave cuff obstruction with conversion to a Duhamel approach.(60) In cases of a dilated Duhamel “spur”, the author has resected the spur with good response.(63) In patients that have had a Soave-type pull-through (endorectal pull-through either minimally invasive transanal approach or traditional transabdominal approach), other authors prefer re-do endorectal pull-through procedure.(59, 64)

There is no consensus regarding the best approach for remedial procedures for patients with an identifiable pathological or anatomic cause of enterocolitis. Furthermore, re-do pull-through operations are relatively uncommon procedures and are best performed by an experienced team. For a more extensive discussion regarding operative strategy for re-do pull-through operations please view the cited references.

In patients with recurrent or refractory HAEC in which no anatomic or pathological etiology has been identified, a number of therapeutic approaches are described below.

Medical Approaches

Antibiotics and Antimicrobials

Despite the appeal of prophylactic antibiotic therapy to prevent recurrent episodes of HAEC, there is no supportive evidence to show efficacy, and furthermore may increase the risk of selecting resistant organisms. However, due to the potential morbidity of early HAEC becoming advanced, many practioners have a low threshold for starting antibiotics at the first signs and symptoms of HAEC.

Sodium Cromoglycate

Sodium cromoglycate is a mast cell stabilizer frequently used in the management of asthma. Rintala and Lindahl were the first to report using sodium cromoglycate to treat 8 patients with either chronic or recurrent HAEC (as described by the authors).(57) Six of eight patients had a favorable response to the treatment with a median follow up of 14 months. Three of the five patients with chronic HAEC improved with a median decrease in daily bowel movements from 6 to 3 and more solid stools. Two of the patients did not respond to sodium cromoglycate after 4 months of treatment at which point it was discontinued. Two of the three patients with recurrent HAEC had an excellent response with complete resolution of symptoms. One patient developed an episode of HAEC after a rotavirus infection. No side effects of sodium cromoglycate were reported. This study found that sodium cromoglycate is an effective treatment modality of patients with chronic or recurrent HAEC. While sodium cromoglycate is used to treat HAEC patients in some centers, to date we can find no follow up studies on the use of this agents.

Surgical approaches

Botulinum toxin therapy

Minkes and Langer evaluated 18 post-surgical HD patients with persistent constipation, obstructive symptoms, or recurrent HAEC, and internal anal sphincter hypertonicity. They treated each patient with intrasphincteric botulinum toxin injections and followed the group prospectively over a 4 year period.(65) In their study, they found 14 patients showed improvement in bowel function, 12 of these longer than 1 month, and 5 longer than six months, although they did not specify the number of patients with enterocolitis or which symptoms improved. Four patients developed transient encopresis that resolved within 3 weeks of treatment and there were no adverse side effects. The authors concluded that this therapy was safe and a less-invasive alternative to myectomy in these patients, and also showed that repeat injections are necessary for recurrent symptoms.

Koivusalo et al, treated a series of 8 post-surgical HD patients with botulinum toxin injections with a median follow up of 19 months.(66) The major presenting symptoms of these patients were: 3 with obstructive symptoms alone, 3 with obstructive symptoms and recurring enterocolitis, 2 with recurring enterocolitis. When focused on only the 5 patients with enterocolitis: one patient had complete resolution of symptoms, two others had significant improvement of enterocolitis but soiling was not eliminated, while the remaining 2 patients had little or no improvement. The authors concluded that while intrasphincteric botox injections were successful in some patients, it was difficult to predict which patients would benefit from this therapy.

Chumpitazi et al. studied a mixed population of 73 children with either surgically repaired HD or internal anal sphincter achalasia (IASA), all of whom developed obstructive symptoms and/or enterocolitis due to inability of the IAS to relax.(67) All of the patients were treated with intrasphincteric botulinum toxin injections with a mean follow up of 32 months. Within the HD group (n=30) there were 13 patients with enterocolitis requiring hospitalization. When the authors studied this subgroup of patients with HAEC, they found a decrease from 2.3+0.6 hospitalizations per year to 1.0+0.3 hospitalizations per year (P=0.06). The authors did not report on specific symptom improvement in this group. However, they found that the long-term response to botox varied according to the underlying diagnosis as children with IAS responded better than those with HD. Their study showed that the factors predicting a favorable long-term outcome were initial short-term improvement after the first botox injection and having IASA rather than HD.

