

## **HISTORICAL PERSPECTIVE IN DIAGNOSIS , SURGICAL PROCEDURES AND COMPLICATIONS OF HIRSCHSPRUNG DISEASE**

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### **INTRODUCTION**

Hirschsprung disease is one of the most familiar disease in pediatric surgical cases, also acknowledged as congenital megacolon. It is happened due to congenital loss of ganglionic cell in the muscular wall of distal part of the gut with resulting loss of peristaltic function in that part of intestine and distension of the colon proximal to the affected segment.

### **Types of Hirschsprung Disease**

Ultra-short segment Hirschsprung disease: only anal canal and terminus rectum is affected.

Short segment Hirschsprung disease: anal canal and whole rectum is aganglionic. (80%)

Long segment Hirschsprung disease: anal canal, rectum and some portion of gut is diseased. (10%)

Total colonic Hirschsprung disease: from anus to full length of colon is diseased. (10%).<sup>[1]</sup>

### **History**

Ruysch, a Dutch anatomist in 1691 gives the primitive description of this disease. He gave description of a 5 year old girl with abdominal discomfort who did not respond to common management and ultimately died. Similarly, Domenics Battani in Italy in 1800 delineated a child whom he followed for 10 years with extreme constipation who finally expired and showed sever colonic dilation at autopsy homogenous with megacolon. Harald Hirschsprung, a Danish pediatric surgeon from Queen Louise children`s hospital, gave the most revealing

and compact description of congenital megacolon at the society of pediatrics in Berlin in 1886. His treatise was titled as “constipation in new born due to dilation and hypertrophy of colon”. He neither offered a treatment nor suggested pathology of this condition. Treves delineated a child with idiopathic distension of colon, he managed the child with colon irrigation and performed a rectosigmoid resection and colostomy. He noted the presence of a “narrow distal rectum” that was the reason of obstruction (a fact that went unestablished for many years). In 1900 Lennander was the first one to propose a neurogenic origin for this disease. The first victorious operation for Hirschsprung’s disease was “the Swenson procedure”.<sup>[2]</sup>

### Pathophysiology

The enteric nervous system is the portion of the autonomic nervous system that directly gives command to GIT. Derived from a multipotent, the neural crest cells, a complete enteric nervous system is required for appropriate gut function. Diseases that arise as a result of defective neural crest cell development are known as neurocristopathies. One such disorder is Hirschsprung disease, also known as intestinal aganglionosis. Hirschsprung disease occurs in 1/5000 live births, and typically presents with the failure to pass meconium, along with abdominal distension and pain that typically requires surgical resection of the aganglionic segment. This disorder is due to interruption of normal neural crest cell migration, growth, maturation, survival and/or apoptosis. The inheritance of Hirschsprung disease is complicated, often non-Mendelian, and specified by variable penetrance. Capacious research has spotted a number of genes that control neural crest cell development in the pathogenesis of Hirschsprung disease including *RET*, *GDNF*, *GFR $\alpha$ 1*, *NRTN*, *EDNRB*, *ET3*, *ZFHX1B*, *PHOX2b*, *SOX10*, and *SHH*. However, mutations in these genes count for only about 50% of occurrences. Although other genetic mutations and combinations of genetic mutations and modifiers mostly contribute to the etiology and pathogenesis of this disease.

The potential of the GI tract to respond to the state of the lumen and gut wall by stimulating peristalsis, regulating blood flow and secretions and thus keep proper physiological balance rests on the enteric nervous system (ENS).<sup>[17]</sup> The ENS is the major part of the peripheral nervous system and functions almost autonomously of the central nervous system<sup>[18]</sup> and is in direct control of the GI system.<sup>[19]</sup> ENS neurons and glia are arranged into ganglia. The enteric ganglia are linked to form two plexuses that extend along the entire length of the gut: on outer side myenteric (Auerbach) plexus running the full length of the gut, and on inner

side submucosal (Meissner) plexus, established only in the small and large intestine. The myenteric plexus grows first and is located between the longitudinal and circular smooth muscle layers, and is involved in motility, while the submucosal plexus, which forms later in gestation, controls motility, blood flow, and the movement of ions across the intestinal epithelium.

