CHAPTER 76
HIRSCHSPRUNG'S DISEASE

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Introduction

Hirschsprung's disease (HSCR or HD) may be defined as a functional intestinal obstruction resulting from the congenital absence of parasympathetic ganglion cells in the myenteric plexus of the distal bowel.

The initial description of congenital aganglionosis (Hirschsprung's disease) by Harald Hirschsprung, heralded as the Father of Danish Paediatrics, in 1886,[1] could not have anticipated the worldwide interest it would evoke. Successful treatment of the condition had to wait for 50 years until the pivotal role of the distal aganglionic segment and its vital role in the pathophysiology of Hirschsprung's disease was identified.[2,3] The development of successful surgical management in the same year[4] has made HSCR one of the success stories of paediatric surgery in the modern era.

Demographics

Hirschsprung's disease is a congenital cause of functional intestinal obstruction mostly diagnosable at birth but often presenting late in resource-poor environments.[5] It has long been regarded as a special condition in Africa, often presenting with advanced disease and malnutrition (the oldest patient we have encountered is 21 years of age). In Africa, patients often present following failure of traditional herbal enemas to afford relief. It may be difficult to separate from other conditions of megacolon, particularly in Africa where it may present in a way similar to other conditions, such as degenerative leiomyopathy. As a result, many believe that there is a special phenotypic expression in Africa. Although difficult to prove, there is a suspected interethnic variation in terms of genetic haplotypes within the promoter region of the REarranged during Transfection (RET) proto-oncogene in African patients. This is based on extrapolated data and has yet to be substantiated in Africa itself.

The HSCR incidence worldwide is approximately 1 in 5,000 live births. This has been substantiated in South Africa, where large series have reported a frequency of approximately 1 patient in every 5,726 live births, with all ethnic groups being affected.[6,7] The male-to-female ratio is approximately 4:1 overall worldwide, but appears to vary between the various ethnic groups represented in South Africa.[6] This ratio was 3.6:1 in caucasians and 3.9:1 in black African patients, but dropped to 2.5:1 in those of mixed descent, where a greater proportion of females were observed. The male-to-female ratio is also affected by the length of the aganglionic segment, which approaches 1:1 in total colonic aganglionosis (TCA). An overall male predominance is apparent, with incomplete gene penetrance and a variable phenotype.

Most babies with HSCR are born to mothers with a normal antenatal history (92%) with the majority having good Apgar scores. HSCR is mostly associated with big babies (average birth weight of 3,129 gm), and has been generally thought to be rare or absent in premature babies. This widely held belief has not been substantiated in recent studies, although our series had 12.2% who weighed less than 2.5 kg at birth, but in only 3 (1.9%) could a gestational age <37 weeks (28, 32, 33 weeks) be documented.

Hirschsprung's disease has been described as a sex-linked heterogonous disorder with various degrees of severity. It has a variable pattern of inheritance, which includes dominant, recessive, and multigenic patterns of transmission.

Associated Anomalies

The reported incidence of HSCR-associated anomalies varies between 5% and 32%, with a mean of 21.1%; no associated link between associated anomalies and familial HSCR transmission has been observed. Twelve percent are associated with chromosomal anomalies; Down syndrome is one of the most frequent (5.82% on average). These genetic variations account for more than 50% of the observed abnormalities associated with HSCR. Other associated anomalies include congenital eye problems and other associated syndromes (e.g., Waardenburg syndrome, sensorineural deafness, neurofibromatosis).

Associated anomalies (see Figure 76.1 for relative frequencies) include gastrointestinal (GIT), central nervous system (CNS), genitourinary (G-U), musculo-skeletal, cardiovascular system (CVS), craniofacial, and skin.
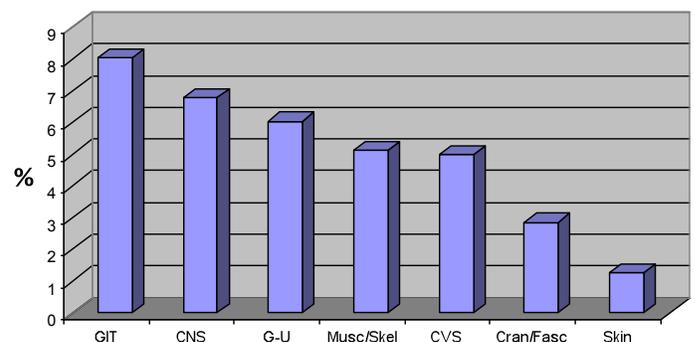

Figure 76.1: Hirschsprung's-associated abnormalities.

