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REVIEW ARTICLE*

HIRSCHSPRUNG'S DISEASE

BY

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In 1887 Hirschsprung of Copenhagen described two patients with a serious condition from which both had died. Later his name was applied to any megacolon, and this resulted in an era of confusion until the work of Swenson and Bill (1948) which led to an understanding of the pathology and a treatment for this serious form in which the normal-looking distal bowel presents an obstruction.

In discussing present views on Hirschsprung's disease this paper will refer to many useful papers without attempting a complete bibliography.

Pathology

Ehrenpreis (1946) showed by barium enemas that there was a 'dysfunction of evacuation' causing secondary dilatation of the colon. Bodian, Stephens and Ward (1949) confirmed aganglionosis of the distal bowel in every case of a series. Isolated reports of such a lesion had been made earlier; for example Dalla Valle (1920, 1924) described the pathology and noted a familial occurrence, and as long ago as 1901 Tittel had described changes in the intramural ganglia. The ganglia are absent from both the submucous and intermuscular plexuses, and their place is taken by whorls of nerve fibres. It was suggested that these fibrils were the pre-ganglionic parasympathetic nerves 'searching' for the absent ganglia. However Kamijo, Hiatt and Koelle (1953) have postulated that these unmyelinated fibres are more likely to be post-ganglionic and suggest that the ganglia are present but situated somewhere nearer the central nervous system, having failed to complete the migration from their site of origin in the dorsal crest. Extensive series show that the rectum and lower part of the sigmoid colon are usually involved, but that about 30% are limited to the rectum and about 15% extend proximally beyond the sigmoid and sometimes even into the small intestine. A very rare group have total aplasia throughout the intestine and in these are no whorls of nerve fibres in the bowel wall (Bodian, Carter and Ward, 1951; Bodian and Carter, 1963; Swenson, 1957; Pagès, 1962). The lesion starts at the lower end of the rectum and extends proximally in every case. 'Skip segments' have been described, but some accounts at least are unconvincing, and if they occur they must be very rare: none were found in the two longest series reported (Swenson, 1957; Wyllie, 1957a).

The bowel proximal to the aganglionic segment enlarges and its muscle hypertrophies in an attempt to overcome the obstruction: this forms the 'megacolon'. The aganglionic bowel which has no co-ordinated peristalsis remains unexpanded, but there is no truly narrow segment. If the segment involves the entire colon, then of course there will be no megacolon. Perhaps 'Congenital Intestinal Aganglionosis' would be the most fitting name for those who dislike eponyms.

Bentley (1962) has revived the idea of a segment so short it cannot be demonstrated radiologically and virtually amounts to an uninnervated internal sphincter which therefore cannot contract and relax in co-ordination; this sphincter is only a development of the lower end of the circular muscle coat and normally receives an innervation descending from the distal intramural ganglia. Further evidence will be awaited with interest, particularly on whether such cases will present with the symptoms of Hirschsprung's disease or those of the 'idiopathic megacolon' or 'rectal inertia' group, of which a few certainly have an early onset for a condition considered generally to be acquired. Duhamel (1963) has recently described a similar 'forme anale' of Hirschsprung's disease, as has Roviralta (1962).

* It is the intention of the Editors from time to time to invite review articles, of which this is the first.

Since the pathological lesion is so limited, the therapeutic test of sphincterotomy is likely to be the most convincing evidence. This procedure has been tried with limited success in the past, but perhaps on wrongly selected cases or too late.

Aetiology

Swenson (1955) suggested there was a failure of development of the pelvic parasympathetic system. But it is not always limited to the distribution of the pelvic autonomic nerves, and the suggested association with bladder neurological defects has not been confirmed. Bodian's suggestion that there is a failure of migration of the cells from the dorsal crest neurectoderm, which normally proceeds craniocaudally, seems more likely.

There is a familial incidence (Dalla Valle, 1924; Bodian and Carter, 1963; Fock and Kostia, 1963) and a sex incidence of about five male to one female in the 'normal' length of segments. The long segments have a higher rate of recurrence in the family, and the recurrences are of the same type, i.e. normal or long segment. There is no marked sex differential in the long segment cases, and this may be related to the greater maturity of the female embryo at the same age.