In summary, intrasphincteric botox injection for the treatment of recurrent HAEC appears to be safe and can be used for multiple injections if symptoms recur. This treatment reduces the number hospitalizations for enterocolitis and can be effective in improving symptoms in some patients, however it is difficult to predict which patients will respond. Some authors have suggested that improvement of symptoms after botox injection predicts favorable response to myectomy/myotomy(65), while others have reported data contradicting this relationship.(67)

Posterior myotomy/myectomy—The transanal posterior myotomy/myectomy procedure was originally described for the definitive treatment of short segment HD by Lynn in 1966.(68) While uncommonly used today for the original purpose, it has been applied to patients with recurrent HAEC after pull-through operation with moderate success. Weber et al. reported 14 patients with recurrent HAEC (10 Soave and 4 Duhamel) who all underwent myectomy as initial treatment, 11 (78%) responded with cessation of diarrhea, improved appetite and weight gain and normal stool pattern.(69) Two of the patients in the Soave group required additional procedures: one required sphincterotomy and the other

underwent conversion to a Duhamel procedure; both responded and were deemed “cured”. One patient in the Duhamel group subsequently required colostomy and eventually died of HAEC. The authors did not report long-term continence data in this group of patients. Wilhaber and colleagues presented a group of 17 patients with recurrent HAEC either with, or without, retained aganglionosis, and showed a 75% response rate with the posterior myotomy/myectomy procedure with 23% having mild soiling.(70) The authors point out that one advantage of the transanal posterior myotomy/myectomy procedure is that it is significantly less invasive than a re-do pull-through operation. In the event that posterior myectomy is not successful in relieving enterocolitis, this does not preclude re-do pull-through operation from being performed. One concern that has been raised regarding this procedure is the risk of incontinence in adulthood. Heikkinen et al, performed long-term follow up (7-17 year) on 14 Finnish patients who underwent posterior myotomy/myectomy procedures as children and found that 4 had occasional or daily mild soiling, and suffered soiling-related social problems.(71)

Internal sphincterotomy—Use of lateral internal sphincterotomy as a treatment for recurrent HAEC due to internal sphincter achalasia or “obstructive symptoms” has been reported with mixed results. Swenson et al. reported its use on 27 patients and abandoned the technique citing no significant benefit.(7) Polley and colleagues reported its application in 3 patients with “successful outcome” but did not include length of follow up, and Blair et al. treated 4 patients and reported complete resolution of enterocolitis episodes.(72, 73) Marty et al. performed 8 internal sphincterotomies but did not report outcome of their patients.(74) The known risk of fecal incontinence with lateral internal sphincterotomy combined with its questionable benefit in these patients, suggests that application of this procedure for the treatment of refractory enterocolitis must be considered with the utmost caution.

Recalcitrant HAEC

For patients with HAEC refractory to both medical treatment and appropriate surgical intervention, the last resort is diversion with either ileostomy of colostomy. Fortunately this is necessary in only a small subset of HAEC patients, often with concomitant developmental delay such as Trisomy 21 or Bardet-Biedl syndrome. While complete diversion is successful in treating HAEC in most of these refractory patients, it has been reported that a few patients continue to have HAEC even after diversion, although this is rare.(9) Interestingly, anecdotal observation of experienced pediatric surgeons have found that for some of these patients this is a prolonged “temporary” diversion until around 5 years of age, when they seem to “outgrow” the HAEC. Some of these children can have their stomas successfully closed without recurrence of enterocolitis. Further research on this group of patients is needed to potentially identify factors that may predict positive or negative outcomes.

