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Phone: 412-648-2037
Fax: 412-648-9020
Email: hslsdoc@pitt.edu

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FUNCTIONAL INTESTINAL OBSTRUCTION ON A CONGENITAL NEUROGENIC BASIS IN INFANCY

WOLF W. ZUELZER, M.D.
AND
JAMES L. WILSON, M.D.
DETROIT

WE REPORT the cases of a number of infants in the first few days and weeks of life who presented the clinical picture of obstructive ileus in the absence of mechanical causes of intestinal obstruction as demonstrated at operation or at autopsy. There is evidence of a familial tendency toward this condition. Our studies on these patients have led us to believe that the obstruction is an entity in which a developmental defect of the intrinsic nervous system in the lower part of the intestinal tract is associated with a disturbance in the propulsive motor function of the bowel. Absence of the nerve cells of the plexus of Auerbach (myenteric plexus) has been reported occasionally in cases with the clinical features of so-called idiopathic megacolon.[1] The association of agenesis of the myenteric plexus with the clinical picture of acute intestinal obstruction seems to have escaped attention, and to our knowledge no previous attempt has been made to describe the condition as a clinical entity with acute and chronic variants.

CLINICAL FEATURES

Our clinical material consists of 11 cases. Nine of the patients were seen by one or both of us, while for 2 only the hospital records were available for study. The pertinent clinical features are summarized in table 1. Analysis of the case histories leads to the following composite picture: The symptoms begin at birth or within the first few days or weeks of life and are essentially those of intestinal obstruc-

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From the Children's Hospital of Michigan and the Departments of Pediatrics and Pathology, Wayne University College of Medicine, Detroit (Dr. Zuelzer), and the Department of Pediatrics and Communicable Disease, University of Michigan Medical School and the University Hospital, Ann Arbor, Mich. (Dr. Wilson).

1. Tiffin, M. E.; Chandler, L. R., and Faber, H. K.: Localized Absence of the Ganglion Cells of the Myenteric Plexus in Congenital Megacolon, Am. J. Dis. Child. **59**:1071 (May) 1940.

tion. Abdominal distention may be present at birth or may develop shortly afterward. Vomiting of the so-called overflow type is usually noted at the onset. Severe constipation is the rule, but it is worth mentioning that several patients were reported to have passed one or two small meconium stools. Unless the symptoms of acute and complete intestinal obstruction compel surgical intervention earlier, periods of ten to fifteen days may elapse without a single bowel movement.

TABLE 1.—*Clinical Features in Eleven Cases of Intestinal Obstruction Without Mechanical Cause*

Case No.	Chief Complaint	Onset of Symptoms	Onset of Complete Obstruction	Physical Findings	Roentgenologic Findings	Operations	Comment
1	Vomiting	Birth	Birth	Signs noncontributory	Gaseous distention	Two exploratory laparotomies	Died
2	Vomiting	Birth	Birth	Signs noncontributory	Gaseous distention	Colostomy, secondary closure of colostomy	Living with colostomy opening
3	Vomiting	Birth	4 wk.	Peristalsis; pattern	Normal position of colon	1. Exploratory laparotomy 2. Colostomy 3. Colostomy closed 4. Second colostomy	Living with colostomy opening
4	Constipation	Birth	2 wk.	Peristalsis	.....	Exploratory laparotomy	Died
5	Vomiting	Birth	.....	Fecal impaction	Gaseous distention	.....	Clinical megacolon; died 4 yr. of age
6	Vomiting	Birth	Birth	No peristalsis	Fluid levels	.....	Died
7	Anorexia	Birth	11 days	Pattern; no peristalsis	Fluid levels	Exploratory laparotomy	Died
8	Vomiting	Birth	Birth	No peristalsis	Noncontributory	Exploratory laparotomy	Died
9	Vomiting	Birth	Birth	Signs noncontributory	Gaseous distention	Exploratory laparotomy	Died
10	Large abdomen	Birth	3 wk.	Intestinal pattern	Fluid levels	.....	Died
11	Distention	Birth	4 mo.	Visible peristalsis	Extreme dilatation of small intestine	Exploratory laparotomy; ileocolostomy; enterostomy	Died

Physical examination reveals distention and tympany of the abdomen and audible, or even visible, peristalsis. In cases of a more protracted course a stepladder pattern may be noted on the abdominal wall. When the distention becomes extreme, the peristaltic activity decreases, and the picture begins to resemble that of paralytic ileus.

Digital examination may reveal the presence of hard, impacted fecal masses in the rectum, and the anal sphincter may appear unduly tight. The feces as a rule are dry, hard and dark brown, are formed into pellets resembling goat feces and are often so firmly impacted that

every attempt at digital removal or evacuation by enema fails. However, in cases of prolonged duration, paradoxic diarrhea may develop and add to the diagnostic difficulties.

The roentgenologic picture varies with the severity, duration and "level" of the obstruction. Like the clinical picture, it is virtually indistinguishable from that typical of ordinary intestinal obstruction. Gaseous distention and fluid levels are commonly seen in "flat plates" of the abdomen (fig. 1 *A*); the films usually suggest obstruction in the terminal portion of the ileum or in some portion of the colon (fig. 1 *B*). If the lumen has been successfully emptied with cleansing enemas, injections of barium sulfate may fail to show any abnormality in the contour or position of the large bowel. This lack of evidence of abnormality does not hold true, however, in protracted cases, in which enlargement of the colon eventually becomes demonstrable. A significant feature in several of our cases was the persistance of firm, dry

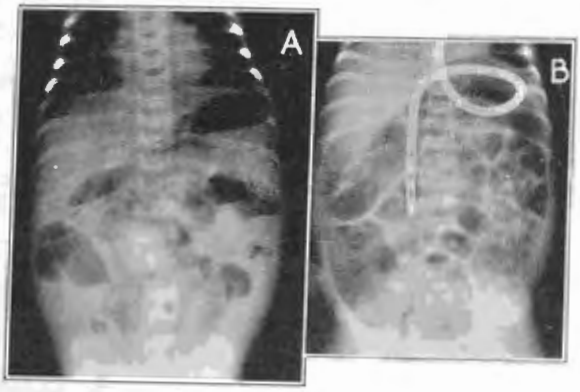

Fig. 1.—*A*, flat roentgenogram of the abdomen of infant R. P. (case 7) at 12 days of age; *B*, flat roentgenogram of the abdomen of infant R. M. (case 2) at 1 day of age.

masses of the barium compound in the colon after a barium sulfate enema. These masses may become impacted and may remain in the colon for weeks and months.

The majority of the patients rapidly progress to the stage at which surgical intervention is deemed necessary, usually in the belief that the symptoms are the result of mechanical obstruction due to a congenital malformation. An exploratory laparotomy is performed, but the surgeon fails to demonstrate any of the mechanical factors which usually are responsible for intestinal obstruction in the early days of life. He may note impacted fecal masses or what he is apt to describe as "spasm" of a segment of the lower intestinal tract, as a rule without abrupt dilation of the proximal segment. Confronted with this unfamiliar situation, the operator is likely to close the wound

without further attempts to relieve the obstruction by surgical means. In every one of our cases in which this course was followed, the patient died eventually of continued obstruction or of a complicating peritonitis or aspiration pneumonia.

Since the clinical problems are complex and our series of patients is short, the entire 11 cases are reported, with pertinent details. The first case illustrates most of the features encountered in the acute cases.

