Congenital aganglionic megacolon (Hirschsprung disease)

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INTRODUCTION

Hirschsprung disease (HD) is a motor disorder of the gut, which is caused by the failure of neural crest cells (precursors of enteric ganglion cells) to migrate completely during intestinal development during fetal life. The resulting aganglionic segment of the colon fails to relax, causing a functional obstruction.

The pathogenesis, diagnosis, and clinical management of HD are discussed below. The emergency complications of HD, including acute obstruction in the neonate, Hirschsprung-associated enterocolitis (HAEC), and volvulus, are discussed in a separate topic review. (See "Emergency complications of Hirschsprung disease".)

EPIDEMIOLOGY

HD occurs in approximately 1 in 5000 live births with an overall male:female ratio of 3:1 to 4:1; when the entire colon is involved, the gender ratio more nearly approaches 1:1 [1-3]. There is familial clustering for nonsyndromic HD, with an overall recurrence risk of approximately 3 percent in siblings for short-segment disease or up to 17 percent if the proband has long-segment disease [4]. This sibling recurrence risk is higher if the proband is a female and is also higher if multiple family members are affected.

PATHOPHYSIOLOGY

The most accepted theory of the cause of HD is that there is a defect in the craniocaudal migration of neuroblasts originating from the neural crest, a process that begins at four weeks of gestation and ends at week 7 with the arrival of neural crest-derived cells at the distal end of the colon [5]. Failure of the cells to reach the distal colon leaves that segment aganglionic and therefore nonfunctional,

resulting in HD. Defects in the differentiation of neuroblasts into ganglion cells and ganglion cell destruction within the intestine may also contribute to the disorder [6].

Genetics — Mutations in several genes have been identified in patients with HD [7,8]. HD is a genetically complex disorder caused by variants in multiple rare genes with low penetrance and variable expression [9]. Thus, individuals with multiple pathogenic variants have substantially increased risk compared with those with fewer pathogenic variants. For nonsyndromic forms, long-segment disease tends to be transmitted by autosomal dominant inheritance and short-segment disease often reflects autosomal recessive or multifactorial inheritance [10].

The predominant gene affected is the *RET* proto-oncogene; mutations in this gene cause a loss of function. More than 20 different mutations in *RET* have been described [11,12]. Coding sequence mutations in *RET* are identified in approximately one-half of all familial cases and approximately one-third of sporadic cases. In one study, *RET* variants were found in 82 percent of patients with total colonic aganglionosis (TCA), compared with 33 percent of those with short-segment disease [13] (see 'Clinical features' below). In addition, certain *RET* polymorphisms are associated with particular phenotypes of HD (short- or long-segment disease) [11]. Most Hirschsprung cases are linked to *RET*, even without an identified coding sequence mutation, suggesting that noncoding variants of this gene play a major role in the disease by causing loss of function of the RET receptor tyrosine kinase that appears to transduce growth and differentiation signals in developing tissues, including those derived from the neural crest. Mouse models have demonstrated that RET protein is necessary for migration, survival, proliferation, and differentiation of the neural crest-derived cells that give rise to the enteric nervous system, and the degree of aganglionosis is proportionate to RET dose [14]. Glial cell line-derived neurotrophic factor (GDNF) and neurturin have been identified as ligands for RET and GDNF, which is essential for both activation of RET and normal enteric nervous system development [15]. Mutations in both GDNF and neurturin have also been identified in patients with HD [7].

The second major gene involved in HD is endothelin receptor *B* (*EDNRB*), which encodes a G-protein-coupled receptor [16]. The proteins encoded by *EDNRB* and its ligand endothelin 3 (*EDN3*) are both involved in the development of neural crest cells.

The mechanisms underlying the strong association between trisomy 21 (Down syndrome) and HD have not been established. It is likely that multiple mechanisms are involved in this association, including specific *RET* variants and variants in the Down syndrome cell adhesion model (*DSCAM*) gene region on chromosome 21 [17,18].

Mutations in other genes have been described in a minority of patients [7]. These genes include *EDN3*, endothelin-converting enzyme (*ECE1*), the gene encoding the Sry-related transcription factor SOX10 (*SOX10*), and the paired-like homeobox 2b (*PHOX2B*) gene [19,20]. A genome-wide association study also identified an association with neuregulin 1 (*NRG1*), a regulator of enteric ganglia precursors [21].

Associated syndromes — HD is associated with chromosomal anomalies, so-called syndromic HD, especially Down syndrome (table 1). Down syndrome is present in 2 to 16 percent of individuals

with HD [22,23]. Conversely, HD occurs in less than 1 percent of individuals with Down syndrome, although the overall risk of HD in Down syndrome is much higher than in the general population [10,24]. (See "Down syndrome: Clinical features and diagnosis", section on 'Gastrointestinal abnormalities'.)

HD is also associated with several different monogenic syndromes (table 2):

- Bardet-Biedl syndrome. (See "Genetic contribution and pathophysiology of obesity", section on 'Bardet-Biedl syndrome'.)
- Cartilage-hair hypoplasia – This is a rare syndrome characterized by short stature, short limbs with increased carrying angle at the elbow, increased lumbar lordosis, ligamentous laxity, scoliosis, and immunodeficiency. Affected infants often present with enterocolitis. (See "Cartilage-hair hypoplasia", section on 'Gastrointestinal abnormalities'.)
- Congenital central hypoventilation syndrome (CCHS). The association of CCHS and HD is known as Haddad syndrome. (See "Congenital central hypoventilation syndrome and other causes of sleep-related hypoventilation in children".)
- Familial dysautonomia (also known as hereditary sensory and autonomic neuropathy type 3, or Riley-Day syndrome). (See "Hereditary sensory and autonomic neuropathies", section on 'HSAN3 (Familial dysautonomia)'.)
- Multiple endocrine neoplasia type 2 (MEN2), which is characterized by medullary thyroid cancer and pheochromocytoma, with or without primary hyperparathyroidism. Type 2A is associated with Hirschsprung disease. (See "Clinical manifestations and diagnosis of multiple endocrine neoplasia type 2".)
- Mowat-Wilson syndrome – This is caused by haploinsufficiency of the *ZEB2* gene (zinc finger E box-binding homeobox 2, also known as *SIP01*) [25-27]. Approximately 50 percent of individuals with Mowat-Wilson syndrome have HD; other features are distinctive facial characteristics, moderate to severe intellectual disability, genitourinary anomalies, and heart defects.
- Smith-Lemli-Opitz syndrome [28-31]. (See "Causes and clinical manifestations of primary adrenal insufficiency in children", section on 'Defects in cholesterol biochemistry'.)
- Waardenburg syndrome – This is an autosomal dominant inherited pigmentary disorder; nearly 100 percent of Waardenburg syndrome type 4 have HD. (See "The genodermatoses: An overview", section on 'Waardenburg syndrome'.)

For trisomy 21, Bardet-Biedl syndrome, and CCHS, *RET* acts as a modifier gene for the Hirschsprung phenotype. Assessment by a clinical geneticist is valuable for all patients with syndromic features or anomalies and also for those with no apparent associated anomalies. (See "Down syndrome: Clinical features and diagnosis", section on 'Gastrointestinal abnormalities' and "Disorders of ventilatory

control", section on 'Congenital central hypoventilation syndrome' and "The genodermatoses: An overview", section on 'Waardenburg syndrome'.)

CLINICAL FEATURES

Types of aganglionosis — In approximately 80 percent of patients, HD affects the rectosigmoid colon (known as short-segment disease) [4,10]. In 15 to 20 percent of patients, the aganglionosis extends proximal to the sigmoid colon (known as long-segment disease). In approximately 5 percent, the entire colon is affected (known as total colonic aganglionosis [TCA]), and, in rare cases, the small bowel may also be involved. Outcomes are generally worse for patients with long-segment as compared with short-segment disease.