HAEC and inflammatory bowel disease

Levin et al, recently reported a series of 8 patients with HD who subsequently developed inflammatory bowel disease (IBD) 4 to 21 years after initial treatment.(15) Six of these patients were given a diagnosis of HAEC that did not improve until it was recognized that they had chronic unregulated bowel inflammation more consistent with IBD. Once appropriate treatment for IBD was started, the patients responded. While the clinical symptoms shared between HAEC and IBD including pain, fever, diarrhea and increased stool frequency were present in some, if not all of the patients; many also had features typical of IBD. These included anemia, elevated ESR, severe perirectal abscess, recto-vaginal fistula post-repair, recurrent peri-stomal fistulae and small bowel-small bowel fistula. Endoscopic findings revealed late inflammatory strictures and the presence of

granulomata on intestinal biopsies. While this group of patients is quite rare, any HD patient with chronic or recurrent HAEC symptoms who also develops these features of IBD, should be worked up using upper and lower GI endoscopy with biopsies, including appropriate inflammatory and serological markers for IBD.

Summary

Application of preventative strategies in high-risk patients, combined with early aggressive treatment of HAEC are the goals of current therapy. While progress has been made, the management of chronic and recurrent HAEC remains challenging for clinicians and patients alike. Only with a better understanding of the biological mechanisms causing HAEC can we develop novel, rational prevention and treatment strategies for HAEC in the future.

References

1. Hirschsprung H. Stuhtragheit Neugeborener infolge Dilatationen und hypertrophie des Colons. Jahruch Kinderheikunde. 1887; 27:1.
2. Pastor AC, Osman F, Teitelbaum DH, Caty MG, Langer JC. Development of a standardized definition for Hirschsprung's-associated enterocolitis: a Delphi analysis. J Pediatr Surg. Jan; 2009 44(1):251–6. [PubMed: 19159752]
3. Murphy F, Puri P. New insights into the pathogenesis of Hirschsprung's associated enterocolitis. Pediatr Surg Int. Oct; 2005 21(10):773–9. [PubMed: 16195910]
4. Pini Prato A, Rossi V, Avanzini S, Mattioli G, Disma N, Jasonni V. Hirschsprung's disease: what about mortality? Pediatric surgery international. May; 2011 27(5):473–8. [PubMed: 21253751]