REPORT OF CASES

CASE 1.—W. N., a white boy, was admitted to the hospital at the age of 4 days, with the chief complaint of "intestinal obstruction."

The patient was born at full term, with a weight at birth of 7 pounds 10 ounces (3,459 Gm.). Delivery was normal. Immediately after birth the infant began to vomit. He was not able to retain any feedings and had only one small bowel movement, a description of which could not be obtained. The family history was noncontributory. The mother's pregnancy had been uneventful. Two older children were both in good health.

Physical Examination.—The infant was well developed, with only slight evidence of dehydration. The heart and lungs appeared normal. The abdomen was hard, decidedly distended and tympanitic; no peristalsis could be heard. A rectal examination was not performed. The temperature on admission was 101.8 F. The laboratory findings were noncontributory.

Course.—The patient received a continuous intravenous infusion of 10 per cent dextrose in isotonic solution of sodium chloride. Wangensteen suction was instituted immediately, and a laparotomy was performed the following day. At operation a large amount of clear, somewhat greenish, fluid was seen in the peritoneal cavity, and the mesentery seemed edematous. The small intestine and the colon as far as the splenic flexure contained considerable amounts of gas. The descending colon appeared contracted, but a catheter passed upward from the anus was readily palpable in the region of the splenic flexure. In the absence of an apparent anatomic cause, no attempt was made to relieve the obstruction by surgical means; the wound was closed, and the patient was returned to the ward in good condition. After operation, Wangensteen suction was continued, but the distention persisted and it was not possible to feed the infant. For five days he passed stools, which were at first pasty and later dark brown and liquid. Thereafter, for the remaining three weeks of his life, the baby never again had a spontaneous bowel movement. However, small, hard, dark fecal masses were occasionally obtained by means of enemas. An infection of the operative wound became apparent during the second week, and it was treated successfully with penicillin and tyrothricin. A "flat plate" of the abdomen one week after the operation revealed pronounced distention of loops of bowel, but it was doubtful whether gas was present in the colon. Three weeks after the original operation a second laparotomy was performed. Again, no anatomic obstruction could be demonstrated, but hard scybala were palpated in the transverse colon and in the sigmoid flexure. The abdominal wound was closed, without further action. The patient withstood this operation well. A few days later attempts were made to produce defecation with mecholyl chloride U.S.P. Although the administration of this drug caused decided slowing of the pulse rate, salivation and urination, rectal examination showed no advance of the fecal mass which had been palpable earlier. Four days after the last operation, spinal anesthesia was induced, without appreciable effect. A week after the operation, a

proctoscopic examination was attempted, but definite resistance was encountered approximately 4.5 cm. above the anus and the examination had to be interrupted because the patient was in poor, shocklike condition. In spite of administration of stimulants, external heat and oxygen, the child died the following evening.

Postmortem Observations.—A complete autopsy was performed twelve hours after death.

The body was that of a well developed and poorly nourished infant. There was considerable pitting edema of the feet and hands. The abdomen was moderately distended. There were two laparotomy wounds, one partially healed, the second of recent origin, with clean, closely approximated edges. A firm, slightly rough mass was palpable in the left flank. On opening the peritoneal cavity multiple, firm adhesions were encountered between loops of small bowel and the parietal peritoneum in the region of the incisions. A small pocket of purulent exudate was present beneath the older incision, on the right side. After separation of the adhesions, which obliterated the entire peritoneal cavity except for the epigastric region, it was noted that the large intestine from the level of the cecum to that of the splenic flexure was greatly enlarged. The descending colon was enlarged to a lesser degree. The sigmoid was somewhat elongated and was matted against the posterior body wall by recent adhesions. The small intestine was not appreciably distended or enlarged.

After further dissection, the lumen of the bowel was opened. There was no intrinsic obstruction at any point. The small intestine was filled with fairly thick, yellow, malodorous, semiliquid material, resembling feces. The large intestine in its proximal portion contained liquid, malodorous, light brown feces in large amounts. Toward the splenic flexure the contents were increasingly solid, and in the descending colon they consisted of large, firm, almost rocklike, dark brown, scybalous masses, which had a homogeneous, dry appearance on cut surface. The largest of these masses measured 3 by 2 by 2 cm. Similar masses were present in the proximal part of the sigmoid colon. The distal part of the sigmoid colon and the rectum were empty. Except for moderate, diffuse atelectasis of both lungs, the gross observations were not otherwise significant.

Microscopic examination revealed a moderate degree of autolysis of the mucous membrane of the lower intestinal tract. Twelve sections were examined from consecutive levels of the duodenum; jejunum; upper, middle and lower portions of the ileum; cecum; ascending and transverse colon; splenic flexure; descending colon; sigmoid; rectum, and anus. Attempts to demonstrate Meissner's plexus in any of these sections were unsuccessful. The demonstration of the myenteric plexus presented no difficulties in any of the sections of the small intestine or of the cecum or ascending colon. In all sections taken from points distal to the hepatic flexure, it was impossible to demonstrate ganglion cells of the myenteric plexus, even by means of serial sections. The borders between the circular and the longitudinal muscle layers were well defined, and small nerve trunks were frequently seen along this line. There was no evidence of scarring or of inflammatory processes in this plane. The muscularis, especially the longitudinal layer, was distinctly increased in thickness in all sections of the colon. In the serosa, various degrees of fibrous thickening, proliferation of fibroblasts and organization of a fibrinous exudate on the surface were noted.

Sections of the lungs showed, in addition to atelectasis, minimal foci of bronchopneumonia. No appreciable change was observed in sections of the pancreas.

The main anatomic diagnoses were: megacolon, agenesis of the myenteric plexus in the distal portion of the colon, status after multiple laparotomies, adhesive

peritonitis, localized peritoneal abscess, pulmonary atelectasis and congestion, terminal bronchopneumonia and malnutrition.

Case 2 illustrates most of the features of cases of the less severe, chronic form. In these cases the course is protracted, and the symptoms of obstruction may be relieved temporarily by the use of enemas. For variable periods the infant may even haye spontaneous, fairly regular bowel movements; but some degree of abdominal distention persists, severe constipation recurs frequently and eventually complete obstruction supervenes unless suitable therapeutic measures have been taken. Roentgenologic studies show progressive enlargement of the colon (fig. 2), and eventually the picture in cases of such protracted course becomes virtually indistinguishable from that of the classic megacolon.

Fig. 2 (case 2).—Study by means of a barium sulfate enema of abdomen of infant R. M. six months after closure of colostomy.

CASE 2.—R. M., a Negro boy, was admitted at the age of 2 days, with the chief complaint of vomiting since birth. He was said to have passed one meconium stool, but no subsequent bowel movement had occurred.

The mother's pregnancy had been uneventful. Delivery was normal and spontaneous at full term. The family history was noncontributory. Four older siblings were said to be in good health.

Physical examination revealed pronounced abdominal distention and tympany. The abdominal organs or masses were not palpable. On rectal examination, a small amount of meconium was obtained, and no obstruction was encountered. Roentgenograms showed only slight distention of the small bowel and considerable distention of the colon, with accumulation of excessive amounts of fecal material. The rectal pouch was not distended.