Clinical presentation

- **Neonatal** – The majority of patients with HD are diagnosed in the neonatal period. Patients present with symptoms of distal intestinal obstruction: bilious emesis, abdominal distension, and failure to pass meconium or stool [32]. The diagnosis is suggested by a delay in passage of the first meconium. By 48 hours of life, 100 percent of normal full-term neonates will pass meconium [33]. In contrast, 45 to 90 percent of infants with HD will fail to pass meconium within the first 48 hours of life [34-36]. However, passage of stool within the first one to two days of life does not exclude the diagnosis. There may be an explosive expulsion of gas and stool after the digital rectal examination (squirt sign or blast sign), which may relieve the obstruction temporarily [37].

  Affected infants also may present initially with enterocolitis, a potentially life-threatening illness in which patients have a sepsis-like picture with fever, vomiting, diarrhea, and abdominal distension, which can progress to toxic megacolon. Patients with enterocolitis require fluid resuscitation, intravenous antibiotic therapy including coverage for anaerobic bacteria, rectal irrigations, and, in rare cases, an emergency colostomy. A rare complication of HD is volvulus, which can affect the sigmoid and, less commonly, the transverse colon and cecum. Even less commonly, HD can present with appendiceal perforation [38]. (See "Emergency complications of Hirschsprung disease".)

- **Postnatal** – Patients with less severe disease (usually because they have short-segment disease) may not be diagnosed until later in infancy or childhood; in approximately 10 percent of individuals, HD is diagnosed after three years of age [39,40]. Such patients typically have a history of chronic constipation and failure to thrive. Although uncommon, HD can be newly diagnosed in adulthood. Patients present with symptoms of abdominal distension and a long history of refractory constipation without fecal incontinence [41,42]. Some of these patients may have "ultrashort-segment Hirschsprung disease" (USSHD), which is described below. (See 'Ultrashort-segment Hirschsprung disease' below and "Functional constipation in infants, children, and adolescents: Clinical features and diagnosis".)

Associated congenital anomalies — Approximately 20 to 25 percent of patients with HD have associated congenital anomalies (figure 1), often but not always in association with one of the syndromes described above.

- **Genitourinary anomalies** – Congenital anomalies of the kidney and urinary tract (CAKUT), including hydronephrosis and renal hypoplasia, are particularly common [22,43,44]. This association is not explained by a simple relationship with RET or GDNF, but these genes could be involved as disease modifiers. In a report of 106 HD patients who underwent routine ultrasonographic screening, CAKUT were found in approximately 20 percent of individuals with nonsyndromic HD and 40 percent of those with syndromic HD [22]. Because of this high frequency, the authors of that report suggested that infants undergo routine ultrasonographic screening for urinary system malformations. (See "Overview of congenital anomalies of the kidney and urinary tract (CAKUT)" and "Evaluation of congenital anomalies of the kidney and urinary tract (CAKUT)".)

- **Visual and hearing impairment** – In one case series, ophthalmologic abnormalities were found in approximately 40 percent of individuals with HD. Most were refractive errors (hyperopia, astigmatism, or myopia), but visual impairment was present in 9.4 percent [22]. Hearing impairment was found in approximately 5 percent of individuals with HD, approximately three times the rate in the general population. The authors suggest routine screening for hearing impairment, using protocols for infants at increased risk. (See "Screening the newborn for hearing loss" and "Hearing loss in children: Screening and evaluation".)

- **Congenital heart disease** – Congenital heart disease is found in approximately 50 percent of individuals with syndromic HD (usually Down syndrome) [22] but is unusual in patients without an associated syndrome [10].

- **Anorectal malformations** – HD may also occur in association with anorectal malformations; the possibility of HD should be considered in patients with anorectal malformations who develop constipation that does not respond to standard treatment and in those with other symptoms suggestive of HD [45].

EVALUATION

HD should be suspected in patients with the clinical symptoms discussed above. A high index of suspicion is appropriate for neonates and infants with a predisposing condition, such as Down syndrome, or for those with a family history of HD (algorithm 1).

Indications for testing

Suspected Hirschsprung disease in neonates

- **High suspicion** – A high suspicion for HD is suggested by the following characteristics in infants <6 months of age:

- Symptoms of intestinal obstruction, including bilious emesis, abdominal distension, and failure to pass stool
- Failure to pass meconium within 48 hours of birth
- Constipation and any of the following:
  - Trisomy 21 (Down syndrome) or other condition known to be associated with HD
  - Family history of HD
  - Physical examination suggestive of HD (abdominal distension, tight anal sphincter, narrowed rectum, or squirt sign on digital examination) (see 'Clinical features' above)

Such infants should have an urgent full evaluation, usually consisting of a contrast enema and rectal suction biopsy (algorithm 1). (See 'Diagnostic testing' below and 'Rectal biopsy' below.)

- **Moderate suspicion** – A moderate level of suspicion for HD is warranted for neonates with a well-documented, moderate delay in passing meconium (>48 hours but <72 hours) but no other symptoms (no abdominal distension, vomiting, or feeding problems).

  Practice varies regarding the management of these infants. They should undergo a careful physical examination and exclusion of other causes of delayed passage of meconium, including anorectal malformations (table 3) (see "Constipation in infants and children: Evaluation", section on 'Physical examination'). They should also be closely observed and evaluated promptly for HD if they develop symptoms of constipation or abdominal distension. It would also be reasonable to perform a contrast enema and suction rectal biopsy in such infants, particularly if close observation cannot be assured. An urgent evaluation is essential if the infant develops symptoms of obstruction or enterocolitis.

Suspected enterocolitis — Urgent evaluation for Hirschsprung-associated enterocolitis (HAEC) is indicated for any neonate or infant who presents with fever, vomiting, abdominal distension, and explosive diarrhea and has known or suspected HD. This includes infants who have undergone surgical repair for HD or those with risk factors such as Down syndrome or a family history of HD. Other concerning symptoms include lethargy or obstipation (table 4) [46]. HAEC seldom occurs in neonates except when the diagnosis of HD is missed or delayed. As an example, the diagnosis of HD or HAEC can be missed in an infant who has an atypical subacute presentation of chronic diarrhea and failure to grow [47].

All such patients should have a rectal examination, performed either with a finger (digital) or with a small-diameter anal dilator; an explosive release of gas during this examination supports a diagnosis of HAEC. The evaluation should also include an abdominal radiograph. The possibility of HAEC is supported by signs of ileus, including air-fluid levels and dilated bowel. A contrast enema should **not** be performed if HAEC is suspected, because of the risk of intestinal perforation.

Evaluation, diagnosis, and management of HAEC are discussed separately. (See "Emergency complications of Hirschsprung disease", section on 'Enterocolitis'.)

Chronic refractory constipation — For older infants and toddlers with chronic refractory constipation (ages six months to three years), the level of suspicion for HD is guided by the history and physical examination:

- For those with failure to thrive and other signs suggestive of HD on physical examination (abdominal distension, narrowed rectum without stool present, tight anal sphincter, or squirt sign on examination), a moderate level of suspicion for HD is warranted. These individuals should be evaluated for HD, but the timing and sequence of diagnostic testing is elective. In this group, anorectal manometry is an excellent screening test if it is available. A normal anorectal inhibitory reflex excludes HD.

- For those with **no** symptoms or signs suggestive of HD, a lesser level of suspicion for HD is warranted. For such patients, it is reasonable to evaluate with a plain radiograph and base further testing on the results. (See 'Abdominal radiograph' below.)