5. Kenny SE, Tam PK, Garcia-Barcelo M. Hirschsprung's disease. Semin Pediatr Surg. Aug; 2010 19(3):194–200. [PubMed: 20610192]
6. Carneiro P, Brereton R, Drake D, Kiely E, Spitz L, Turnock R. Enterocolitis in Hirschsprung's disease. Pediatric surgery international. 1992; 7(5):356–60.
7. Swenson O, Sherman JO, Fisher JH, Cohen E. The treatment and postoperative complications of congenital megacolon: A 25 year followup. Annals of surgery. Sep; 1975 182(3):266–73. [Research Support, U.S. Gov't, P.H.S.]. [PubMed: 1164055]
8. Vieten D, Spicer R. Enterocolitis complicating Hirschsprung's disease. Semin Pediatr Surg. Nov; 2004 13(4):263–72. [PubMed: 15660320]
9. Surana R, Quinn F, Puri P. Evaluation of risk factors in the development of enterocolitis complicating Hirschsprung's disease. Pediatric surgery international. 1994; 9(4):234–6.
10. Teitelbaum DH, Qualman SJ, Caniano DA. Hirschsprung's disease. Identification of risk factors for enterocolitis. Ann Surg. Mar; 1988 207(3):240–4. [PubMed: 2964227]
11. Haricharan RN, Seo JM, Kelly DR, Mroczek-Musulman EC, Aprahamian CJ, Morgan TL, et al. Older age at diagnosis of Hirschsprung disease decreases risk of postoperative enterocolitis, but resection of additional ganglionated bowel does not. J Pediatr Surg. Jun; 2008 43(6):1115–23. [PubMed: 18558193]
12. Hanimann B, Inderbitzin D, Briner J, Sacher P. Clinical relevance of Hirschsprung-associated neuronal intestinal dysplasia (HANID). Eur J Pediatr Surg. 1992; 2(3):147–9. [PubMed: 1498103]
13. Hackam DJ, Filler RM, Pearl RH. Enterocolitis after the surgical treatment of Hirschsprung's disease: risk factors and financial impact. J Pediatr Surg. Jun; 1998 33(6):830–3. [PubMed: 9660207]
14. Melendez E, Goldstein AM, Sagar P, Badizadegan K. Case records of the Massachusetts General Hospital. Case 3-2012. A newborn boy with vomiting, diarrhea, and abdominal distention. N Engl J Med. Jan 26; 2012 366(4):361–72. [Case Reports Clinical Conference]. [PubMed: 22276826]
15. Levin DN, Marcon MA, Rintala RJ, Jacobson D, Langer JC. Inflammatory bowel disease manifesting after surgical treatment for hirschsprung disease. Journal of pediatric gastroenterology and nutrition. Feb.2012
16. Luis LA, Encinas JL, Avila LF, Andrés AM, Burgos L, Fernández A, et al. [Hirschsprung disease: lessons learned from the last 100 cases]. Cir Pediatr. Jul; 2006 19(3):177–81. [PubMed: 17240952]