Although Hirschsprung's disease is described in association with several congenital abnormalities, there are two main reasons for their significance:

1. The majority may be attributed to abnormal genetic development signalling, yielding clues as to the genetic background of HSCR and its pathogenesis.

2. The influence of these associated anomalies on prognosis.

Familial Transmission

HSCR has a well-documented inherited familial predisposition (2.4–9%) and has also been reported in mono- and dizygotic twins. Affected families are known to carry an approximately 200 times higher risk of recurrence.[8] No significant difference is noted between male and female probands, but in our series, 50% of male TCA patients had a family history, transmitted through a female sibling in only two cases.

An association also exists between aganglionosis extending beyond the rectosigmoid and a family history (59% of familial versus 26% of the nonfamilial), with the frequency of TCA being significantly higher (P< 0.01) in the familial group. In addition, HSCR may recur in 15–21% of families with long-segment aganglionosis (L-HSCR), and as high as 50% in patients with ultra-long-segment aganglionosis (Zuelzer's disease). In our series, a progression of the length of segment was also observed in succeeding generations in two families.

The pattern of inheritance appears to vary in terms of the length of the affected segment, long-segment Hirschsprung's disease being considered to have an autosomal dominant inheritance pattern with incomplete penetrance (mostly RET; see nest section), whereas short-segment Hirschsprung's disease appears to be transmitted in an autosomal recessive manner or due to multiplicative effects of a number of involved genes.[9] In addition, several known associated syndromes are also inherited in an autosomal dominant manner.

Aetiology/Pathophysiology

The normal migration of neuroblasts in a cephalo-caudal direction within the bowel reaches the rectum by 12 weeks. Should the normal development be disturbed, a part of the colon will lack the normal ganglion cells and result in a functional loss of coordinated peristalsis, as occurs in HSCR.

At a molecular level, HSCR essentially appears to result from disruption of normal signalling during development. As a result, the cues controlling the migration of the neural crest cells go awry, resulting in aganglionosis of the distal bowel.

Current evidence would appear to support a large genetic component in HSCR aetiology. The patterns of conditions associated with HSCR have already been of great value in revealing many of the genetic components of the condition. Known genetic variations have been identified in at least 12% of HSCR cases which is higher than the expected in the normal population. Although much progress has been made in assessing possible mechanisms by which this gene malfunction may be involved in the pathogenesis of HSCR, the aetiology of HSCR is complex probably involving both genetic and microenvironmental influences in the development of the clinical phenotype. The extent of the complexity is shown by the number of genes implicated in its pathogenesis (at least nine). This is hardly surprising, as the signals governing cell migration and development in the embryo are extraordinarily complicated, and signalling molecules are notorious for crosstalk and redundancy.

Although the reason for the incomplete migration and development of ganglion cells is as yet not completely clear, the identification of major susceptibility genes (namely, the REarranged during Transfection (RET) gene and the Endothelin B receptor gene (EDNRB) and other genetic variations) have helped in understanding the aetiology of the condition. Ongoing research has identified a number additional HSCR susceptability genes (the EDNRB ligand EDN 3, the glial cell line derived neurotrophic factor (GDNF) situated at chromosome 5p12-13, and its related GFRα). In addition, the recently described association with PHOX2B and the SOX-10 gene on chromosome 22q13 and appears to synergise with the endothelin system in very long aganglionic segments.

Pathology

Hirschsprung's disease results in a functional obstruction of the bowel with dilatation of the proximal colon and hypertrophy of the muscles (i.e., megacolon).