A Levin tube was placed in the stomach, and Wangensteen suction was instituted. The patient expelled large amounts of flatus. On the following day, he passed, first, several small meconium stools and, later, large, brown, liquid stools. The distention diminished, and it was soon possible to feed him by mouth. He

continued to have spontaneous bowel movements, which changed from dark brown to soft yellow. During the second week in the hospital the baby refused his formula, vomited and had an increased number of loose, yellow stools, but these symptoms subsided and he was discharged at the age of 25 days.

He was readmitted nine days later, at the approximate age of 1 month, because he had had no bowel movement since his discharge from the hospital. At this time the abdomen was again distended, and a moderate degree of gaseous distention in the stomach and colon was demonstrable in roentgenograms. The administration of an enema resulted in the return of small, hard masses of fecal material. On administration of a mixture of liquid petrolatum U.S.P., water and a synthetic wetting agent,[2] spontaneous bowel movements occurred, and the patient was discharged after five days.

He returned for the third time at the age of 4 months. During most of the interval he had had a bowel movement approximately every other day. The stools were described as hard and constipated. During the last week he had failed to pass any stool in spite of enemas and laxatives administered by the mother. For the last day he had vomited after each feeding. Examination revealed that the abdomen was distended but soft, and peristalsis was audible. Roentgenograms of the abdomen at this time showed pronounced distention of loops of bowel, which appeared to be mainly of the small intestine. The stomach was likewise greatly distended. This time the use of enemas and administration of liquid petrolatum U.S.P. and "aerosol" by mouth were unsuccessful. Abdominal distention and vomiting increased in spite of the use of Wangensteen suction and rectal tubes. Spinal anesthesia was administered but did not result in peristalsis, although cutaneous anesthesia to the level of the third dorsal vertebra was demonstrated. In spite of the parenteral administration of fluids, the child's condition rapidly became critical, and two days after his admission an emergency enterostomy and colostomy were performed. There was little drainage from the enterostomy opening, but twenty-four hours later, when the colostomy loop was opened, large amounts of yellow fecal material escaped and the distention was relieved. However, the distal colostomy loop contained firm fecal masses, which persisted for three weeks in spite of frequent attempts to evacuate them with manipulation and enemas. Nevertheless, the patient's general condition improved and he began to eat and to gain weight.

At the age of 5 months he was discharged to the Children's Hospital Convalescent Home in Farmington, Mich., where he remained for nearly a year. While there, he gained weight steadily and passed three to four soft stools daily through the colostomy opening. He was readmitted to the hospital at the age of 14 months for further study. At this time the colostomy loop seemed to be functioning well, but there was a slight prolapse and the surrounding skin showed superficial erosions. A gastrointestinal series of roentgenograms showed no abnormalities of the stomach and small intestine. Twenty-four hours after the ingestion of the barium sulfate meal, the barium was contained entirely in the colon, and the site of the colostomy was seen to be the junction of the descending colon and the sigmoid flexure. Injection of barium sulfate into the distal segment from below showed no abnormalities in size or contour in that portion of the colon. Four days after this procedure was carried out, hard masses of the barium compounds were still present in the rectum, and this material could not be flushed out from above or

2. "Aerosol" (dibutyl sodium sulfosuccinate) is manufactured by American Cyanimid & Chemical Corp., New York.

below until a rectal tube was pushed through the entire distal segment. The dry, caked barium was then removed digitally and by irrigation through the tube.

A few days later rubber balloons were inserted into the proximal and distal ends of the colostomy loop. Peristaltic waves were readily demonstrated in a water manometer connected with the balloon in the proximal portion of the colon. There were no fluctuations in pressure in the balloon inserted into the distal part of the colon. When the pressure in the rectum was raised by insertion of a balloon inflated to produce a pressure of 40 mm. of mercury, there was no change in pressure in the upper end of the distal segment of the colon, as measured by a second balloon. In the proximal portion of the colon, however, there was definite evidence of a reflex, since defecation occurred through the colostomy opening when the pressure in the rectum was raised.

After a month's observation, an appendicostomy was performed; simultaneously, the colostomy loop was excised, with end to end anastomosis of the two segments of colon.

The specimens of the appendix and of the excised portion of the colon were fixed in Zenker's fluid and examined by means of serial sections. Microscopic examination of the appendix revealed nothing unusual. There were numerous well preserved ganglion cells in the myenteric plexus. In three longitudinal sections of the excised portion of the colon, it was impossible to demonstrate a single ganglion cell in the myenteric plexus, but numerous small nerve trunks were seen at the border between the inner and the outer muscle coat.

After the operation, the patient did not receive food or fluids by mouth for eight days. He was then given a liquid and shortly afterward a soft diet, and on the tenth postoperative day he had a soft, liquid, yellow spontaneous stool. A few days later the appendicostomy tube slipped out; immediately afterward abdominal distention was noted, and there was vomiting. Relief was obtained with the use of Wangensteen suction, and formed stools followed the administration of an enema. Thereafter, the patient had fairly regular soft or liquid stools for approximately one week, but there was a persistent tendency to abdominal distention. Three weeks after the operation a barium sulfate enema was administered. Roentgenograms obtained at this time showed definite enlargement of the proximal portion of the colon to the site of the previous colostomy. The rectum and sigmoid appeared well contracted. For four days after the barium enema no stools were passed, and twelve days afterward considerable amounts of the barium compound were still present in the colon, despite the use of daily enemas, colonic irrigations and phenolphthalein. A moderate degree of abdominal enlargement was present on the child's discharge from the hospital, nearly two months after the operation, but it was possible with the help of daily enemas and phenolphthalein to obtain stools almost every day.

The patient was last seen three months later, at the age of 19 months. According to the mother, he had been in good health since the last discharge from the hospital. He was taking phenolphthalein, and his diet had been supplemented with large amounts of prune juice and prune pulp. He had spontaneous bowel movements almost every day, but once or twice a week an enema was required. He was eating well, weighed 25 pounds (11.3 Kg.) and appeared well nourished and well developed. The abdomen seemed slightly large but had good muscular tone. The circumference of the abdomen was 21 inches (53 cm.); that of the chest, 19 inches (48 cm.). Fluoroscopic examination after cleansing enemas showed extreme gaseous distention of the colon. Barium sulfate given by enema was observed to pass rapidly through the rectum and sigmoid colon. There seemed to be some obstruction near the junction of the sigmoid and the descending colon. During

a long period of observation, the barium did not pass the splenic flexure, but roentgenograms taken subsequently showed a mixture of barium compound, gas and fecal material in the greatly dilated transverse colon, in the cecum and in the ascending colon. A check-up roentgenogram taken two weeks later showed substantial amounts of barium sulfate still retained in the colon.

In this case a diagnosis of agenesis of the myenteric plexus was made before operation and confirmed by histologic examination of a portion of the colon. The segmental character of the defect was evident from the fact that ganglion cells were demonstrated in the appendix. The extent of the defect could not be established. There is no question that this patient's life was saved by the colostomy. Closure of the colostomy loop was frankly experimental. It had been anticipated that intestinal obstruction would recur. It is impossible to determine whether by accident the entire defective segment had been removed, but in view of the poor motility demonstrated in the distal segment it is unlikely that this occurred. Perhaps partial evacuation had become possible. The peristaltic forces in the proximal segment of the colon were adequate for partial evacuation after shortening of the inactive segment. Although this patient seemed headed for further difficulties, the results were, nevertheless, encouraging.

In the next case it was not possible to restore the continuity of the lumen after colostomy without producing recurrent obstruction.

