Pediatric Surgery

Hirschsprung's D isease

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In 1986, an international panel met in Calcutta to take stock of the advances that had taken place in our understanding of Hirschsprung's disease (HD). .This disease was described exactly one hundred years earlier by Harald Hirschsprung, Professor of Pediatrics at the University of Copenhagen in a paper entitled "Sluggishness of stool in the newborn resulting from dilatation and hypertrophy of the colon". The disease began to be known eponymously as Hirschsprung's disease, although Hirschsprung was not the first to describe this condition and nor did he know anything about its pathogenesis or its treatment(l).

In 1948 came a double breakthrough. Orvar Swenson, then the junior most member of the surgical team at the Boston Children's Hospital, showed by a special radiological technique that in all 20 of his patients with HD, there was an area of spasm in the rectosigmoid or rectum at the lower limit of the area of dilatation of the colon. He then proceeded to treat one of them by resecting this segment of narrow bowel and anastomosing the dilated and hypertrophied bowel above to the anal canal, thereby effecting a permanent cure. At about the same time, other workers(2) demonstrated that ganglion cells were absent in the intrinsic plexuses of all the spastic segments examined. Thus, the megacolon was shown to be the effect and not the cause of the disease.

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It thus became possible to define HD as a disease in which resistance is offered to the onward passage of bowel contents by a segment of distal bowel in which there is a congenital absence of ganglion cells. The length of the segment affected may vary from the proximal centimeter of the anal canal to the entire intestine. The intensity of the resistance may also vary and is not directly related to the length of segment affected. The disease commonly extends proximally up to the rectum and sigmoid, and the colon above is dilated and hypertrophied. However, in about 20% of patients, the aganglionosis extends further. When the aganglionosis affects the entire colon, there is no segment of megacolon, but this is a rare condition.

Prior to 1967, my experience with HD was limited to 6 patients. Five were very sick neonates with huge abdominal distension, constipation and vomiting; they all died after a right transverse colostomy. The only survivor was managed conservatively till the age of 18 months. Our earlier patients were mostly older children-stunted, malnourished, pot-bellied, constipated and miserable with episodes of diarrhea, vomiting and respiratory infections. Many of them would be taken away because the family would not agree to surgery, more specifically to colostomy. Later, we began to see infants and then neonates. Although a few of the neonates presented soon after birth in good shape, the majority were desperately ill with enterocolitis, pneumoperitoneum, unrelieved obstruction and

septicemia. In the period 1968 to 1973, 13 neonates died before any surgical procedure could be carried out; colostomy was done in 10, of these 7 died and only 3 could be prepared for definitive surgery. We also began to see adults. They fell into one of two categories; either they had survived inspite of neglect, or they had been managing reasonably well with conservative treatment but realized that earning a living or finding a spouse would not be possible without surgical correction.

Diagnosis

For the diagnosis of HD the conventional diagnostic parameters are elaborated below.

1. *History and Clinical Exami nation*

In the neonate, the diagnosis of HD is suggested by the history of delayed passage of meconium, abdominal distension and vomiting. In fact, meconium may not be passed at all and the obstruction may be complete. More often, the obstruction is relieved by the passage of a finger into the anorectum, a flatus tube, a suppository, a paan leaf stalk, an enema or bowel wash. It may recur instantly or after some time. The distended bowel may at times perforate, either spontaneously or during attempted decompression by a tube. The constipation may be replaced by severe diarrhea with toxemia, dehydration and electrolyte depletion. Unrelieved abdominal distension leads to respiratory complications.

Later, patients come with a history of recurrent obstructive episodes and remissions. An obstructive episode may be followed by an episode of severe diarrhea with dehydration and toxemia, or may progress to complete obstruction. Remissions may become shorter and the recurrences more and more severe. On the other hand, patients may reach a state of compensation and present with failure to thrive, protein-energy malnutrition and intercurrent infection.

By a thorough clinical examination, other common causes of intestinal obstruction like anorectal malformations, anal fissures, stenosis and space occupying lesions can be excluded. It is also possible to diagnose functional disorders like prematurity, hypothyroidism, Down's syndrome and spinal cord malformations; however, any one of these may co-exist with HD.

2. Radiology

A plain X-ray abdomen shows distended loops of bowel above the aganglionic zone, or air filled megacolon terminating in a narrow cone. The diagnosis of the disease as well as its extent is confirmed when barium enema is performed on unprepared bowel under fluoroscopic vision. This shows: *(a)* Disparity in caliber between the proximal dilated and the distal narrow segment of colon; *(b) A* cone at the junction between the two; and *(c)* Retention of contrast in the bowel even at 24 hours. A radiologist who only occasionally handles small patients will need the support of the surgeon during the study. An accurate .diagnosis will not be reached in about 10% of cases, particularly in neonates where the transition from the dilated to collapsed segment may not be very pronounced.

3. *Ano-rectal Manometry*

The normal internal anal sphincter responds to rectal distension by an initial contraction followed by relaxation. In HD, the contraction is sustained and not followed by any relaxation. The disease can be excluded if a normal response is obtained. A transducerised manometer developed by Varma *et al.(3)* can be used for this purpose but the results are far superior with the state of the art computerized re-

cording equipment presently available.