Macroscopically, HSCR features a narrow aganglionic segment and a transitional zone, and then the dilated proximal portion with a thickened bowel wall as a result of hypertrophy of the muscular wall of the intestine.

HD classically affects the rectum and sigmoid (70%), but can also involve a long portion of colon and can affect the entire large bowel. In 20% of cases, a long segment of colon is affected, with the total colon being aganglionic in 8–10%.

Extensive ultra-long aganglionosis with extensive small bowel involvement is uncommon, occurring in <2%.

The functional abnormality always includes the internal anal sphincter and extends proximally for short or long distances, depending on the type.

HSCR, although regarded at one stage as a relatively easy diagnosis, has on occasion become "one of the most difficult diagnoses in Paediatric Surgery",[10] mainly due to difficulties in interpreting the histological, clinical, and radiological findings.

Histologic Diagnosis

The classic histological picture of Hirschsprung's disease is the absence of ganglion cells in intramuscular myenteric (Auerbach's) plexus and the submucosal Meissner's plexus. In addition, proliferation of peripheral nerves may also be seen in the affected bowel.

The method of suction biopsy initially described by Helen Noblett[11] allows specimens of the submucosal and mucosal layers to be obtained with minimal discomfort and without anaesthesia. A number of innovations to the biopsy forceps over the years have culminated in the availability of a superior tool with disposable capsules for specimen taking. This method, although reliable, is underutilized due to the expense of the disposable capsules. A more durable tool of the old-fashioned type is still manufactured, but can be difficult to locate (one possible source can be found at http://www.Trewavis.com.au/).

Biopsy specimens are taken at 2 and 4 cm (3 and 5 cm in older children). Failure to obtain adequate diagnostic yield on rectal suction biopsy will necessitate a full thickness biopsy, which causes problems during surgical procedures that require mucosal stripping (e.g., endorectal pull-through procedures). The biopsy specimens are then snap frozen and sectioned into slices ±15 μm thick.

Acetylcholinesterase Increase

Acetylcholinesterase (AChE) staining techniques remain the investigation of choice to evaluate suction biopsies to show an increased activity in the parasympathetic nerves of the affected zone as well as neurofibrils within the lamina propria and muscularis mucosa (Figure 76.1). This technique remains the gold standard on rectal suction biopsies in Europe and many parts of the world.

Because AChE staining techniques are mostly confined to specialized centres, many pathology units in Africa have a problem in obtaining access and rely on H&E (hematoxylin and eosin) staining, which may present difficulties in identifying immature ganglion cells from plasma cells or lymphocytes.

Interpretation of AChE staining may be influenced by the different patterns of AChE seen (particularly in neonates). The classic type A staining shows prominent AChE positive nerve fibrils throughout the lamina propria. The type B pattern shows similar AChE neurofibrils in the muscularis mucosa and neighbouring lamina propria.[12] Patients demonstrating the type B histochemical pattern may go on to display typical type A patterns after a few weeks.

Other immunohistochemical staining methods abound. NADPH-d immunocytochemistry yields a blue identification of both submucosal and myenteric ganglia.

The morphologic diagnosis of HSCR therefore rests on the following:

• Absence of ganglion cells in the submucosal layer (and/or intermyenteric (Auerbach's) plexus)

• Presence of the enlarged peripheral nerve trunks in the submucosa

• Increased AChE staining—proliferation of neurofibrils in the lamina propria and the muscularis mucosa (absent in normally innervated intestine; see Figure 76.2)
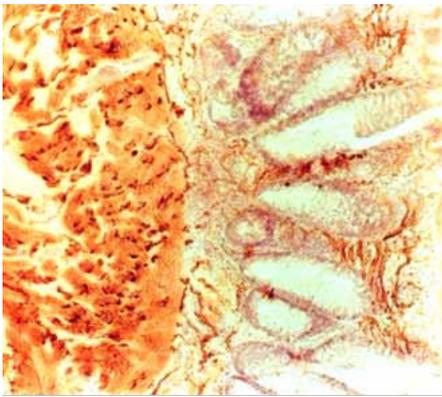
Figure 76.2: Acetylcholinesterase stain (Meier-Rüge), showing neurofibrils within the lamina propria in Hirschsprung's disease.