CASE 3.—L. L.,[3] a white girl, was first seen at Henry Ford Hospital at the age of 4 weeks, with the chief complaint of constipation and vomiting. There had been severe constipation since birth. The bowels had moved only every two or three days, and stools were hard and small. The infant had lost weight, and on the day prior to her admission had begun to vomit. The family history was of interest in that there had been 2 other children in the family who had died in early infancy after operations for intestinal obstruction. In addition, the mother had 2 normal, living children.

Physical examination revealed that the infant was poorly nourished, dehydrated and acutely ill. The abdomen was conspicuously distended, and there was patterning of the intestinal loops on the anterior abdominal wall. Loud borborygmi were heard. A barium sulfate enema showed normal position and outline of the colon. An exploratory laparotomy was performed and no intrinsic or extrinsic anatomic cause of obstruction was demonstrated, but a large, firm mass of fecal material was present in the sigmoid. This mass was broken up through manipulation and partly extracted by rectum.

After operation, the vomiting ceased. The child began to eat well and had spontaneous bowel movements. However, a week later there was recurrence of vomiting, and the large intestine again seemed to be filled with firm feces. Attempts to evacuate the colon and to prevent distention by daily colonic irrigations and enemas proved futile. Severe abdominal distention developed, and the child's condition became critical, in spite of the usual supportive measures. Fluoroscopic studies a week after the operation still showed residues of barium in the colon.

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3. Records of this case were obtained from Dr. Joseph A. Johnston, of Henry Ford Hospital, Detroit.

As a last resort, a transverse colostomy was performed. Thereafter the infant's condition improved remarkably, and she began to gain weight. The mass of barium compound remained in the sigmoid colon in spite of frequent attempts to flush it out through the colostomy opening. The child was discharged and thrived at home for six months. She was then readmitted for the purpose of closing the colostomy opening. However, by means of inserting rubber balloons into the large intestine, it was demonstrated that the motility of the distal segment was poor. A cork inserted into the distal end of the colostomy loop failed to travel in the direction of the anus. It was felt, therefore, that the motility of the distal segment of the colon was too poor, and closure of the colostomy opening was not carried out.

Four months later the patient was transferred to the University Hospital, Ann Arbor, Mich., where she was first seen by one of us (J.L.W.). At this time she was 1 year old. Her general condition and nutritional status were good. The parents requested closure of the colostomy opening, and, after due consideration, the operation was carried out. The results were unfortunate. Distention appeared; peristaltic waves and intestinal patterning were noted on the abdominal wall, and the child began to vomit. It was evident that the large intestine was not functioning normally, and, as an emergency measure, a second colostomy was carried out. This procedure was followed by remarkable improvement, although when last seen the patient had not fully recovered from the effects of the last operation. In this instance, relief from obstruction could be obtained only by colostomy, and at the time of writing it appears that the patient cannot live without a permanent artificial opening.

One of the most interesting features of the condition is the familial tendency. It was noted in the case just described. The next 5 cases which we report here were those of brothers and sisters in a family of 12 children. Because of the extraordinary features, the history of this family is given in some detail.

CASE 4.—The father, born in 1907, gave a history of severe constipation since birth and stated that because of this he had been seriously ill as a young child on at least three occasions. He was still constipated but was otherwise well when last seen in 1944.

The mother was born in 1909. At the time that a detailed history was obtained, in 1944, she stated that she had had heart trouble and asthma for a number of years. She had frequent attacks characterized by numbness and cyanosis of the hands and feet. She also claimed to have a nervous condition which caused spells of aphasia. Her gallbladder had been removed at another hospital. She admitted being a heavy smoker but denied being alcoholic. Her first child, born in 1929, had always been healthy.

P. P., the second child, was born in 1930. She was admitted at the age of 2 weeks, with the chief complaint of constipation. She had not had a bowel movement since birth, and enemas had resulted only in the passage of small, yellow, hard feces. She had vomited frequently during the last four days.

Physical examination revealed extreme abdominal distention and tympany, and peristaltic waves were visible on the abdominal wall. No masses or viscera were palpable. The laboratory data were noncontributory.

An exploratory laparotomy was performed, with the use of local anesthesia. The surgeon described the descending and sigmoid colon as being in a state of spasm but stated that the lumen was intact, and a tube passed through the rectum during the operation could be traced to the splenic flexure. It was felt that no

operative repair was needed, and the wound was closed. After operation the signs of intestinal obstruction continued undiminished. Fever developed, and the patient died six days after admission. Permission for autopsy was refused.

The third child of this family, born in 1931, was said to have had epilepsy for a number of years, and in early childhood he had lacked control of the bowel and bladder. Later, this condition had improved, and, at the age of 12 years, the child was considered by his parents to be in good health.

The fourth child was entirely well. The fifth child had died at the age of seven months of "pneumonia" and blood poisoning. The sixth child had been normal.

CASE 5.—K. P., the seventh child of this family, was born in 1938. She was admitted to the hospital at the age of 1½ months because of frequent vomiting, abdominal distention and alternating constipation and diarrhea since birth.

Physical examination revealed pronounced abdominal distention and a hard mass in the left lower quadrant, which proved to be inspissated feces. After the use of enemas, the patient began having daily spontaneous bowel movements and the vomiting ceased, but the abdomen remained distended; the question of congenital megacolon was raised.

The patient was next seen at the age of 20 months. Abdominal distention had never disappeared and recently had again become severe. The stools had always been grayish and hard as a rock. Roentgenographic studies showed distinct enlargement of the colon. Under treatment with mecholyl chloride U.S.P. and neostigmine methylsulfate U.S.P., there was considerable improvement. The abdomen remained moderately distended, however, and the child complained of frequent abdominal pain. She was not seen again until she was 4 years old. At this time she was poorly nourished. The abdomen was extremely distended and tympanitic, and an intestinal pattern with occasional peristaltic waves could be seen on the abdominal wall. There were moderate enlargement of the tonsils and of the anterior cervical lymph nodes, caries of the teeth and evidence of mild, healing rickets. Examination of the urine revealed 4 to 8 red blood cells, 30 to 40 white blood cells per high power field and occasional granular casts in the uncentrifuged specimen. The blood showed the presence of a mild anemia. Roentgenograms of the abdomen showed gaseous distention of the colon and, to a lesser extent, of the small bowel. Fluoroscopic examination revealed two opaque bodies in the pelvis. Studies with barium sulfate showed a constriction at the level of the rectosigmoid junction with pronounced dilatation of the proximal segment of the colon. Sigmoidoscopic examination revealed narrowing of the lumen of the sigmoid, without change in the appearance of the mucous membrane. When a catheter was passed beyond the constriction, large amount of gas and "loose" feces were obtained, and the abdomen became deflated and fairly soft. Spinal anesthesia failed to produce defecation or relaxation of the constriction, as observed fluoroscopically with the help of barium sulfate enemas. Mecholyl chloride, given over a period of three weeks, failed to relieve the constipation or distention, and neostigmine methylsulfate was likewise ineffective. However, with frequent cleansing enemas, the abdominal distention was fairly well controlled. Suddenly, one morning the child, who previously had been in good health, went into a shocklike condition when placed on the bed pan. Pallor, profuse sweating, vomiting and abdominal pain were present, and she became stuporous and died within an hour. Autopsy was not performed.