A similar clinical and pathological picture is seen in adults in South America as a result of degeneration due to the infestation of Chagas' disease (Ferreira-Santos, 1961).

Pharmacology and Physiology

Swenson, Rheinlander and Diamond (1949) and Hiatt (1951) showed failure of propulsion waves in the aganglionic segment. Ward (unpublished data) pointed out that the concept of a 'spastic' or narrowed segment was inaccurate: it is rather an unexpanded segment that may relax or contract *en masse* without progressive waves. Trounce and Nightingale (1960) showed that strips of the aganglionic muscle nevertheless showed a response to nicotine and suggested that the acetylcholine-producing structures presumably present might be the whorls of non-medullated nerve fibres. Kamijo *et al.* (1953) have also studied the response to drugs. Callaghan (1962, unpublished data) has observed that the internal sphincter does not relax reflexly as in the normal defaecation reflex. This would fit in with the findings of Swenson, Fisher and Scott (1960) that internal sphincterotomy relieves residual symptoms after resection; but Schuster, Hendrix and Mendeloff (1963) using an indirect method consider that they have demonstrated a normal reflex relaxation.

An isolated observation of Davidson and Bauer (1958) is of great interest. The colon above the aganglionic bowel was shown to exhibit the usual types of contraction. After Swenson's operation the same piece of bowel brought down to take the place of the excised rectum then showed typical contractions of a rectum. Could this be due to the alteration in resulting pressures depending on the proximity of the anal sphincters? Much remains to be discovered in order to explain, for example, the intermittent nature of the symptoms of a persistent congenital defect and the fact that the severity of symptoms, though often related to the length of the segment, is by no means always so.

Clinical Picture

The child with the 'classical' picture of Hirschsprung's disease is now recognized to be a survivor of a relatively mild form. The mortality of congenital intestinal aganglionosis is at least 50% in the first year of life (Bodian *et al.*, 1949; Eek and Knutrud, 1962), and few reach adult life untreated. It has become customary to recognize clinical groups (Wyllie, 1957a; Roviralta and Casasa, 1962), and more and more are recognized in infancy or even the neonatal period as paediatricians become aware of the early symptomatology and the dangers of delay in diagnosis and treatment.

The symptoms almost always date back to the neonatal period. Obstruction is revealed by abdominal distension, absolute constipation or delayed passage of meconium, and vomiting. This may settle spontaneously or, dramatically, on rectal examination.

Group I: Neonatal obstruction persisting until relieved by colostomy. Most of these are the longer segments, and in the longest ileostomy may be necessary.

Group II: Recurring obstructive episodes during infancy until relieved by colostomy. This is probably the largest group.

Group III: Recurring obstructive episodes during infancy responding to rectal washouts so that the infants remain fit for a primary definitive operation.

Group IV: Mild (or *very* occasionally absent) symptoms in infancy, presenting later as typically stunted, wasted children with chronic obstruction—a huge gaseous distension of the abdomen with visible and audible peristalsis contrasting with the wasted limbs and buttocks. They are prone to recurrent chest infections and obstructive crises of enterocolitis with increased distension and diarrhoea. They do not soil themselves except during these crises; being basically an obstructive disease there is no overflow incontinence. It should be noted that as the obstruction is not complete faeces may occasionally be present in the rectum at the time of examina-

tion although the ampulla will not be widely dilated as in the rectal inertia syndrome. Wyllie found the rectum to be empty at the first examination in four-fifths of 152 cases.

In rare cases the symptoms and constipation may settle down over a few years, presumably as the hypertrophy of the colonic muscle 'compensates' for the obstruction. However, such patients are still at risk, and the author has already seen one later develop an acute obstructive crisis with enterocolitis and peripheral circulatory failure, and another whose sigmoid colon perforated in young adult life.

Group V: Attacks of diarrhoea with distension in early infancy. These cases with enterocolitis are easily mistaken for gastro-enteritis and the underlying obstructive lesion can be missed. Unless this obstruction is relieved by washouts or colostomy the mortality is high.

The natural history of the disease as recounted above justifies the advice that no diagnosed case should be discharged from hospital without operation, either a temporary colostomy or a primary definitive procedure.