Clinical Features

The clinical evaluation of the patient remains the most important diagnostic step in the diagnosis of HSCR.

History

A delay in passage of meconium is the most important neonatal observation. Normal babies pass meconium within 24 hours, and a small percentage will also pass meconium by 48 hours. A significant delay in the passage of meconium after birth indicates a congenital cause. Any baby who has a delay in the passage of meconium of more than 24 hours or who passes little meconium should be investigated for HSCR.

Other signs in the neonate are a functional intestinal obstruction and bile-stained vomiting, often from day 2. In the older child in Africa, the main complaints are abdominal distention, constipation, wasting, diarrhoea, and retardation in growth.

A family history of HSCR or severe constipation are other significant factors. A family history is present in 4%, with a 61% possibility of a long segment. Other associated anomalies account for 16% of the cases of HSCR.

Physical Presentation

The clinical presentation depends not only on the length of the aganglionosis but also the age of the patient.

Neonate (50–80%)

- Most cases (>90%) present with signs in the neonatal period but are sometimes overlooked in poorly resourced health situations.

- In Africa, the number of neonatal diagnoses made may be as low as 10%.

- Intestinal obstruction presents with bile-stained vomiting and abdominal distention (often by day 2).

- Delayed passage of meconium is a presenting feature in more than 80% of patients with Hirschsprung's disease.

- Hirschsprung's-associated enterocolitis (HAEC) (16%) presents with bloody diarrhoea and mucus associated with abdominal distention and vomiting. The majority of cases of enterocolitis present during 2–4 weeks after birth. This is an important diagnosis because it accounts for 53% of the mortality arising from Hirschsprung's disease.

Older child (+10–50%)

- Some patients have early onset of mild constipation followed by acute low intestinal obstruction. The early onset of chronic constipation (often since birth) is an indication to exclude HSCR. Stools when passed are irregular and passed with great difficulty.

- Abdominal distention occurs in almost 100% (may be marked).

- Megacolon of the proximal colon is a classic sign of HSCR.

- The child does not develop normally and is often thin and malnourished.

- In contrast to the rectal findings in chronic constipation, the rectum is often empty on examination in HSCR and should the examining finger push beyond the aganglionic zone, there is an explosive evacuation of soft stool.

- Hirschsprung's-associated enterocolitis can also occur in the older patient or after surgery. This may lead to toxic megacolon.

- Secondary urogenital problems may occur in patients as a result of the chronic obstruction (e.g., vesicoureteric reflux, hydronephrosis).

Diagnostic Investigations

History and Examination

Look for clinical features of HSCR.

Abdominal X-rays

The diagnostic accuracy of abdominal x-rays is 52%.

- Look for signs of low intestinal obstruction and distended bowel loops of different calibres (Figure 76.3).

- Erect plates can demonstrate in fluid levels.

- A lateral view may demonstrate the narrow rectum.

Figure 76.3: Abdominal radiograph showing a low intestinal obstruction and varying distended bowel loops.

Contrast Enema

- A contrast enema is diagnostic in two-thirds of patients if low pressures are used. Irrigation of the colon before the contrast must not be performed as it may result in possible decompression of the megacolon or the distended bowel.

- The narrow aganglionic segment is shown with a dilated proximal bowel segment, and a transitional zone is diagnostic.

- Care must be taken not to apply pressure in neonates, as the bowel can easily be distended (Figure 76.4).

Figure 76.4: Underfilled contrast enema showing a narrow distal segment and distended proximal bowel (right).

- The aganglionic segment may be irregular, demonstrating a saw-tooth appearance, probably as a result of muscular fasciculations.

- A delay in the clearing of contrast (barium sulphate) within 24 hours is also a reliable sign, and a follow-up x-ray should be performed the following day.