4. Histology

The diagnosis is clinched if ganglion cells are shown to be absent in areas where they should be present. Material obtained by suction biopsies from the ano-rectal junction allows a study of the submucous plexus; ganglion cells should normally be seen beyond 1.5 to 2 cm from the anal verge. The myenteric plexus can be reached only by a formal operation under general anesthesia; the ganglion cells here are normally larger and more numerous and hence it is easier for the pathologist to spot their absence.

The extent of the disease can be confirmed during laparotomy; the myenteric plexus from different segments of bowel are examined by obtaining pieces that include serosa and muscularis. Selection of the segment of bowel for histological examination is made after a macroscopic study of the loops. The presence or absence of ganglion cells can be reported on frozen sections. If reliable frozen section facilities are not available, the surgeon has to proceed on the basis of macroscopic findings and re-operate if examination of paraffin section proves him wrong.

5. *Newer Diagnostic Tools'*

These can be grouped under:

(a) Histochemical Methods: Significant increase of acetylcholinesterase activity in the nerve fibers of the lamina propria, muscularis mucosae and circular muscles of the bowel in the absence of ganglion cells has been seen in HD. A small mucosal biopsy at and above the pectinate line is sufficient to confirm the diagnosis after appropriate preparation and staining(4). Ganglion cells can be demonstrated by lactate dehydrogenase; with the use of succinic dehydrogenase, mature and immature cells can be differentiated(5).

(b) Immunocytoche mical Methods: A number of antibodies have been used to identify specific nerve fibers and neurotransmittors notably neuropeptide Y, vasoactive intestinal peptide and substance P. Similarly, ganglion cells can be identified by neuron specific antibodies like enolase and D7(6,7).

With the new diagnostic tools a number of Hirschsprung's like disorders have been identified. These include intestinal neuronal dysplasia(5,8) hypoganglio-nosis(9), internal sphincter achalasia(10), neonatal hollow visceral myopathy(11), and degenerative leiomyopathy(12). The first two conditions have been shown to co-exist with classical HD.

Management in the Neonate

Neonatal HD has to be managed as an emergency if there is enterocolitis, perforation or complete obstruction.

Enterocolitis is initially treated by decompression of the bowel using a soft wide flatus tube and irrigations with normal saline, together with intravenous fluids, antibiotics and parenteral nutrition.

We recommend immediate laparotomy and proximal decompression by the simplest possible method for complete obstruction or colonic perforation, and encourage the surgeon to do this on the spot rather than transfer if this involves delay; a routine right upper quadrant colostomy is recommended. The other neonates should be transferred to a pediatric surgery service.

If the obstruction has been relieved temporarily by conservative means and the cone is thought to be low down in the rectum or anal canal, we perform anorectal myectomy. The details of this operation are described elsewhere(13). Absence of gan-

glion cells in the lower half of a muscle strip removed from the upper anal canal and lower rectum confirms the diagnosis. Cure can be predicted if ganglion cells are found at the top end of the strip. In our experience, ganglion cells were absent throughout in all the 17 neonates examined. Of these 14 were relieved of constipation and have not required further operations; 2 had temporary improvement and could be prepared for a pullthrough and one was lost to follow up.

In all other situations, a planned colostomy is done. In the patients with the cone clearly identified at the rectum or lower sigmoid, a left lower quadrant incision is used. In all other situations the abdomen is opened by a paramedian incision. Exploration confirms the absence of lesions other than HD. The bowel if greatly distended is decompressed either through a flatus tube via the anus or through the amputated appendix. Samples are then taken for histological study. If the cone is not clearly identifiable, examination of frozen sections is most valuable.

In the last decade, there were 3 patients with total colonic aganglionosis; an ileostomy was done but none could be prepared for definitive surgery. In all the other 34 the disease was confined to the colon and colostomy was done about 4 to 6 cm. proximal to the cone; a loop colostomy with a skin bridge was done in most patients, a few had a divided colostomy. There were 3 postcolostomy deaths, all in low weight babies who had pneumoperitoneum, septicemia and enterocolitis. One baby is known to have died after being sent home and three have been lost to follow-up. All the others have had definitive surgery and are doing well; five of these had presented with pneumoperitoneum.

Two alternative methods of managing neonatal HD need to be considered. The first is conservative, namely bowel washes and laxatives till the baby is fit for an elective pullthrough. We have done this twice but our physician colleagues have often conducted this treatment themselves and involved us only when the patients reached a satisfactory weight. The other is to carry out a neonatal pullthrough which we have done successfully but only twice.

Management in the Postneonatal Period

The majority of patients were treated by abdomino-perineal pullthrough. Before advising this, we have asked ourselves two questions: *(i)* Could a lesser procedure suffice? and *(ii)* Is the patient fit for pull through?

(i) Anorectal myectomy has been done on 55 patients either because the Barium enema was inconclusive or showed a cone low down. This operation gave the diagnosis in all cases, cured 40, and offered palliation to the rest. There was no mortality and minimum morbidity.

