Colonic Inertia Disorders in Pediatrics

Colonic inertia disorders in pediatrics include a large number of conditions with diverse etiologies and different pathophysiologic mechanisms (Table 1). Of all of these, we selected those that are most common, have more social impact, and have more clinical importance for surgeons.

Idiopathic Constipation

Definition and Terminology

Idiopathic constipation is the incapacity or difficulty to pass stool regularly and efficiently. The cause of this condition is unknown. We intentionally use the term *idiopathic* because we believe that, even when there are many proposed explanations for the cause of this condition, none of these explanations have scientific basis. In agreement with Benjamin Disraeli, we believe that "to be conscious that you are ignorant is a great step to knowledge."[1]

Incidence, Relevance, and Social Impact

Idiopathic constipation is by far the most common defecation disorder and the most common colonic motility disorder in children. This condition affects an enormous pediatric population and represents a common cause for surgical consultation.[2-4] It is relevant not only because it affects millions of Americans but also because it is extremely incapacitating in its most serious forms. In fact, it produces a form of fecal incontinence that is known as encopresis or overflow pseudo-incontinence. The most serious type of constipation cannot be differentiated from a very serious motility disorder called *intestinal pseudo-obstruction* that carries a significant mortality rate.[5,6]

Causes and Pathogenesis

Although the cause of idiopathic constipation is unknown, the literature presents many potential causes for the disease. Most of the proposed explanations have no solid scientific basis, however. There are many

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TABLE 1. Cause of colonic inertia disorders in pediatrics

Isolated defects
Idiopathic constipation
Colonic aganglionosis (Hirschsprung's disease)
Other conditions
Intestinal neuronal dysplasia (IND)
Intestinal pseudo-obstruction
Visceral neuropathies
Visceral myopathies
Consecutive to systemic diseases
Scleroderma, lupus, diabetes mellitus
Hypothyroidism, hyperthyroidism
Lead poisoning
Drugs: Opiates, anticholinergic ganglion blockers, aluminum, and calcium-containing antacids
Central nervous system depression and hypoxia
Neuromuscular disease, muscular dystrophy
"Prune belly" syndrome
Mental retardation
Multiple endocrine neoplasia 2B syndrome
Disturbed neuromuscular innervation
Spina bifida, meningomyelocele
Paraplegia
Postpolio
Sacral spinal cord tumor

publications that discuss dietary disorders as a cause of constipation.[7,8] There is no question that the different types of food that we ingest have either a laxative or constipating effect on the body. In addition, there are personal idiosyncracies that explain why one type of food may act as a laxative for one individual and as constipating for another individual. We recognize that diet is important to regulate colonic motility, but the therapeutic value of the diet is negligible in the most serious forms of constipation. Thousands of patients have mild forms of constipation that are treated successfully with diet. However, the type of patient that is referred to the surgeon has a much more serious form of this condition, a form that does not respond to dietary treatment.

Many authorities have tried to explain the problem of idiopathic constipation on a psychologic basis.[9-14] Very interesting psychodynamic mechanisms have been proposed. Strict, demanding parents who impose rigid rules on a child during the toilet training process may provoke psychologic disturbances that result in idiopathic constipation. Children, then, supposedly, retain the stool to manipulate the parents to achieve their own purposes. Many of these interesting mechanisms have an element of truth, but we do not believe that they can explain the severe

forms of constipation in patients with a giant megacolon, a megabladder, and serious nutritional and developmental disturbances. In addition, it is certainly not easy to retain the stool voluntarily when an otherwise autonomous rectosigmoid has normal peristalsis. On the other hand, we believe that most patients with idiopathic constipation have a secondary psychologic component. This is true for most medical and surgical conditions. Individuals who have an incapacity to empty the colon will have serious psychologic distress. In addition, the passing of large, hard pieces of stool may provoke pain, which will make the patient afraid to have bowel movements. This may complicate the problem of constipation, but we do not believe this is the original cause.

Surgeons, on the other hand, have proposed different potential mechanisms to explain this problem. For instance, a rather simplistic explanation is that there is a lack of relaxation of the internal sphincter, also known as achalasia.[15-17] This is a very attractive and appealing idea. In other words, a simplistic logic dictates that incontinence means lack of sphincter, therefore, constipation means too much sphincter. However, the diagnosis of this achalasia of the internal sphincter is based mainly on manometric studies.[18-22] Unfortunately, rectal manometry is rather unreliable when analyzed and scrutinized carefully. Traditionally, rectal manometry is performed by the placement of a balloon in the rectum when the pressure of the anal canal is being measured. When the rectal balloon is inflated under normal circumstances, there is a drop in the intra-anal canal pressure. This is well known in the literature as an anorectal reflex. When the pressure does not drop in the anal canal, it is considered abnormal and a sign of a lack of relaxation of the internal sphincter. This is also considered diagnostic for Hirschsprung's disease.

If the patient's rectum has no ganglion cells, the diagnosis of Hirschsprung's disease is confirmed. On the other hand, if the rectal biopsy shows ganglion cells, the patient then receives the diagnosis of achalasia of the internal sphincter. In cases of Hirschsprung's disease, the treatment is well established and accepted. In cases of achalasia of the internal sphincter, the treatment proposed by many authorities is a myectomy or internal sphincterectomy, which is a controversial procedure.[23-25] The whole issue becomes more controversial when the rectal manometry is scrutinized critically. The pressure recorded in the lumen of the anal canal, supposedly given by the internal sphincter, in reality is generated both by the internal (smooth muscle) and by the striated voluntary muscle mechanism (external sphincter and levator) that surrounds the lower rectum and the anal canal around the area of the internal sphincter.[26,27]

We have been unable to find a publication that clarifies this serious flaw in the interpretation of manometric studies.

How do we know that the pressure in the anal canal is not the primary result of the contraction of the voluntary sphincter mechanism? The original manometric studies that were performed in animals used muscle relaxants, which kept the voluntary muscle mechanism paralyzed. Any changes in the pressure of the anal canal under those circumstances could be attributed to the effect of the smooth muscle (internal sphincter). However, none of the clinical studies that have been published have been performed with the use of muscle relaxants. In addition, the inflation of a balloon in the rectum is assumed to produce tension on the rectal walls that triggers some form of mechanism that produces, as a final result, a drop of pressure in the lumen of the anal canal. However, the problem with constipated patients is that they have different degrees of megarectosigmoid. Sometimes the megarectum is minimal, and sometimes it is giant. The sizes of the balloons that are used in manometric studies are never big enough to stretch giant rectosigmoids. As a result, it is conceivable that the inflation of a regular balloon is not enough to stretch the rectal wall in patients with megarectum and may produce false-negative relaxation reflexes.

We do not use the sphincter myotomies that are proposed for the treatment of internal sphincter achalasia[23-25] because the descriptions of the surgical technique are not accurate and because the precise anatomic limits of the internal sphincter are not well documented. Most importantly, the results of such operations have not been uniformly good.[28]

There are many publications that favor the idea that intestinal neuronal dysplasia (IND) may be the explanation for the abnormal colon motility that is observed in patients who are constipated.[29-34] We are rather skeptical about this. A critical, comprehensive evaluation of the literature on IND was conducted[35]; the most obvious impression that we obtained from this review was that there is no basic agreement among pathologists about how to establish this specific histologic diagnosis. In addition, topographic studies that describe the extension of this histologic disorder in different patients are missing. For a surgeon to propose a rational treatment for this condition, the surgeon should know the extent of the affected bowel that would be resected and, in theory, that will cure the patient. This has never been accomplished. In addition, the symptoms of patients with IND vary from patient to patient. The treatments vary from laxatives to enemas to different types of resections, and the follow-up of the patients has not been consistent. To complicate the problem even more, some patients recover spontaneously. We believe that neuronal

intestinal dysplasia represents an interesting histologic disorder that deserves further scientific evaluation.

Hypoganglionosis has also been invoked as a potential explanation for patients with severe constipation. This is based on biopsy specimens that were taken from specimens of dilated colon. However, as far as we know, the number of ganglion cells remains constant through our lifetime. If that is true and the colon becomes larger and larger as the constipation problem gets worse, it is conceivable that a specimen taken from the colon from a giant megasigmoid will show relatively fewer ganglion cells, which could explain a diagnosis of (relative) hypoganglionosis.

Many surgeons believe that many patients with idiopathic constipation may have ultra short Hirschsprung's disease.[36,37] They believe that some patients may have a very short area above the anal canal with absent ganglion cells that produces constipation and that may explain the reason that the rectum is dilated all the way down to the anal canal. Again, this is also an attractive but controversial explanation. The problem with this concept is that normal individuals have an area of aganglionosis above the pectinate line. The length of that area has not been described accurately. There have been attempts to determine the extent of this area, but these studies have not been comprehensive.[38,39] A study that determines the length of normal aganglionosis in premature infants, newborns, preschool children, school-aged children, adolescents, and adults has not been performed.

Once the diagnosis of ultra short-segment Hirschsprung's disease has been established, the proposed treatment is a posterior rectal myectomy. There is no explanation about why such an operation may improve the symptoms in these patients. In addition, the results of these operations are debatable.[28]

More recently, we have learned about new potential explanations for colonic hypomotility. A deficiency of substance P immunoreactivity in the colonic nerve fibers of some children with severe constipation has been proposed.[40] In addition, abnormalities were found in the colon when it was studied with monoclonal antineurofilament antibodies.[41] Another very interesting finding was an increased plasma level of pancreatic polypeptide and a decreased plasma level of motilin in children with encopresis.[42] All of these new possibilities deserve future investigation.

We recognize that we do not yet know the cause of this condition. We believe that these patients are born with a form of hypomotility disorder, with different degrees of severity and a wide spectrum of symptoms.[43,44] At the benign end of the spectrum, some patients have a minor form of constipation that is treatable with diet alone. At the other extreme, we

encounter patients with severe forms of constipation that may overlap clinically with a serious condition known as intestinal pseudo-obstruction, and they may even die. In the very severe form of this condition, patients frequently have not only the incapacity to empty the rectum but also the incapacity to empty the bladder, without any recognizable spinal or neurologic abnormality. They have some form of severe autonomic disorder of unknown origin.

The concept of a spectrum of disease cannot be over-emphasized. Most of the proposed treatments for constipation[45-50] do not take this into consideration, but rather they are standard therapeutic protocols that render good results in a percentage of cases but that always leave a group of patients who do not respond.[51-59] This group (that we call medically intractable) represents the most serious portion of the spectrum.

Natural History and Clinical Manifestations

Although we do not know the cause of idiopathic constipation, we have learned a great deal about its natural history. Idiopathic constipation is a self-perpetuating and self-aggravating disease. A patient who has a certain degree of constipation and who is not treated adequately goes through life only partially emptying the colon, leaving larger and larger amounts of stool inside the rectosigmoid, which results in greater degrees of megasigmoid.

Most surgeons accept the common clinical fact that the dilatation of a hollow viscus produces poor peristalsis. Constipation, or fecal retention, that produces megacolon then exacerbates the constipation (Fig 1). In addition, the passage of large, hard pieces of stool may produce painful anal lacerations (fissures) that result in a reluctance by the patient to have bowel movements. Consequently, if the patient was born with a certain degree of constipation, as time goes by and the patient does not receive proper treatment, the constipation worsens and becomes an increasingly serious problem.

We believe that this condition is mostly incurable, which means that these patients must be followed for life. The lack of understanding and acceptance of this fact, we think, explains the high recurrence rates reported in the literature.[51-59] Treatments are provided frequently on a temporary basis[45-50]; then they are tapered or interrupted, followed by a subsequent recurrence. This creates frustration for patients and parents and may contribute to the well-known pattern of patients going to many doctors or clinics seeking for a solution. Sometimes, colostomies or enemas are performed, and the patients are followed with contrast studies to monitor the degree of colonic dilatation. Once the distal colon regains

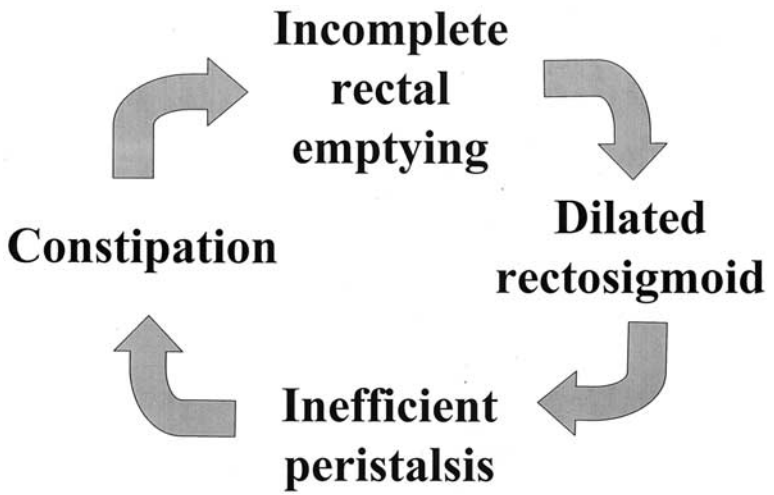

FIG 1. Cycle of constipation and megarectum.

a normal caliber, the physician assumes that the patient is cured; the colostomy is closed, or the enemas are discontinued, and there is a predictable return of the symptoms.