Manometry

In normal people, distention of the rectum results in the reflex relaxation of the internal sphincter (rectosphincteric reflex; see Figure 76.5). This is absent on manometry in patients with Hirschsprung's disease.
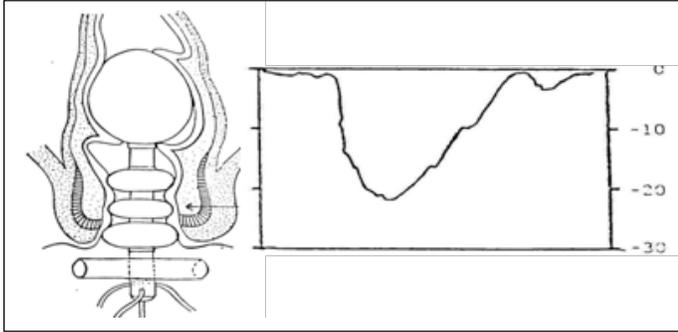

Figure 76.5: Manometric tracing showing normal rectosphincteric reflex.

Rectal Biopsy

See the section in this chapter on Pathology.

Differential Diagnosis

Differential diagnosis includes the following:

- Small left colon syndrome, particularly in diabetic mothers

- Meconium plug syndrome in neonates.

- Chronic idiopathic intestinal pseudo-obstruction (CIIP, or CHIPS)

- Other dysganglionosis of the gastrointestinal tract

- African degenerative leiomyopathy (ADL)[13]

- Acquired megacolon (generally at >1 year of age), resulting from anal fissure, anal or rectal stricture, anorectal malformations, tumour, or psychogenic reasons

Management

The standard surgical management of Hirschsprung's disease varies among centres.

The initial aim of management is to confirm the diagnosis. The patient is resuscitated and antibiotics are given (some children with enterocolitis have clostridium difficile infection).

The second aim is to correct the problem (i.e., relieve the intestinal obstruction) by means of definitive surgery. The aim of definitive surgery is to resect the abnormal aganglionic bowel and to anastomose normally ganglionated bowel to the rectum without affecting continence. Fluid and electrolyte losses are corrected and antibiotics commenced, if required.

Principles of Surgical Management and Results

A defunctioning colostomy (colostomy located at site of normal ganglionated bowel as determined by the presence of ganglion cells on frozen section) is the traditional way of relieving obstruction. This is then followed by a definitive pull-through procedure 3 to 9 months later.

Although a covering colostomy appears to decrease the incidence of infection, complications from the colostomy are not uncommon, including skin excoriation and bleeding from the stoma and prolapse.

In modern practice, temporary decompression is first attempted by means of washouts with warm saline. Should this be successful, it can be continued until definitive surgery can be performed. The recent swing to management by bowel irrigation techniques allows for early one-age surgery to be performed at a much earlier stage (mostly still within the neonatal period). Colostomy may still be necessary in resistant cases or if nursing care is unreliable.

Definitive pull-through surgical procedures have undergone numerous modifications since the original description by Swenson. Most of these modifications are based on the original concept described in 1948 by Swenson and Bill[4] and adhere to the principle of removing the functionally obstructive segment of aganglionic bowel and reanastomosis. In recent years, the endorectal pull-through (ERP) described by Soave[14] has gained popularity.

Neonatal Pull-Through

The current trend is for primary anal ERP either as a primary procedure or as a laparoscopically assisted pull-through procedure once the patient has been stabilized. Many argue for the latter because the laparoscope allows for histological mapping to identify the level of the transitional zone by biopsy It appears to make the procedure considerably easier in the neonate.

It would appear that neonatal pull-through is a safe and feasible method of treatment of Hirschsprung's disease and is suitable for those patients diagnosed in the neonatal period. Unfortunately, this applies to fewer HSCR cases in much of Africa. The remainder, who present with grossly distended megacolon, are probably best managed by surgical diversion of the faecal stream, allowing the chronically distended bowel to return to a normal calibre lumen before definitive surgical correction.