Diagnostic testing — Rectal biopsy is the gold standard for diagnosis. Before proceeding to rectal biopsy, we typically perform noninvasive tests to support the likely diagnosis, contrast enema, or anorectal manometry. Each of these procedures has advantages and disadvantages related to availability, technical expertise, radiation exposure, and invasiveness [48]. The diagnostic steps depend on the level of suspicion for HD, age of the child, whether there is concern about HAEC (which requires emergency management), and on the available resources and institutional/clinician preference (algorithm 1).

In our practice, we generally perform a barium enema rather than suction biopsy as the initial diagnostic procedure. If a clear transition zone is seen on barium enema, the study is virtually pathognomonic of HD and helps the surgeon plan the operative approach. If a transition zone is not seen, HD cannot be entirely excluded. We always confirm the diagnosis by biopsy even when the barium enema shows typical features of HD.

Some providers start the evaluation with anorectal manometry, followed by rectal suction biopsy if the findings are abnormal.

Contrast enema — In infants with suspected HD, a contrast enema can support the diagnosis of HD; it is performed without stool cleanout ("unprepped"). However, this test is not sufficient to exclude the diagnosis of HD, especially in newborns or other individuals with a high clinical suspicion for the disease [49,50]. The rectum and colon may look relatively normal in cases of long-segment or total colonic HD. A contrast enema is also useful for presurgical planning because it may help the surgeon to localize the transition zone and determine the length of the aganglionic segment [48], although the location of the transition zone on imaging does not always match its true pathologic location [51].

The presence of a "transition zone," which represents the change from the normal caliber/narrowed rectum (aganglionic segment) to the dilated colon proximal to the aganglionic region, is virtually pathognomonic of HD (image 1). Despite this high degree of certainty, we always confirm the diagnosis by rectal biopsy. The transition zone usually is in the rectosigmoid area and is seen best in

the early lateral and oblique views. In patients with total colonic involvement, the entire colon may appear relatively normal, but dilated loops of distal small bowel may be visible [52]. If a transition zone is not clearly detected, a follow-up postevacuation film 24 hours later may reveal residual retained contrast in the colon, which is suggestive of the diagnosis [53]. The rectosigmoid index (RSI), the ratio between the diameter of the rectum and the sigmoid colon, is typically >1 in normal children. Reversal of this ratio, although less often noted than a transition zone, is a useful sign of HD in infants and older children [54,55].

The use of contrast enema for diagnosis of HD is limited by false-negative results, which render this test less sensitive than rectal suction biopsy and anorectal manometry for the diagnosis of HD (table 5) [48,56]. As an example, a digital rectal examination within a few days prior to the contrast enema may dilate the rectum and cause a false-negative result. Similarly, classic radiographic findings such as inversion of the RSI may not be evident in studies performed in the early newborn period or in premature infants [57]. Therefore, a normal contrast enema is not sufficient to exclude the diagnosis of HD in a neonate with a high clinical suspicion of disease. In a single-center retrospective study of newborns who were clinically suspected to have HD, 32 percent of those who had inconclusive findings on contrast enema were ultimately diagnosed with HD, compared with 2.5 percent of those with negative findings on contrast enema [49]. However, in patients with a low clinical suspicion of HD, a contrast enema provides good evidence to exclude the diagnosis. This was shown in a study that compared 50 children who presented with constipation and were diagnosed with HD with a concurrent cohort of 50 patients with idiopathic constipation [58]. Significantly more patients with HD experienced delayed passage of meconium, abdominal distension, and vomiting and had a transition zone identified on a contrast enema. The presence of at least one of these findings was identified in every patient diagnosed with HD compared with 64 percent of patients with idiopathic constipation. Thus, the authors suggest that rectal biopsy may be avoided in children with constipation who lack all of these clinical and radiologic features.

Anorectal manometry — Anorectal manometry sometimes is a very useful aid in the diagnosis and is especially helpful in patients with ultrashort-segment Hirschsprung disease (USSHD). It is helpful as a screening test because a clearly normal study demonstrating relaxation of the internal anal sphincter with distension of the rectum excludes the diagnosis of HD. Lack of relaxation of the internal anal sphincter with balloon rectal distension is suggestive of HD, but false positives can occur. Anorectal manometry has a positive predictive value that is reported to be 75 to 95 percent but is less accurate in infants younger than one month of age and those with longstanding chronic constipation [56,59,60]. (See "Constipation in infants and children: Evaluation", section on 'Anorectal manometry'.)

Rectal biopsy — A suction rectal biopsy can be done at the bedside or in an ambulatory setting without the need for general anesthesia. A biopsy should be taken 2 cm above the level of the dentate line to avoid the 1 to 2 cm zone of physiologic hypoganglionosis or aganglionosis that is normally present. A second biopsy should be taken proximal to the first one. Although adequate tissue is obtained for analysis in the majority of infants and toddlers, in children above age three years, the rate of adequate tissue declines progressively from 88 percent to 70 and 45 percent (in adolescents) [61-

63]. Repeat suction biopsies, grasp-forceps biopsies, or full-thickness biopsies under general anesthesia can be performed if the initial biopsy is nondiagnostic (ie, if insufficient tissue is obtained).

The diagnosis of HD is established if ganglion cells are absent in the rectal biopsy, provided that the tissue sample is adequate (picture 1). Supportive findings include the presence of hypertrophic nerve fibers, increased acetylcholinesterase activity or staining in the muscularis mucosae, and decreased or absent calretinin-immunoreactive fibers in the lamina propria [64-67]. Excessively thickened nerve fibers may not appear until after eight weeks of age [68]. (See 'Diagnosis' below.)

A normal rectal biopsy virtually excludes HD, provided that the biopsy samples are obtained from the correct site and contain at least a small amount of muscularis mucosae. Thus, a rectal suction biopsy is more sensitive and specific than contrast enema and anorectal manometry for the diagnosis of HD for children up to three years of age (table 5) [48,56].

Abdominal radiograph — A plain abdominal radiograph is not helpful in excluding the diagnosis of HD, except perhaps for patients in whom there is a low suspicion of disease (eg, children with moderate refractory constipation and normal anorectal examination). If a plain radiograph is performed, the possibility of HD is suggested by signs of distal intestinal obstruction, ie, decreased or absent air in the rectum and dilated bowel loops proximal to the aganglionic region. Occasionally, careful review of the plain radiographs may reveal the transition zone even when it is not visible on the contrast enema [69].

DIAGNOSIS

HD is suspected based on clinical features described above, usually supported by contrast enema or anorectal manometry. (See 'Contrast enema' above and 'Anorectal manometry' above.)

The diagnosis is established by rectal biopsy (a rectal suction biopsy and/or a full-thickness biopsy). **Absence of ganglia** on the suction biopsy confirms the diagnosis of HD, provided that the sample is adequate, meaning that the biopsies were obtained from the correct site and contain at least a small amount of muscularis mucosae. If ganglia are seen in an appropriately performed suction biopsy, HD is virtually excluded. (See 'Rectal biopsy' above.)

DIFFERENTIAL DIAGNOSIS

Other disorders that may present with intestinal obstruction in a newborn infant include:

- Gastrointestinal malformations, including intestinal atresia, duplication cysts, or malrotation. (See "Intestinal atresia" and "Intestinal malrotation in children".)
- Meconium ileus due to cystic fibrosis. (See "Cystic fibrosis: Overview of gastrointestinal disease", section on 'Meconium ileus'.)

- Multiple endocrine neoplasia type 2 (MEN2). Type 2A is associated with Hirschsprung disease, whereas type 2B may be associated with ganglioneuromatosis, skeletal deformations, and Marfanoid habitus. (See "Clinical manifestations and diagnosis of multiple endocrine neoplasia type 2".)