There is still no general acceptance of the occurrence of an extremely short aganglionic segment involving little more than the internal sphincter. Bentley (1962) and Duhamel (1963) have suggested that such a *forme anale* might present as an intractable constipation with a dilated rectum resembling rectal inertia or idiopathic megacolon syndrome.

Diagnosis

The clinical picture described above contrasts clearly with that of chronic constipation and megacolon due to other causes. The syndrome variously called idiopathic megacolon, terminal reservoir or rectal inertia usually presents later in the 'training period' with the faecal masses palpable in the flat abdomen. Rectal examination reveals a grossly dilated ampulla full of faeces right down to the anus. In severer cases overflow diarrhoea occurs but very rarely is there any risk to health or life in this asocial condition. It is basically one of constipation rather than of obstruction as in aganglionosis.

Prompt treatment of incipient attacks of obstruction by an astute mother may minimize the symptoms in true Hirschsprung's disease, and other uncommon conditions may mimic it to an extent, making clinical diagnosis difficult. Coekin and Gairdner (1960) described as 'congenital constipation' a group that have the symptoms of rectal inertia, yet these date from birth.

The meconium plug syndrome (Zachary, 1957; Clatworthy, Howard and Lloyd, 1956) may simulate the neonatal symptoms of aganglionosis but these do not recur after passage of the plug. Rarely one sees mildly obstructive symptoms in the neonatal period, which settle spontaneously and are not associated with aganglionosis. Occasional cases are described of a persistent amotility of histologically normal gut, which causes a clinical imitation of severe Hirschsprung's disease in every particular except the bowel sounds which are absent instead of increased, and usually end fatally (Nixon, 1961a). Confirmation may be required and barium enema or biopsy will provide this.

Radiology

The barium enema requires to be performed in a special manner. The bowel is not prepared, so that the barium can be observed running up from the undilated rectum into the dilated 'megacolon' through the typical cone of transition. At this stage the examination should cease. If the megacolon is filled with large amounts of barium its inspissation may increase the symptoms, and water may be absorbed so quickly that fatal water intoxication has occurred (Jolleys, 1952). If the bowel has been washed out during the few days before the examination, the colon may be so deflated as to hide the contrast in diameter at the cone of transition, and the diagnosis will be missed. Some schools rely on observation of evacuation (or rather its failure) in long-delayed films in this situation. In the few cases involving the whole colon and yet being clinically mild the enema may mislead. For the colon will be of the same diameter throughout and the enema is unlikely to reach the cone in the ileum.

Rectal Biopsy

Rectal biopsy will always confirm the diagnosis. There are several techniques: Bodian (1960) preferred a relatively large biopsy of mucosa and submucosa while others prefer a deeper biopsy allowing examination of the intermuscular plexus (Swenson, Fisher and MacMahon, 1955; Bill, Creighton and Stevenson, 1957; Hiatt, 1958). In practice any difficulty in interpreting a biopsy is usually due to the provision of inadequate tissue by the use of biopsy forceps such as are used to examine tumours. Shandling (1961) finds such specimens satisfactory, but many pathologists are unwilling to commit themselves on such small specimens, and a more elaborate procedure is preferred.

It should be noted that while an adequate biopsy will always give the diagnosis it gives no information about the extent of the lesion whereas the barium enema will. Furthermore, the biopsy scar may cause some inconvenience by splitting at the

definitive operation, and it need not be considered a routine requirement.

Treatment

Definitive treatment is always by operation to deal with the aganglionic segment and the most firmly established is that of Swenson and Bill (1948) in which the segment is resected by an abdomino-anal pull-through technique. Urgent primary treatment may be required to save life depending on the manner of presentation.

Should the newborn baby have acute obstruction the passage of the examining finger per rectum may stimulate the passage of meconium and flatus. If not, a rectal washout with normal saline (after diagnostic barium enema) may do so. The daily use of washouts may keep the baby fit and gaining weight when some would operate at about 6 weeks of age (Nixon, 1961b). Others, including Swenson (1957) and Browne (1955), believe that a colostomy should always be performed in cases presenting in infancy, leaving the definitive operation until the baby weighs 25 lb. (11·3 kg.) or so. Swenson considers this safer though his figures do not seem conclusive, and Wyllie (1957b) found no convincing evidence in the first 152 cases of the Great Ormond Street series. Since colostomy is not an entirely benign procedure (MacMahon, Cohen and Eckstein, 1963), this point is worthy of further consideration. All who treat this disease would surely agree that when the diagnosis is suspected it should be confirmed, and operation, either colostomy or definitive, should be performed before the baby is allowed home lest the baby succumb to a crisis of enterocolitis.