The major disadvantage of the one-stage neonatal pull-through procedure is that the determination of normal bowel is entirely dependant on frozen section histopathological evaluation. An expert pathological service is essential for this procedure to be carried out safely; the time taken for this procedure may vary but may add considerable delay. In addition, longer aganglionic segments present certain technical difficulties, resulting in a significant number of conversions to standard operative procedures.

Definitive Surgical Procedures

Five surgical procedures have received reasonably wide acceptance.

Swenson Procedure

This was the original operation described by Swenson in 1948. It involves resection of the aganglionic segment deep into the pelvis and direct end-to-end anastomosis of the proximal colon to the anorectal canal.

Duhamel Procedure

In the Duhamel procedure (retrorectal pull-through), the lower but aganglionic rectum is retained and the ganglionated bowel brought posteriorly and anastomosed to the aganglionic remnant in a side-to-side anastomosis.

Soave Procedure

The Soave procedure (extramucosal endorectal pull-through), along with its variations, is the most frequently performed procedure in the world for short-segment Hirschsprung's disease. See Figure 76.6. It has more recently been popularized as a laparoscopic-assisted or anal approach.

The procedure involves an extramucosal resection of a retained aganglionic rectal segment. The rectal mucosa is removed and a muscular cuff retained. The ganglionated colon is brought through this cuff and anastomosed to the dentate line in the rectum, thus forming an endorectal pull-through.

Rehbein Procedure

Largely abandoned, the Rehbein procedure (deep anterior resection) involves bringing the proximal ganglionic colon into the pelvis and anastomosed to the rectal stump by means of an end-to-end anastomosis higher than in the other operations (i.e., at the level of the levator ani muscle). It is very similar to the low anterior resection performed in adults.
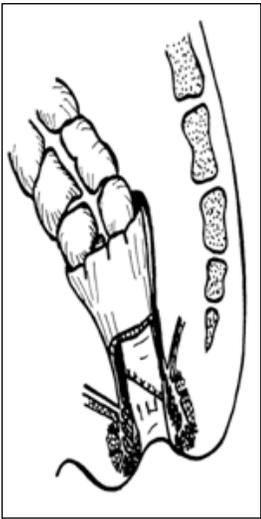
Figure 76.6: Soave procedure.

Transanal Pull-Through

The transanal pull-through approach is through the anus, thus avoiding abdominal scars. It is currently in vogue in many parts of the world, being mostly suited to a short aganglionic segment. It is similar to the Soave procedure, but is performed in reverse through the anus.

The technique involves the patient being placed in lithotomy and the rectum irrigated until clean. Retraction sutures are placed to expose the rectal mucosa and open the anus. Submucosal dissection is commenced 3–5 mm from the dentate line and the cut line controlled by multiple fine traction sutures. Following the completion of the submucosal dissection, the rectum is transected. The dissection is continued proximally until the peritoneal reflection where the sigmoid colon is mobilized and delivered. Following histological confirmation of ganglion cells in the proximal bowel, the aganglionic segment is resected, and a sutured anastomosis is performed. Many recommend a laparoscopic first stage to mobilize the bowel and perform biopsies to facilitate the resection margins.

Postoperative Complications of Hirschsprung's Surgery

Early postoperative complications appear to occur at a similar rate regardless of the age at surgery. The majority of reports of neonatal correction of Hirschsprung's disease describe initial experiences, and a paucity of long term-data exists. The Toronto group[15] have shown that the complication rate of single-stage repair was unaffected by whether the repair was performed prior to or later than the neonatal period, and the short-term outcome was similar for those weighing less than 4 kg.

There is a paucity of long-term evaluations, although one large study[16] reported a 6% incidence of postoperative enterocolitis and a 4% stricture rate. The overall long-term development of function (continence, sexual, and psychological) remains largely unevaluated.

Early Complications

Early postoperative complications include anastomotic insufficiency, stenosis, prolonged ileus, adhesive obstruction, intestinal obstruction, and retraction of the neorectum. Wound sepsis may be present to varying degrees, and other complications of sepsis or pelvic or presacral abscesses may be evident. Acidosis may be associated with excessive fluid and electrolyte losses in long-segment disease, and enterocolitis associated with Hirschsprung's disease may be present. Early complications following the Soave procedure are a reported higher rate of anastomotic leakage (4–7.7%) and stenosis (9.4–23.7%) compared with other procedures.