- Disorders causing chronic intestinal pseudo-obstruction, including intestinal neuronal dysplasia. (See "Chronic intestinal pseudo-obstruction", section on 'Genetic' and "Functional constipation in infants, children, and adolescents: Clinical features and diagnosis", section on 'Other causes'.)

- Meconium plug syndrome, a condition that occurs in up to 1:500 newborns and is due to colonic dysmotility or abnormal consistency of meconium, leading to obstipation in the newborn. A contrast enema is both diagnostic and therapeutic. However, approximately 15 percent of infants with meconium plug syndrome also have HD, so a full diagnostic evaluation for HD, including rectal suction biopsy, is warranted [70].

- Small left colon syndrome, which typically occurs in infants of diabetic mothers and appears to be due to transient left colon dysmotility, leading to delayed passage of stool. A contrast enema makes the diagnosis, showing a contracted left colon, and the problem usually resolves on its own after a few days. These neonates should undergo rectal biopsy ensure they do not have HD.

These disorders can be distinguished from HD by their clinical features and the presence of ganglia on a rectal suction biopsy.

In older infants and children, the main consideration in the differential diagnosis is functional constipation. Other possibilities include anorectal anomalies, internal anal sphincter achalasia, hypothyroidism, and chronic intestinal pseudo-obstruction (see "Functional constipation in infants, children, and adolescents: Clinical features and diagnosis"). Classical HD also should be distinguished from ultrashort-segment Hirschsprung disease (USSHD), as discussed below. (See 'Ultrashort-segment Hirschsprung disease' below.)

MANAGEMENT

Surgical correction — The mainstay of treatment is surgery. The goals are to resect the affected segment of the colon, bring the normal ganglionic bowel down close to the anus, and preserve internal anal sphincter function. Many surgical techniques have been developed. The choice among them usually is based upon surgeon preference since the overall complication rates and long-term results are similar [37,71].

The traditional operation was an abdominoperineal pull-through in two or three stages, in which patients initially underwent a diverting colostomy (to allow the dilated bowel to decompress) with definitive repair performed later. However, most centers now perform the procedure in one stage, an approach that does not appear to increase complication rates [37,72-74]. Laparoscopic-assisted and transanal repairs are commonplace and now preferred over the open procedures in most centers. The

outcome seems to be equivalent to the traditional abdominoperineal pull-through, with the added benefits of earlier resumption of full feeds, less pain, shorter hospitalization, and less conspicuous scars [75-78]. In a systematic review and meta-analysis comparing totally transanal, endorectal, and laparoscopic-assisted pull-through, operative time was found to be shorter for the transanal procedure [79]. However, the incidence of serious complications such as enterocolitis, incontinence, and chronic constipation did not differ between the two procedures. The frequency of postoperative internal anal sphincter defects identified by endosonography was also higher in patients undergoing a transanal approach (69 versus 19 percent). These findings should be confirmed with data from other centers and with different lengths of follow-up to fully understand the implications of this operative approach.

Patients with ultrashort-segment Hirschsprung disease (USSHD) may not require a pull-through operation. (See 'Ultrashort-segment Hirschsprung disease' below.)

Treatment of the emergency complications of HD, including acute bowel obstruction, enterocolitis, and volvulus, is discussed separately. (See "Emergency complications of Hirschsprung disease".)

Further evaluation for associated anomalies — The clinician should be alert for signs or symptoms of congenital anomalies in patients with suspected HD. For all patients with HD, and particularly those with syndromic HD, genitourinary anomalies, hearing impairment, and visual impairment are common (figure 1). In light of the high rate of urinary tract anomalies in both nonsyndromic (20 percent) and syndromic (40 percent) HD, some experts recommend ultrasonographic screening for urinary system malformations in all patients with HD [22], but practice varies. (See 'Associated congenital anomalies' above.)

Assessment by a clinical geneticist is valuable for all patients with syndromic features or anomalies and also for those with no apparent associated anomalies. Genetic screening for multiple endocrine neoplasia type 2A (MEN2A) may be offered to families of infants with HD and particularly for those with a family history of MEN2 or related neoplasms in first-degree relatives. (See 'Associated syndromes' above and 'Associated congenital anomalies' above and "Clinical manifestations and diagnosis of multiple endocrine neoplasia type 2", section on 'Genetic screening'.)

ULTRASHORT-SEGMENT HIRSCHSPRUNG DISEASE

The term "ultrashort-segment Hirschsprung disease" (USSHD) is sometimes used to describe a form characterized by a very short segment of aganglionosis extending 2 to 4 cm proximal to the internal anal sphincter. Most experts agree that this form exists, although there is some controversy on this point.

The clinical picture is similar to the classical short-segment HD (which involves most or all of the rectum and part of the sigmoid colon), except that the degree of constipation may be less severe and the complications of growth retardation and enterocolitis are less likely to develop. On contrast enema, the rectum may be dilated down to the internal sphincter and there may not be a visible

transition zone. If anorectal manometry is performed, the anorectal inhibitory reflex is absent, as it is in the other forms of HD. The lack of anorectal relaxation is the physiologic basis for the clinical features.

The diagnosis of USSHD is established by taking two biopsies:

- A biopsy taken just proximal to the dentate line that shows aganglionosis – This distinguishes USSHD from internal anal sphincter achalasia (which has similar findings on anorectal manometry, but in achalasia, ganglion cells are present). (See "Functional constipation in infants, children, and adolescents: Clinical features and diagnosis", section on 'Internal anal sphincter achalasia'.)
- A biopsy taken approximately 4 cm above the internal sphincter that shows normal ganglion cells – This biopsy distinguishes USSHD from classical HD, in which ganglion cells would be absent.

It is important to distinguish patients with USSHD from those with typical HD because patients with USSHD may not require a pull-through operation. Some patients with USSHD respond to bowel management with diet, stool softeners, and laxatives. Others respond to botulinum toxin injections. If these measures fail, a myomectomy should be considered, removing a 0.5 to 1.0 cm-wide strip of inner circular muscle in the posterior midline, from the level of the internal anal sphincter to the level of the normal ganglionated bowel.

OUTCOME

Abnormalities of bowel function are common after definitive surgery for HD, although quality of life is generally good [80-87]. The most common long-term complications are constipation, fecal incontinence, and enterocolitis. Fecal incontinence has the greatest impact on quality of life. Patients with trisomy 21 or other syndromes are more likely to have constipation or incontinence [88]. Total colonic aganglionosis (TCA) has a much higher rate of complications and mortality before and after definitive treatment compared with the more common forms of HD, in which a smaller portion of the colon is affected [89]. TCA also has a much higher risk for enterocolitis and poor functional results, including incontinence after surgery. Some patients, especially those with residual aganglionosis or stricture formation, may benefit from a redo pull-through procedure [90].

Constipation — Constipation or persistent obstructive symptoms, which include vomiting, bloating, borborygmi, abdominal distension, and severe constipation, occur in 10 to 30 percent of patients after operative repair for HD [91]. This can be caused by mechanical obstruction (eg, stricture), persistent or acquired aganglionosis, a colonic motility disorder (eg, intestinal neuronal dysplasia), increased internal anal sphincter tone, or nonspecific colonic dysmotility/stool-withholding behavior [92]. The diagnostic evaluation typically includes a radiographic contrast study to evaluate for stricture, rectal suction biopsy to evaluate for persistent aganglionosis, and an assessment of motility (eg, radiopaque marker study).

Guidelines for the management of postoperative obstructive symptoms in children with HD have been published by the American Pediatric Surgical Association [91]. If increased internal anal sphincter tone is suspected, a trial of botulinum toxin injection may be helpful (algorithm 2) [93]. In many cases, obstructive symptoms improve or resolve with time [83].

