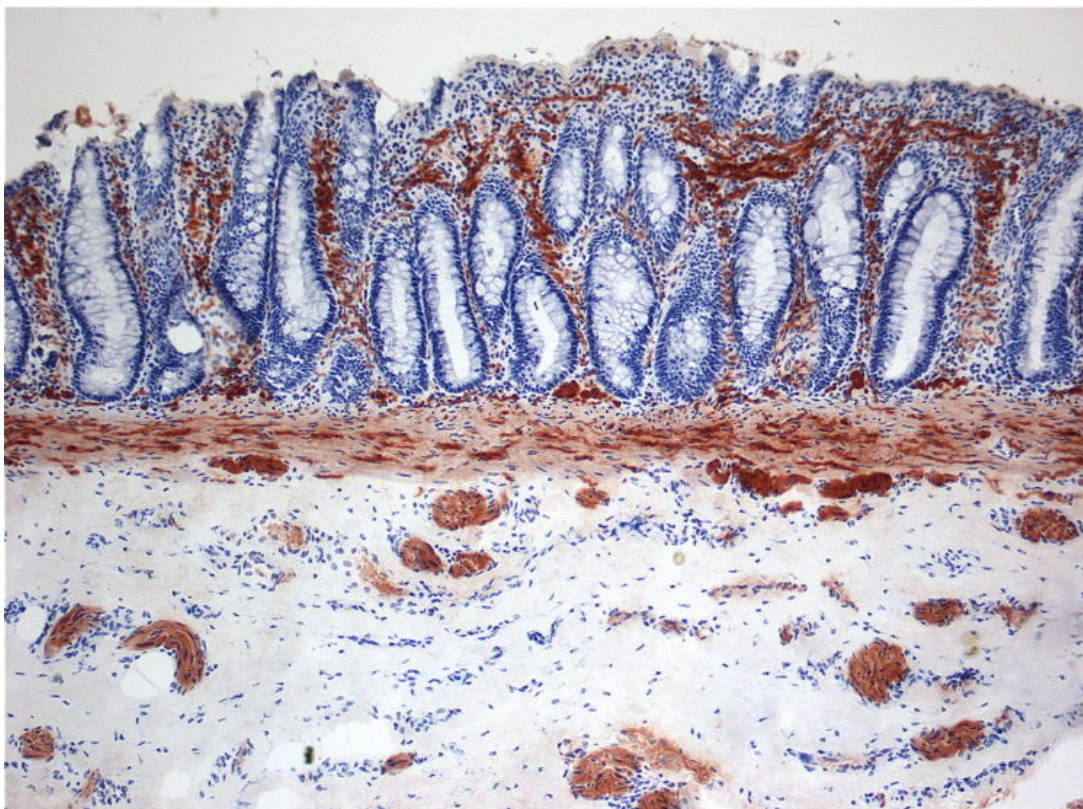


# Hirschsprung Disease (Congenital Aganglionic Megacolon) — Symptoms and Causes

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**Pediatric Hirschsprung Disease occurs when there is an absence of the ganglionic layer in the myenteric layer of the anus and the submucosa of the colon. This leads to the failure of relaxation of the colon, delayed passage of meconium, abdominal distension and constipation. Laboratory investigations are helpful if the patient develops enterocolitis where leukocytosis might be evident. Barium enema studies and histologic examination of biopsies confirm the diagnosis of Hirschsprung disease, and surgical resection of the aganglionic part of the colon is the current treatment of choice.**



## Definition of Hirschsprung Disease

Hirschsprung disease is a **birth defect characterized by the absence of nerve cells in the distal colon**, resulting in functional obstruction. It is a developmental disorder present in newborn characterized by the inability to defecate meconium within 24-48 hours of birth due to absent ganglions in the distal colon. This results in large nonfunctional distal intestines usually in the rectum, but it can also involve the colon and

the ileum.

## Epidemiology of Hirschsprung Disease

Pediatric Hirschsprung disease has an incidence of about **1 per 5,000** live births, making it a common etiology of delayed passing of meconium. Hirschsprung disease is associated with some **life-threatening complications** such as intestinal obstruction, proximal dilatation of the intestines, thinning and infection of the intestines leading to enterocolitis. These complications are responsible for a **mortality rate of 30%**.

The disease is uncommon in premature infants. In the current scenario 90 % of cases are diagnosed in the newborn period.

Pediatric Hirschsprung disease is **more common among males** with a 4:1 ratio. By 2 years, all patients with Hirschsprung disease are already diagnosed.

### The distribution of intestine involvement varies with:

- Terminal rectum only involved in 10% of the cases
- Sigmoid colon involvement in 65%
- Proximal colon involvement in 10%
- Entire colon with small bowel involvement in 10-15%

Segmental aganglionosis is rare and when evident acquired aganglionosis should be suspected.

It occurs in all races, 3 times more among Asian-Americans. The disease affects Caucasian children more than African Americans.