Late Complications

It is essential that the operative details are available in the assessment of long-term complications, so that like can be compared with like. The evolving nature of the surgery of Hirschsprung's disease should be borne in mind, as it has evolved from the original three-stage procedure to a two-stage and now one-stage (mostly neonatal) pull-through (often laparoscopic assisted). These technical advances have largely altered the nature and frequency of early complications, and it would appear from available evidence that the newer modifications give a lower incidence of enterocolitis and stricture formation. Reliable data and evaluation of late complications are largely unavailable regarding constipation incidence, continence, social integration, and sexual function, among others.

It is generally recognised that the major long-term complications in the postoperative period following Hirschsprung's surgery are constipation and Hirschsprung's-associated enterocolitis. The long-term incidence of constipation approaches 9% following almost all surgical procedures, but this figure may be considerably influenced by certain procedures with a well-established higher incidence of constipation (e.g., the Rehbein procedure). The incidence of postoperative constipation is one of the most practical methods of measuring successful therapy, although its assessment is often highly subjective. The true incidence may , in fact, be hidden, due the fact that many patients receive some form of treatment (e.g., stool softeners, etc.). Postsurgical obstructive symptoms must be separated from HAEC because diarrhoea and enterocolitis may persist into the postoperative period (especially following extensive gastrointestinal (GI) involvement such as TCA). The incidence of HAEC may also be influenced by obstruction due to the presence of stenosis or cuff strictures.

Constipation and obstructive symptoms may be related to a number of possible causes, which include a residual aganglionic segment, sphincter achalasia, associated dysganglionosis of the enteric nervous system, strictures, restrictive cuff following ERP, retained spur following Duhamel procedures, "acquired" aganglionosis, and other functional causes. Most large series include a small number of patients with incomplete resection of the aganglionic segment (namely, 2.2% for the Soave procedure; 3.6% and 3.8% for the Swenson and Rehbein techniques, respectively; and 1.2% following the Duhamel procedure), and repeat biopsies may be required to ascertain the status of the pull-through segment.

In many cases of postsurgical obstructive symptoms, failure to identify a cause on routine clinical and pathologic investigations suggests some degree of sphincter achalasia due to the failure of the internal sphincter to relax. Sphincter achalasia may be difficult to treat, and previous attempts at repeated anal dilatation have had mixed success. We have found the topical application of a glyceryltrinitrate paste to be fairly effective, and it is a cheap alternative to the injection of botulin toxin advocated by some.

Although the majority of patients do well following the modified surgical techniques currently employed for treating HSCR, some patients experience some degree of lack of control on follow-up. The incidence of incontinence following the ERP technique appears to be low, although sufficient long-term follow-up is as yet not available to assess the long-term outcome of neonatal or the transanal ERP techniques. Intermittent soiling may be associated with constipation, diarrhea, and a faeculoma, thus appearing to be related to overflow rather than inadequate sphincters. Some may be attributed to ill-advised sphincterotomy (largely historical).

There is a reported incidence of 0–9.7% of patients with genitourinary symptoms such as enuresis, incontinence of urine, dysuria, and impotence. The possibility that this could have resulted from damage to pelvic nerves (especially with techniques involving extensive pelvic dissection) has largely been confined to historical series. It has also

been suggested that these symptoms may be related to psychological disturbances associated with long periods of hospitalization and trauma.

A relationship with perirectal abscess formation has been reported, and postoperative septic complications resulting in subsequent perianal fistulas appear to be uncommon, although they have been reported in isolated cases following the Swenson, Duhamel, and Soave procedures.[17]

Mortality, although uncommon, has been reported in 1.5–2.8%, depending on the surgical procedure employed. This can be partly influenced by HAEC and Down syndrome (where the mortality rate approaches 26%).[18,19]

Management of Special Problems

Enterocolitis management
Avoid surgery in the acute stage of HAEC because it may result in an increased incidence of complications. Management of HAEC includes resuscitation, antibiotics, decompression (6-hourly), and colostomy when stabilized.