Gut motility is controlled by collective mechanisms including neural, such as the enteric ganglia, and nonneural, such as the interstitial cells of Cajal (ICC).<sup>[20][21]</sup> Interstitial cells of Cajal works as pacemaker cells creating and transmitting slow waves that result to smooth muscle contraction in the gut.<sup>[20]</sup> The deprivation of enteric ganglion cells of the myenteric and submucosal plexi along variable length of the GI tract causes Hirschsprung disease (HSCR),<sup>[22]</sup> which is characterized by constant contraction of the aganglionic bowel that result to intestinal obstruction and dilatation of proximal intestinal portion (megacolon). The portion of the bowel proximate to the aganglionic region with diminished enteric neuronal quantity termed the transition zone, and it is always cranial to the aganglionic region.<sup>[23]</sup> Hypoganglionosis and aganglionosis of the distal gut can be caused by limiting enteric progenitor cells.<sup>[24][25]</sup> The zone of aganglionosis leads to tonic contraction of the involved segment, causing obstructive symptoms.<sup>[3][26]</sup>

### **Clinical presentation**

Mostly neonates are presented with a distended abdomen, the delayed passage of meconium (more than 24 hours), and vomiting.<sup>[4]</sup>

The symptoms differ with the age of the child and the severity of the disease. In the newborns, bilious vomiting, abdominal distension, unable to pass meconium or abnormal stool frequency are common.

- Burst of stool after per rectal examination is the classical finding. History of constipation with repeated rectal irrigation and foul smell feces can be found in the older children in undiagnosed cases, there may be repeated episodes of fecal impaction or acute life threatening enterocolitis. Enterocolitis may be the presenting feature in up to 12% patients of HD. It remains as the major cause of death and the mortality rate can be as high as 20-50%. The disease etiology is still uncertain, but evidences propose that the intestinal microbiota may play a significant role in the development of HD and Hirschsprung associated enterocolitis (HAEC). The infection and colonization by particular intestinal bacteria may be injurious to the intestinal barrier, microenvironment

and the immune responses, leading to repeated HAEC. A current study has reported that probiotics significantly reduce the prevalence and drop the extremity of HAEC.<sup>[8]</sup>

- Nearly fifty percent of all infants with Hirschsprung disease have a history of delayed first passage of meconium (beyond age 36 h), and nearly fifty percent of infants with delayed first passage of meconium have Hirschsprung disease. A family history of same condition is present in about 30 percent of reported cases.
- Unlike children suffering functional constipation, children with Hirschsprung disease rarely undergo soiling and overflow incontinence.
- Children with Hirschsprung disease may be ill nourished. Nutrition deprivation leads to the untimely satiety, abdominal discomfort, and distention associated with chronic constipation.
- Typical presentation of older infant and children are chronic constipation. This constipation often is intractable to standard treatment protocols and may need daily basis enema therapy.

Enterocolitis can be life threatening complication associated with Hirschsprung disease. Common presentation of enterocolitis are abdominal pain, fever, foul-smelling diarrhea or bloody diarrhea, as well as vomiting. If not identified timely, enterocolitis may lead to sepsis, transmural intestinal necrosis, and perforation.<sup>[6]</sup>

Another severe form of HD, but fortunately uncommon, Total colonic aganglionosis (TCA) is a severe and rare type of HD. Roughly it occurs in 2-13% of all patients with the disease and involves the entire colon, but may extend proximally into variable lengths of small bowel. Delay diagnosis of TCA often occurs, due to minor complaints; this delay however increases the risk of dreadful outcomes, predominately perforation, enterocolitis, sepsis and death, extending up to 20 - 50%.<sup>[9]</sup>