17. Ziad F, Katchy KC, Al Ramadan S, Alexander S, Kumar S. Clinicopathological features in 102 cases of Hirschsprung disease. Ann Saudi Med. May-Jun;2006 26(3):200–4. 2006. [PubMed: 16861859]
18. Suita S, Taguchi T, Ieiri S, Nakatsuji T. Hirschsprung's disease in Japan: analysis of 3852 patients based on a nationwide survey in 30 years. J Pediatr Surg. Jan; 2005 40(1):197–201. discussion -2. [PubMed: 15868585]
19. Engum SA, Petrites M, Rescorla FJ, Grosfeld JL, Morrison AM, Engles D. Familial Hirschsprung's disease: 20 cases in 12 kindreds. J Pediatr Surg. Oct; 1993 28(10):1286–90. [PubMed: 8263688]
20. Travassos D, van Herwaarden-Lindeboom M, van der Zee DC. Hirschsprung's disease in children with Down syndrome: a comparative study. Eur J Pediatr Surg. Aug; 2011 21(4):220–3. [PubMed: 21351043]
21. Bandré E, Kaboré RA, Ouedraogo I, Soré O, Tapsoba T, Bambara C, et al. Hirschsprung's disease: management problem in a developing country. Afr J Paediatr Surg. Sep-Dec;2010 7(3):166–8. 2010. [PubMed: 20859022]
22. Ieiri S, Higashi M, Teshiba R, Saeki I, Esumi G, Akiyoshi J, et al. Clinical features of Hirschsprung's disease associated with Down syndrome: a 30-year retrospective nationwide survey in Japan. J Pediatr Surg. Dec; 2009 44(12):2347–51. [PubMed: 20006024]
23. Morabito A, Lall A, Gull S, Mohee A, Bianchi A. The impact of Down's syndrome on the immediate and long-term outcomes of children with Hirschsprung's disease. Pediatric surgery international. Feb; 2006 22(2):179–81. [PubMed: 16362310]
24. Menezes M, Puri P. Long-term clinical outcome in patients with Hirschsprung's disease and associated Down's syndrome. J Pediatr Surg. May; 2005 40(5):810–2. [PubMed: 15937820]
25. Teitelbaum D, Qualman S, Caniano D. Hirschsprung's disease. Identification of risk factors for enterocolitis. Ann Surg. 1988; 207(3):240–4. [PubMed: 2964227]
26. Berger S, Ziebell P, OFFsler M, Hofmann-von Kap-herr S. Congenital malformations and perinatal morbidity associated with intestinal neuronal dysplasia. Pediatric surgery international. Sep; 1998 13(7):474–9. [PubMed: 9716673]
27. Elhalaby EA, Teitelbaum DH, Coran AG, Heidelberger KP. Enterocolitis associated with Hirschsprung's disease: a clinical histopathological correlative study. J Pediatr Surg. Jul; 1995 30(7):1023–6. discussion 6-7. [PubMed: 7472925]
28. Reding R, de Ville de Goyet J, Gosseye S, Clapuyt P, Sokal E, Buts JP, et al. Hirschsprung's disease: a 20-year experience. J Pediatr Surg. Aug; 1997 32(8):1221–5. [PubMed: 9269974]
29. Elhalaby EA, Coran AG, Blane CE, Hirschl RB, Teitelbaum DH. Enterocolitis associated with Hirschsprung's disease: a clinical-radiological characterization based on 168 patients. J Pediatr Surg. Jan; 1995 30(1):76–83. [PubMed: 7722836]
30. Teitelbaum DH, Coran AG. Enterocolitis. Semin Pediatr Surg. Aug; 1998 7(3):162–9. [PubMed: 9718654]
31. Thomas DW, Greer FR. Nutrition AAoPCo, American Academy of Pediatrics Section on Gastroenterology Hp, and Nutrition. Probiotics and prebiotics in pediatrics. Pediatrics. Dec; 2010 126(6):1217–31. [PubMed: 21115585]
32. Wang Q, Dong J, Zhu Y. Probiotic supplement reduces risk of necrotizing enterocolitis and mortality in preterm very low-birth-weight infants: an updated meta-analysis of 20 randomized, controlled trials. J Pediatr Surg. Jan; 2012 47(1):241–8. [PubMed: 22244424]
33. Guandalini S. Update on the role of probiotics in the therapy of pediatric inflammatory bowel disease. Expert Rev Clin Immunol. Jan; 2010 6(1):47–54. [PubMed: 20383890]
34. Shen DH, Shi CR, Chen JJ, Yu SY, Wu Y, Yan WB. Detection of intestinal bifidobacteria and lactobacilli in patients with Hirschsprung's disease associated enterocolitis. World J Pediatr. Aug; 2009 5(3):201–5. [PubMed: 19693464]
35. Herek O. Saccharomyces boulardii: a possible addition to the standard treatment and prophylaxis of enterocolitis in Hirschsprung's disease ? Pediatric surgery international. Sep.2002 18(5-6):567. [PubMed: 12415416]
36. Bill AHCN. The enterocolitis of Hirschsprung's disease. 1962; 103:70–4.