Total colonic aganglionosis
Total colonic aganglionosis poses special problems due to the length of the bowel involved. It is usually treated by means of an ileostomy, a subsequent anal pull-through procedure with preservation of some aganglionic bowel, and anastomosis by means of a long side-to-side anastomosis.

Other
Obstructive symptoms may occur in the postoperative phase with recurrent episodes of abdominal distention associated with watery diarrhea.

Prognosis and Outcome

Ethical Issues
- Hirschsprung's disease is surgically correctable, and the majority of patients with the disease can live productive, satisfying lives.

- Physical growth and development generally approximate normal.

- Intellectual function is mostly good.

- Most HSCR patients (93%) achieve acceptable anorectal function, given sufficient time to adjust.

- Long-term functional results are excellent in some, good in the majority, and poor in approximately 15–30%.

- Functional results depend on the length of aganglionosis, procedure performed, surgical complications, social circumstances, family support, and associated anomalies, among other factors.

- Psychological problems may be magnified in those with poor support systems.

- Ethical issues do arise in cases of very long aganglionic segments, leading to intestinal failure.

- Ethical issues may be pertinent in certain disabling associated anomalies.

- Genetic counselling (if not handled correctly) also has the potential for giving rise to ethical issues, but should not be handled in isolation.

Genetic Counselling and Prevention
Although genetic factors are clearly implicated in the aetiology of HSCR, no clear pattern of inheritance exists, and autosomal dominant, recessive, and multigenic patterns have all been reported. This all strongly suggests a multifactorial and multigenic HSCR aetiology, and the majority of HSCR cases can be classified as complex genetic disorders for which familial aggregation is observed with variable Mendelian inheritance. Genetic counselling via pedigree analysis alone is particularly difficult in such a multifactorial condition, as it may be affected by a number of other unrelated factors (e.g., small family size, poor history, and adoption, as well as the lack of an identifiable genetic mutation). As a result, practical therapeutic interventions still appear to be mostly unattainable.

Nevertheless, apart from being an integral part of the ethics surrounding DNA testing, genetic counselling has become highly sought by families at risk. It is currently mostly carried out on empiric grounds. This will help to drive the process forward and DNA analysis of at least the major susceptibility genes in the family is an achievable goal. Should a major genetic defect be detected in this manner, the door is open for foetal genetic testing and evaluation of risk.

Key Summary Points

1. Hirschsprung's disease (HSCR) occurs in 1 out of every 5,000 live births worldwide.

2. HSCR is a functional intestinal obstruction occurring most frequently in large, term babies.

3. The male-to-female ratio is approximately 4:1 overall, but approaches 1:1 in long-segment Hirschsprung's disease (L-HSCR).

4. The aetiology is multifactorial, with genetics playing a major role.

5. The family recurrence varies between 4% and 9%.

6. The main susceptability gene is the REarranged during Transfection (RET) gene on chromosome 10 (10q22), but at least nine other genes have been implicated (including the Endothelin B receptor (EDNRB)).

7. The disease is caused by the congenital absence of ganglion cells (aganglionosis) in the distal bowel (histopathologically).

8. Aganglionosis may be confined to the rectosigmoid area in >70% (short-segment; S-HSCR).

9. Aganglionosis may extend up the large bowel for varying lengths (long-segment; L-HSCR) and may involve the entire colon (total colonic aganglionosis, or TCA), and even up the small bowel.

10. The majority of affected patients present with delay in the passage of meconium after birth, constipation, and abdominal distention.

11. Hirschsprung's-associated enterocolitis (HAEC) is a serious complication that contributes to morbidity and mortality.

12. Surgery involves relief of intestinal obstruction, confirming the diagnosis, and a corrective pull-through surgical procedure.

13. The majority of patients with Hirschsprung's disease are surgically correctable and can live productive, satisfying lives.

14. Most HSCR patients (93%) achieve acceptable anorectal function, given sufficient time to adjust.

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