Siting of the colostomy is important and bad placing can mar the definitive operation. Stephens (1951) and Browne (1955) preferred a right transverse colostomy defunctioning the distal colon during resection and requiring later closure. Although usually very successful and rendering complications of the later resection less serious, it has some disadvantages. In the longer segment cases it may so fix the bowel as to necessitate subtotal colectomy instead of a less extensive resection. When performed in the neonatal period it may so effectively defunction the sigmoid colon that the loop fails to develop and its vessels become too short to reach the bottom of the pelvis. Swenson prefers to site the colostomy just above the cone of transition to aganglionic bowel: thus all the ganglionic bowel remains in use and develops normally. The colostomy is taken down and pulled through the anus at the definitive operation so that this is not protected by defunctioning of the bowel. Long segments reaching into the right half of the colon in particular may become proximally dilated by foetal impaction of meconium, giving a misleading appearance of a cone below the true level of transition. In the absence of facilities for frozen section biopsies it may be wiser to perform an ileostomy as the urgent procedure in such cases.

In children presenting after infancy it will more often be possible to prepare for primary resection without preliminary colostomy. Washouts are used and care must be taken that a proper technique avoids the risk of potentially fatal water intoxication. Insoluble sulphonamides to reduce the intestinal flora are usually preferred to wide spectrum antibiotics which introduce the risk of superinfection.

The abdomino-anal pull-through operation originally described by Swenson and Bill (1948) (Fig. 1a) is of proved value over a long follow-up period. Browne (1955) introduced a useful modification to avoid having to open the bowel within the abdomen. Swenson (1957) reported the results of 200 operations up to 10 years after operation. The results for general health and bowel control were excellent with no frank incontinence. The early mortality was only 3%, though a later additional 3% due to crises of enterocolitis came as a surprise. Furthermore, adult patients were found to be fertile or potentially fertile. Wyllie (1957b) reported on 152 cases from Great Ormond Street with a similar mortality. A thorough inquiry into bowel habit revealed a higher proportion of residual troubles, up to 40%: most of these were slight and only elicited from satisfied patients and parents by detailed questioning, but there were 14% with an important degree of soiling. Hiatt (1958) found 16% of 150 cases had 'mild continuing problems' but no mortality. It is often said that the bad results of Swenson's operation are the results of bad operating. There seems much truth in this. Certainly the oft-repeated statement that the operation risks urinary incontinence and impotence can only be based on misunderstanding of the correct technique. It is a tedious, testing operation whose wide differences from the commoner type of resection suited to cancer surgery are not always appreciated. For example the few (seven) strictures in Wyllie's series seemed clearly related to ischaemic necrosis of bowel, in turn the result of unsatisfactory mobilization of its blood supply. However, it does not seem to the present author that soiling, uncommon as it is, can be reliably related to technical errors. Callaghan (1962, unpublished data) has found the sphincter pressure in such cases lower than the rectal contraction pressure, the reverse of the normal. This may point to damage by over-