37. Sheth J, Nour S, Dickinson F. CT images of Hirschsprung's associated enterocolitis: a rare finding. Arch Dis Child. Oct.2009 94(10):816. [PubMed: 19770200]
38. Cheung CR. 'Significant value' of CT scan in diagnosis of Hirschsprung's associated enterocolitis. Arch Dis Child. Apr.2010 95(4):314. [PubMed: 20335246]
39. Lane V, Sugarman ID. Investigation of rectal bleeding in children. Paediatrics and Child Health. 2010; 20(10):465–72.
40. Brook I. Pseudomembranous colitis in children. Journal of gastroenterology and hepatology. 2005; 20(2):182–6. [PubMed: 15683418]
41. Belknap WM. Hirschsprung's disease. Current Treatment Options in Gastroenterology. 2003; 6(3): 247–56. [PubMed: 12744824]
42. Brearly S, Armstrong GR, Nairn R, Gornall P, Currie AB, Buick RG, et al. Pseudomembranous colitis: a lethal complication of Hirschsprung's disease unrelated to antibiotic usage. J Pediatr Surg. Mar; 1987 22(3):257–9. [PubMed: 3559870]
43. Levitt MA, Dickie B, Pena A. Evaluation and treatment of the patient with Hirschsprung disease who is not doing well after a pull-through procedure. Semin Pediatr Surg. May; 2010 19(2):146–53. [PubMed: 20307851]
44. Langer JC. Hirschsprung disease. Fundamentals of Pediatric Surgery. 2011:475.
45. Núñez R, Torres A, Agulla E, Moreno C, Marín D, Santamaría JI. [Rectal irrigation and bowel decontamination for the prevention of postoperative enterocolitis in Hirschsprung's disease]. Cir Pediatr. Apr; 2007 20(2):96–100. [PubMed: 17650719]
46. Herek O. A new colonic lavage method for infants with Hirschsprung's disease. Pediatr Surg Int. Nov.2001 17(8):671. [PubMed: 11727068]
47. Bradnock T, Walker G. Evolution in the management of Hirschsprung's disease in the UK and Ireland: a national survey of practice revisited. Annals of The Royal College of Surgeons of England. 2011; 93(1):34–8. [PubMed: 20738896]
48. Fujimoto T, Puri P. Persistence of enterocolitis following diversion of faecal stream in Hirschsprung's disease. Pediatric surgery international. 1988; 3(2):141–6.
49. Gao Y, Li G, Zhang X, Xu Q, Guo Z, Zheng B, et al. Primary transanal rectosigmoidectomy for Hirschsprung's disease: Preliminary results in the initial 33 cases. J Pediatr Surg. Dec; 2001 36(12):1816–9. [PubMed: 11733913]
50. Temple SJ, Shawyer A, Langer JC. Is daily dilatation by parents necessary after surgery for Hirschsprung disease and anorectal malformations? J Pediatr Surg. Jan; 2012 47(1):209–12. [PubMed: 22244419]
51. Diseth TH, Egeland T, Emblem R. Effects of anal invasive treatment and incontinence on mental health and psychosocial functioning of adolescents with Hirschsprung's disease and low anorectal anomalies. J Pediatr Surg. Mar; 1998 33(3):468–75. [PubMed: 9537559]
52. Tiryaki T, Demirbağ S, Atayurt H, Cetinkurşun S. Topical nitric oxide treatment after pull through operations for Hirschsprung disease. Journal of pediatric gastroenterology and nutrition. Mar; 2005 40(3):390–2. [PubMed: 15735503]
53. Marty TL, Seo T, Sullivan JJ, Matlak ME, Black RE, Johnson DG. Rectal irrigations for the prevention of postoperative enterocolitis in Hirschsprung's disease. J Pediatr Surg. May; 1995 30(5):652–4. [PubMed: 7623219]
54. De Filippo C, Pini-Prato A, Mattioli G, Avanzini S, Rapuzzi G, Cavalieri D, et al. Genomics approach to the analysis of bacterial communities dynamics in Hirschsprung's disease-associated enterocolitis: a pilot study. Pediatr Surg Int. May; 2010 26(5):465–71. [PubMed: 20306059]
55. Chong PP, Chieng DC, Low LY, Hafeez A, Shamsudin MN, Seow HF, et al. Recurrent candidaemia in a neonate with Hirschsprung's disease: fluconazole resistance and genetic relatedness of eight Candida tropicalis isolates. Journal of medical microbiology. Apr; 2006 55(Pt 4):423–8. [Case Reports Research Support, Non-U.S. Gov't]. [PubMed: 16533990]
56. Morinville V, McDonald J. Clostridium difficile-associated diarrhea in 200 Canadian children. Can J Gastroenterol. Aug; 2005 19(8):497–501. [PubMed: 16107901]
57. Rintala RJ, Lindahl H. Sodium cromoglycate in the management of chronic or recurrent enterocolitis in patients with Hirschsprung's disease. J Pediatr Surg. Jul; 2001 36(7):1032–5. [PubMed: 11431770]