Another controversy about this condition is the time of the initiation of the symptoms. Many physicians believe that this problem starts during the toilet training process.[45-50] It is true that this is the time when the symptoms become more evident. However, we believe that the motility disorder is present since birth. Babies who are breast fed may not show symptoms because of the well-known laxative effect of the human breast milk. When breast feeding is discontinued and the patient receives formulas and other kind of foods, the symptoms become obvious. When babies have constipation problems while breast feeding, one must assume that the patient will have a severe constipation that will worsen with time. Many times, the parents tell us that the problem started in the preschool years. However, when we inquire specifically about the bowel movement pattern since birth, we frequently find evidence of constipation from very early in life. Actually, the parents remember most vividly the episode of the first fecal impaction, and they refer to that event as the initiation of symptoms.

The definition of constipation is another problem. Many pediatricians believe that normal individuals can go 2 to 3 days without a bowel movement throughout life without having any significant implications. That is true for many individuals. However, when that principle is applied

to a patient who has demonstrated idiopathic constipation, that concept interferes with an effective treatment and leads to the development of the vicious cycle that we have described already (Fig 1). In other words, the parents and the pediatrician become tolerant and flexible, which allows the patient to go 1 or several days without a bowel movement, which results in a larger colon with the consequences already mentioned.

Constipation in infants is manifested by difficult, sometimes painful bowel movements, the presence of hard stool, the passing of large, bloody pieces of stool, and periods of 2 to 3 days without passing stool. When these babies receive laxatives, sometimes the parents must increase the amount of laxatives to the point of producing diarrhea before the baby can pass stool. Even with liquid stool, the parents describe that the babies are incapable of having bowel movements without some form of rectal stimulation.

The presence of a fissure is often the first worrisome sign. It produces painful bowel movements that make the patient a stool retainer. Holding the stool for several days produces stool retention, which favors the hardening of the stool; eventually, however, the patient will pass a larger and harder piece of stool that will re-open the fissure, thereby creating a vicious cycle. If the patient has the mild form of this condition, it is usually successfully treated by the pediatrician who may prescribe a diet with a high content of fiber and/or laxative types of food. If this alone is not sufficient, then the pediatrician usually prescribes stool softeners and/or active ingredient types of laxatives. The recommended dosages may be effective for many patients but not for others, which is understandable given the spectrum of this disease.

Fecal impaction is a stressful event that is defined as a condition of retained stool for several days, crampy abdominal pain, and sometimes tenesmus. Rectal examination discloses the presence of a large mass of rock-hard stool located very low in the rectum. When laxatives are prescribed to a patient who has fecal impaction, the result is exacerbation of the abdominal pain and sometimes vomiting. This is a consequence of an increased colonic peristalsis (produced by the laxative) that acts against a colonic obstruction that is produced by the fecal impaction. Sometimes, in spite of the impaction, the patient may pass liquid stool, which is a phenomenon known as paradoxic diarrhea; the liquid stool passes around the solid fecal matter, but the impaction persists. A fecal impaction does not represent a failure of treatment for 1 or 2 days. It must be conceived and understood as failure or lack of treatment for days or weeks.

Constipation is recognized and diagnosed by most practitioners when

they learn that a patient has difficulty passing stool or when the patient has gone 1, 2, or 3 days without passing any stool. There is another form of constipation that is not recognized by most physicians. In this form, the patient passes many bowel movements during the day but in very small amounts. The stool is very sticky and thick and eventually becomes only a smearing or soiling of the underwear. This is also constipation.

Soiling of the underwear without the patient's awareness is an ominous sign of bad constipation. A patient at an age of bowel control soils the underwear day and night and basically does not have spontaneous bowel movements. This phenomenon is known as encopresis. These patients behave as fecally incontinent individuals. This condition is also termed overflow pseudo-incontinence. When the constipation is treated adequately, most of these pseudo-incontinent children regain complete bowel control. Very occasionally, the patient continues to behave as incontinent in spite of an effective treatment. In those patients, one must suspect and exclude either an innervation problem (such as spina bifida or tethered cord) or a serious psychologic disorder.

Soiling is a socially incapacitating phenomenon. The patients are rejected at school. The classmates point their fingers and stay away from the child because of the odor. The patient is unaware of the smell, which is a very well-known phenomenon in individuals with unpleasant odor due to different reasons. This problem is complicated because the parents believe that the patient is intentionally trying to upset them by sitting at home in the living room, obviously smelling very badly, and not doing anything to solve the problem. In fact, the patient does not perceive the bad odor. The emotional interrelations in the family are seriously affected, and that is when the psychologic problems become worse. We do not believe that the patients do this intentionally. We believe that, if an individual wanted to manipulate the parents, the individual could select many other ways to do so. Nobody wants to have stool-stained underwear or to smell and then be rejected by society. By the time these patients come for surgical consultation, they are withdrawn, shy, negative, and reluctant to be examined by the surgeon. They usually have been subjected to many painful rectal examinations. They have scars from previous fissures in the anus. The family is usually in distress. These patients have also been subjected to biofeedback, behavior modification, psychologic, and sometimes psychiatric consultations, without positive results. The family may put a lot of emphasis on the lack of cooperation from the patient and make the patient feel guilty.

Mild forms of constipation usually are treated successfully by pediatricians and gastroenterologists. This group of patients with medically

intractable forms of constipation represents a real challenge. They usually are referred for a surgical consultation when medical therapy has failed.

Diagnosis

The diagnosis of idiopathic constipation is a clinical one. The symptoms described earlier are very reliable to establish this diagnosis. In addition, if a patient manifests these symptoms, the patient has high likelihood of idiopathic constipation. Patients with Hirschsprung's disease do not soil; in addition, when left unattended without surgical treatment, these patients are at risk of dying. Those patients who survive are frequently malnourished and have a history of episodes of enterocolitis. Patients with idiopathic constipation do not have real enterocolitis. Sometimes they experience episodes of distention and vomiting, similar to enterocolitis; they are actually fecally impacted, and they also have viral gastroenteritis that produces a severe crampy abdominal pain and diarrhea around the impaction. In cases of real enterocolitis in Hirschsprung's disease, the patients become extremely toxic and lethargic and may die.

A contrast enema performed with a hydrosoluble material (never barium) is the most valuable diagnostic study to confirm the diagnosis of idiopathic constipation. The characteristic image of a contrast enema in a child with a megarectosigmoid is shown in Fig 2. The dilatation of the colon extends all the way down to the level of the levator mechanism, which is recognized because it coincides with the pubococcygeal line. The lack of dilatation of the rectum below the levator mechanism (pubococcygeal line) should not be interpreted as a transition zone or nondilated aganglionic bowel. Under normal circumstances, the anal canal and that part of the rectum below the levator mechanism are collapsed by the effect of the striated muscle tone from the sphincter mechanism. The rectum above the anal canal and the sigmoid are extremely dilated. This provokes an image that has been described many times in the literature as a posterior shelf. This posterior shelf has been interpreted by other authorities as evidence of an anteriorly located anus.[60-63] Many surgeons adopted this concept and treat patients on the basis of that idea. We believe that this diagnosis has not been substantiated and that there are not enough cases that have been studied systematically and followed on a long-term basis.

A real anteriorly located anus should be defined as an otherwise normal anus, surrounded by sphincter mechanism in its entire circumference, with a normal caliber and normal pectinate line that is located anteriorly. If we accept that definition, we can say that we have never encountered this condition. Although we cannot say that this condition does not exist,

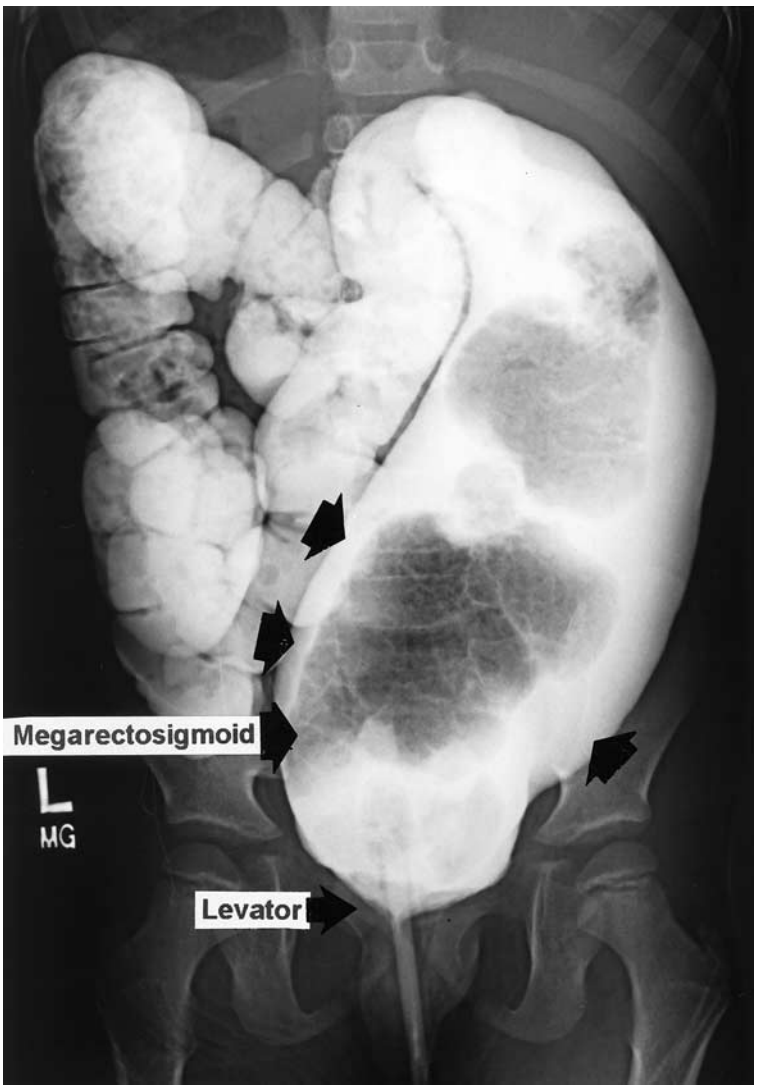

FIG 2. Radiologic image of a contrast enema in a patient with idiopathic constipation. The rectosigmoid dilatation extends all the way down to the lower rectum.

at least we can say that it must be extremely rare. On the other hand, there is one congenital condition that does have the anal opening located anteriorly. We call that condition "rectoperineal fistula." The orifice is abnormally narrow; it is not surrounded by sphincter mechanism in its entire circumference and does not have a normal pectinate line. The

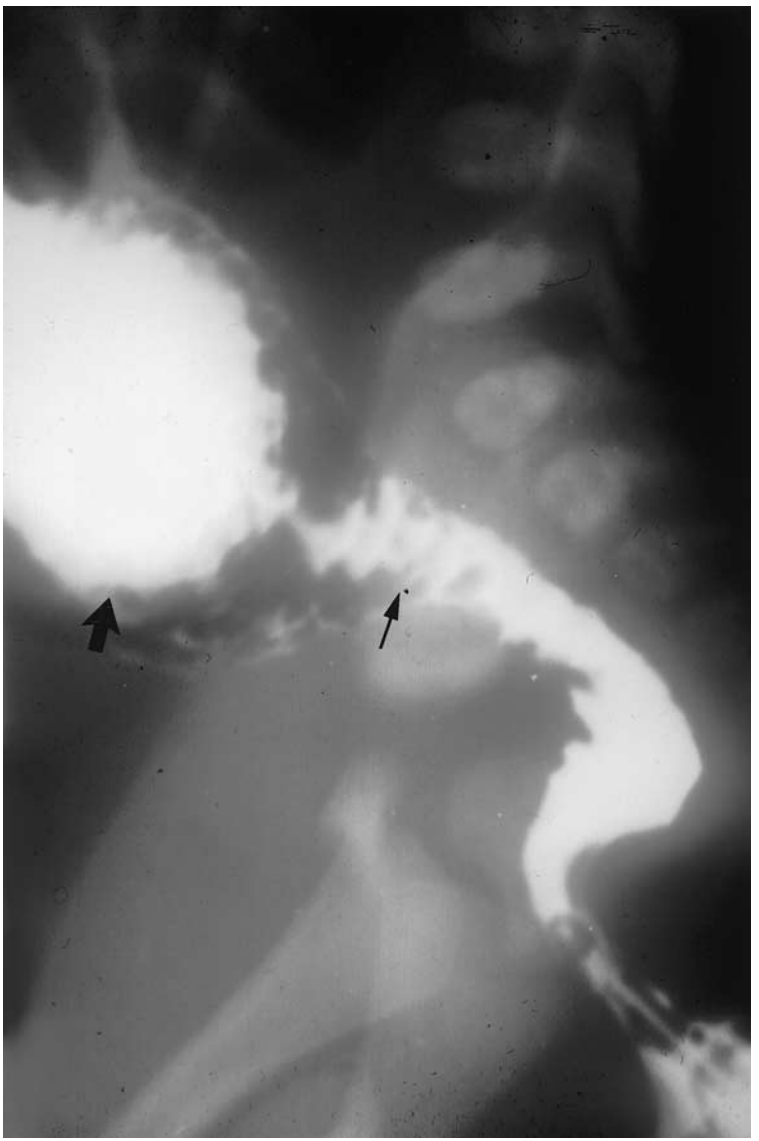

FIG 3. Radiologic image of a contrast enema in a patient with Hirschsprung's disease. The *distal narrow* portion represents the aganglionic segment. The dilated proximal colon (*large arrow*) is normoganglionic. Between these areas, the transition zone (*small arrow*) is seen.

operative treatment of that condition consists of moving the orifice back to be placed within the center of the sphincter mechanism, thereby creating an anus of a normal caliber.[64] These children also have a

tendency to be constipated. The treatment of these patients must follow the same principles used for those with idiopathic constipation, but in addition, the surgeon must be sure that the patient does not have an anal stricture.