Total colonic HD with an isolated ileal perforation in the neonatal period, as the first presentation, is very unusual, especially in infants.<sup>[9]</sup>

Toxic megacolon is demarcated as an acute dilatation of the colon related with clinical evidence of toxemia. Major presenting symptoms are abdominal distension, constipation, reduced bowel sounds and toxic symptoms such as fever, tachycardia, or hypotension. Though this is most commonly related with ulcerative colitis, it may be associated with variety of other conditions, like Crohn's disease, amoebic colitis, pseudomembranous colitis,

cholera, and bacillary dysentery. TM (Toxic Megacolon) complicating HD is comparatively rare. Constipation is a common childhood issue. HD should not be ignored as a cause of constipation at any age. Active steps should be taken to diagnose the disease. Early diagnosis can reduce the serious and life threatening complication.<sup>[8]</sup>

Up to 30% of patients with HSCR also have other congenital abnormalities, such as velocardiofacial defects, congenital heart defects, gastrointestinal tract malformations, CNS abnormalities, genitourinary problems, craniofacial malformations, and spina bifida. Moreover, 2–15% of HSCR cases are linked with Down's syndrome.<sup>[3]</sup>

### Diagnosis

In the suspected cases there will be history of delayed or failure of passing meconium. The diagnosis of HD can be made by different ways. In plain x-ray abdomen there will be a picture of intestinal obstruction and predominately helpful in manifestation of perforation.<sup>[1]</sup> However, initial diagnostic procedure is a contrast enema. This will demonstrate the transition zone between normal (dilated) bowel and the narrow aganglionic bowel. This transition zone is noticed in 70–90% of patients. The rectosigmoid ratio is applied to assess the transition zone. A rectosigmoid ratio more than 1 is normal. A stool-filled cranial portion of bowel will reduce the rectum to sigmoid ratio. Anorectal manometry may also help with the diagnosis. With anorectal manometry, clinicians observe an absent recto anal inhibitory reflex.<sup>[3]</sup>

Rectosigmoid index is derived by dividing the widest diameter of the rectum by the widest diameter of the sigmoid loop when the colon is completely distended by the contrast medium. The normal rectosigmoid index is  $\geq 1$ . In typical length HD the rectosigmoid index is less or equal to 1.<sup>[5]</sup>

Full thickness biopsy, as a classic approach, was acquired by an skilled pediatric surgeon at three location (2, 5, and 7 cm) apart above dentate line. Proximal and distal ends of biopsy specimens were tagged for pathologist. Full thickness biopsy is a gold standard method.

Mucosal irregularity and irregular segmentation were the unique radiologic findings with the specificity about 100%. Transitional zone was the most precise radiologic finding with the sensitivity about 80%.

Anorectalmanometry is helpful specifically in the older child to differentiate Hirschsprung's disease and the other causes of constipation.<sup>[8]</sup>

The gold standard method for diagnosis of HD is a rectal biopsy. It is feasible to obtain a submucosal rectal suction biopsy without anesthesia.<sup>[3]</sup> Rectal suction biopsy was collected from mucosa at the level of 2-3 cm superior to dentate line.<sup>[7][27]</sup> Analysis of the biopsy specimen is performed. On analysis of biopsy an absence of ganglion cells and hypertrophic nerve trunks are seen. However, anorectalmanometry has some technical problems like small size of neonatal rectum, mobility during measurement, and suitable balloon size compared to rectum.<sup>[8]</sup>