Enterocolitis — Despite surgical repair, Hirschsprung-associated enterocolitis (HAEC) is a major cause of postoperative morbidity and occasional mortality, with postoperative incidence rates as high as 45 percent [46,88,94-96]. It usually occurs within the first year after surgical repair [95]. HAEC is also more common in long-segment disease, especially TCA.

The risk for HAEC appears to be increased in patients with an anastomotic stricture, suggesting that intestinal stasis may have a role in the etiology [95]. HAEC is more likely to develop after the pull-through operation if there is histologic evidence of inflammation in the resected colon [97]. The risk is also increased in patients with long-segment disease, particularly for patients with TCA [94,98,99]; such patients also have increased risks for perianal excoriations, electrolyte imbalance, and anastomotic leak as compared with patients with rectosigmoid disease [100]. The risk for these problems tends to improve with time after surgery. A few reports have suggested an association between HAEC and subsequent development of Crohn disease [101]. The risk factors, clinical presentation, and management of HAEC are discussed in greater detail separately. (See "Emergency complications of Hirschsprung disease", section on 'Enterocolitis'.)

Incontinence — Diarrhea and incontinence are seen commonly during the early postoperative period, but they seem to improve with time [102]. Loss of water-absorptive surface area from colonic resection and anal sphincter dysfunction are likely etiologic factors. The latter may be due to damage to the anal canal and internal sphincter during the pull-through operation [103,104]. Improvement of bowel function occurs in the majority of patients with frequency of stools and continence improving with age [76,80,94,98,102,105,106]. In most patients, there is a rapid decrease in stool frequency during the first six months postoperatively, with a slower decline over the next several years [76].

Long-term follow-up reveals that approximately 75 to 95 percent of patients achieve a stool frequency of five or fewer stools per day [98,105,106]. Some patients may have persistent problems with constipation and fecal soiling [98,105-107]. In one long-term study, 42 percent of patients had occasional soiling and 12 percent had frequent soiling [88]. Most patients with Down syndrome and HD have disturbances of bowel function (soiling, recurrent enterocolitis) over the long term, and some revert to a permanent colostomy [88,108]. Those with total colonic HD have more fecal soiling, but for most patients with HD, the disease-specific quality of life tends to improve as time passes [82,109].

Urologic and sexual outcomes — Urologic and sexual complications, specifically urinary incontinence and erectile dysfunction, have been reported after surgery for HD [110-112]. A study suggests they are no more common than in matched controls [110]. However, caution is appropriate since urinary and sexual dysfunction are known to occur after other types of pelvic surgery and because these problems may not be recognized until years after surgery. Prospective documentation of urologic and sexual outcomes in all Hirschsprung cases has been suggested [111].

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Hirschsprung disease (The Basics)")

SUMMARY AND RECOMMENDATIONS

- Hirschsprung disease (HD) is caused by congenital absence of ganglion cells in the distal rectum and extends for a variable distance proximally. It affects the rectum and part of the sigmoid colon in approximately 80 percent of patients, but it also can involve more proximal segments, the entire colon, or (in rare cases) most of the small bowel. There is an increased risk for HD among patients with trisomy 21 and several other genetic syndromes (table 2). Assessment by a clinical geneticist is valuable for all patients with syndromic features or anomalies, as well as for those with no apparent associated anomalies. (See 'Introduction' above and 'Associated syndromes' above.)

- For all patients with HD, and particularly those with syndromic HD, genitourinary anomalies, hearing impairment, and visual impairment are common (figure 1). Congenital heart disease is common among those with syndromic HD. The clinician should be alert for signs or symptoms of congenital anomalies in patients with suspected HD. Some authors have suggested routine screening for congenital anomalies of the kidney and urinary tract (CAKUT) and for hearing impairment. (See 'Associated congenital anomalies' above.)

- The majority of patients with HD are diagnosed in the neonatal period when they present with symptoms of distal intestinal obstruction, including bilious emesis, abdominal distension, and failure to pass stool. A high index of suspicion is appropriate for infants with a predisposing condition such as Down syndrome or for those with a family history of HD. Patients with less severe (short-segment or ultrashort-segment) HD may not be diagnosed until later in infancy or childhood. Such patients typically have a history of chronic constipation and failure to thrive. (See 'Clinical features' above.)

- An urgent full evaluation for HD is appropriate for newborns or young infants (<6 months old) with the following features:

    - Symptoms of obstruction (bilious emesis, abdominal distension, and failure to pass stool)
    - Failure to pass meconium within 48 hours of birth
    - Constipation and trisomy 21 or other condition known to be associated with HD, or a family history of HD
    - Constipation and physical examination suggestive of HD (tight anal sphincter; narrowed, empty rectum; or squirt sign on digital examination)

  (See 'Suspected Hirschsprung disease in neonates' above.)

- Occasionally, affected infants may present with enterocolitis, a potentially life-threatening illness in which patients have a sepsis-like picture with fever, vomiting, diarrhea, and abdominal distension, which can progress to toxic megacolon. (See 'Clinical features' above and "Emergency complications of Hirschsprung disease".)

- Definitive diagnosis of HD is made by rectal biopsy, which may be supported by findings on abdominal radiographs, contrast enema, or anorectal manometry. The diagnostic steps depend on the level of suspicion for HD, whether there is concern about Hirschsprung-associated enterocolitis (HAEC; which requires emergency management), age of the child, and on the available resources and institutional/clinician preference (algorithm 1). (See 'Evaluation' above and 'Diagnosis' above.)

- The treatment for HD is surgical resection of the aganglionic segment of bowel. The normal ganglionic bowel is brought down and anastomosed just proximal to the anus, and injury to the anal sphincter is avoided. (See 'Management' above.)

- Abnormalities of bowel function are common after definitive surgery for HD, although overall quality of life is generally good. The most common long-term complications are constipation and fecal incontinence. Postoperative enterocolitis may also occur and is a medical emergency. (See 'Outcome' above and "Emergency complications of Hirschsprung disease".)

- The term "ultrashort-segment Hirschsprung disease" (USSHD) is sometimes used to describe a form of HD characterized by a very short-segment of aganglionosis extending 2 to 4 cm proximal to the internal anal sphincter. The clinical picture is similar to the classical short-segment HD (which involves most or all of the rectum and part of the sigmoid colon), except that the degree of constipation may be less severe. It is important to distinguish patients with USSHD from those with typical HD because they may not require a pull-through operation. (See 'Ultrashort-segment Hirschsprung disease' above.)

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GRAPHICS

Chromosomal abnormalities associated with Hirschsprung disease

Chromosomal abnormality	Features	Chromosomal locus (gene symbol)	Percent of individuals with this disorder who have Hirschsprung disease
Down syndrome	Intellectual disability, short stature, congenital heart disease, craniofacial features	Trisomy 21	0.6 to 3%
Deletion 10q	Intellectual disability, hypotonia	del 10q11.2 (*RET*)	Unknown
Deletion 13q	Intellectual disability, growth failure, craniofacial features	del 13q22 (*EDNRB*)	Unknown
Deletion 2q22	Intellectual disability, microcephaly, craniofacial features, seizures	del 2q22 (*ZFHX1B*)	Unknown