The contrast enema in patients with idiopathic constipation shows different degrees of dilatation of the rectosigmoid, as expected in this spectrum of disease. Most interestingly, there is a dramatic size discrepancy between a normal transverse and descending colon and the very dilated megarectosigmoid (Fig 2). These changes are actually the reverse from what we see in cases of Hirschsprung's disease (Fig 3). Here, the colon in this last condition is dilated only proximal to the aganglionic segment, which remains nondilated. The more localized the dilatation of the rectosigmoid in cases of idiopathic constipation, the better the results of a surgical resection. Generalized dilatation of the entire colon is not a good prognostic sign, because those patients do not respond well to segmental resections of the colon.

We formally contraindicate the use of barium in these diagnostic studies. The term *barium enema* is widely used. In addition, adult radiologists like to use barium because it lines the mucosa and allows an accurate diagnosis of mucosal abnormalities and/or polyps. In these patients, on the other hand, we are not looking for mucosal abnormalities; we want to see the degree and extension of the dilatation of the colon. In addition, barium tends to stay in the colon and becomes petrified. Fecal impaction with barium is much more difficult to clean than impaction with hard feces.

Rectal biopsy specimens are usually taken with the specific purpose of identifying Hirschsprung's disease. For many years, the rectal biopsy was part of our routine in the study of these patients. Now, we find that study unnecessary when the clinical picture and the radiologic images are characteristic. At the present time therefore we only perform biopsies when there is a suspicious image of aganglionosis in the contrast enema or when the patient behaves clinically in a way similar to a patient with Hirschsprung's disease. If the patient has episodes that may simulate enterocolitis and does not soil, we must suspect Hirschsprung's disease. If the rectal examination shows an empty rectum and still the patient is impacted above the reach of our finger, one must suspect Hirschsprung's disease and take a biopsy specimen.

Rectal manometry is used by many practitioners.[15-22] We performed this study many times in the past with unreliable results. In addition, there

are many reasons that rectal manometry is not helpful in the diagnosis of these patients.

Because these patients have a hypomotility disorder, the most rational study to be performed should be the one that would evaluate the colonic motility. Unfortunately, the motility of the colon is not easily evaluated. Colonic manometry has been performed by placing balloons at different levels in the colon and recording the waves of contraction.[44,65,66] Others have performed recordings of the electrical activity of the colon.[67,68] This is a sophisticated study that is performed by only a few gastroenterologists who are interested in the subject. The results of this study may suggest what we already know, that some parts of the colon move better than others. We look forward to the improvement of the accuracy of these studies and hope that eventually these studies will determine accurately the part of the colon that should be resected.

Histologic studies of the colon in patients with idiopathic constipation mainly show hypertrophic smooth muscle in the area of the dilated colon. We do not know the significance of this finding. One would expect that hypertrophic smooth muscle would produce high-power peristaltic waves; actually, the exact opposite is the case. The dilated part of the colon is usually atonic and aperistaltic.

Another radiologic study involves the use of radiomarkers that are ingested by the patient and followed through the entire gastrointestinal tract.[69-72] The information that this study provides is already known clinically (ie, the colon moves slowly). Therefore, we do not feel that it really contributes to the treatment of these patients.

Treatment

Medical Treatment. For the mild forms of constipation, pediatricians and pediatric gastroenterologists use dietary measures.[7,8] If this alone is not sufficient, they use stool softeners. If that is not enough, they use active ingredient type of laxatives and or enemas.[45-59] They also refer the patients to psychologists[9-14] or subject them to behavior modification[73-79] and biofeedback types of treatments.[80-82] This last treatment modality is also controversial, and the results have been disappointing.[83,84] We do not have experience with those treatment modalities, but we believe that they may have a role in the treatment of the moderate forms of constipation. We concentrate our attention on the treatment of those patients with severe forms of constipation that are resistant to the treatments already mentioned.

Many of these patients receive drugs (such as cisapride) that are designed to increase the motility of the colon.[85-87] We have not seen any positive effect of these drugs on severe forms of constipation. More recently, there are surgeons and physicians who advocate the use of botulinum toxin injected in the anal sphincter to produce relaxation.[88-90] The use of this medication is based on the presumption that these patients have a lack of sphincter relaxation to explain the constipation phenomenon. The number of patients who have been treated in this fashion and the follow-up of them has not been sufficient to draw any definitive conclusions. In addition, we favor the idea that these patients have a motility disorder of the colon, rather than a lack of relaxation of the internal sphincter.

Our treatment protocol for these patients with severe forms of idiopathic constipation includes a trial of medical treatment. If the condition does not respond to this treatment, then we offer the patient a specific type of operation. When the patients come to our clinic, the parents of the patients feel frustrated by the fact that we offer them a medical treatment that they think the patient has already received and not responded to positively. We try to convince the parents that, although we will be using the same medications (laxatives), we are going to use them with the use of a different protocol. The difference is that we will adapt the dosage to the patient's response. We assume (and we are usually right) that the patient received less laxative than required. In addition, we monitor the patient's response radiologically. We adjust the daily laxative dosage and also obtain abdominal radiographs every day to evaluate objectively the degree of fecal impaction.

Disimpaction.—When patients come for consultation, they are usually impacted. We explain to the parents that the disimpaction process is going to be cumbersome and very uncomfortable for both the parents and the patient. The routine includes the administration of 3 enemas per day. The first enema of the day includes the use of phosphate (Fleet; C.B. Fleet Co, Inc. Lynchburg, Va): 1 adult Fleet for patients older than 12 years of age, 1 pediatric Fleet for patients between 4 and 12 years of age, and one half of a pediatric Fleet for patients younger than 4 years of age, plus 500 mL of saline solution for patients younger than 4 years of age or 1 liter of saline solution for patients older than 4 years of age. The second and third enemas of the day include only the saline solution and no Fleet. We try to avoid the overuse of Fleet enemas because of the risk of absorption of phosphate, which can lead to hypocalcemia. The parents administer this treatment for 3 consecutive days. If they believe at some point that the

patient is disimpacted, based on the observation of the patient passing an enormous amount of stool, they bring the patient back to our clinic so that we can obtain an abdominal radiograph to determine whether the colon is really empty of stool. Many times the patient passes a large amount of stool, and the parents believe that the patient is disimpacted, but the patient actually is not. That is the reason that we have adopted the routine of obtaining radiographs to evaluate the amount of stool that remains in the colon. If the patient goes 3 days subjected to this triple enema per day regime and is still impacted, then we admit the patient to the hospital, continue administering the 3 same enemas, but in addition, we administer a balanced electrolyte solution called Golytely (Braintree Laboratories, Braintree, Mass) through a nasogastric tube at a rate of 25 mL per kilogram per hour for 4 hours. Every 4 hours, the patient is evaluated. If there is any question about the presence of hard stool in the abdomen, an abdominal radiograph is obtained to be sure that the patient is disimpacted. The patient receives intravenous fluids and remains with nothing by mouth during the administration of Golytely. If the patient goes 3 days with this regime and is still impacted, we believe that the patient should go to the operating room for disimpaction under anesthesia. It is important to remember not to prescribe laxatives to a patient who is fecally impacted. To do so may provoke vomiting and severe abdominal pain. In addition, the patient will become reluctant to take laxatives for fear of those symptoms. That is the reason that we emphasize first to disimpact and then to administer laxatives.

Determination of the Laxative Requirement in a Disimpacted Patient.— Once the patient has been disimpacted, we administer an arbitrary amount of laxative, usually senna derivative. We determine the initial amount based on the information that the parents give us about the previous response to laxatives. We prescribe the amount that we think is going to work and watch the patient for the next 24 hours. If the patient does not have a bowel movement in the 24 hours after the administration of the laxative, the amount of laxative was not sufficient. We then increase the amount of laxative, but we also administer an enema to remove the stool that was produced during the previous 24 hours. The basic rule is that the stool in these extremely constipated patients should never remain in the rectosigmoid more than 24 hours because if it stays there it will become hard and it will be more difficult to expel in the following days.

We continue the routine of increasing the amount of laxatives and administering an enema every night until we achieve our goal, which is to produce bowel movements and empty the colon completely. The day that the patient has a bowel movement (which is usually with diarrhea),

we obtain a radiograph to be sure that the bowel movement was effective (ie, the patient completely emptied the rectosigmoid). If the patient passed stool but did not empty completely, we continue increasing the amount of laxatives.

Because we are dealing with a spectrum type of disease, we find patients with laxative requirements much larger than one might expect. Occasionally, in the process of increasing the amount of laxatives, we find patients who vomit before reaching any positive effect. In these patients, we may try a different medication to see whether it is better tolerated. Some patients vomit all kind of laxatives, feel very sick, and have severe cramps, and we never reach the amount of laxative capable of producing a bowel movement that empties the colon. That patient is considered intractable and therefore a candidate for a surgical intervention. Most of the time, however, we find the dosage that the patient needs to empty the colon completely, as demonstrated radiologically. Once we have reached that amount, we expect the patient to stop soiling. If the patient soils at this stage, we order a magnetic resonance study of the spine and radiographs of the sacrum. If these are normal, we consider that that patient may have an important psychologic and/or even psychiatric condition. Under those circumstances, we offer that patient the administration of a daily enema as a way to avoid impaction and to avoid soiling during the time that the patient receives adequate psychiatric help.

Most of the time, however, we are successful in reaching the amount of laxative that the patient needs, and the patient remains clean. At this point, the patient and the parents have the opportunity to evaluate the quality of life that they will have with that kind of treatment. We explain to them that the treatment will most likely be needed for life. In fact, as time goes by and the patient grows, the patient may need more laxatives. At that time, after giving the family and the patient a few days or weeks to evaluate the quality of life that they have with this kind of treatment, we discuss with the parents the option of surgery. We explain that, because we do not know the origin of this condition, we do not have a rational treatment to cure these patients. However, we have an operation that provides symptomatic improvement, sometimes to the point that they do not need laxatives and can live a normal life. Because this is a quality of life issue at this point, we respect the feelings of the parents and the patients.

Surgical Treatment.

Sphincter Myotomy.—Sphincter myotomy has many advocates.[23-25] For the reasons that we have discussed already, we do not perform this kind of operation.

Sigmoid Resection and Other Types of Colectomy.—Partial or total colectomies have been performed,[91-95] with variable results. Most surgeons recognize that bowel resection represents a palliative alternative in most cases. According to our concept of a spectrum, some patients benefit more than others from these operations. The challenge for us is to learn to discriminate between those patients who will benefit from those patients who will not.[92] We look forward to more accurate preoperative evaluations.

For the last 14 years, we have been performing a sigmoid resection for the treatment of these conditions.[96] A very dilated megarectosigmoid is shown in Fig 4. The resected megasigmoid and the anastomosis of the descending colon to the rectum are also shown in Fig 4. An intraoperative view of this operation is shown in Fig 5.

During the same time period, we have seen and followed 237 patients with idiopathic constipation. Seventeen of them elected to have operation. We also treated 315 patients with constipation and ARMs. From this last group, 53 patients elected to undergo a sigmoid resection. All but 2 patients improved with this operation. One of the patients who did not improve received a colostomy, which did not alleviate the symptoms, and subsequently the condition worsened. The diagnosis of intestinal pseudo-obstruction was established, and the patient now has an ileostomy. Another patient is still constipated for unknown reasons.

The degree of improvement in these patients, however, varied from one patient to another, which follows with our conviction that these patients are part of a wide spectrum. Approximately 10% of patients did not require any more laxatives and have bowel movements every day with no soiling. Thirty percent of patients decreased the laxative requirement by 80%. The remaining 60% of patients decreased the laxative requirement by 40%.

All of these patients must be followed closely because we are aware of the fact that we are not curing this condition entirely. The rectum that we are leaving behind is most likely abnormal. We assume that it has whatever abnormality affects the rest of the colon; therefore, the patients require long-term follow-up.

Another alternative could be to resect the rectosigmoid (including the rectum) down to the pectinate line in a similar manner as we do for patients with Hirschsprung's disease and to anastomose the nondilated colon that we assume has normal motility to the rectum above the pectinate line. We have not performed this operation because we do not want to increase the morbidity of these interventions.

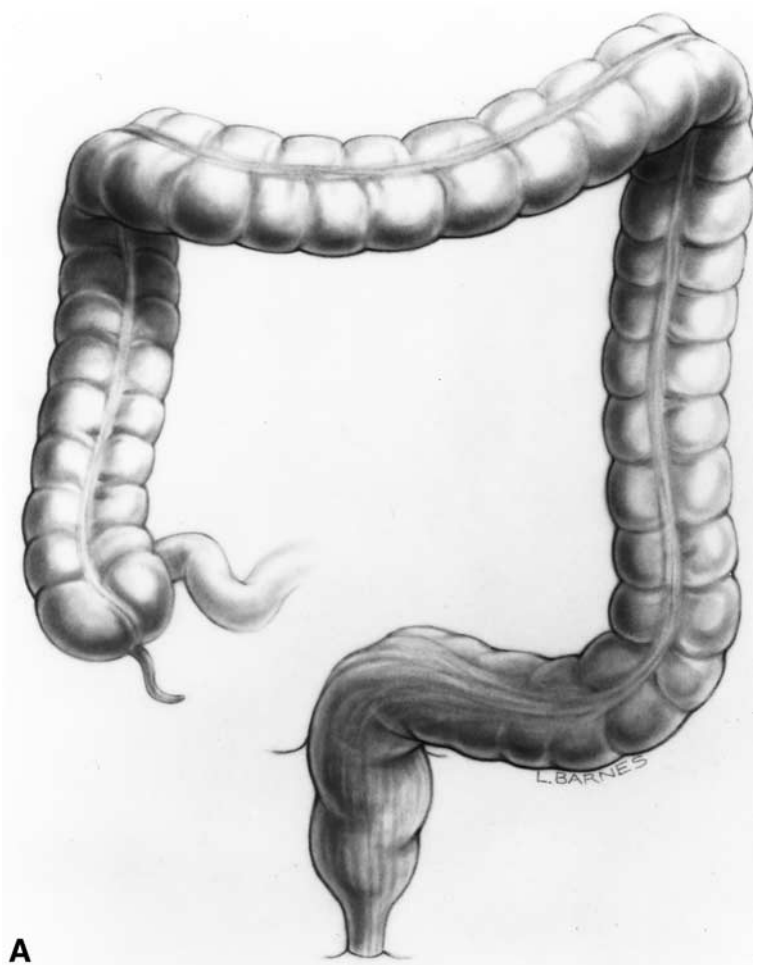

FIG 4. Diagram illustrates the concept of a sigmoid resection. **A**, Normal sized colon. **B**, Megasigmoid and lines of resection. **C**, Operation performed.