## Etiology of Pediatric Hirschsprung Disease

The exact etiology of Hirschsprung disease is unknown, but the etiology is thought to be:

**Familial aggregation in 15% of cases** is evident. The disease is associated with a mutation in three genes i.e. RET gene in chromosome 10, endothelial receptor B gene in chromosome 13 and endothelial 3 genes in chromosome 20.

**Sporadic in etiology is seen in the majority with causes such as decreased nitric oxide synthase activity**, or quantitative deficiency, being associated with an increased risk of pediatric Hirschsprung disease, **pyloric stenosis**, and other gastrointestinal motility disorders.

Research studies reveal the mother's health history or lifestyle during pregnancy may impose the chance of development of the disease in the infant.

## Pathophysiology of Pediatric Hirschsprung Disease

Patients with Hirschsprung disease do not have enteric neurons in their rectum and colon which causes a **loss of peristaltic waves and constipation**. Enteric neurons form from the neural crest and migrate with the **vagus nerve** down to the intestine. By 8 weeks of gestation, the ganglionic neurons have reached the proximal colon, and by 12 weeks of gestation the rectum.

Any arrest in this normal migration or presence of a hostile environment that destroys the ganglionic cells will lead to the absence of enteric neurons in the rectum and distal colon

and will result in pediatric Hirschsprung disease.

Research studies reveal that mutation in the genes, RET, GDNF, GFR $\alpha$ 1, NRTN, EDNRB, ET3, ZFH1B, PHOX2b, SOX10, and SHH are present in approximately 50% of Hirschsprung disease patients.

## Clinical Presentation of Pediatric Hirschsprung Disease

Hirschsprung disease may present in any of the following three ways:

1. Delayed passage of meconium in newborns
2. Frank intestinal obstruction with bilious vomiting, obstipation, and abdominal dilatation
3. Enterocolitis

Newborns with Hirschsprung disease have **delayed passage of meconium** after 48 hours of life and **abdominal distension**. Family history is positive in one-third of the cases. Patients with Hirschsprung disease do not have soiling or overflow incontinence. Chronic abdominal distension leads to **early satiety** which can eventually result in **malnutrition**. Patients may represent slow growth with slowness in gaining weight.

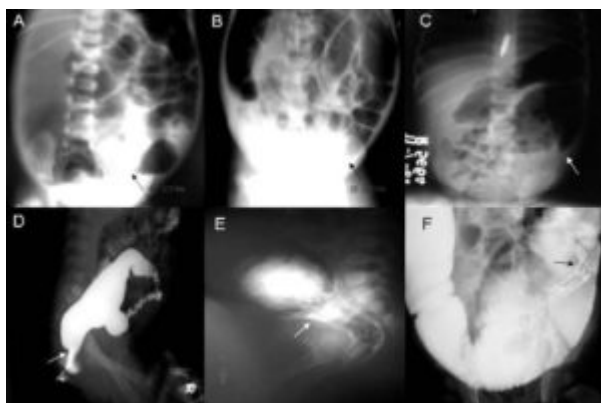
Older infants develop **chronic constipation** and become dependent on **daily enemas** for the induction of bowel movement. Patients with Hirschsprung disease can develop **enterocolitis** which presents with abdominal pain, fever, and bloody [diarrhea](#). Enterocolitis in this group of patients can be fatal.

Physical examination usually reveals **abdominal distension** with possible **palpation of the colonic loops**. Additionally, forceful expulsion of fecal material after the rectal examination is common. The rectum is usually empty on a rectal examination.

<b>Neonates</b>	<b>Older Infants</b>
Failure to pass meconium	Chronic constipation
Distended abdomen	Dilation of proximal bowel
Emesis	Failure to thrive
Feeding intolerance	Sepsis with gastroenteritis

## Diagnosis of Hirschsprung Disease

Laboratory investigations are not helpful in patients with Hirschsprung disease unless they develop a fever or severe abdominal pain; signs of enterocolitis. In enterocolitis, patients could have **leukocytosis** or **bacteremia**.



**Image:** "A: Plain abdominal radiograph showing a PARTZ at rectosigmoid, arrow. B: Plain abdominal radiograph showing a PARTZ at midsigmoid, arrow. C: Plain abdominal radiograph showing a PARTZ at descending colon, arrow. D: Contrast enema showing a CETZ at rectosigmoid, arrow. E: Contrast enema showing a CETZ at midsigmoid, arrow. F: Contrast enema showing a CETZ at descending colon, arrow. PARTZ, Plain abdominal transition zone; CETZ, Contrast enema transition zone." by Pratap et al. BMC Pediatrics 2007 7:5 doi:10.1186/1471-2431-7-5. License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

Patients with an uncomplicated presentation usually benefit the most from imaging studies in the diagnostic work-up. As, in any case of bowel obstruction, an **abdominal x-ray** is indicated. Abdominal x-ray shows **megacolon**, **small bowel obstruction**, and/or **multiple fluid-gas-levels**.