CASE 6.—T. P., born in 1940, was the ninth child in the family. The eighth child, 2½ years old at the time, was well. The patient was admitted at the age of 2 days, with the chief complaint of vomiting. Birth and delivery had been normal, and the mother's health during pregnancy had been good. The child

had begun to vomit almost immediately after birth, and this had continued until the time of admission to the hospital. The vomitus was at first greenish and later orange-brown. There had been no bowel movement and only a small "spot" had been passed after an enema was given at home.

Physical examination revealed a large, well developed infant, with evident dehydration and loss of weight. A malodorous, greenish yellow material was oozing from the mouth. The abdomen was moderately distended and tympanitic. There was no visible peristalsis. Rectal examination revealed no masses, but after withdrawal of the finger a large stool, which was described as liquid meconium, was passed. After admission to the hospital, the patient continued to pass dark green, liquid meconium stools and to have vomiting of the overflow type. No fluids were given by mouth. A Levin tube was passed through the stomach, and Wangensteen suction was instituted. A roentgenogram of the abdomen showed extreme gaseous distention of numerous loops of small bowel, but fluoroscopic examination and roentgenograms made after a barium sulfate enema demonstrated no abnormality in structure or in motility of the colon. Eighteen hours after the infant's admission, cyanosis developed; the child began to cough up bright red, frothy blood and died shortly afterward, at the age of 3 days.

At autopsy no intestinal obstruction was observed. Multiple hemorrhages involved the kidneys, adrenal glands, lungs and brain, and the diagnosis of hemorrhagic disease of the newborn was made. Sections of the bowel were not available for examination.

Case 7.—R. P., the tenth child, born in 1941, was admitted to the hospital at the age of 12 days because of refusal of feedings since birth and abdominal distention for one day. He had seemed normal at birth, but from the beginning he had refused the breast and taken water only poorly. He had no bowel movement until the fifth day of life, when he passed a small amount of meconium after a glycerin suppository had been given. At this time he began to vomit greenish material and acted as though he had abdominal pain. With the help of daily suppositories, he had a small, black stool every day, but on the day before his admission the abdomen became distended. The extremities were cyanotic, and the child began to hiccup and vomited brownish, malodorous material.

Physical examination showed that the infant was critically ill, with severe abdominal distention. There was patterning of the intestinal loops on the abdominal wall, but peristalsis was not audible. Rectal examination showed an essentially normal condition. Roentgenograms of the abdomen showed numerous gas-filled loops of small bowel with fluid levels, suggesting an obstruction near the ileocecal valve. Abdominal paracentesis yielded a small amount of cloudy yellow fluid, which contained a few white and red bood cells, but no organisms, and which yielded no growth on culture.

The patient was given sodium sulfadiazine, dextrose in isotonic solution of sodium chloride and transfusions of whole blood. In spite of Wangensteen suction, the abdomen remained distended, and five days after admission an exploratory laparotomy was performed. At operation, the ileum and the entire colon down to the level of the sigmoid were seen to be greatly distended, and the small bowel appeared cyanotic, but its color improved. In the sigmoid colon, firm masses were palpable, which appeared to be impacted feces. It was also noted that the bladder was large and distended. An ileostomy was performed, but the child's postoperative condition was poor, and he died two days afterward, considerable edema having developed.

A limited autopsy was performed seventeen hours after death. The body was that of a well developed, poorly nourished white boy. There was edema of the

face, the scrotum and the left lower extremity. A clean operative incision was present over the right side of the abdomen, with a rubber drain inserted near the lower end. On opening the abdominal cavity, 20 cc. of slightly turbid, amber, thin fluid was seen. A Wetzel type of ileostomy had been performed in the lowermost loop of ileum. The peritoneal surfaces were smooth except for some roughness and yellow and red discoloration of the serosa of the cecum and the ascending colon. The caliber of the colon decreased gradually up to the splenic flexure; up to this point the lumen contained sticky brown fecal material, and the mucous membrane was diffusely reddened and here and there showed shallow ulcerations. The descending colon and the upper rectum contained large, firm scybala of the consistency of fecoliths, averaging 2 cm. in length and 0.8 cm. in diameter. These masses were dark brown and on cut surface appeared laminated. The rectal ampulla was empty. Dissection of the upper intestinal tract revealed no significant abnormality. The position of the abdominal organs was normal.

Microscopic examination of sections from the cecum and the ascending colon revealed well preserved ganglion cells and myenteric plexus, except in areas of ulceration. Here only the serosa and a few fibers of the outer muscle layer were preserved and the region of the plexus, together with the inner muscular layer, was destroyed. In sections of the sigmoid and rectum no ulceration was present. Both muscle layers were intact. Between them small nerve trunks could be identified, but no ganglion cells were seen, although there was little evidence of autolysis. Sections of the pancreas showed normal structure.

The anatomic diagnoses were fecal impaction in the sigmoid and rectum, dilatation and hypertrophy of the colon, multiple subacute ulcers of the cecum and ascending colon, status after laparotomy and Wetzel ileostomy and acute peritonitis, terminal.

CASE 8.—C. P., the eleventh child, born in 1944, was admitted to the hospital when 2 days old, with the chief complaint of abdominal distention and vomiting since birth. The prenatal history was noncontributory. Delivery was normal and spontaneous, and the child weighed 9½ pounds (4,309 Gm.). As soon as she was fed she began to vomit, and she then frequently vomited between meals. The vomitus was greenish. The abdomen rapidly became distended. There was no information as to whether meconium or stools had been passed.

Physical examination revealed that the infant was well nourished and well developed, but appeared dehydrated and acutely ill. The abdomen was greatly distended, and no masses or organs were palpable. No peristaltic movements could be heard. The laboratory data were noncontributory.

An exploratory laparotomy was performed with the patient under general anesthesia on the day after admission to the hospital. At operation a small amount of free fluid in the abdominal cavity was encountered. The surgeon described the small bowel as slightly dilated and the ileum as discolored, "suggesting a circulatory disturbance." There was, however, no demonstrable obstruction of the lumen, and gas could be moved from the ileum into the large intestine. The operator was unfamiliar with the family history and did not attempt to relieve the condition by surgical means, and the abdomen was closed.

The postoperative course was stormy, with an infection of the abdominal wound. Feedings by mouth were resumed on the third postoperative day, but a few days later had to be discontinued again because of recurrent and severe abdominal distention. The child again vomited and passed liquid, brown, malodorous stools. The distention increased. The general condition deteriorated, and the child died on the twelfth postoperative day.

A limited autopsy was performed four and a half hours after death. External examination of the body showed nothing unusual other than the presence of an operative incision and some discoloration of the skin over the abdomen. The wound itself appeared clean. The peritoneal cavity contained approximately 100 cc. of malodorous, turbid, brownish, thin material, which resembled feces, and the peritoneal surfaces throughout were dull, rough, reddened and matted together with fibrin, with multiple pockets containing brownish exudate. The adhesions had caused considerable kinking and spur formation, but on cautious dissection the small and large intestine were shown to have a continuous and adequate lumen. The large intestine, from the level of the ileocecal valve to the level of the sigmoid flexure, appeared increased in caliber and in the thickness of the wall. The lumen of the colon contained malodorous, brownish material, similar to that seen in the free peritoneal cavity. The liver was extremely enlarged and engorged and pitted on pressure. The thoracic organs were not unusual except for mild, diffuse pulmonary atelectasis.