The sigmoid resection and anastomosis between the descending colon and the rectum is an operation that takes approximately 3 hours. The patient stays in the hospital 3 to 4 days and does not require a colostomy. We put emphasis on a strict preoperative bowel preparation, mainly mechanical. The complications that are observed in this group of patients include 1 patient who had a partial dehiscence of the anastomosis 1 week after operation. The patient went to an emergency room complaining of abdominal pain, and somebody did a rectal examination that presumably

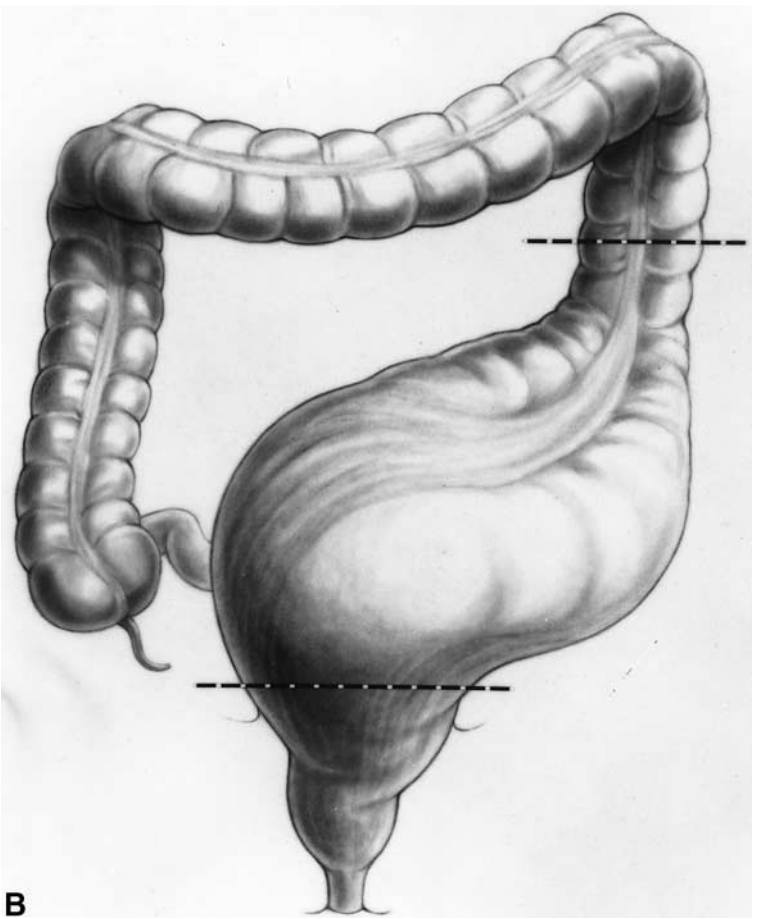

FIG 4. Continued.

could have provoked a perforation, although we are not sure. The patient required a colostomy, which was closed 2 months later.

The most dilated part of the colon is resected because we assume that it is the part of the colon that is the most seriously affected. We assumed that the nondilated part of the colon has a normal motility; that is why we use the nondilated part of the colon to anastomose to the rectum. In retrospect, those patients who improved the most were the same patients who had a more localized form of megarectosigmoid (Fig 6). Patients with more generalized forms of dilated colon did not respond as well. The question that remains, then, is whether we should perform a resection of a longer segment of colon in these patients.

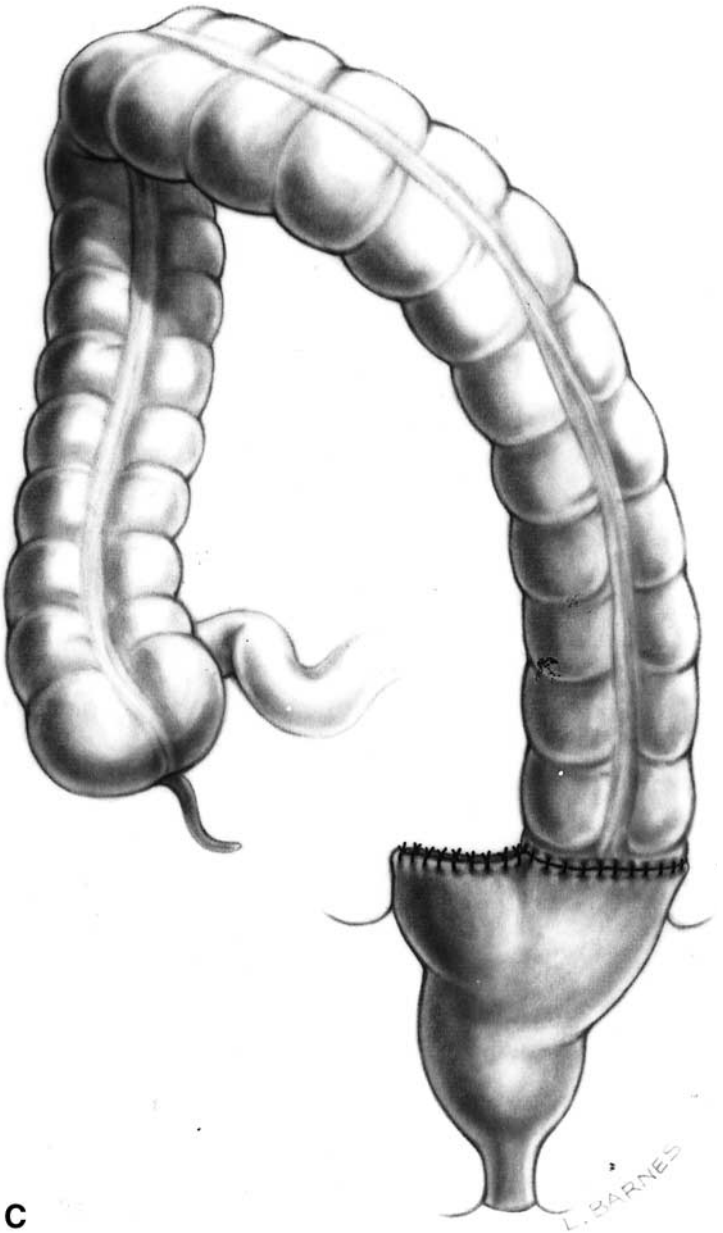

FIG 4. Continued.

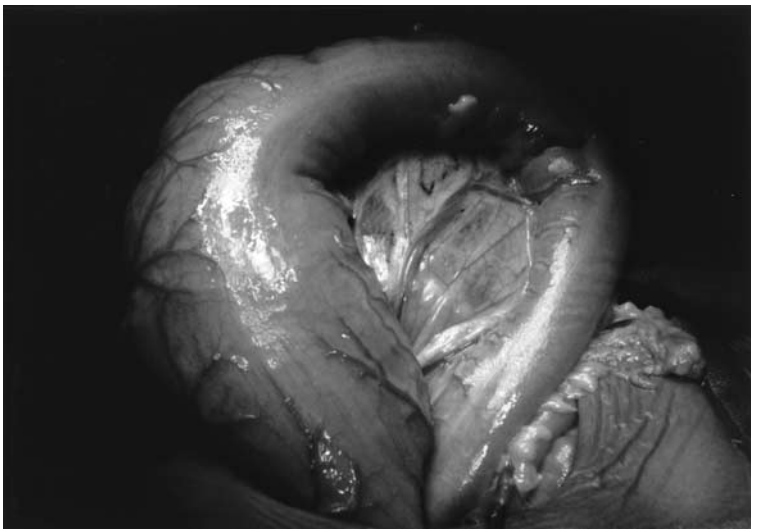

FIG 5. Operative field during a sigmoid resection.

The administration of antegrade enemas through a continent appendicostomy or a button cecostomy is becoming popular.[97,98] We think that this modality of treatment represents a useful alternative for patients who are treated with enemas only, because those antegrade enemas are only a different route of administration of enemas. The overwhelming majority of our patients are treated with laxatives, with or without a sigmoid resection, and therefore do not need continent appendicostomies.

We hope that in the future, a more serious, scientific approach will be applied to this condition. Modern modalities of scientific technology should be used to study this condition. Most likely, there are histologic abnormalities that escape our eye with current histologic techniques. Also, we hope that the motility studies of the colon will reach a degree of perfection that will make them more reliable and more useful from the clinical point of view. Eventually, genetics will have a role in the prevention of this condition because entire families can be affected.

Constipation Problems in Patients with Anorectal Malformations

The most common sequela observed in patients who were born with an ARM is constipation. Approximately 37.6% of all patients have some degrees of constipation. Besides all the uncomfortable and sometimes

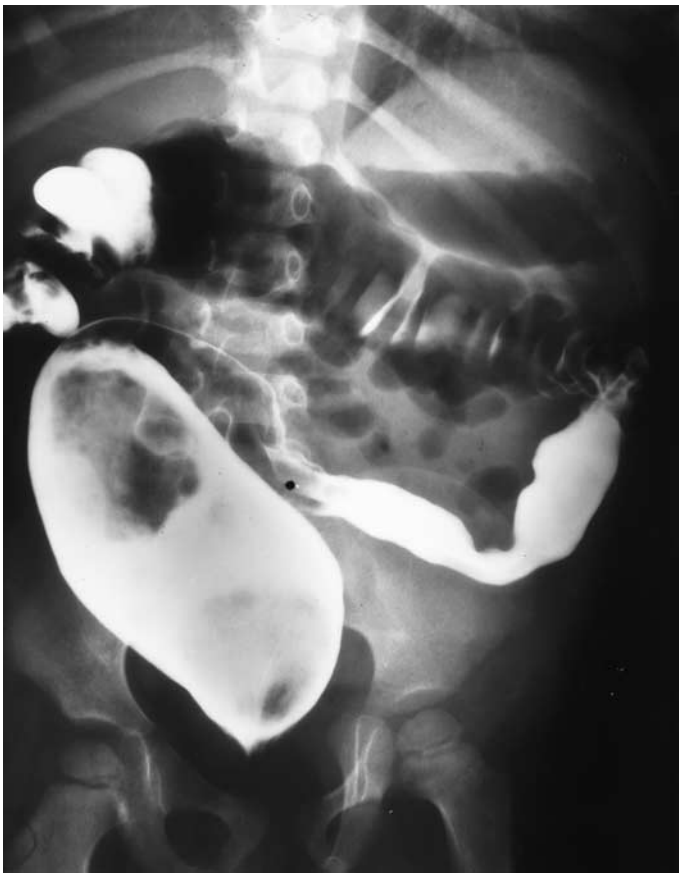

FIG 6. Contrast enema demonstrates a very localized form of megasigmoid.

painful symptoms of constipation, these patients, when not treated properly, experience overflow pseudoincontinence. The second most common sequela observed in children with ARM is fecal incontinence.[99] Unfortunately, the overflow pseudo-incontinence phenomenon is not well known. Consequently, most patients with ARM and overflow pseudoincontinence are not detected and live many years assuming that they have real incontinence. Some of them even receive operations designed for patients who are fecally incontinent. These operations do not help them, but rather make them worse. In reality, an adequate treatment of constipation shows that these patients are fecally continent.

Before 1980, most patients who were born with high ARM were subjected to an abdominoperineal endorectal pull-through type of opera-

tion.[100] This type of procedure, by definition, included the resection of the rectosigmoid and the pull-through of the descending colon down to the perineum. Those patients are now adults and do not have constipation but rather have a tendency to diarrhea. Contrast enemas show a nondilated colon that runs straight from the splenic flexure down to the perineum with an obvious absent rectosigmoid. One can see colonic haustrations in the pelvis, near the anus (Fig 7). Unfortunately, the most of those patients are fecally incontinent. They have the worst type of incontinence that is associated with a tendency to diarrhea or colonic hypermotility. We consider this the worst type of incontinence because it is the most difficult to treat.[101]

In 1980, we started repairing ARMs with a posterior sagittal approach.[102,103] Today, this approach is used in most centers. The posterior sagittal anorectoplasty includes the preservation of the original rectosigmoid of the patient. Most of these patients have constipation.

