Hirschsprung’s Disease: Stimulating surgical investigation for over a century

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Since Harald Hirschsprung’s classical description of congenital megacolon in 1886, Hirschsprung’s disease has challenged pediatric surgeons to the present day, spurring a century of pathological and surgical investigations. Initially the focus was on the megacolon, which could reach spectacular dimensions. It was not until 1949 when Boston surgeon Ovar Swenson demonstrated the absence of peristalsis in the rectosigmoid that the pathogenesis was established and rational surgical strategies could be devised.

First description

Frederick Ruysch first described Hirschsprung’s disease in 1691 as the phenomena of an extremely dilated colon.\(^1\),\(^2\) However, this disease was eponymously named after Harald Hirschsprung (Figure 1) who presented the first comprehensive description of the clinical histories of two infants with fatal constipation at the Society of Pediatrics in Berlin in 1886. In his original description Hirschsprung describes the pathologic appearance of the colon from an 11 month old child as “not only dilated, but the wall is also greatly hypertrophied, especially the muscle layer.”\(^3\),\(^4\) Although there were a handful of prior reports on congenital megacolon, Hirschsprung’s classical descriptions officially recognized this disease entity in the medical community. Few diseases in pediatric surgery has stirred as much disagreement and misunderstanding as the pathophysiology and optimal treatment of Hirschsprung’s disease.

Pathogenesis debated

Following Hirschsprung’s publication many prominent surgeon-scientists offered their opinions. There were three major theories regarding the etiology of Hirschsprung’s disease. Hirschsprung and his associate Mya, who first coined the term “congenital megacolon,” put forth the malformation hypothesis. They believed congenital dilatation and hypertrophy of the colon was the root cause of this disease.

Marfan and Treves were among those who thought that the colon became obstructed by some kind of mechanical obstruction. The redundant and dilated colon, particularly the sigmoid, caused enlargement of the rest of the colon present in their patients. In 1905 Perthes offered evidence that the colon formed valves that led to a functional obstruction.\(^5\)

In 1900 Lennander began to venture close to the current view when he proposed that a deficiency in the innervation of the bowel as the cause of colonic obstruction.\(^6\) Given the knowledge of the time he saw two possible neurogenic causes: Parasympathetic inhibition and sympathetic hyperfunction. Evidence for parasympathetic inhibition was experimental evidence of megacolon developing following resection of parasympathetic nerves distal to the colon in animals in 1926.\(^7\) Clinical observations in the 1930s reported colonic dilatation developing in patients treated with atropine, at the time interpreted as evidence of autonomic dysfunction as contributing to Hirschsprung’s disease.\(^8\)

Theories in practice

The debate on pathogenesis had a practical basis – it would dictate a rational surgical solution. Based on Hirschsprung’s view the 19th century solution was surgical resection of the
dilated colon. However, the distal segment still presented a functional obstruction. It is no surprise that nearly all patients so treated failed to improve and many died. Still, those ascribing to Hirschsprung’s malformation theory continued to resect the dilated colon into the early 20th century. Other operations included removal of rectal valves or folds that would be created by crimped loops of bowel and bypass operations to exclude problematic segments of the colon.4

Those who held a neurogenic basis for the disease tried to improve colonic peristalsis. Lennander observed an enterprising attempt to pass electrical current through an enema in a 4-year-old boy. The boy passed stool, perhaps out of a desire not to have the procedure repeated as the faradization itself can be extremely painful.

Addressing the supposed parasympathetic deficiency, others proposed parasympathomimetic drugs. Law and colleagues in 1940 administered acetyl-beta-methylcholine bromide to treat Hirschsprung’s disease. Despite the toxicity of his treatment, he believed his treatment was a success.9

On the other end of the autonomic nervous system, lumbar sympathectomy received attention during the 20s and 30s. Telford and Haxton reported improvement in constipation following treatment with spinal anesthesia and lumbar sympathectomy in patients with spastic paraplegia.10 The latter operation was advocated by Ladd and Gross in their landmark text in 1941.11 Despite some successes, failure was more common.

Intestinal peristalsis and innervation

In 1901 Tittel focused on the intrinsic nervous system in the first histologic study of Hirschsprung’s disease.12 He found that the colon lacked nerve plexuses, although the innervation to the ileum appeared normal. Given the current understanding of the disease, it comes as no surprise that his findings were refuted at that time. Other investigators found ganglion cells in the colons in their specimens, in retrospect clearly coming from patients with short segment disease or with functional constipation.

The debate resurfaced in 1940 when Tiffin and co-workers called attention to the absence of ganglion cells in the myenteric plexus of a patient with congenital megacolon.13 Despite these findings, opinions regarding the significance of the absence of ganglion cells were slow to change. As late as 1970 Ehrenpreis argued that the lack of ganglion cells was as a result of colonic dilation instead of the cause.4

Orvar Swenson

Educated at Harvard Medical School and with residency training from the Peter Bent Brigham hospital, Orvar Swenson (Figure 2) was recruited in 1945 to set up a surgical research laboratory at The Children’s Hospital by its chief of surgery, William E. Ladd. Swenson became particularly interested in children who were slowly dying with megacolon without an effective treatment.