Graphic 101015 Version 3.0

Monogenic syndromes associated with Hirschsprung disease

Syndrome	Features	Mode of inheritance	Chromosomal locus/gene symbol	Percent of individuals with this disorder who have Hirschsprung disease
Bardet-Biedl syndrome	Retinal dystrophy, obesity, intellectual disability, polydactyly, hypogenitalism, renal abnormalities	AR	At least 11 loci/genes	2 to 10%*
Cartilage-hair hypoplasia	Short-limbed dwarfism, sparse hair, immune defects	AR	9p21-p12/*RMRP*	7 to 9%
Congenital central hypoventilation syndrome	Hypoxia, reduced ventilatory drive, neuroblastoma	Variable	4p12/*PHOX2B* 10q11.2/*RET* 5p13.1-p12/*GDNF* 20q13.2-q13.3/*EDN3* 11p13/*BDNF*	20%
Familial dysautonomia (Riley-Day syndrome)	Sensory and autonomic dysfunction (including abnormal sweat, tear, and saliva production)	AR	9q31/*IKBKAP*	Unknown
Fryns syndrome	Distal digital hypoplasia, diaphragmatic hernia, CHD, craniofacial, intellectual disability	AR	Unknown	Unknown
Goldberg-Shprintzen syndrome	Craniofacial, microcephaly, intellectual disability, PMG	AR	10q22.1/*KIAA1279* Others?	Common
Intestinal neuronal dysplasia	Abnormal intestinal innervation with giant ganglia	Unknown	Unknown	≤20%*
L1 syndrome	Intellectual disability, hydrocephalus, ACC, adducted thumbs	XLR	Xq28/*L1CAM*	Rare
MEN2A/FMTC	MTC, pheochromocytoma, hyperparathyroidism ¶	AD	10q11.2/*RET*	≤1%
MEN2B	MTC, pheochromocytoma, mucosal and intestinal neuromas, skeletal abnormalities, corneal changes	AD	10q11.2/*RET*	Rare
Mowat-Wilson syndrome	Intellectual disability, microcephaly, craniofacial, CHD, ACC, epilepsy, short stature	AD	2q22/*ZFHX1B*	41 to 71%
Neurofibromatosis 1	Café-au-lait macules, neurofibromas, Lisch nodules	AD	17q11.2/*NF1* 5p13.1-p12/*GDNF*?	Unknown
Smith-Lemli-Opitz syndrome	Intellectual disability, hypospadias, 2/3 syndactyly, CHD, craniofacial	AR	11q12-q13/*DHCR7*	Unknown
Waardenburg syndrome type 4 (Waardenburg-Shah syndrome)	Pigmentary abnormalities, deafness	AR (usually)	13q22/*EDNRB* 20q13.2-q13.3/*EDN3*	Common
		AD	22q13/*SOX10*	Almost 100%

AR: autosomal recessive; *RMRP*: RNAse mitochondrial RNA processing gene; *PHOX2B*: paired-like homeobox 2B gene; *RET*: RET proto-oncogene; *GDNF*: glial cell line-derived neurotrophic factor gene; *EDN3*: endothelin 3 gene; *BDNF*: brain-derived neurotrophic factor gene; *IKBKAP*: inhibitor of kappa light polypeptide gene enhancer gene; CHD: congenital heart disease; PMG: polymicrogyria; ACC: agenesis of the corpus callosum; XLR: X-linked recessive; *L1CAM*: L1 cell adhesion molecule gene; MEN2A: multiple endocrine neoplasia type 2A; FMTC: familial medullary thyroid cancer; MTC: medullary thyroid carcinoma; AD: autosomal dominant; MEN2B: multiple endocrine neoplasia type 2B; *ZFHX1B*: zinc finger homeobox protein 1b gene; *NF1*: neurofibromin 1 gene; *DHCR7*: 7-dehydrocholesterol reductase gene; *EDNRB*: endothelin receptor type b gene, *SOX10*: Sry-box 10 gene.

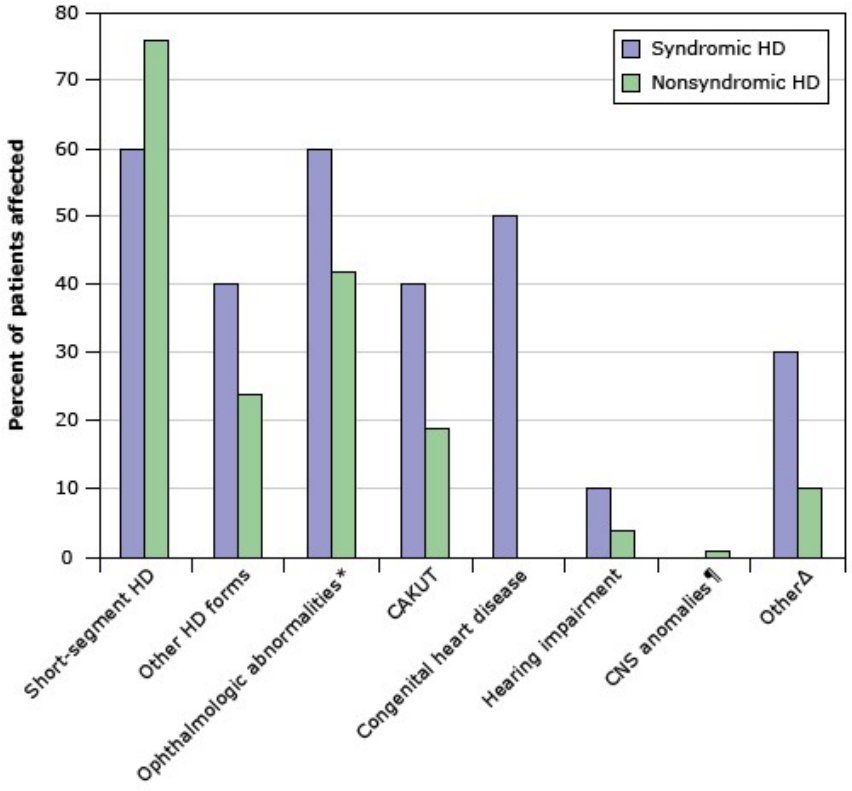
* Limited data are available.

¶ In FMTC, affected individuals do not have pheochromocytoma or hyperparathyroidism.

Parisi, MA (updated December 2006). Hirschsprung Disease Overview. In: GeneReviews at GeneTests: Medical Genetics Information Resource (database online). Copyright © University of Washington, Seattle. 1997-2010. Available at http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=hirschsprung-ov. Accessed May 31, 2010.

Graphic 73215 Version 9.0

Frequency of congenital anomalies in Hirschsprung disease



Data from a study of 106 patients with HD who underwent systematic screening for congenital anomalies. Syndromic HD represented 9.4% of patients and included Down syndrome (6.6% of all patients), Turner syndrome, cat-eye syndrome, and congenital central hypoventilation syndromes.

HD: Hirschsprung disease; CAKUT: congenital anomalies of the kidney and urinary tract; CNS: central nervous system.

* Ophthalmologic abnormalities were mostly refractive errors (hyperopia, astigmatism, or myopia), strabismus, or amblyopia. No major ocular anomalies were detected. Visual impairment was present in 9.4%.