In our series of more than 1300 patients with ARM who underwent operation with a posterior sagittal approach, 75% have voluntary bowel movements and 25% have fecal incontinence. The association of true fecal incontinence (as opposed to overflow pseudo-incontinence) with constipation makes the medical treatment (bowel treatment) much easier. The key in the treatment consists of finding the type of enema that is capable of cleaning the colon completely every day. Once this has been achieved, the patient remains completely clean for 24 hours (in between enemas) simply because of slow colonic motility and a giant, floppy, reservoir.[101]

Causes and Contributing Factors

Current techniques to repair ARM include the separation of the rectum from the genitourinary tract, plus dissection and mobilization of the rectum to be placed within the limits of the available sphincter. This major rectal dissection has been blamed for the lack of motility of the rectosigmoid that leads to the constipation of these patients. However, for this to be true, one would expect that those patients who are subjected to more extensive dissection would experience a worse degree of constipation. In other words, those patients with higher malformations (higher rectum) require more dissection and more mobilization; therefore, they should experience the most severe degree of constipation. In contrast, those patients with very benign (very low) defects require minimal dissection and mobilization and should experience minimal constipation. Paradoxically, the retrospective analysis of our cases shows the opposite to be true.[99] The higher the malformation, the worse the prognosis for

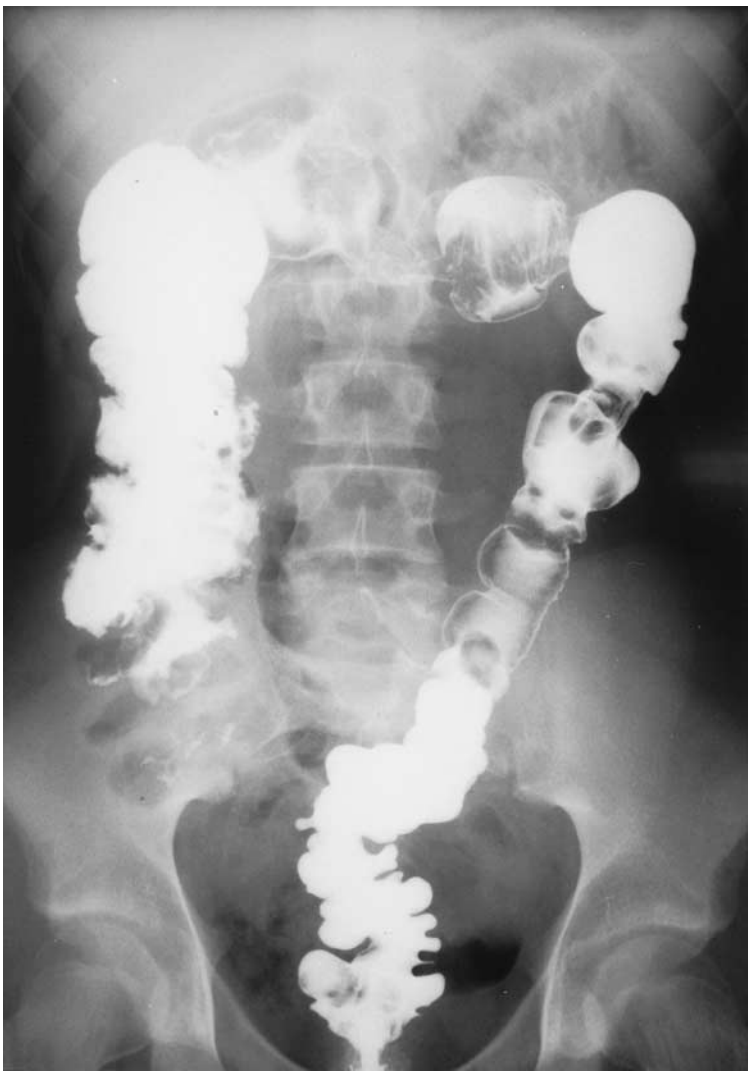

FIG 7. Contrast enema demonstrates no rectosigmoid.

bowel control, but the less chance of constipation. The lower the malformation, the higher the chance of achieving bowel control, but the higher the chance of constipation. This fact deserves future investigation. On the basis of the observation of multiple prenatal ultrasound scans from our patients, we have evidence that babies with ARM have a dilated rectosigmoid before birth. We believe that in utero colonic dilatation

gives these patients a degree of constipation after birth. This problem can be exacerbated or minimized after birth, depending on the treatment that is provided to the patient.

The most obvious factor that may aggravate a problem of constipation is an anal stricture, which can be prevented by the performance of a technically correct operation, with special emphasis to avoid ischemia of the mobilized rectum and to avoid excessive tension on the anastomosis. It is also very important to follow a specific protocol of anal dilatations after operation. During the repair of an ARM, the rectum is placed within the limits of the sphincter. At the end of the operation, particularly in patients with good sphincters, the anus looks closed because of the effect of the surrounding sphincteric mechanism. Under those circumstances, it is easy to understand that the anus will heal closed unless it is dilated. Our protocol of anal dilatations has been published previously.[99] It basically consists of daily passage of metallic dilators, gradually increasing the caliber until reaching the size considered normal for the patient's age. After that, the frequency of dilatations is gradually decreased over a period of months to avoid stricture.

A retrospective analysis of our series of 1300 ARM cases, seeking factors that could promote or exacerbate constipation, revealed some interesting and unexpected facts. Most patients who underwent operation came to our institution with a colostomy already in place. That gave us the opportunity to find out whether the type of colostomy played a role in the determination of the degree of constipation. We found that patients with a descending or sigmoid colostomy with separated stomas, have less constipation and had a less dilated rectosigmoid, particularly if it had been irrigated and maintained empty of meconium. Patients with loop colostomies that allowed the passing of stool from the proximal into the distal limb had a very dilated rectosigmoid that was impacted with stool (Fig 8); after the repair and after the colostomy had been closed, these patients experienced severe constipation.

The old rule was again confirmed: "A dilated hollow viscus has a poor peristalsis." Moreover, patients with transverse colostomies experienced very severe megarectosigmoid, particularly if they had a loop colostomy. We learned that it is very difficult to irrigate and clean a rectosigmoid through a stoma that had been created in the transverse colon. The distal colon remains very small (microcolon), and yet the rectosigmoid becomes progressively more distended giving a characteristic appearance (Fig 9). The degree of rectosigmoid dilatation was greater the longer the length of time that the patient remained with the colostomy before the main repair.

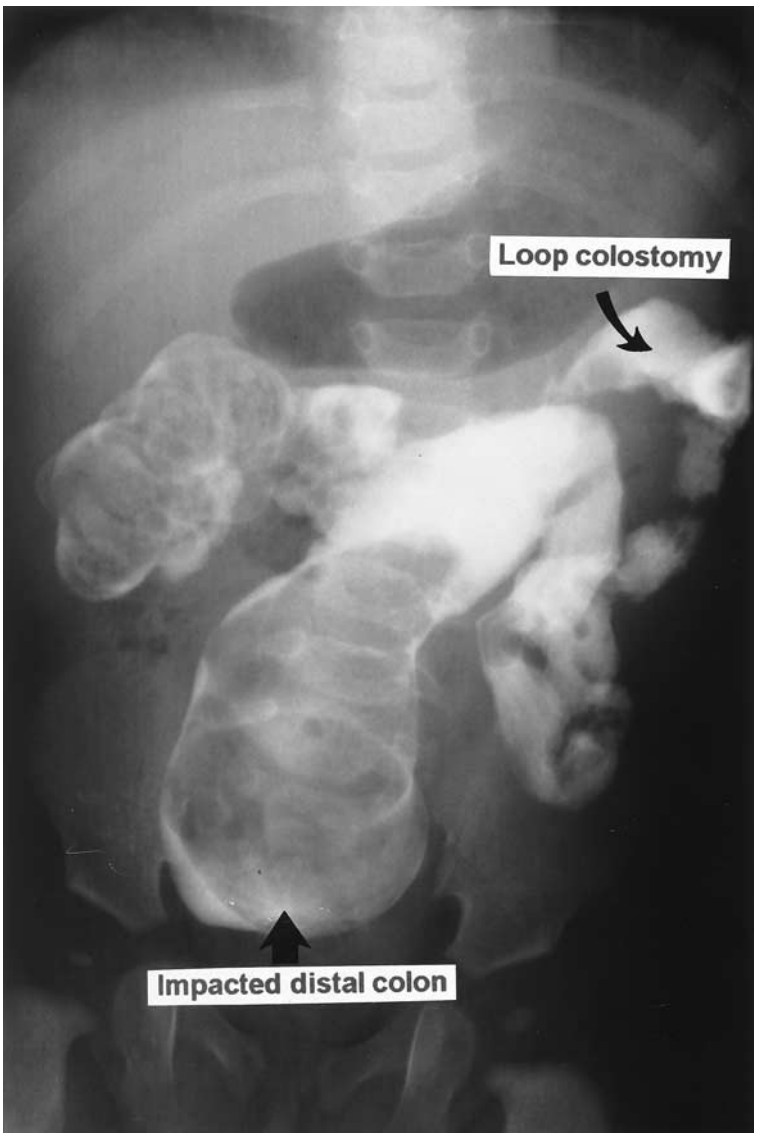

FIG 8. Impacted distal rectosigmoid caused by a loop colostomy.

Again, the more dilated the rectosigmoid, the more severe the constipation that the patient experienced.

The literature indicates that Hirschsprung's disease occurs more frequently in patients with ARM than in the rest of the population.[104] The analysis of our series does not support this conclusion, however. We were

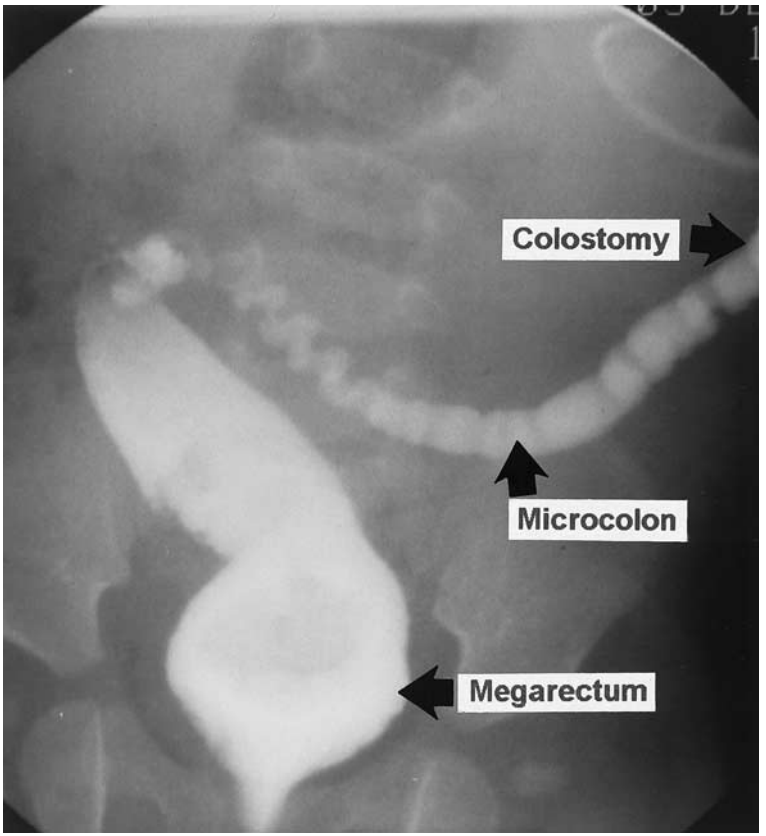

FIG 9. Characteristic image of a microcolon with megasigmoid in a patient with a transverse colostomy.

able to find only 2 demonstrated cases of Hirschsprung's disease in our series. On the other hand, besides the 1300 patients who underwent operation, we have seen and medically treated another 400 patients who underwent operation elsewhere. Many of these patients experienced severe constipation. The responsible surgeons suspected Hirschsprung's disease and frequently took biopsy specimens, which most often excluded aganglionosis. In 3 cases, however, the biopsy showed no ganglion cells; the surgeons accepted this finding as evidence of Hirschsprung's disease and performed an abdominoperineal resection and pull-through. That procedure cured the problem of constipation but unfortunately rendered those patients fecally incontinent. We suspect that those patients did not have Hirschsprung's disease because clinically they behaved like patients with idiopathic constipation. They never had an episode of enterocolitis;

their rectum was dilated all the way down to the anal canal; they soiled, and the biopsy did not show hypertrophic nerves, which is another important histologic component that is expected in a patient with Hirschsprung's disease. In summary, we believe that Hirschsprung's disease is not more common in patients with ARM than in the general population, and we suspect that such an association is being overdiagnosed.

Perhaps, the most important aggravating phenomenon in the pathogenesis of constipation is the self-aggravation that occurs when constipation is not suspected; consequently, it is not treated early and efficiently. Many surgeons consider their responsibility finished after they have repaired the malformation and closed the colostomy. In addition, they do not alert the parents about the risk of the patient experiencing constipation and about the self-aggravating characteristic of the disorder. In addition, pediatricians are not alerted to this problem. This may have very serious consequences, particularly in patients who were born with a benign ARM with an excellent functional prognosis. Some of them are left unattended, and the colon gradually enlarges to reach giant dimensions. When they reach the age of bowel control, they continue to experience encopresis; and unfortunately, they are frequently treated as if they were fecally incontinent. Sometimes they are even subjected to operations to improve bowel control, which actually worsens the problem of constipation.

Treatment

The medical treatment of patients experiencing constipation and ARM is not different from the treatment described earlier for patients with idiopathic constipation. The only difference resides in the indications for a sigmoid resection. Basically, we feel that a sigmoid resection in a constipated patient with real fecal incontinence is contraindicated. We must keep in mind that, when treating patients who are fecally incontinent, it is much easier to implement our bowel treatment program by keeping a patient artificially clean when that patient is constipated and has a dilated, floppy colon compared with the situation when the patient is incontinent and has a tendency to diarrhea. In the first situation (incontinence and constipation), the goal of the treatment is to find, by trial and error, the type of enema that is capable of cleaning the rectosigmoid completely every day. Once that is achieved, the patient will remain completely clean for 1 or 2 days because of, in part, the floppy, aperistaltic rectosigmoid. In the second situation (incontinent with tendency to diarrhea), the treatment is more complicated because it requires not only finding the type of enema that will clean the colon but also

finding a way to paralyze the colon or at least to decrease its peristalsis to guarantee that the patient remains clean in between enemas.[101] Therefore, we consider the possibility of a sigmoid resection only after we have demonstrated that the patient is fecally continent.