## TREATMENT

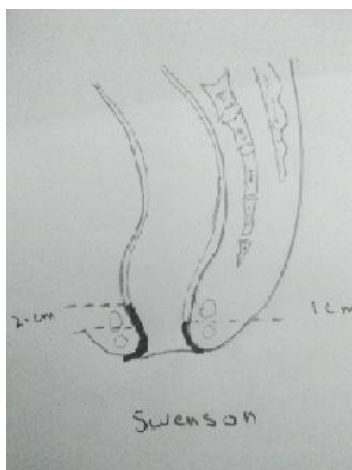
### Preoperative treatment

Infants with Hirschsprung disease will have therapeutic surgery within the first few weeks of life or months later, depending on their overall built, and proportion of colonic distension. The major aim of preoperative management is to prevent enterocolitis and to lessen colonic distension. Infants who do not undergo an ostomy require daily rectal irrigation to avoid enterocolitis until they are prepared for surgery. Rectal irrigation with 10 to 20 mL/kg of warm 0.9% normal saline solution can be performed at home by the parents to ease passage of stool and to decompress the rectum. A large-bore rubber catheter is utilized and permits efflux of the 0.9% sodium chloride solution and stool.<sup>[10]</sup>

## SURGICAL TREATMENT

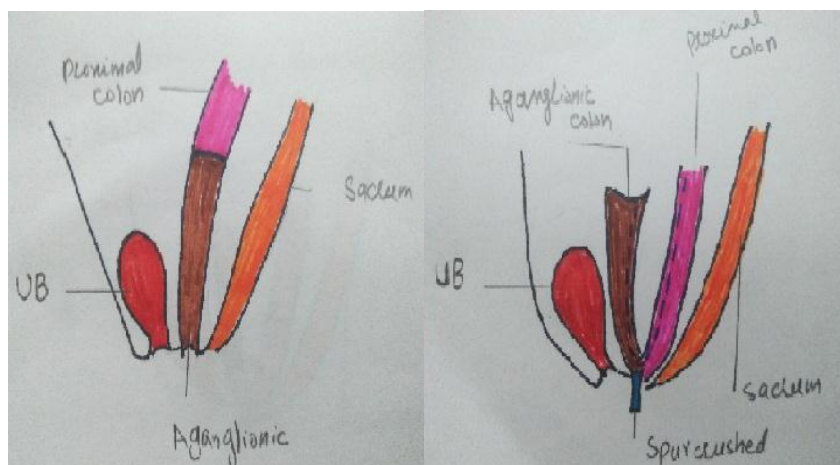
### Swenson procedure

Ovar Swenson narrated the first surgical procedure to Hirschsprung disease in 1940. The pull through procedure comprised of freeing the abnormal distal colon from within the pelvis by very careful sharp extra rectal dissection down to 2cm above the dentate line in anal canal, in order to prevent sphincter injury and execute end to end anastomosis. Defective segment is completely detached, proximal ganglionated colon and anal canal are left in the normal anatomical position.<sup>[12]</sup>



### Modified Duhamel operation

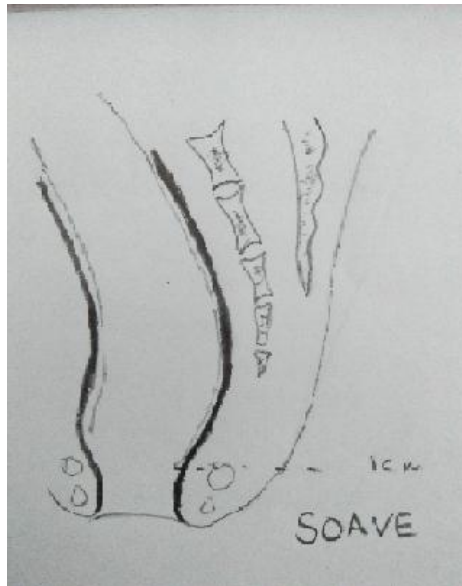
In this operation resection of upper portion of the rectum and a segment of colon; anastomosis of colon to posterior portion of the lower rectum and crushing the spurs to generate the rectal pouch. It is practically simple and a retro-rectal pull through. A new pouch is formed by anterior part of aganglionic rectum and by ganglionic proximal pulled down colonic segment. Biopsy should be obtained from proximal pull down to see for confirmation of ganglions. Pulled down proximal colon is sutured to full thickness posterior anal canal just superior to the dentate line. Spur between two colonic segments is crushed by Kocher's forceps or specialized instrument to generate a solitary pouch.<sup>[1]</sup>