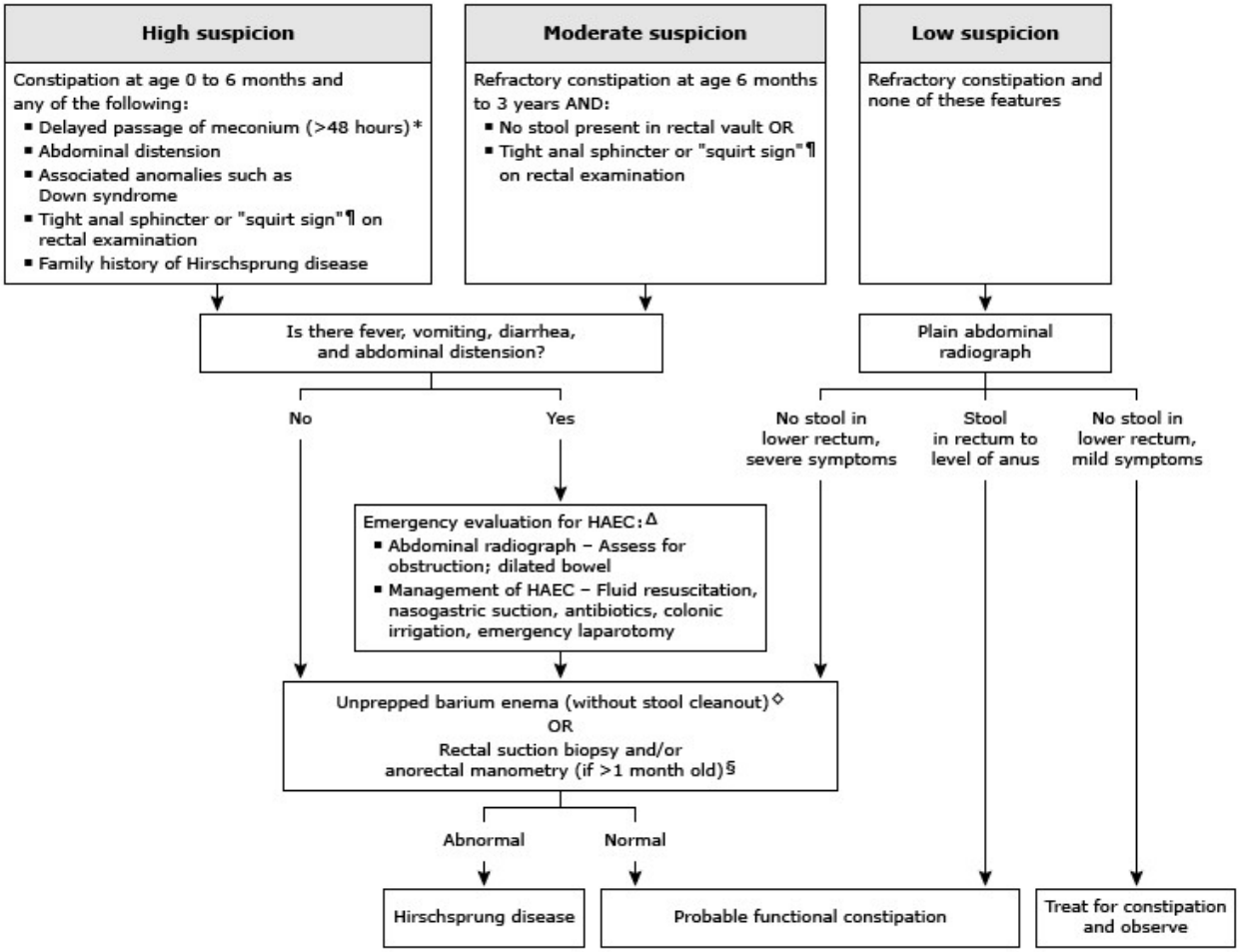
¶ CNS anomalies included agenesis of the corpus callosum; no other major brain abnormalities were detected.

Δ Other anomalies included metabolic issues (growth hormone deficiency, hypothyroidism, or precocious puberty), gastrointestinal anomalies (atresia, pancreas anularis or malrotation), familial medullary thyroid carcinoma, cryptorchidism, epilepsy, and cleft palate.

Data from Pini Prato A, Rossi V, Mosconi M, et al. A prospective observational study of associated anomalies in Hirschsprung's disease. Orphanet Journal of Rare Diseases. 2013; 8:184.

Graphic 100632 Version 2.0

Assessment for Hirschsprung disease in infants and young children



HAEC: Hirschsprung-associated enterocolitis.

* A moderate level of suspicion is also warranted for neonates with well-documented delay in passing meconium but **no** other signs, symptoms, or risk factors for Hirschsprung disease. Practice varies regarding the evaluation of these infants. At a minimum, they should undergo a careful physical examination and exclusion of other causes of delayed passage of meconium, including anorectal malformations, and should be closely observed and evaluated promptly for Hirschsprung disease if they develop symptoms of constipation or abdominal distension.

¶ The "squirt sign" is a forceful expulsion of gas and stool as the finger is withdrawn from the anus after the digital rectal examination, particularly in infants.

Δ For more details on the evaluation and management of HAEC, refer to UpToDate content on emergency complications of Hirschsprung disease.

◊ In our practice, we generally perform a barium enema rather than suction biopsy as the initial diagnostic procedure; if a clear transition zone is seen, the study is virtually pathognomonic of Hirschsprung disease and helps the surgeon plan the level of resection preoperatively. We always confirm the diagnosis by biopsy even when the barium enema shows typical features of Hirschsprung disease. Even if a transition zone is not seen, Hirschsprung disease cannot be entirely excluded. The barium enema may have false-negative results if performed within 24 hours of a digital rectal examination.

§ Some providers proceed to an anorectal manometry and/or rectal suction biopsy without a barium enema. If ganglia are seen in an appropriately performed suction biopsy, Hirschsprung disease is excluded. Lack of ganglia on the suction biopsy is suspicious for Hirschsprung disease, but the diagnosis may have to be confirmed by a full-thickness rectal biopsy if the pathologist considers the suction biopsy to be an inadequate sample. Similarly, normal results of anorectal manometry can exclude Hirschsprung disease, but abnormal results should be confirmed by biopsy. Anorectal manometry is less accurate in infants under 1 month of age.

Graphic 51156 Version 7.0

Diagnoses to consider in infants and children with delayed passage of meconium

Condition	Comments
Hirschsprung disease	Abdominal distension and vomiting are common. On digital examination, typical findings are a tight anal canal with empty rectum, often with an explosive "squirt" of soft stool when the finger is withdrawn. On contrast enema, a transition zone may be seen but often is not visible in newborns.
Intestinal obstruction	Consider atresia, webs, or volvulus. Obstruction may be present even in infants who pass meconium.
Meconium ileus	Symptoms often begin on second day of life. Most patients with meconium ileus have cystic fibrosis.
Meconium plug syndrome	Caused by colonic dysmotility or abnormal meconium consistency, leading to obstipation in the newborn. A contrast enema is both diagnostic and therapeutic. Some patients with meconium plug syndrome have Hirschsprung disease.
Functional ileus	Occurs in setting of prematurity, sepsis, respiratory distress, pneumonia, or electrolyte disturbances.
Small left colon*	Barium enema shows small-caliber left colon. Increased incidence with maternal diabetes.
Drugs administered to mother before delivery	Magnesium sulfate ($MgSO_4$), opiates, or ganglionic-blocking agents.
Hypothyroidism	Infants with hypothyroidism also may have prolonged jaundice, lethargy, and low body temperature.
Other	Rare disorders associated with intestinal pseudo-obstruction, including megacystis-microcolon-intestinal hypoperistalsis (Berdon) syndrome.

* Similar findings may occur in infants with Hirschsprung disease, so affected infants should be observed closely and evaluated for Hirschsprung disease, if appropriate.

Data from: Tunnessen WJ. Constipation and fecal retention. In: Signs and Symptoms in Pediatrics, 3rd ed, Lippincott, Williams & Wilkins, Philadelphia 1999. p.518.