The problem of overflow pseudo-incontinence must be suspected during an evaluation of a patient who was born with a benign condition, for which a good functional result is expected. The patient has a normal sacrum and a normal lumbar spine. The patient experiences severe constipation that has not been treated properly and comes for consultation for, what the family believes is, fecal incontinence. That patient must be disimpacted first. Then, over a period of several days, we determine the amount of laxative that is necessary to empty the colon completely, as demonstrated by an abdominal radiograph. Once this has been achieved, we find out whether the patient has bowel control. If the patient is truly incontinent and constipated, the patient must receive the bowel treatment. On the other hand, if the patient has bowel control, the patient must receive the determined dosage of laxative on a permanent basis with an option for a sigmoid resection that will make the treatment easier by decreasing the laxative requirements significantly.

Colonic Motility and Bowel Control

For an individual to have bowel control, it is necessary to have 3 important anatomic and physiologic elements: sensation, sphincter mechanism, and colonic and rectosigmoid motility. We will not elaborate on the importance of the first 2 elements, because their relevance is obvious; there is plenty of literature on this subject, and such discussion is beyond the scope of this monograph.

The relevance of rectosigmoid and colonic motility in bowel control has been largely underestimated. Several clinical situations have convinced us of the importance of colonic motility in fecal continence. The first and most common clinical situation is the one already mentioned several times, overflow pseudo-incontinence. Patients with this problem behave as if they are fecally incontinent although they have fecal impaction and yet are totally continent when disimpacted. This situation occurs both in patients with and without ARMs and illustrates how colonic inertia may relate to fecal incontinence.

Another, less common but more impressive, clinical situation is represented by patients who have had severe damage to the anus and rectum that provoked a total destruction of the sphincter mechanism and the anal canal (this structure contains the nerve endings that provide exquisite sensation, so important for bowel control). These patients are

without sensation and without sphincters. Yet, some of them behave as fecally continent individuals, provided they do not have a colonic motility disorder. When the injury did not affect the motility of the rectosigmoid, they remained having 1 or 2 well-formed bowel movements every day at a predictable expected time (as most normal human beings), and they remain completely clean in between bowel movements. It becomes clear that they are not normal when something affects their colonic motility, giving them diarrhea or unexpected bowel movements. This situation illustrates a frequently unrecognized concept: an individual can live a normal life and be socially accepted, without anal sphincter or sensation, provided that individual has an anatomically and functionally normal colon.

We take advantage of this situation when implementing our bowel treatment program in patients with fecal incontinence. An enema empties the rectosigmoid, which is the first step of the treatment. The second step consists of decreasing the motility of (or even paralyzing) the colon by dietary and/or pharmacologic means. This guarantees the cleanness of the patient.

The third common clinical situation that illustrates the importance of motility in bowel continence is in patients who have lost their entire colon and undergone an ileoanal anastomosis, with or without a pouch. Most patients achieve bowel control when subjected to a technically correct operation, but many patients have continence problems even when they have normal sensation and a normal sphincter mechanism.

In conclusion, we have tried to give examples that illustrate the importance of motility in bowel control. We may even speculate that, in theory, we could efficiently treat a problem of fecal incontinence by the administration of a pharmacologic agent that could provoke a controlled wave of sigmoid peristalsis (bowel movement) followed by the administration of another agent that could paralyze the colon, which would keep the patient clean, provided that the patient had the capacity to form solid stool.

Colonic Aganglionosis (Hirschsprung's Disease)

Colonic aganglionosis, also known as Hirschsprung's disease, is a common problem with which all pediatric surgeons are familiar. It is a condition that is treated successfully in most patients but still represents a therapeutic challenge in many cases.

The first clinical description was in 1691 when Fredrick Ruysch described the autopsy of a child who died with what appeared to be a congenital megacolon.[105-107] Harold Hirschsprung in 1886 at the Pediat-

ric Congress in Berlin described an infant with this condition[108,109]; the first reference to the underlying pathophysiologic features was by Tittle,[110] who noted the underlying condition to be related to the absence of ganglion cells. Tiffin and colleagues[111] in 1940 described the disturbed peristalsis of the aganglionic intestine; Zuelzer and Wilson[112] in 1948 and Robertson and Kernohan[113] in 1938 were able to correlate the functional disturbance of the distal colon with aganglionosis. Swenson and colleagues[114] described the keys to the radiologic diagnosis, and the first rational surgical approach was reported by Swenson and Bill[115] in 1949. Modifications of this technique, such as the Duhamel[116] approach and the Soave[117] operation were developed to avoid some of the complications that had been encountered with the Swenson method but were based on the same principles of repair that involved the resection of the aganglionic segment of bowel and pull-through of the normoganglionic and nondilated colon.

Pathophysiologic Features

Partial or complete functional colonic obstruction that is associated with the absence of intramural ganglion cells describes the basis of Hirschsprung's disease. The aganglionic portion of the colon is always located distally, but the length of aganglionosis varies.

The spectrum of the manifestations with this disease is determined by the extent of aganglionosis. The most common type (occurring in two thirds of patients) is one in which the aganglionic segment includes the rectum and sigmoid colon.[118] Long-segment Hirschsprung's disease occurs in approximately 10% of cases.[118] In this situation, the aganglionic portion may extend to any level between the hepatic flexure and the descending colon. Total colonic aganglionosis, also occurring in approximately 10% of patients,[118] is a serious condition in which the entire colon is aganglionic, frequently including a portion of the terminal ileum. The so-called "ultra short" Hirschsprung's disease is an entity not agreed on by all authors. It is frequently difficult to differentiate from functional idiopathic constipation.

Typically, the aganglionic portion of the colon appears narrow when compared with the proximal distended portion. The aganglionic segment has an absence of intramural, submucosal, and intermuscular ganglion cells. In addition, the nerve fibers are increased in size and prominence. The proximal, normally innervated, portion of the colon is usually distended, and its wall is thickened because of muscle hypertrophy. Mucosal ulcerations can also be present. Between these 2 areas is a transition zone, which histologically is usually hypoganglionic.

In addition to the finding of aganglionosis that defines Hirschsprung's disease, there is an increase in acetylcholinesterase in the aganglionic colon.[119,120] With the use of acetylcholinesterase staining, a significant increase in the number of oversized nerve fibers in the muscularis mucosa, the lamina propria, and the submucosa can be observed.

It is believed that, in patients with Hirschsprung's disease, an arrest occurs in the craniocaudal migration of the neuroenteric ganglion cells from the neural crest into the upper gastrointestinal tract, down through the vagal fibers, and along the distal intestine.[121] As a result, ganglion cells are missing from Auerbach's myenteric plexus (located between the circular and longitudinal layers of bowel wall), Henle's plexus (in the deep submucosa), and also in Meissner's plexus (in the superficial submucosa). Normally, the ganglia act as a final common pathway for both sympathetic and parasympathetic influences. Their absence may produce uncoordinated contractions of the affected bowel. Lack of propulsive peristalsis, mass contraction of the aganglionic segment, lack of relaxation of the bowel, and spasm of the internal sphincter have all been demonstrated.[122-125] Nitric oxide has been considered a neurotransmitter that is responsible for the inhibitory action that is elicited by the intrinsic enteric nerves. A lack of nitric oxide synthase (the enzyme required for nitric oxide production) has been demonstrated in the myenteric plexus of the aganglionic segment.[126,127]

The clinical impact of these pathophysiologic events is partial or total functional colonic obstruction, although the extent of aganglionosis and the severity of symptoms do not necessarily correlate. All of these abnormalities explain the reason that there is a functional colonic obstruction. However, there are other very important functional abnormalities that affect patients with Hirschsprung's disease that are not well understood. The fecal stasis that results from the functional obstruction produces not only characteristic signs of colonic obstruction but also leads to a serious bacterial proliferation with the production of toxins that produces a condition called enterocolitis, which can be lethal. Fecal stasis by itself would produce the clinical situation known in patients with idiopathic constipation and not lead to the serious complication of enterocolitis. Clearly, there is some other factor that may represent a local immunologic deficiency of the intestine. It is this clinical condition that is unique to Hirschsprung's disease.

The incidence of Hirschsprung's disease is 1 per 5000 births.[118] The disease appears to be more common in white patients, and boys are more frequently affected than girls.[118] The inheritance pattern is multifactorial. A sibling sister of an affected boy has a 0.6% chance of having

Hirschsprung's disease. A brother of an affected girl with long-segment disease has an 18% risk.[128] Down's syndrome is found in 5% of patients with Hirschsprung's disease.[129]

A deletion in the long arm of chromosome 10 has been identified in patients with Hirschsprung's disease,[130] and this deletion appears to overlap the region of the RET proto-oncogene. Patients with multiple endocrine neoplasia (MEN 2A) also have a deletion of this proto-oncogene.[116] Investigators are rapidly making progress in defining the genetic basis of this disease.[131-137]

Clinical Manifestations

Infants with Hirschsprung's disease usually become symptomatic during the first 24 to 48 hours of their life. Occasionally a child may have minimal or absent clinical manifestations during the first days or weeks and exhibit intermittent bouts of symptoms later in life. Most patients are diagnosed in their first year of life.

Abdominal distension, delayed passage of meconium, and vomiting are the most frequent observations. A spontaneous or induced explosive passage of liquid stool and gas often occurs, which dramatically improves the baby's condition. Symptoms recur after an asymptomatic period, which may last hours to days. Stools are frequently liquid and are foul smelling.

The infant may become very ill from enterocolitis that includes sepsis and hypovolemia. This severe, potentially lethal, condition should not be confused with gastroenteritis. The patient experiences abdominal distension, vomiting, explosive bouts of gas, foul-smelling liquid stools, proliferation of unusual anaerobic bacteria (*Clostridium difficile*), toxemia, lethargy, and sometimes death. On rare occasion, necrosis proximal to the aganglionic segment can occur. Enterocolitis carries a significant mortality rate if not treated quickly. Patients with Hirschsprung's disease that goes undiagnosed and therefore untreated have a high mortality rate.

Other causes of intestinal obstruction in the newborn must be excluded. Meconium plug syndrome is the most frequent condition, with manifestations similar to Hirschsprung's disease. The expulsion of a plug of meconium with resolution of symptoms and the absence of other signs that are characteristic of Hirschsprung's disease helps establish the diagnosis. Meconium ileus (another condition on the differential diagnosis list) is manifested by a clinical picture of intestinal obstruction and a characteristic image of "ground glass" on the abdominal radiograph. A family history of cystic fibrosis may be present. Once the meconium is cleared, symptoms tend to resolve, at least temporarily. Small left colon

syndrome (more common in a baby whose mother has diabetes mellitus) can be detected by contrast enema, which demonstrates a narrow left colon to the level of the splenic flexure. Symptoms usually improve after the contrast study and resolve over several weeks. Hypothyroidism, adrenal insufficiency, cerebral injury, and ileus that results from prenatal drug exposure can be confused with Hirschsprung's disease.

Patients who survive with inadequate treatment or with relatively mild symptoms ultimately experience severe constipation, with an enormously distended abdomen. The proximal colon is huge and full of inspissated fecal matter. At this stage, the diagnosis may be confused with chronic idiopathic constipation.

In contrast to Hirschsprung's disease, patients with idiopathic constipation usually become symptomatic after the sixth month of life, do not vomit, never experience enterocolitis, and do not become seriously ill. These patients often experience overflow pseudo-incontinence or encopresis (constant, chronic soiling). Rectal examination of these patients reveals severe impaction, which is in contrast with patients with Hirschsprung's disease in whom the rectal vault is often empty.

Diagnosis

A high index of suspicion is needed to establish the diagnosis of Hirschsprung's disease in the newborn period. The clinician who evaluates a newborn with abdominal distension, failure to pass meconium, and explosive diarrhea after rectal examination should suspect Hirschsprung's disease and proceed with an evaluation.

The plain radiograph of a neonate with a distended colon is hard to differentiate from one with distended small intestine. Air fluid levels can be present but are a nonspecific finding. A contrast enema with dilute barium or water-soluble material is the most valuable radiologic study for the establishment of the diagnosis of Hirschsprung's disease. The contrast enema is performed without a bowel preparation, and the contrast injection is controlled by hand with a syringe. It is vital that the catheter not be introduced beyond the limit of the anal canal, because the tip may reach the distended colon and result in injection above the aganglionic segment. The study may show a distended proximal colon, the transition zone, and a nondistended distal rectosigmoid (Fig 3).

The older the patient, the more obvious the size difference between the normal ganglionic intestine and the abnormal aganglionic one. Sometimes the typical changes are not present during the neonatal period. The contrast enema is less accurate in infants with very short aganglionosis or when the entire colon is involved. In the latter situation (total colonic

aganglionosis), the contrast study may reveal a short colon, with retraction of the hepatic and splenic flexures and straightening of the sigmoid.

Anorectal manometry has been used for the diagnosis of Hirschsprung's disease.[138,139] The principle behind this technique depends on relaxation of the internal sphincter when the rectum is distended with a balloon that leads to a measured fall in the anal canal pressure. In patients with Hirschsprung's disease, this expected reflex is absent.[124] However, this test has several significant limitations. It is difficult to perform in the newborn; in older children with a large rectal vault that is the size of the balloon, it may be inadequate to distend the rectum, therefore giving inaccurate recordings.