In a 2003 interview he remembered a young child with abdominal distention who was believed to have inflammatory bowel disease. Ladd performed a colostomy and the patient’s distention resolved.14 Swenson knew that Sidney Farber, pathologist and famed cancer researcher, had equipment to measure intestinal peristalsis. He used it to study intestinal peristalsis through the child’s colostomy. Surprisingly, his tracings demonstrated active contractions, where tracings in the colon distal to the stoma demonstrated no peristalsis. Swenson thus made the crucial discovery that patients with Hirschsprung’s disease, rather than a mechanical obstruction, had a functional one.14

He reviewed the contrast studies of megacolon patients with Edward Neuhauser, radiologist at The Children’s Hospital. Most of the colon were hugely dilated, but they couldn’t make out the rectum and sigmoid in the studies. Swenson proposed placing contrast into the rectum as an enema.14 They found that the rectum and sigmoid in many of the patients were patent but normal in caliber, compared with the much larger distended proximal to that level. This finding would become the standard imaging study for the diagnosis of Hirschsprung’s disease.15

Knowing that children with megacolon improved after colostomy, surgeons at The Children’s Hospital began to do the procedure only to find that obstruction recurred when the stoma was later closed. Swenson decided for his next patient...
with megacolon he would bring the stoma down to a level as close to the anus as possible, in effect performing a colo-anal anastomosis above the dentate line, the procedure that would later be known as the Swenson procedure.\(^{16}\)

Swenson faced extensive criticism when he explained what he planned to do. He recalls being told, “You’re going to ruin these patients; they’ll have urinary incontinence; they’re going to have sexual problems.”\(^{14}\) Robert Gross, who had assumed the position of chief of surgery upon Ladd’s retirement, tried to take over care of Swenson’ patient. The mother refused and Swenson went on with the operation. The child did well, and Swenson went on to do the procedure on six other megacolon patients languishing on the hospital wards.\(^{14}\)

Five of the six did well. One did not. Repeating the barium enema, there was an area of constriction that had been left behind. Swenson had the crucial idea of doing an intraoperative biopsy to confirm the presence of ganglion cells at the level of the bowel being connected to the anorectum. In yet another innovation that would define the management of the disease was to perform a rectal biopsy to confirm the diagnosis. “Well hell, the thing to do is to do a rectal biopsy!” he remembered thinking.\(^{14}\) The test would become standard in the diagnosis of Hirschsprung’s disease and a necessary part of its intraoperative management.\(^{16}\)

Discussing the idea with Gross, however, was a mistake. The chief became angry. “Swenson,” he said, “I forbid you to do this either on your own patients or on a ward patient in this hospital. You’ll end up with a lot of infection and trouble that I don’t want.”\(^{14}\) Swenson went on to do the biopsies. And within months he was out of a job, his office taken away from him by Gross.\(^{14}\) He moved across town to the Floating Hospital for Children at Tufts University School of Medicine and continued to treat generations of children with megacolon.\(^{17}\)

Other operations

Once Swenson demonstrated the pathophysiology of Hirschsprung’s disease and devised an effective surgical approach, other surgeons devised successful operations that addressed some of the difficulties posed by his procedure. Despite its success the Swenson procedure was an extensive and difficult operation that had a high mortality when performed in infants. Surgeons were concerned that the deep pelvic dissection around the anorectum risked anastomotic leak, incontinence, and sexual dysfunction.

In 1956 Duhamel proposed excluding the rectum, bypassing it by bringing the ganglionated segment to the posterior aspect of the anorectum through the retrorectal space. The retained anorectum and the pulled through segment was connected side-to-side by crushing the two using a pair of clamps left in place, handles emerging from the child’s anus until the walls annealed weeks later.\(^{16}\) Modifications to the Duhamel procedure included placing the anastomosis above the internal sphincter to address postoperative soiling\(^{16}\) and the use of stapling devices to connect the native anorectum with the pulled through segment, saving the infant the hassle of having clamps dangling from his or her anus.\(^{19}\)

In 1962 Soave described the technique of separating the mucosal layer of the anorectum from the seromuscular layer and bringing the ganglionated segment through the sleeve of muscularis that remained.\(^{20}\) The technique had been devised by Sabiston and Ravitch in 1947\(^{21}\) and had been applied to an adult patient with Hirschsprung’s disease by Yancey 10 years previously in 1952.\(^{22}\) Soave left the pulled through colon hanging out the infant’s anus for 10 days to facilitate adherence of the pulled through colon to the mucosa of the anorectum before it was trimmed away. Boley did away with that step by everting the mucosal remnant and bringing the pulled through segment out with it, allowing a direct anastomosis outside the perineum.\(^{23}\) Another technique for resecting the rectosigmoid was proposed by Rehbein in 1958, in effect doing a low anterior resection less extensive than Swenson’s original operation.\(^{23}\)

With improvements in the anesthetic and critical care of newborn infants, surgeons began to perform pull through procedures earlier in infancy and finally in the newborn period. Cilley and Coran began to do one-stage pull through procedures routinely in the first weeks of life in 1994.\(^{25}\) In 1998, De la Torre-Mondragon and Ortega-Salgado described a single stage transanal pull-through procedure by starting a submucosal dissection just above the dentate line, in effect doing a Soave procedure from below. A muscular sleeve thus is created to allow mobilization of the rectum and sigmoid colon down and out of the anus, full thickness biopsies obtained to identify the transition zone. Once ganglion cells are identified, the ganglionated segment is sutured to the rim of anal mucosa. One patient was under one month of age, another was a month-and-a-half, demonstrating that the procedure was appropriate in infants.\(^{26}\)

Conclusion

The 130-year history of Hirschsprung’s disease exemplifies the perseverance and dedication of surgeon-scientists to investigate its pathology and to pursue a rational basis for appropriate surgical management. Swenson’s fresh interpretations of what he was observing in his patients, the originality of his use of diagnostic biopsy and imaging, and his bold surgical solution combine to form one of the landmark achievements of a single individual in pediatric surgery. Research into the molecular genetics of Hirschsprung’s disease has brought the understanding of the pathology of the condition into the modern era.\(^{27}\)
References


Legend

1. Harald Hirschsprung.

2. Orvar Swenson. Digital Collections and Archives, Tufts University.