Microscopic examination of sections from the proximal portion of the intestinal tract revealed nothing of significance except for evidence of peritonitis. In the large intestine it was difficult to find ganglion cells in the myenteric plexus, even in sections of the cecum, but a few such cells were demonstrable in the transverse colon. None could be demonstrated in sections of the descending and sigmoid colon. Sections of the rectum were not available. The pancreas had an essentially normal appearance. The picture in the section of the liver was that of enormous engorgement of the sinusoids, with thinning and often rupture of the polygonal cell cords.

The anatomic diagnoses were: spastic ileus, clinical; agenesis of the myenteric plexus in the colon; fecal peritonitis; multiple peritoneal adhesions, and acute congestion of liver.

We present briefly the histories in the 3 remaining cases in our group.

CASE 9.—S. W., a 6 day old Negro boy, was admitted with the history of having vomited bile-stained material since birth.

Physical examination revealed evidence of moderate dehydration. There was no appreciable distention of the abdomen, and no note was made concerning the presence or absence of audible peristalsis. A flat roentgenogram of the abdomen showed gas-distended loops of bowel, mainly on the left side of the abdomen. On fluoroscopic examination, barium sulfate given by mouth was seen to enter the duodenum. On the second day in the hospital an exploratory laparotomy was performed. The entire jejunum and ileum was delivered. The jejunum was moderately dilated, and there was gradual narrowing of the lumen. In the region of the ileocecal valve, the lower part of the ileum and the entire colon were described as the size of a lead pencil. It was difficult to force intestinal contents into the narrow portion of the small intestine, but no frank atresia could be demonstrated. No surgical attempt to circumvent the obstruction was made, and the patient was returned to the ward, where he continued to vomit. At no time did he pass stools. On the second postoperative day, 0.5 mg. of mecholyl chloride was given subcutaneously, without appreciable effect. A purulent discharge from the operative area was noted shortly afterward, and there was almost continuous regurgitation of blackish or greenish liquid, even though no attempt was made to give the child fluids by mouth. The child's condition deteriorated steadily, and he died on the fifth postoperative day.

A complete autopsy was performed five hours after death. On opening the abdomen, a generalized peritonitis was observed, with pockets of purulent exudate in each lower quadrant. There was pronounced dilatation of the stomach, jejunum and upper portion of the ileum. Approximately 22 cm. from the ileocecal valve, the lumen of the ileum narrowed abruptly, and at this place the musculature appeared thick. Both the lower portion of the ileum and the entire colon were of small caliber. A rubber catheter inserted in the ileum well above the point of obstruction passed easily to the level of the ileocecal valve; when the bowel was opened, the lumen was seen to be intact. There was no anomaly of the mesenteric insertion. Examination of the lungs showed multiple areas of bronchopneumonia. The remainder of the gross observations were noncontributory.

Microscopic examination confirmed the impression of thickening of the musculature of the ileum at the level of the obstruction. In sections of the small intestine taken from levels above the narrow portion, numerous nests of ganglion cells were readily demonstrated in the myenteric plexus. Below this level, in the terminal portion of the ileum and in the entire colon, careful examination by means of serial sections failed to disclose the presence of ganglion cells at any level. The main anatomic diagnoses were: localized muscular hypertrophy of the ileum, agenesis of the myenteric plexus in the terminal portion of the ileum and the colon, status after laparotomy, localized purulent peritonitis and aspiration pneumonia.

CASE 10.—L. W., a white boy, was admitted to the hospital at the age of 3 weeks because of vomiting and constipation. At birth the child was said to have been blue for approximately forty-five minutes, and the abdomen was swollen. Because of the latter symptom the child was taken to another hospital on the third day of life and, while there, was treated for two weeks with enemas and the use of rectal tubes. On his discharge the parents were told treatment with enemas would have to be continued. At home the patient did well for two days only, and then he began to vomit fecal material and to refuse all feedings. It was learned that he had never had a spontaneous bowel movement.

On admission the patient was acutely ill, poorly developed and poorly nourished. The abdomen was enormously distended, but no viscera could be palpated through the abdominal wall. Review of the roentgenograms taken at the other hospital, representing a gastrointestinal series, showed normal passage of barium through the small bowel and extreme gaseous distention of the colon to the level of the rectosigmoid junction. At this point the lumen appeared narrow but not completely occluded. Further roentgenograms taken with a colonic tube in place showed gas and fluid levels in the intestinal tract.

The abdominal distention improved with the use of Wangensteen suction and of rectal tubes. Rectal dilatation was performed, and a no. 4½ sigmoidoscope was passed. When a catheter was passed upward 8 inches (20 cm.) from the anus, a thick, liquid stool was obtained. A rectal tube was left in place for three days, and thereafter the abdominal distention disappeared. The patient had numerous spontaneous stools, and the vomiting ceased. For several weeks the child continued to have spontaneous bowel movements. He began to gain weight slowly on a high caloric intake. However, because of occasional vomiting, a gastrointestinal series of roentgenograms was again made and the passage of barium proceeded normally. However, a few days afterward the abdomen again became severely distended, and the child's general condition declined. A staircase pattern became visible on the abdominal wall, but no peristalsis was audible. Neostigmine methylsulfate was without appreciable effect on the distention, and the use of rectal tubes and turpentine stupes was resorted to. There

was considerable dyspnea, which was not relieved with oxygen therapy. Suddenly a shocklike condition, with mottling of the skin, developed, and the child died at the age of 2½ months.

A complete autopsy was performed nine hours after death. There was evidence of malnutrition and edema of the lower extremities. The peritoneal surfaces were smooth and glistening, and the situs of the abdominal organs was normal. There was, however, considerable enlargement of the colon, with increase in caliber and in thickness and length as well. The ascending and descending colon was redundant, and the sigmoid was likewise elongated. At the rectosigmoid junction there was a sharp angulation; the rectum appeared narrow, but there was no evidence of anatomic obstruction. The lumen of the colon contained large amounts of thick, yellowish gray feces.

Microscopic examination showed absence of the ganglion cells in the myenteric plexus and below the level of the rectosigmoid junction. In the proximal portion of the colon such cells were readily demonstrated at all levels. The anatomic diagnoses were: megacolon, agenesis of the myenteric plexus and malnutrition.

CASE 11.—B. M., a white girl 5 months old, entered the hospital because of severe constipation and abdominal distention since birth. One month prior to her admission the abdominal distention had become so severe that she had been taken to another hospital, where the distention was reduced by the use of numerous enemas. Several weeks later she had returned to that hospital for further treatment. At that time all feedings were stopped and fluids were given only by the intravenous route. This procedure had resulted in the relief of the distention for a time, but when feedings were started again the distention recurred to an even severer degree. The stools had always been infrequent and hard in consistency, and for the last twelve days she had had no movements at all. During the last month she had vomited intermittently.

On examination the child appeared fairly well nourished and not acutely ill, but there were severe abdominal distention and visible peristalsis. Roentgenograms of the abdomen showed tremendous dilatation of the small bowel. By means of enemas with iodized oil U. S. P., it was demonstrated that the large bowel was of normal size but contained much fecal material. Treatment with numerous enemas was without success. The distention increased and was relieved only with the use of Wangensteen suction. A small amount of iodized oil U. S. P. was introduced through the Wangensteen tube and was seen to turn back and forth at a point estimated to be 80 inches (203 cm.) below the pylorus. The oil did not move from this point for several hours, and it was felt that there was definite obstruction of the terminal portion of the ileum.