### Soave Procedure

This procedure is consisted of making a circumferential cut via the muscular coat of the colon at the pelvic peritoneal reflection. Moving in an intramural plane, the mucosa is isolated from the muscular coat till the anal canal. The freed mucosa is excised and the proximal normal colon is pulled through this conserved viable spastic aganglionic muscular sleeve. A

telescoping type of anastomosis is created that adds an extra layer of colonic wall at the anastomosis site. Marks, paediatric surgeon, trimmed the sleeve posteriorly, this procedure is extensively practiced nowadays. Moreover Boley modified the method by creating an extra pelvic anastomosis between the anal canal mucosa and the mucosa of the normal colon.<sup>[12]</sup>



### **Laparoscopic pull through**

Laparoscopy in HD was being performed in 1992 and initially it was confined to biopsy, followed by a minilaprotomy and pull through procedure.<sup>[15]</sup>

The prime laparoscopic approach to pull through surgery was stated in 1995 by George son. A laparoscopic biopsy is performed to recognise the transition zone that followed by laparoscopic mobilization of rectum below the peritoneal reflection and than endoscopic dissection of the colon and rectum. A short mucosal dissection starting at the dentate line is practiced and the rectum is then prolapsed through the anus with the anastomosis done transanally.

This procedure has been linked with shorter hospital stay and early outcome to open procedures.<sup>[4]</sup>

### ***One-Stage Trans anal Endorectal Pull- through Procedure***

In this procedure anal canal was exposed with Loan-Star anal retractor. A circumferential row of sutures was embedded proximately 0.5 to 1 cm above the dentate line. The rectal mucosa was dissected just distant to the traction sutures and lifted circumferentially utilizing refined



diathermy needle to create the submucosal plane after that dissection was smoothly extended proximally by adopting blunt dissection and cauterization of submucosal invading vessels. The traction on mucosal tube aided proximal extension of mucosal dissection till the level proximal to peritoneal reflection (roughly 10 to 15 cm above the dentate line). Four stay sutures were inserted to handle the upper end of muscular cuff, which was dissected circumferentially permitting exposure of the full-thickness sigmoid colon. Mobilization of the colon was continued as proximal to the grossly evident or histologically affirmed transition zone as feasible by dividing the rectosigmoid vessels after cauterizing them. The extensive seromuscular cuff was inverted outside the anus and reduced to less than 5 cm in length before reverting it to its normal position. After excision of the aganglionic segment, the normally innervated bowel was pulled through the muscular cuff and anastomosed to the remaining mucosa superior to the dentate line.<sup>[11]</sup>

The Trans anal technique has scanty complications, fewer analgesia and is linked with decrease hospital stay and early feeding.<sup>[4]</sup>

According to international pediatric endosurgery guidelines for laproscopic approach in 2004, implementation of laproscopy enabled the surgeon to cautiously use the approach of pull through while omitting the considerable root of morbidity, which consists of colostomy and its complications. Post-operative abrupt and delayed problems for example wound dehiscence, wound infection and intestinal adhesion obstruction. Laproscopic procedure averts the internal and external scarring. There is brisk recovery and minor perianal excoriation. Overstretching and injury of anal sphincter during rectal dissection exclusively in neonates, which progressively recover with time and this can be prevented by a laproscopic rectal dissection procedure.<sup>[16]</sup>

### **Long segment Hirschsprung Disease**

There are following procedures for long segment Hirschsprung disease such as straight pull through, colon patch, J-pouch construction, Martin's procedure and Kimura procedure etc.<sup>[4]</sup>