(ii) Patients judged unfit for a primary pullthrough were treated by a preliminary colostomy. The colostomy was done 5 to 10 cm. proximal to the cone; the cone was obvious and frozen section study was not generally required. It was done on 37 patients in the last decade. Twenty-four were under the age of 1 year. Of these, 8 had pneumoperitoneum, 4 had complete obstruction, 2 had enterocolitis and 10 had protein energy malnutrition. Of the children over 1 yr of age, 2 had complete obstruction, 1 had tuberculosis and 2 had protein energy malnutrition. All the 8 children over the age of 4 years had an enormously distended proximal bowel. Two infants died from septicemia and peritonitis; all the others had a successful pullthrough later.

We have done 157 pull throughts so far, 65 in the first 15 years and 92 in the second

15 years. Data regarding age at pull through and type of pull through done together with results have been published elsewhere(14).

The important observations from our experience are *(Table I):*

1. Eleven of the 12 deaths took place in the first phase.
2. In the first phase a variety of methods of pullthrough were practiced, but in the second phase Duhamel's operation was done in all cases.
3. The number of pull throughs done on patients in the different age group above the age of one year are more or less similar in the 2 phases, but many more patients below the age of 1 year were submitted to pullthrough in the second phase.

Today when we have covered a century after the publication of Hirschsprung's paper, most of the problems presented by this disease appear to have been solved. However, there are three which still continue to baffle us, namely: (i) The management of total colonic aganglionosis; *(ii)* The diagnosis and management of Hirschsprung's-like diseases; and *(iii).* The uncertain long term results after pullthrough. According to Molenaar (15) one in every ten patients have serious defecation disorders of unknown cause; this can be eliminated once "there is greater insight into the link between pathophysiology of the phenotype and mutation pattern in the gene."

REFERENCES

1. Ehrenpresis T. 'Hirschsprung's Disease'. Chicago, Year Book Medical Publishers Inc, 1970; pp 14-15.
2. Ehrenpresis T. 'Hirschsprung's Diseases'. Chicago, Year Book Medical Publishers Inc, 1970; pp 21-22.
3. Varma KK, Hunt TW, Stephens FD. The anomanometer—its use in the assessment of continence and in the diagnosis of Hirschsprung's disease. Aust NZ J Surg 1972; 42:185-192.
4. Meier-Ruge W, Lutterbeck PM, Scharli A, *et al.* Acetylcholinesterase activity in suction rectal biopsies of the rectum in the di-

TABLE I–*Results of Management of Hirschsprung's Disease.*

	First phase (1966-1980)			Second phase (1981-1995)		
	Uneventful	Non-lethal complications	Deaths	Uneventful	Non-lethal complications	Deaths
Age group (yr)						
<1	4	2	–	28	7	–
1-4	22	8	10	34	3	1
>4	13	5	1	19	–	–
Operation						
Duhamel	24	4	5	81	10	1
Ikeda	3	5	2	–	–	–
Swenson	8	2	2	–	–	–
Soave	6	2	2	–	–	–

agnosis of Hirschsprung's Disease. J PediatrSurg 1972; 7: 11-17.

5. Meier-Ruge WA, Schmidt PC, Stoss F. In testinal neuronal dysplasia and its morphometric evidences. Pediatr Surg Int 1995; 10: 447-453.

6. Tarn PKH. An immunoche mical study with neuron-specific enolase and substance P of human enteric innervation—deviations in Hirschsprung's Disease and Pyloric stenosis. J Pediatr Surg 1986; 21: 227-232.

7. Puri P, Fujimoto T. Diagnosis of allied functio nal bowel disorders using monoclonal antibodies and electron microscopy. J Pediatr Surg 1988; 23: 546-554.

8. Kobayashi H, Hirakawa H, Puri P. What are the diagnostic criteria for intestinal neuronal dysplasia? Pediatr Surg Int 1995; 10: 459-464.

9. Munakata K, Okabe I, Morita K. Hypoganglionosis. Pediatr Surg Int 1992; 7:8-11.

10. Fujim oto T, Puri P, Miyano T. Abnormal peptidergic innervation in internal sphincter achalasia. Pediatr Surg Int 1992; 7:12-17.

11. Puri P, Tsuji M. Megacystis-microcolon-intestinal hypoperistalsis syndrome (neonatal hollow visceral myopathy). Pediatr Surg Int 1992; 7:18-22.

12. Rode H, Moore SW, Kaschula ROC, Brown RA, Cywes S. Degenerative leiomyopathy in children. A clinicopathological study. Pediatr Surg Int 1992; 7: 23-29.

13. Chatterjee SK, Banerjee S. Is anorectal myectomy a good operation for short segment Hirschsprung's disease? J Indian Assoc Paed Surg 1995; i: 21-24.

14. Chatterjee SK, Chakraborty AK, Basu AK, Banerjee S. Abdominoperineal pull-through for Hirschsprung's Disease-A 30 years experience. J Indian Assoc Paed Surg 1996; 1:17-22.

15. Molenaar JC. Pathogenetic aspects of Hirschsprung's Disease. Br J Surg 1995; 82:145-147.