If the patient is not feverish, and they do not have acute abdominal pain, they can undergo a **barium enema study**. Barium enema can easily define the aganglionic from normally innervated colon.

The aganglionic part is usually collapsed, while the normal part is dilated and appears to be normal. This investigation is more useful in infants rather than neonates because neonates do not have enough time to develop dilatation of the normal colonic segment above the obstruction level.

The non-distended rectum is a useful diagnostic sign of Hirschsprung disease detected on barium enema imaging.

Patients with less severe Hirschsprung disease usually present with **chronic constipation**, without clear findings on radiography. In these patients, **rectal manometry** is useful as it shows the failure of **anorectal sphincter relaxation**.

The gold standard diagnostic test to confirm Hirschsprung disease is a **histologic examination** of a biopsy. **Rectal biopsy** shows the absence of ganglion cells in the submucous plexus. **Acetylcholinesterase staining** shows hypertrophied nerve trunks throughout the layers of the bowel. Although calretinin staining is more accurate than acetylcholinesterase staining for diagnosis of congenital aganglionosis.

#### Clinical tests for Hirschsprung's disease

Test	What it shows
Rectal suction biopsy (gold standard)	Absence of ganglion cells
Contrast enema	'Transition zone' between narrow aganglionic distal bowel and distended normal bowel proximal to it
Anorectal manography	Failure of internal anal sphincter relaxation when the rectum is distended with balloon.

# Treatment of Hirschsprung Disease

Patients with **acute intestinal obstruction** can be **dehydrated** due to third-space fluid loss and should be rehydrated. During fluid replacement therapy, enteric feeding should be discontinued and intestinal and gastric decompression might be indicated. Intravenous administration of balanced salt solutions may be helpful to prevent electrolyte imbalances.

**Intestinal decompression** is done by **rectal examination** or **rectal saline irrigation**, both result in the expulsion of the fecal material. In some patients, gastric decompression might be indicated if the upper gastrointestinal obstruction is suspected. **Gastric decompression** is achieved by the placement of a **nasogastric tube**.

If the patient is feverish, have leukocytosis or shows signs of enterocolitis, **broad-spectrum antibiotics** are indicated.

These measurements are only temporary. For the treatment of Hirschsprung disease, surgical management is the only definitive option.

Several forms of surgery exist for the management of Hirschsprung disease and the choice of the procedure is dependent on the patient's age, expectations and comorbidities. Additionally, the **length of the aganglionic segment** is an important factor in defining the type and extent of surgical intervention.

A **single pull-through surgery** is preferred in the majority of the patients, especially in neonates. In single pull-through surgery, the aganglionic segment is resected and the normal healthy colon is anastomosed to the anal cavity above the **dentate gyrus**. This procedure can be performed **laparoscopically** or in **open surgery**.

The availability of a good pathologist is essential to make sure that a single pull-through surgery is going to work because multiple biopsies from the anus and rectum need to be examined to define the distal and proximal levels that are normally innervated for the anastomosis to be done at their level.

Patients with **severe colonic distension**, **megacolon** or **enterocolitis** are candidates for a **two-step surgery**. The first step is to perform a **colostomy**, which is followed by a **pull-through procedure** once the patient is stable enough. This picture usually happens when the diagnosis is delayed, which means that this procedure is usually more common among infants and not newborns with Hirschsprung disease.

Another surgery that can be adopted in the treatment of Hirschsprung disease is ostomy surgery, a surgical procedure that reroutes the normal movement of the stool out of the body when a part of the bowel is removed. During either procedure, the surgeon may remove all or part of the colon, called a colectomy. A removable external collection pouch, called an ostomy pouch or ostomy appliance, is attached to the stoma and worn outside the body to collect the stool. The child or caregiver will need to empty the pouch several times each day.

Although most children with Hirschsprung disease do not need ostomy surgery, a child sick from Hirschsprung disease may need ostomy surgery to get better before undergoing the pull-through procedure. This gives the inflamed areas of the intestine time to heal.

In the acute phase after surgery and preoperatively, it is recommended for the infant to be **breastfed** or to at least receive breast milk and **not cow milk**. It is believed that

breast milk decreases the risk of constipation in infants in general, and in patients with Hirschsprung disease in particular.

Patients with a two-step procedure might need to **limit their physical activity** after the leveled colostomy. On the other hand, patients who undergo a one-step pull-through procedure usually recover faster and can go back to their routine physical activities earlier.

The patient often gets constipated after surgery. They are given laxatives and when they grow older enough to eat solid food, a high-fiber diet with plenty of water is recommended to enhance bowel movement and avoid dehydration.

In those patients whose growth is slow due to Hirschsprung Disease improves well after surgery. As their constipation and bowel movement improves, they eat well and drink well, with a relative effect on their growth. Both the surgery is effective in bringing a good impact on growth aspects of the child.

## References

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[Pediatric Hirschsprung Disease](#) via medscape.com

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