### **Complications**

Post-operative issues include wound infections, intra-abdominal bleeding, intestinal perforation, bowel obstruction recto vesical and rectovaginal fistulas and enterocolitis etc.<sup>[4]</sup> About 60% of patients have complications after corrective surgery. In the prompt postoperative interval, 50% of patients have fecal soiling and diarrhea independent to

obstruction, which usually return to normal over several months. This can be managed with fiber to give bulk to stool and loperamide to decelerate colonic transit. During this transition, young children may have extreme perianal excoriation that can be cured with a barrier cream such as zinc oxide.<sup>[10]</sup>

Long-term obstructive complications promote constipation can result from anastomotic stricture, achalasia of the anal sphincter, or residual aganglionosis. Patients can also have fecal incontinence of varying extents, or intermittent enterocolitis. Children with these long-term complications needs a multidisciplinary strategy coordinated care with a pediatric gastroenterologist, pediatric surgeon, nutritionist, psychologist, and the primary care provider.<sup>[10]</sup>

- *Anastomotic stricture* can arise due to stenosis of the rectal cuff or from anastomotic seepage. Anastomotic stricture has been prevented and/or cured with daily anal dilation at home by the parents using an anal dilator or digital manipulation. However, predominantly in older children, this routine can cause psychosocial problems. Temple observed that weekly anal dilation in the surgeon's office let parents remain in the role of protector and was just as effective as daily dilations.
- *Anal sphincter achalasia*, or persistent neurogenic spasm of the internal sphincter, is illustrated by constipation and fecal incontinence. The pediatric surgeon will inject botulinum toxin (Botox) injections for achalasia. Basson and colleagues observed that Botox injections had a 36% achievement ratio (in 4 out of 11 patients with Hirschsprung disease) for achalasia. Instead, anal sphincter achalasia can be managed with topical nitrous oxide or posterior myomectomy. Areas of residual aganglionosis may be overlooked in the initial surgery because of patchy areas of normal bowel at the transition zone. If reason of chronic constipation is residual aganglionosis, a repeat pull-through operation or a permanent colostomy may be obligatory.
- Constipation from obstruction can be treated with meticulous bowel management with fiber, adequate oral hydration, and laxatives. For patients with serious constipation, the Malone antegrade colonic enema procedure, permitting colonic irrigation from the ileocecal junction, had a 100% achievement rate in 10 patients with Hirschsprung disease, and offers autonomy for older children.
- *Fecal soiling*, even not severe, can have a remarkable psychosocial effect on children with Hirschsprung disease, triggering embarrassment and social isolation. Odd anal sensation due to residual aganglionosis or as a sequela to surgery. Soiling turns into a

problem when the anal sphincter is damaged during surgical procedure or secondary to constipation with overflow incontinence. Soiling improves with time; though, this is a postoperative trouble to some degree for more than 50% of patients during childhood.<sup>[4]</sup> Remarkable impairment of fecal control is prevalent after transanalendorectal pull through in HD patients during childhood but symptoms lessen with age. However, impairment of emotional and sexual domains may be common in adulthood.<sup>[14]</sup>

- *Enterocolitis* can be recurrent and hard to treat long-term. Elhalaby and fellows observed that recurrent postoperative enterocolitis occurred in 38% of patients who had enterocolitis preoperatively. Enterocolitis must be managed with urgent resuscitation, bowel rest, antibiotics, and a diverting colostomy if required.<sup>[10]</sup>

Children should follow up at least they are beyond toilet training process in order to recognize and offer early treatment of these dilemmas. Nevertheless of most of these issues resolve after the 5 year of age and greater number of cases report fair outcomes. Patients with long segment disease, down syndrome and comorbidities have poor experimental outcomes.<sup>[4]</sup>

## CONCLUSION

Timely detection and treatment of the disease will promote better quality of life and may deter potentially deadly complications. In an infant or young child with stubborn constipation from birth, which is resilient to conservative management, Hirschsprung's disease is a diagnosis which needs to be ruled out.<sup>[13]</sup> All the methods described above had complications. Proper management of complications will drop the degree of severity and offer much better life.

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