Graphic 82181 Version 8.0

Suggested categorization and management of patients with suspected or established Hirschsprung-associated enterocolitis

APSA categorization	Typical presenting symptoms	Typical radiographic features	Recommended treatment (do all of the following)	Possible additional measures
Possible HAEC (grade I)	Anorexia, diarrhea, mild abdominal distention	Normal radiograph or mild signs of ileus	▪ Oral hydration ▪ Oral metronidazole	▪ Rectal irrigations
Definite HAEC (grade II)	One or more of the following*: ▪ Explosive diarrhea ▪ Fever, tachycardia, or lethargy ▪ Moderate abdominal distention and/or tenderness ▪ Explosive gas/stool on rectal examination	May include: ▪ Signs of ileus, including air-fluid levels and dilated loops of bowel ▪ Distension of the proximal colon, with rectosigmoid cutoff ¶	▪ Clear liquids or hold feeds ▪ IV hydration ▪ Metronidazole (oral or IV) ▪ Broad-spectrum antibiotic coverage Δ (in addition to metronidazole) ▪ Rectal irrigations	▪ Nasogastric decompression ◊
Severe HAEC (grade III)	Symptoms of grade II (above), PLUS: ▪ Obstipation ▪ Poor perfusion ▪ Hypotension ▪ Altered consciousness/mentation ▪ Marked abdominal distension ▪ Signs of peritonitis	Signs of grade II (above), PLUS possible: ▪ Pneumatosis intestinalis ▪ Pneumoperitoneum (rare)	▪ Hold feeds ▪ Metronidazole (IV), AND ▪ Broad-spectrum IV antibiotics Δ ▪ IV hydration ▪ Rectal irrigations	▪ Nasogastric decompression ◊ ▪ Possible surgical intervention §

HAEC: Hirschsprung-associated enterocolitis; APSA: American Pediatric Surgical Association; IV: intravenous.

* A particularly high suspicion for HAEC is appropriate for patients with a prior history of this disorder.

¶ On plain radiograph, HAEC is specifically suggested by distension of the proximal colon and absence of air in the distal rectosigmoid colon, with an abrupt cutoff at the level of the pelvic brim.

Δ Broad-spectrum antibiotic coverage might consist of IV ampicillin with gentamicin, or IV piperacillin/tazobactam.

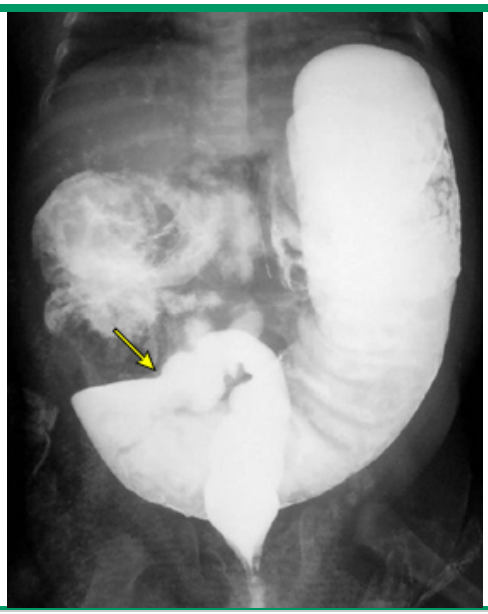
◊ Patients with marked abdominal distension should be treated with nasogastric decompression as well as holding of feeds.

§ Patients who develop pneumoperitoneum may require surgical exploration. Patients with severe HAEC who fail to improve with maximal medical management may require surgery with proximal bowel diversion.

Adapted from Gosain A, Frykman PK, Cowles RA, et al. Guidelines for the diagnosis and management of Hirschsprung-associated enterocolitis. Pediatr Surg Int 2017; 33:517.

Graphic 114001 Version 3.0

Barium enema in Hirschsprung disease



Barium enema of an infant with Hirschsprung disease, showing the transition zone (arrow) between the lower aganglionic bowel and the normal colon above.

Courtesy of George D Ferry, MD.

Graphic 59877 Version 5.0

Comparison of sensitivity and specificity for rectal suction biopsy, contrast enema, and anorectal manometry in the diagnosis of Hirschsprung disease in children*

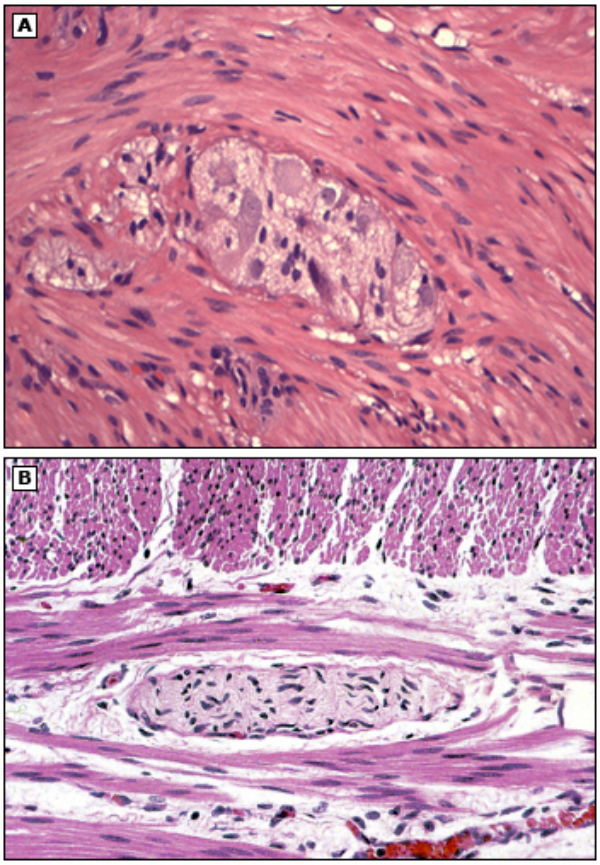
Test	Sensitivity	Specificity
Rectal suction biopsy	93%	100%
	(95% CI, 77-98 percent)	(95% CI, 96-100 percent)
Contrast enema	76%	97%
	(95% CI, 57-89 percent)	(95% CI, 91-99 percent)
Anorectal manometry	83%	93%
	(95% CI, 63-93 percent)	(95% CI, 85-97 percent)

* Diagnosis was confirmed by full-thickness rectal biopsy and exluded by clinical follow-up for at least 6 months.

Data from: De Lorijn, F, Reitsma, JB, Voskuijl, WP, et al. Diagnosis of Hirschsprung's disease: a prospective, comparative accuracy study of common tests. J Pediatr 2005; 146:787.

Graphic 65223 Version 4.0

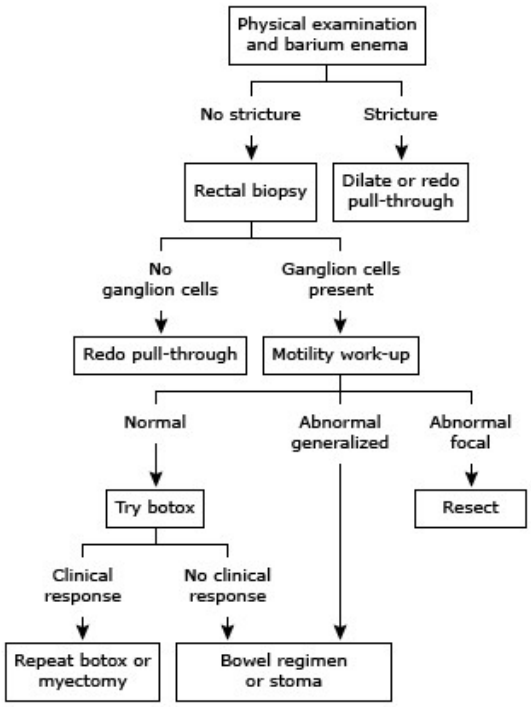
Hirschsprung disease



(A) Normal: Hematoxylin and eosin (H&E) staining section of rectal tissue shows a normal myenteric ganglion containing many neurons that are easily identified as large cells with nucleus containing prominent nucleoli and amphophilic cytoplasm due with Nissl granules.
(B) Hirschsprung disease: A rectal biopsy specimen from a patient with Hirschsprung disease shows a hypertrophic nerve in the myenteric plexus and an absence of ganglion cells.

Graphic 53381 Version 7.0

Algorithm for the diagnosis and management of the child with obstructive symptoms after a pull-through operation for Hirschsprung disease



Botox: botulinum toxin injection products (in the anal sphincter).

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Graphic 78219 Version 3.0

Contributor Disclosures

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