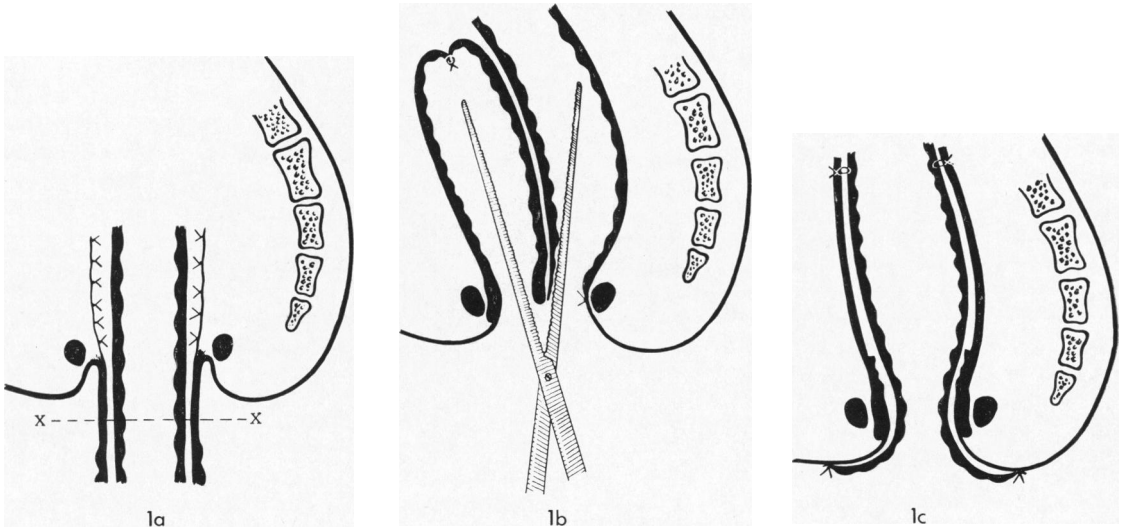

FIG. 1a.—Swenson type operation. Rectum mobilized on the muscle coat with temporary prolapse through the anus during excision of segment and anastomosis.

FIG. 1b.—Original Duhamel operation. Upper end of rectum divided and closed. Remainder of aganglionic segment excised and proximal colon drawn down behind rectum and out through incision in posterior half of anus between internal and external sphincters. Application of crushing clamps to adjacent walls of rectum and colon converts to a single chamber with sensitive rectum anteriorly and propulsive colon posteriorly.

FIG. 1c.—Endorectal pull-through operation (Simonsen, Soave, Nixon). Upper end of rectum divided down through muscle coats only and intact mucosa stripped as far as anal canal. Division of lower end of mucosal tube and anganglionic segment drawn out of anus through intact muscular tube of rectum. Excess trimmed back to anus after two weeks for colon to unite with denuded interior of rectum.

stretching during the pull-through or to interference with innervation in the absence of obvious technical errors.

In 1957 Daintree Johnson, Davis and Evans gave what amounted to a 62-year follow-up of a Swenson-type operation. In 1898 Sir Frederick Treves described his treatment of a 5-year-old girl with megacolon. He discussed two types of megacolon: the one appearing to have an obstructive origin in the distal undilated bowel, and the other arising as a result of habitual constipation. The girl had been relieved of obstructive attacks by colostomy, and he then carried out an abdomino-anal pull-through procedure 'excising the anus' along with the bowel below the colostomy. At the age of 67 years she came to the Royal Free Hospital with intestinal obstruction caused by a band to the caecum and relieved by division of this band. In spite of a patulous anus she had remained continent throughout her life.

On the basis of considerably smaller experience, others have expressed dissatisfaction with the procedure. Certainly the consequences of an inadequate or unsatisfactory Swenson operation can be serious or even irremediable, and an easier operation would be welcome. None of the other operations has yet proved itself in a long-term follow-up of similar size, but they certainly merit consideration.

David State (1952) advised an anterior resection reaching down only to the peritoneal reflection but carrying back the resection beyond the limit of dilatation of the colon. This seemed irrational for it removed the secondarily affected bowel without removing all the aganglionic bowel. Indeed, Wyllie pointed out that in one-third of the Great Ormond Street series the entire aganglionic segment was below the peritoneal reflection and would have been left intact by such an operation. However, State's 10-year follow-up (1963) was surprisingly good, though in discussion of his paper it seemed that his criteria selected the more suitable cases for the method. Rehbein and von Zimmermann (1960) also reported good results but some of their patients required repeated bougienage, and follow-up barium enemas showed the colon to be more dilated (whereas Stephens' (1951) follow-up of Swenson's recto-sigmoidectomy showed post-operative reduction of the dilatation). While the results are not so good as to have encouraged wider use of the procedure, perhaps the most surprising thing, considering the pathology of the disease, is that it *ever* succeeds—for

a residual rectal segment shorter than this after a badly-executed Swenson procedure can produce severe residual symptoms.