A laparotomy was done, and the small bowel was observed to be greatly distended except for the terminal 6 inches (15 cm.) of the ileum, which appeared of normal caliber. No intrinsic or extrinsic obstruction of the bowel could be seen, and it was possible to push fecal material and gas through the lumen at every point. For this reason, no further operative procedure was carried out. The child's immediate postoperative condition was good, and the distention was relieved by means of suction. As soon as feedings were started again, four days after the operation, abdominal distention recurred, and it was evident that there was an intestinal obstruction of some kind. An anastomosis was made between the lower part of the ileum and the transverse colon; but two days after the second operation the child's condition took a sudden turn for the worse, the abdominal distention became extreme and the child died soon afterward.

An autopsy, performed by the department of pathology of the University Hospital, revealed fibrinopurulent peritonitis, extreme distention of the jejunum and

proximal portion of the ileum and moderate distention of the cecum and colon. There was no abnormality in the situs or the attachment of the abdominal viscera. Obtaining of proof of a defect in the enteric nervous system was not undertaken in this case.

PATHOLOGIC STUDY

In 7 of the 9 fatal cases autopsy was performed. In 5 of these cases the autopsy was done by one of us (W.W.Z.), while in the other 2 cases only written reports were available. A surgical specimen was obtained from 1 of the 2 patients who survived.

The gross postmortem observations were not uniform, but in no case was a mechanical cause of intestinal obstruction seen, although this point was always carefully investigated by cautious dissection, by exploration of the mesentery and peritoneum for anomalous insertion

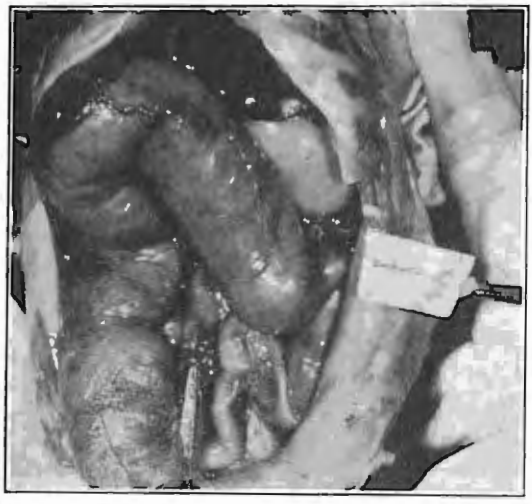

Fig. 3 (case 1).—Appearance of large bowel of infant W. N. at autopsy. Note the dilatation of the proximal part of the colon.

or abnormal bands or adhesions and by probing and flushing of the lumen prior to opening the bowel. Adhesions, when present, were fresh and were accounted for by terminal peritonitis. In spite of the absence of gross mechanical causes, the existence of obstruction was obvious (fig. 3). In the 6 cases in which attention was paid to this point, a definite "level of obstruction" could be recognized at autopsy. From the dilatation of the proximal segment and the relatively small size of the distal portion of the bowel, interference with the passage of contents through the lumen appeared to exist at the level of the ileocecal valve in 2 cases, in the lower descending colon in 1 case and in the rectosigmoid junction in the 3 others. In 1 surviving patient the observations at operation and the roentgenologic signs also indicated obstruction at the level of the rectosigmoid junction.

The dilatation of the lumen above the "obstruction" in the cases in which autopsy was performed was sometimes fairly abrupt, sometimes more gradual. In several instances the change in caliber corresponded to a change in the character of the fecal contents, which tended to be liquid in the proximal portions with a gradual transition to a solid consistency in the distal direction. Immediately below the "obstruction" the feces were hard and obviously impacted. Sometimes distinct pressure ulcers were observed in the mucous membrane surrounding these hard scybala, while proximally the lining was grossly intact.

Even in this small series of cases, an interesting correlation was suggested between the size of the large intestine proximal to the "obstruction" and the length of the patient's survival (table 2). In

TABLE 2.—*Pathologic Observations in Eleven Cases of Intestinal Obstruction*

Case No.	Observations at Laparotomy	Age at Death	Megacolon	Level of Obstruction as Observed at Autopsy	Ganglion Cells in Myenteric Plexus
1	Distention; scybala in colon	1 month	+	Descending colon	Absent in distal part of colon
2	Distention; scybala in colon	Living; enterostomy with secondary closure	+	Rectosigmoid	Absent in descending colon
3	Impaction in sigmoid	Enterostomy; living	?	Sigmoid	?
4	Spasm of colon	19 days	?	Descending colon	?
5	.....	4 yr.	+	?	?
6	.....	3 days	—	?	?
7	Cyanotic ileum	14 days	+	Sigmoid; rectum	Absent in rectum
8	Discolored ileum	15 days	—	Lower part of ileum	Absent in colon
9	Constricted ileum	11 days	—	Lower part of ileum	Absent in colon
10	.....	2½ mo.	+	Rectosigmoid	Absent in rectum
11	Dilated small intestine and colon	5 mo.	?	?	?

cases in which death occurred shortly after birth dilatation was noted, but there was no frank megacolon in the sense of fixed anatomic enlargement of the colon. In those cases in which the infant lived beyond the age of 1 month, enlargement of the colon with increase in the caliber, as well as in the thickness of the wall, was increasingly evident at autopsy. In 2 additional cases, in which autopsy was not performed, studies with barium sulfate showed a definite megacolon.

In 4 cases purulent peritonitis was present at autopsy. In not all these cases had a laparotomy been performed. In each case it was evident, however, that the peritonitis was a late complication which did not account for the earlier symptoms of intestinal obstruction. Except for such conditions as aspiration pneumonia, otitis media and evidence of malnutrition in the older infants, the observations at autopsy were noncontributory. The central nervous system showed no gross

abnormality in any case in which it could be examined. The abdominal sympathetic ganglions were dissected in only 1 case, in which nothing unusual was observed.