Rectal biopsy is the procedure that is used to confirm this diagnosis on the basis of the absence of ganglion cells and the presence of excess nonmyelinated nerves. The specimen must be taken above the normal zone of aganglionosis that all normal individuals have and that ends approximately 1.5 cm above the dentate line. Full-thickness rectal biopsy in older children and suction rectal biopsy in newborns usually gives adequate tissue to make the diagnosis. The specimen must include mucosa and submucosa. An accurate histologic diagnosis of Hirschsprung's disease can only be established by an experienced pathologist. Errors in the establishment of this diagnosis are not uncommon and can lead to serious complications from incorrect treatment.

Some centers assess the amount of acetylcholinesterase in the biopsy specimen as a diagnostic alternative. An absence of nicotinamide adenine dinucleotide phosphate–containing neurons and an increase in acetylcholinesterase-containing nerve bundles are characteristic of Hirschsprung's disease.[140] In addition, authors have mentioned nitric oxide synthase as a candidate neurotransmitter that may be responsible for relaxation of the internal anal sphincter.[141]

Medical Treatment

Bowel irrigation with saline solution is an extremely valuable procedure for the emergency treatment of distension and vomiting. The act of decompressing the bowel with irrigations may produce dramatic improvement in a very ill infant. Irrigations can be continued until the time of definitive surgical intervention. Irrigations are also valuable for treating enterocolitis, which can occur both before and after surgical treatment.

Surgical Treatment

Colostomy. Decompression with colostomy is the traditional initial treatment after the diagnosis of Hirschsprung's disease is made. In most

centers today, primary pull-through is performed without colostomy. However, the colostomy in this disease is still very valuable for the patient, under certain conditions. In particular, patients who are very ill initially may need urgent colostomy, and patients who undergo operation in centers without the ability to perform histologic evaluation on an emergent basis may also require colostomy.

The colostomy addresses the emergency situation of bowel distension and provides protection for the future pull-through. A right transverse colostomy is an effective and safe method for decompression of the colon in most patients. It is very unlikely that the stoma will be in an aganglionic segment. It is particularly useful in the emergency situation, if the radiologic determination is unreliable or if frozen section pathologic examination is unavailable. Of course, the major risk of this type of colostomy occurs if the patient has long-segment disease. When the definitive procedure is performed, the colostomy may interfere with the pull-through because of the short length of bowel that remains between the stoma and the transition zone.

Many surgeons advocate the creation of the colostomy just above the transition zone. This obligates the surgeon to pull the colostomy down at the time of the definitive repair, depriving the patients of the protection of proximal diversion. This approach does limit the number of procedures to 2, as opposed to the situation of a right transverse colostomy which requires a third stage colostomy closure.

The trend has been away from the use of initial colostomy and toward definitive surgical procedures in the newborn period, with a 1-stage repair that has been shown to be feasible without increased operative mortality rate.[142-148] The long-term effects of this approach (including late constipation, enterocolitis, and fecal incontinence) remain to be established.

Definitive Operations.

Swenson Procedure.—The Swenson procedure involves placing the child in lithotomy position and entering the abdomen through a Pfannenstiel, hockey-stick incision. The aganglionic colon is resected, including the dilated portion of bowel. The aganglionic area is mobilized below the peritoneal floor by precise dissection as close as possible to the rectal wall down to the level of the levator ani muscle. The middle hemorrhoidal vessels are ligated, and electrocautery is used to dissect the perirectal vasculature. The aganglionic bowel is resected above the pectinate line. The normoganglionic bowel is mobilized, which preserves its blood supply and a transanal hand-sewn anastomosis is performed to the rectum, 1 to 2 cm above the pectinate line.[115]

Duhamel Procedure.—The Duhamel[116] procedure was developed to avoid the extensive pelvic dissection that is required in the Swenson operation. The aganglionic rectum is preserved, and the bowel is divided and closed at the peritoneal reflection. Normal ganglionic bowel, above the most dilated portion, is pulled through a presacral retrorectal space created by blunt dissection. The posterior rectal wall is incised above the dentate line, entering the previously dissected retrorectal space. The ganglionic bowel is then pulled through the rectal incision, and a stapler or 2 crushing clamps are used to create the anastomosis between the posterior rectal wall and the anterior wall of the normoganglionic bowel. The anastomosis between the colon and the aganglionic rectum must be wide, and the rectal stump must be as small as possible to avoid fecal accumulation.

Soave Procedure.—In the Soave[117] procedure, the surgeon removes the aganglionic rectosigmoid by an endorectal dissection down to a point located 1 to 2 cm above the pectinate line, theoretically minimizing the risk of pelvic nerve injury that is associated with the Swenson procedure. The normally innervated colon is passed through the rectosigmoid muscular cuff. Originally this operation was performed without a colostomy and left a portion of the pulled through colon protruding outside the anal skin margin. This colon was excised at a second operation 1 week later. Boley modified this procedure into a 1-stage operation by performing a primary anastomosis.[149]

Primary Pull-through.—In 1980, So and colleagues,[142] from our institution, presented a series of patients with Hirschsprung's disease who underwent a 1-stage endorectal approach in the newborn period. Their results suggested that 1-stage operative repair is feasible in children and neonates and has many advantages (such as the elimination of the need for additional anesthesia, surgical procedures, and the possible complications of a colostomy). Subsequent to this pioneering effort, several series that used the 1-stage approach have been reported.[143-148,150]

Laparoscopic and "Incisionless" Approaches.—With the recent advances in laparoscopic techniques and instrumentation, laparoscopic pull-through procedures are becoming common.[151,152] Georgeson and colleagues[153,154] in 1995 introduced the primary laparoscopic pull-through for Hirschsprung's disease. Using this approach, the abdominal incision that is used in the conventional approach is avoided; there is a more rapid return of bowel function, a shorter postoperative recovery, and excellent cosmetic results. This technique involves a seromuscular biopsy to confirm the location of ganglionic bowel, followed by laparoscopic mobilization of the distal colon.[154] Rectal mobilization is completed with

a transanal mucosectomy. The technique appears to reduce the perioperative complications and postoperative recovery time dramatically. The technique is learned quickly and has been performed in multiple centers with consistently good results.

De la Torre and Mondragon[155] in 1998 and Langer and colleagues[156,157] in 1999 reported a 1-stage pull-through procedure that can be performed successfully with the use of a purely transanal approach without an intraperitoneal dissection. If the transition zone is in the rectosigmoid, which is the case in most patients, the entire operation can be performed transanally and is truly incisionless. If the normoganglionic bowel cannot be reached transanally, the operation can be completed with laparoscopy or laparotomy.

We have experience at our center with the use of the endorectal procedure. We have also used the posterior sagittal approach in 49 patients who were referred to us after having an attempted, but failed, operation at another institution. These patients have catastrophic operative complications that include infections, dehiscence, retraction, abscesses, and fistula formation to the genitourinary neighboring structures or to the perianal skin.

We have found the posterior sagittal approach to be an excellent way to restore the anatomic features in these patients. On the basis of this experience, we decided to use the posterior approach in 29 primary operations. We were very impressed by the excellent exposure that enabled us to resect the aganglionic and dilated bowel, pull down and anastomose the normoganglionic nondilated bowel to the rectum, above the pectinate line, in a very accurate way, that preserved normal bowel control in all patients. We moved to performing this same operation without a protective colostomy in the last 9 patients in this series. Three patients experienced postoperative rectocutaneous midline fistula, which healed uneventfully after the creation and subsequent closure of a colostomy.

We concluded that the posterior sagittal approach is an excellent way to repair the rectum in this condition, particularly in secondary procedures, but the patients require a protective colostomy. Currently, for a newborn with Hirschsprung's disease, we avoid the posterior sagittal incision altogether and perform the full-thickness rectal mobilization exclusively transanally with the baby in prone position, without performing a colostomy.

Total Colonic Aganglionosis

Martin[158] in 1968 described a technique for treating total colonic aganglionosis in Hirschsprung's disease that uses the aganglionic portion

of the colon and takes advantage of its water resorptive capacity. An ileostomy was performed at the time of diagnosis, and the definitive operation was performed at 1 year of age. The ganglionic terminal ileum was pulled down through the retrorectal (presacral) space, as described for the Duhamel procedure. The small bowel was brought through the incised opening in the posterior rectal wall and the end of the ileum was then sutured to the opening in the posterior rectal wall. A stapler was used to remove a triangular-shaped segment of the common wall between the rectum and small bowel. Up to this point, the procedure was not different from that of the Duhamel operation. The next step consisted of the creation of a long side-to-side anastomosis between the distal ileum and rectum, sigmoid, and descending colon up to the level of the splenic flexure. The proximal aganglionic intestine was excised.

Kimura and colleagues[159] advocated a staged approach. The first operation consists of an ileostomy, and the second stage is a side-to-side ileo-ascending colon anastomosis. At the final stage, the terminal ileum (with the right colon as a free patch) is pulled down with either a Swenson, Duhamel, or Soave technique. Their goal, similar to Martin's, was to take advantage of the water absorption capacity of the right colon and also to try to create a reservoir to decrease the excessive number of bowel movements.

Total colonic aganglionosis continues to be a formidable therapeutic challenge. First, the low incidence of this variant does not allow for any single surgeon, perhaps with the exception of Martin, to accumulate a significant series to draw valid conclusions regarding the best way to treat this serious condition. Martin's idea and its variants[159,160] were based on the assumption that an aganglionic patch will absorb water and will create a reservoir that will help to form solid stools and to decrease the excessive number of bowel movements.

Although it is true that some patients fare reasonably well after being subjected to that kind of operation, many more patients have a difficult short- and long-term course, with many problems and a poor quality of life. In fact, many patients who were referred to us and who have had operation at other institutions, not only do not absorb water through those patches but actually experience a form of secretory diarrhea that is only controlled by the resection of the pouch. Some patients have excessive fluid losses; a diverting proximal ileostomy that left the pouch in situ did not improve the problem, and the resection of the pouch immediately alleviated the problem. We have encountered 5 such patients. Other authorities also believe that those patches do not represent an advantage

for the patient and agree with the idea of performing a straight end-to-end anastomosis between the terminal ileum with normal ganglion cells and the rectum 2 centimeters above the pectinate line.[145,147]

Under the best circumstances, these unfortunate patients all have a difficult life. In addition, in an era of competition between pediatric surgeons to perform major operations earlier and earlier, these babies undergo operation early in life and experience the most severe forms of diaper rash, which gives them and their parents very poor quality of life. These issues rarely receive adequate discussion.

It also appears that the longer the segment of aganglionosis, the higher the chance of experiencing enterocolitis, which adds more problems for these patients. As a result, we perform the main repair in cases of total colonic aganglionosis after the patient becomes toilet trained for urine (usually after 3 years of age). The presence of an ileostomy upsets the parents and the surgeon, but the babies are usually happy and thriving. When the operation is performed at that age in a toilet-trained patient, it becomes easier to control the stool when it comes in the form of multiple liquid bowel movements.

Ultra Short-segment Aganglionosis

The treatment of ultra short Hirschsprung's disease is a matter of considerable controversy. Anorectal myectomy, which is reported to be a posterior internal anal sphincterotomy, has been advocated.[23,161-166] The results have not been consistently satisfactory, and there is no clear rationale to support this operation.

There is evidence that a dilated hollow viscus looses its normal effective peristalsis.[167-172] This is true, both in the gastrointestinal tract and in the urinary tract.[173,174] Our experience in the reoperation of 49 cases of Hirschsprung's disease provided evidence of the importance of this concept. Leaving dilated normoganglionic bowel results in severe postoperative constipation.

Short- and Long-term Problems

In spite of many triumphant reports, we are far from curing Hirschsprung's disease. It is conceivable that we are biased by the fact that a large number of patients are referred to us after a failed previous operation. The recent therapeutic advances, including the primary approach without a colostomy, the laparoscopic approach, and the transanal operation are welcome because they tend to decrease suffering in these patients. Yet the real challenge remains the same. These novel approaches did not impact on the main short- and long-term problems of these

patients. We believe that these postoperative sequelae should be the center of our attention and the motivation for future scientific studies. We have divided these sequelae into 3 categories: preventable, nonpreventable, and partially preventable.

Preventable Sequelae. This is the most important group of problems. The consequences of a technical error or lack of experience in the performance of these procedures generally are considered unacceptable. These include dehiscence, retraction, and stricture of the rectal anastomosis. These complications occur most likely as a consequence of a combination of ischemia and excessive tension. They can be avoided by a meticulous observation of the vessels that provide the blood supply of the pulled through bowel to decide which vessels must be divided to gain length without compromising the blood supply.

Rectourethral or Rectovaginal Fistulae.—We have been unable to find the explanation for these bad complications when we read the operative reports of such patients who have been referred to our center. Obviously, the surgeon was unaware that he was working in the wrong territory when the injury occurred. A basic principle is to perform the dissection and resection of the aganglionic bowel, staying as close as possible to the bowel wall when performing a full-thickness type of dissection.

Rectocutaneous Fistula and/or Recurrent Pelvic Abscesses.—These complications are due to the presence of trapped bowel mucosa in the pelvis or in the seromuscular cuff that was left after endorectal operations and occur mainly in patients who were treated with endorectal techniques. Chronic fecal impaction of the remaining rectosigmoid aganglionic pouch is the most common postoperative sequela that we have encountered after a Duhamel operation.