In 1956 Duhamel reported on his ingenious 'retrorectal transanal' pull-through. Fig. 1b illustrates the principle of the operation. It is a simple operation which Duhamel advises as an immediate urgent procedure as safe as colostomy, though most of its proponents apart from Roviralta who has simplified the technique (1962) do not advise its use in the presence of obstruction. Several advantages are claimed. First, there is no need for the careful dissection of the rectum, which is alleged to endanger the pelvic nerves. Certainly this shortens the procedure, though the large series of Swenson operations already mentioned show that proper technique reliably avoids any risk to the nerves. Secondly, it avoids the risks of an anastomosis. Leaks and infections nevertheless have occurred after the procedure, and it seems likely that whether the junction is achieved by suture anastomosis or spur crushing clamps it is ischaemia that causes breakdown, due to the need to mobilize the bowel down to the pelvic floor in both operations. A further advantage claimed is that the anterior 'rectal' half of the neorectum retains rectal sensation and that this might avoid some of the post-operative troubles with control that may occur after rectosigmoidectomy. This seems a sound observation. It was also suggested that the destruction of the internal sphincter would avoid the residual symptoms occurring as a result of inability to relax the uninnervated sphincter. While this seems to be correct, experience shows that this may be achieved at the cost of soiling. Eek and Knutrud (1962) and Louw (1961) obtained good results with this operation, but Kostia (1962) had 10 soilers out of 25 operations. Many were under 4 years old, and he felt the absence of serious complications made the operation preferable.

Grob (1960) modified the procedure bringing the colon into the rectum above the anal sphincter to avoid such soiling, and Duhamel (1963) now advises bringing the bowel through about halfway up the internal sphincter. This type of operation has its own complication in the tendency to form an anterior pouch of rectum with constipation and overflow incontinence, though Duhamel believes this can be avoided by care in dividing the septum to the apex of the rectal pouch. Nor is it yet proven that a hemi-circumference of peristalsing bowel will remain adequate over many years.

There is wide agreement that whatever its status as a procedure of choice, the Duhamel-Grob is the best secondary operation for a 'failed Swenson'. Remobilization of the rectum below the pelvic floor for a second pull-through has a disastrous effect on the blood supply of the dilated segment.

Soave (1963) briefly reported the successful results of treatment of 22 cases by a submucous resection (Fig. 1c) stimulated by the similar technique for rectal agenesis used by Rehbein (1959) and Romualdi (1961). The easy plane of separation between submucosa and muscle has been exploited for other conditions, yet it is not widely appreciated. The present writer, independently, has used the technique on chosen cases since 1958 with good results to date, and Simonsen, Habr and Gazal (1960) reported on a similar technique. Simple and safe as is this operation, details of technique and aftercare are of importance in avoiding complications, and further experience needs to be gained.

At the 1963 meeting of the British Association of Paediatric Surgeons, Knutrud (unpublished data) commented favourably on a simplification of Swenson's operation devised by Grob. The anterior and lateral dissection of the rectum are not performed so that an oblique anastomosis results, and apparently this can be made low enough posteriorly to avoid residual troubles.

Enterocolitis in Hirschsprung's disease merits special comment. Clinically the child has a grossly distended abdomen with diarrhoea and probably vomiting. Untreated, the child may die of fluid and electrolyte loss within 24 hours: it is the cause of the crises in which untreated patients may die. Bill and Chapman (1962) have confirmed Swenson *et al.*'s (1960) opinion that the basic trouble is obstruction. Emptying the bowel by passage of rectal tubes, washouts and even colostomy with rapid fluid replacement allow rapid recovery. Intravenous fluid replacement without evacuation will often fail to cure the condition. It is now realized that this condition can also recur after apparently successful operation, so that it behoves paediatricians and practitioners to bear in mind the urgency of treatment of distension and diarrhoea in these children. Internal sphincterotomy is usually successful in reducing the severity of the attacks, if not always eliminating them. The aetiology is not clear. Bacterial cultures reveal no pathogens, and if the condition is not promptly treated it proceeds to necrosis of the mucosa, suggesting a vascular lesion.

In summary of treatment one may say that the great advance that Swenson's work seemed to offer has been confirmed by experience, yet the proliferation of alternative procedures shows that there is room for further simplification and safety in technique for general use. The dangers, especially of enterocolitis, in apparently 'compensated' cases are recognized as justifying operation in all cases.

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