58. Bagwell CE, Langham MR Jr. Mahaffey SM, Talbert JL, Shandling B. Pseudomembranous colitis following resection for Hirschsprung's disease. J Pediatr Surg. Oct; 1992 27(10):1261–4. [Case Reports]. [PubMed: 1403498]
59. Teitelbaum DH, Coran AG. Reoperative surgery for Hirschsprung's disease. Semin Pediatr Surg. May; 2003 12(2):124–31. [Review]. [PubMed: 12728399]
60. Langer JC. Persistent obstructive symptoms after surgery for Hirschsprung's disease: development of a diagnostic and therapeutic algorithm. J Pediatr Surg. Oct; 2004 39(10):1458–62. [PubMed: 15486887]
61. Chumpitazi BP, Nurko S. Defecation disorders in children after surgery for Hirschsprung disease. Journal of pediatric gastroenterology and nutrition. Jul; 2011 53(1):75–9. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. [PubMed: 21694540]
62. Estevao-Costa J, Fragoso AC, Campos M, Soares-Oliveira M, Carvalho JL. An approach to minimize postoperative enterocolitis in Hirschsprung's disease. J Pediatr Surg. Oct; 2006 41(10): 1704–7. [Research Support, Non-U.S. Gov't]. [PubMed: 17011273]
63. Dasgupta R, Langer JC. Evaluation and management of persistent problems after surgery for Hirschsprung disease in a child. Journal of pediatric gastroenterology and nutrition. Jan; 2008 46(1):13–9. [Review]. [PubMed: 18162828]
64. Pini-Prato A, Mattioli G, Giunta C, Avanzini S, Magillo P, Bisio GM, et al. Redo surgery in Hirschsprung disease: what did we learn? Unicentric experience on 70 patients. J Pediatr Surg. Apr; 2010 45(4):747–54. [PubMed: 20385282]
65. Minkes RK, Langer JC. A prospective study of botulinum toxin for internal anal sphincter hypertonicity in children with Hirschsprung's disease. J Pediatr Surg. Dec; 2000 35(12):1733–6. [PubMed: 11101725]
66. Koivusalo AI, Pakarinen MP, Rintala RJ. Botox injection treatment for anal outlet obstruction in patients with internal anal sphincter achalasia and Hirschsprung's disease. Pediatr Surg Int. Oct; 2009 25(10):873–6. [PubMed: 19662428]
67. Chumpitazi BP, Fishman SJ, Nurko S. Long-term clinical outcome after botulinum toxin injection in children with nonrelaxing internal anal sphincter. The American journal of gastroenterology. Apr; 2009 104(4):976–83. [Comparative Study]. [PubMed: 19259081]
68. Lynn HB. Rectal myectomy for aganglionic megacolon. Mayo Clinic proceedings Mayo Clinic. May; 1966 41(5):289–95. [Case Reports]. [PubMed: 5932614]
69. Weber TR, Fortuna RS, Silen ML, Dillon PA. Reoperation for Hirschsprung's disease. J Pediatr Surg. Jan; 1999 34(1):153–6. discussion 6-7. [PubMed: 10022162]
70. Wildhaber BE, Pakarinen M, Rintala RJ, Coran AG, Teitelbaum DH. Posterior myotomy/ myectomy for persistent stooling problems in Hirschsprung's disease. J Pediatr Surg. Jun; 2004 39(6):920–6. discussion -6. [PubMed: 15185226]
71. Heikkinen M, Lindahl H, Rintala RJ. Long-term outcome after internal sphincter myectomy for internal sphincter achalasia. Pediatric surgery international. Feb; 2005 21(2):84–7. [PubMed: 15616817]
72. Polley TZ Jr. Coran AG, Wesley JR. A ten-year experience with ninety-two cases of Hirschsprung's disease. Including sixty-seven consecutive endorectal pull-through procedures. Annals of surgery. Sep; 1985 202(3):349–55. [PubMed: 4037907]
73. Blair GK, Murphy JJ, Fraser GC. Internal sphincterotomy in post-pull-through Hirschsprung's disease. J Pediatr Surg. 1996; 31(6):843–5. [PubMed: 8783119]
74. Marty TL, Seo T, Matlak ME, Sullivan JJ, Black RE, Johnson DG. Gastrointestinal function after surgical correction of Hirschsprung's disease: long-term follow-up in 135 patients. J Pediatr Surg. May; 1995 30(5):655–8. [PubMed: 7623220]