Fecal Incontinence.—Fecal incontinence is an unacceptable and unfortunate complication in patients who undergo operation for Hirschsprung's disease. Regardless of the type of procedure that is preferred by a surgeon, bowel control can be preserved if a series of basic technical rules are followed. The anal canal and a portion of 2 cm of the lower rectum must be preserved intact, because in that area resides the exquisite sensation so necessary for fecal continence and because preservation of that segment will guarantee preservation of the sphincter mechanism.

Nonpreventable Sequelae.

Postoperative Enterocolitis.—Even with a technically correct operation, enterocolitis may occur after the operation.[175-178] Most surgeons with substantial experience in the treatment of Hirschsprung's disease have been through the frustrating experience of some patients experienc-

ing enterocolitis, whereas other patients who undergo the operation with the same technique behave like normal children.

We do not know the cause of this serious complication. However, we are familiar with some of the predisposing factors, including stasis. This reflects a serious dysmotility disorder of the normoganglionic bowel. In theory, the resection of the aganglionic bowel and the anastomosis of a normoganglionic colon to the lower rectum should cure these patients, and in fact, it does in many of them, yet many others obviously have problems.

Now we know that Hirschsprung's disease is more than just aganglionosis. Normoganglionic bowel is frequently not normal bowel; it is dysmotile; therefore, the patient is incapable of emptying the colon. In addition, there is probably a degree of a local immunologic disorder that allows the proliferation of unusual bacteria such as *C difficile*.

We have been unable to identify the normal ganglionic colon that will behave abnormally and will have enterocolitis. Current histologic techniques do not allow us to detect any special abnormalities. IND has been proposed as a possible explanation.[179,180] However, this has not been always substantiated, and further studies are required for clarification. The dysmotility disorder can be manifested clinically when 1 of these patients is subjected to a colostomy for serious enterocolitis. With the same portion of colon that has enterocolitis connected to the abdominal wall in what could be called a "low pressure" system (because there is no resistance to the emptying of the colon into the stoma bag), the symptoms disappear. As soon as the colostomy is closed and the same normoganglionic colon is reconnected to the rectum, the symptoms reappear. The difference is that the colon must empty only by overcoming the resistance of the natural sphincter mechanism in what could be called a "high pressure" system. Because of this feature, some authors have proposed a posterior myectomy[181,182] to treat enterocolitis. The results of this treatment have been highly controversial. Conceivably, those myectomies may produce a degree of decreased sphincter tone that may facilitate the emptying of the colon. However, fecal incontinence is a potential complication of that kind of treatment.[28,183]

The treatment that we offer to children with enterocolitis includes decompression of the colon by the use of colonic irrigations and the administration of oral metronidazole in an attempt to avoid the overgrowth of undesirable bacteria, specifically *C difficile*. This treatment dramatically alleviates the acute symptoms and may save the patient's life. However, it may or may not eradicate the problem.

Even when the concept and the rationale behind the colonic irrigation are extremely simplistic, we frequently see a confusion among nurses and practitioners in the understanding of the difference between an irrigation and an enema. This confusion may result in serious problems for the patient. An enema involves the administration of a fluid through the rectum with the expectation of promoting, as a response, the emptying of the colon. This is true in the case of an individual with normal or near-normal colonic motility. Patients who have enterocolitis have a very abnormal motility. The administration of an enema will only contribute to the overdistention and will aggravate the problem.

A colonic irrigation, in contrast, consists in the passing of a large caliber (22F-26F) rubber tube through the rectum and into the colon; small amounts of normal saline solution are infused through the lumen of the tube with the purpose of clearing its lumen to allow the liquid fecal matter to come out through the lumen of the same tube. This maneuver is repeated several times, moving and rotating the tube into different positions to try to evacuate the colon completely. In the acute stage of this condition, we repeat the irrigations as frequently as demanded by the patient's abdominal distention and clinical condition.

Simultaneously, the patient receives a large amount of intravenous fluids to restore his intravascular volume and electrolyte imbalance. The patient is maintained receiving nothing by mouth until the condition is considered stable (usually 24-48 hours). Then the patient is discharged on irrigations 3 times per day and metronidazole (at one half of the therapeutic oral dosage). Over the following weeks, the frequency of irrigations is tapered, and the amount of metronidazole is reduced. In most cases, the treatment can be discontinued over a period of 3 months. In other patients, unfortunately, the treatment continues for longer periods of time, because every time an attempt is made to discontinue treatment, the symptoms return. At that point, the alternative for the patient is to continue the treatment for an indefinite period of time, to have a colostomy performed, or to be subjected to another pull-through that will resect another arbitrarily determined portion of normoganglionic colon, with the hope that the new pulled-through bowel will perform better in terms of emptying. Unfortunately, no guarantees can be made about the prognosis for these patients.

Partially Preventable Sequelae. Constipation is included in this category. We have evidence that some patients who underwent operation for Hirschsprung's disease underwent resection of the aganglionic segment and pull-through of a normoganglionic but dilated colon. Those patients

had postoperative constipation. We think that this could have been prevented by resecting not only the aganglionic bowel, but also the dilated portion proximal to it. However, the problem seems to be more complicated, because 10% of patients in our own series have constipation despite our emphasis on the resection of the dilated colon. Constipation should be treated aggressively to avoid the vicious cycle of constipation provoking megacolon, which in turn provokes more constipation.

Other Conditions

Intestinal Neuronal Dysplasia (IND)

IND is a histologic disorder that has been described to include hypertrophy of ganglion cells,[184] normal ganglion cells,[185] immature ganglia and hypoganglionosis,[186] hyperplasia of the submucous and myenteric plexi with formation of giant ganglia, hypoplasia or aplasia of sympathetic innervation of the myenteric plexus,[187] increased acetylcholinesterase positive nerve fibers around submucosal vessels, and increased acetylcholinesterase positive nerve fibers in the lamina propria. This histologic disorder has been reported to be responsible for symptoms that include abdominal distension, constipation, and enterocolitis, with or without aganglionosis. IND has been reported to predominate in the rectosigmoid region but can involve the entire colon and small intestine. For surgeons, it is always vital to correlate symptoms to the histologic findings because it is resection of the histologically abnormal tissue that is expected to cure a condition. Surgeons require not only a histologic diagnosis but also a topographic diagnosis so that they can perform a rational procedure. Unfortunately, IND does not meet these criteria. For example, patients with Hirschsprung's disease who have been subjected to a technically correct operation may still experience constipation or enterocolitis after the procedure. The normoganglionic bowel in this situation does not function normally because it has the histologic abnormality, IND. This is an appealing concept; however, nowhere in the literature have we found descriptions of the precise extension of the histologic abnormality as to be able to determine what bowel segments should be resected. In addition, we could not find follow-up information for these patients.

Patients with IND have been subjected to several types of treatment, including medical treatment with laxatives, enemas, and total parenteral nutrition.[33,34,188-193] Many types of operative interventions have been used that include total or partial resection of the affected bowel,[183,189,191,194-196] resection of a coexistent aganglionic segment, leaving

the IND-affected bowel untouched,[197-201] resection of the aganglionic segment with partial resection of the IND-affected bowel,[33,185,191,202] sphinctermyectomy,[191,198] and the creation of short- and long-term colostomies.[184,187,189,198] Once again, specific descriptions of what was resected anatomically, how extensive was the IND, and follow-up results are absent from these reports.

The results obtained from this variety of treatments have been very discordant.[35] Therefore, caution should be observed when the diagnosis of IND is made, and a conservative approach to surgery should be taken. We have found that most patients who were referred to us with the diagnosis of IND will respond to bowel treatment techniques and do not require surgical intervention.

Another controversial issue regarding IND involves the discrepancy in the literature in the histologic criteria used by pathologists. Symptoms are disparate from 1 report to another, and there is a wide range in the severity and presence of symptoms (such as diarrhea, constipation, vomiting, and distension). The most significant problem is no consistent topographic description; therefore, the proposed treatments cannot be correlated with a specific anatomic diagnosis.[34,35,184-187,189,193,196,198-201,203-205] In addition, several authors believe that patients can have spontaneous resolution of symptoms.[162,189,192,198]

These patients must have some definable pathophysiologic state that we simply have not identified yet. Once this pathophysiologic state is defined, we may be able to understand many of the bowel motility disorders for which we do not have a satisfactory explanation.[35] At present, there is no rational justification, based on a histologic diagnosis of IND, to make therapeutic decisions. It is clear that IND is a subject that requires a systematic scientific approach. Correlation between the histologic features and the symptoms is vital to find a rationale for treatment.

Intestinal Pseudo-obstruction

At the most severe end of the spectrum of children with motility problems are those children who are referred to in the literature as having chronic idiopathic intestinal pseudo-obstruction. This refers to a very serious, poorly defined, and sometimes lethal condition that is characterized by chronic or intermittent bouts of functional intestinal obstruction. Many terms have been used to describe intestinal pseudo-obstruction (such as chronic adynamic ileus, pseudo-Hirschsprung's disease, adynamic bowel syndrome, familial visceral myopathy, and megacystic-microcolon-intestinal hypoperistalsis syndrome).[206-217]

Many theories have been invoked to explain this clinical entity. The definition of this disorder varies widely among authors, and there are no clear distinctions of this clinical entity in the literature. The proposed explanation for this clinical syndrome includes abnormalities of the intestinal nervous system (visceral neuropathies) or abnormalities that are caused by problems with the intestinal smooth muscle (visceral myopathies). The motility problems can be primary or a consequence of other systemic disorders and can occur with a familial or spontaneous pattern.[210,213-216,218,219]

The histologic findings range from a normal appearance to specific abnormalities that are described as muscle fibrosis, vacuolar degeneration, disorganization of myofilaments, or an arrest in the maturation of the myenteric plexus.[220]

In addition to idiopathic causes, intestinal pseudo-obstruction has been described as associated with Down's syndrome, neurofibromatosis, multiple endocrine neoplasia 2B, Russell-Silver syndrome, Duchenne muscular dystrophy, viral gastroenteritis, and prematurity.[220] Secondary causes have been described, such as infections like Chagas' disease, which is caused by *Trypanosoma cruzi*, a parasite which has been demonstrated to affect the myenteric plexus. Drug-induced pseudo-obstruction can be encountered in pediatric patients and can occur in a newborn with prenatal transplacental drug exposure or with prolonged ingestion of narcotics. In addition, abnormalities of intestinal smooth muscle may result from fibrosis, which can occur in certain collagen vascular diseases.

Symptoms can be related to the upper or lower intestinal tract and vary depending on how severely a patient is affected. In the worst cases, the mortality rate is high. The impairment of intestinal motility manifests as recurrent episodes of intestinal obstruction and can include symptoms of vomiting, abdominal pain and distension, failure to thrive, and severe constipation. Intestinal bacterial overgrowth is a common finding. More than one half of affected infants have symptoms within the first few days of life. Older children, who usually have less severe symptoms, may have a history of dysphagia, nausea, abdominal distension, or constipation.

There is no evidence of mechanical or anatomic obstruction. The most severe cases of idiopathic constipation can sometimes follow a serious and worsening clinical course that eventually leads to the extension of the hypomotility that is proximal to the colon. At that point, the patient can be considered to have intestinal pseudo-obstruction. The urologic system can be abnormal, and dilatation of the bladder or ureters can occur.

When a surgeon is asked to evaluate such a patient, the primary responsibility is to make sure there is no anatomic mechanical obstruction. Contrast studies can make this distinction, but sometimes patients require a laparotomy to exclude an anatomic explanation definitively.

The goals of treatment are to alleviate symptoms. Most medical treatments (which essentially are medications that try to promote bowel peristalsis) fail. Surgical interventions are usually necessary and involve diversions to help obstructive symptoms and are tailored to the specific clinical situation. Such diversions may include colostomy, ileostomy, jejunostomy, and gastrostomy. Another important role of the surgeon is to perform biopsies to help find a histologic explanation. Small-bowel transplantation has even been performed in severe cases.[221,222] Many patients require total parenteral nutrition; in fact, before the use of total parenteral nutrition, many of these patients died of malnutrition. Total parenteral nutrition extended the life expectancy of infants with this condition so that a clinical description was possible.[5]

Megacystis-microcolon-intestinal hypoperistalsis syndrome or hollow viscus myopathy syndrome affects a well-defined subset of patients with intestinal pseudo-obstruction.[223-225] It affects neonates and involves poor small intestinal motility, an absence of stool in the colon, megacystis, hydronephrosis, lax abdominal-wall musculature, incomplete intestinal rotation, and microcolon. Girls are affected more commonly than boys, and an autosomal recessive pattern of inheritance has been suggested.[225] Pathologic examination of the involved organs demonstrates increased numbers of ganglion cells, but ganglion cell number can decrease as the disease progresses. Electron microscopic evaluation shows a thinning of the longitudinal muscle coat, with extra connective tissue.[224] The speculated causes of this syndrome include visceral myopathy, imbalance in gut peptides, defective autonomic inhibitory neurotransmitter activity, and destruction of hollow viscus smooth muscle and neural elements by an in utero inflammatory process.[220] Treatment includes decompressive and drainage procedures for the intestinal and urinary tract. Patients require long-term parenteral nutrition; the mortality rate is high (87%). Most patients die by age 6 months.

In the literature, there is no clear definition of the spectrum of the disease, and authors may group benign cases with very severe ones and consider both benign and severe cases as intestinal pseudo-obstruction. There is no uniform approach to treatment, and the results of treatment and long-term follow-up are difficult to find in the literature. We emphasize that this is a rare condition, with serious clinical sequelae, that

may be fatal. This is an area of clinical practice that requires much work, both in defining the pathophysiologic features and devising treatments that, at this point, can only be considered palliative.

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