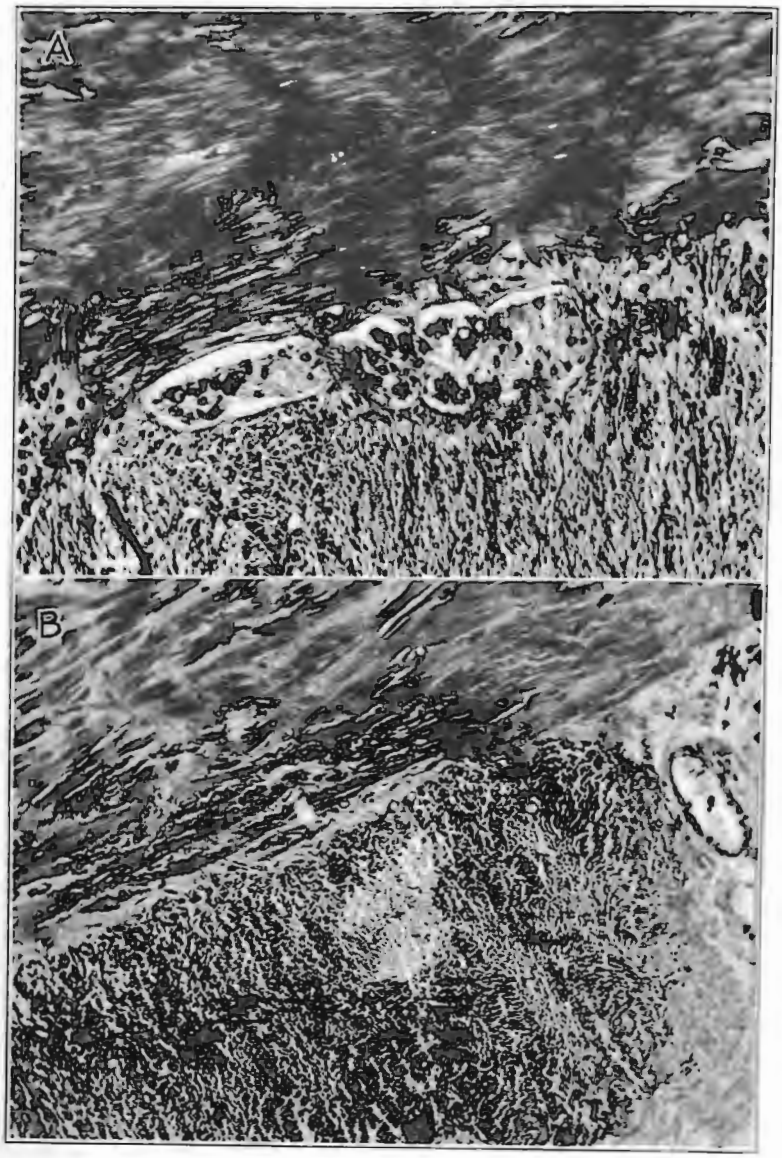

Fig. 4.—*A*, representative section of large intestine from normal control, showing nests of ganglion cells between longitudinal and circular muscle layers; *B* (case 1), representative section of large intestine of infant W. N., showing absence of myenteric plexus.

A complete microscopic study of the gastrointestinal tract was carried out in 5 of the fatal cases. Sections taken from successive levels of the intestinal tract were fixed and stained in the usual manner and compared with sections from 10 control cases of infants in the same age range with presumably normal bowel function. In addition, the surgical specimens from the descending colon and the appendix in case 2 were available. The sections on the average were 1.5 to 2.0 cm. long and were cut longitudinally, that is, parallel to the axis of the bowel.

In the control cases, the ganglion cells of the myenteric plexus were readily demonstrable at every level of the small and large intestine, even when autolysis of the mucosa was pronounced. These cells were irregularly spaced; but in every section at least several nests could be demonstrated, and usually they were abundant (fig. 4 *A*). In sections of the intestinal tract of our patients, ganglion cells were also readily demonstrable in the proximal portions of the intestinal tract. Distally, none could be found, even with the help of serial sections (fig. 4 *B*), although a plexus of nerve fibers was readily seen at the boundary between the internal and the external muscle layer. The appendix in case 2 contained numerous well developed ganglion cells, but none were seen in sections of the descending colon.

It is interesting that a fairly accurate correlation seemed to exist between the levels of the "obstruction" as determined at autopsy or at operation and the levels in which absence of the myenteric plexus was demonstrable. The inclusion of surgical material and the comparison of the sections with those from higher levels of the intestine and with sections from control cases convinced us that our inability to demonstrate ganglion cells was not the result of postmortem changes or of artefacts.

FUNCTIONAL TESTS

Our observations on the motor function of the intestine in our cases are far from adequate. In many cases the nature of the condition was not recognized during life, and often clinical emergencies precluded detailed studies. Our ideas were not crystallized at the beginning of this study but developed gradually with each new case, and we omitted many observations we now wish we had made. We present the few available data concerning intestinal motility (table 3) as a basis for future investigation, rather than as a finished study with definite conclusions.

The failure of spinal anesthesia to induce peristalsis or defecation in the cases in which this test was carried out seems of particular interest. The peristaltic activity resulting from this procedure in cases of "idiopathic" megacolon is generally regarded as evidence of an imbalance in the nervous regulation of the motility of the colon, with undue preponderance of sympathetic influences.

The failure to produce appreciable motor activity in the colon by eliminating sympathetic stimulation in our cases is in keeping with our assumption that the motor disturbance in our cases was related to the absence of parasympathetic motor neurons in the intestinal wall. The negative results obtained with parasympathomimetic drugs, such as mecholyl and neostigmine, even when used to the limits of tolerance, point in the same direction. However, we are not yet prepared to regard such negative effects as significant in diagnosis. In 1 case a complicating peritonitis may have interfered with the response to spinal anesthesia, and we feel that a greater number of observations is required before our results can be properly interpreted.

In 2 cases colostomy openings offered the opportunity for direct investigation of colonic motility. In both cases the studies revealed virtually complete lack of motility of any kind in the distal segment, while proximal to the site of the "obstruction" lively contractions were

TABLE 3.—*Functional Tests*

Case No.	Effect of Neostigmine Methylsulfate	Effect of Mecholyl Chloride	Effect of Spinal Anesthesia	Mechanical Tracings of Intestinal Motility
1	.....	No effect	No effect	.....
2	.....	.....	No effect	Absence of motility in affected segment of colon
3	.....	.....	.....	Absence of motility in affected segment of colon
5	Questionable	No effect	No effect	.....
10	No effect	.....	.....	.....

demonstrable. An artificial bolus inserted into the distal segment failed to travel toward the rectum. This demonstration was in keeping with the observations of residues of barium in the rectum for weeks after the administration of a barium sulfate enema.

Our observations need to be extended and confirmed. The correlation between the clinical and the pathologic observations in this group of patients suggests a causal relation between the disturbance in intestinal motility and the absence of nerve cells in the enteric plexus. At present it seems unwise, however, to attempt a detailed interpretation of our observations in terms of the physiology of intestinal motor function. The regulation of the various types of intestinal motility is a highly complex process, with many details yet to be clarified. In the intact organism the functions of the enteric nervous system are modified by central influences mediated by the extrinsic nerves, and probably by the properties of the musculature of the intestine.[4] As yet, physiologists have been unable to define the exact role of each of

4. Kuntz, A.: The Autonomic Nervous System, Philadelphia, Lea & Febiger, 1945.

these factors or to assign specific functions to the enteric nervous system. The study of the myenteric plexus is beset with technical difficulties, and no experiment has been devised which would be comparable to the elimination of its nerve cells in the intact animal.[5] It is probable that certain types of intestinal motility are myogenic,[6] but it would be impossible to state to what extent the propulsive function of the bowel could be carried out in the absence of local or central nerve influences.[7] Coordinated movements, such as peristalsis and other reflex-like reactions of the intestine, would seem to require neural regulation, and there is considerable evidence,[8] but no final proof, that these reactions are initiated by the cells of the enteric nervous system and abolished when the cells are eliminated. At present it may be safely said only that in the absence of the myenteric plexus serious interference with intestinal motility can be expected and that in the cases described here a profound functional disturbance was evident. It would seem appropriate in the future to consider patients such as ours as subjects for basic physiologic studies, and it may be that physiologists will be able to draw valid conclusions regarding the function of the enteric nervous system from an experiment of nature which they cannot duplicate in the laboratory.

DIAGNOSIS

It is evident that the condition which we have described offers many diagnostic problems. In the acute cases the sure preoperative differentiation from the ordinary mechanical obstruction will be impossible. The only clue which might differentiate the condition from mechanical obstruction is its familial incidence. In several of our cases, however, the information obtained about the siblings who had probably had the same condition as the patients was equivocal, and only by implication could we assume that similar defects had been encountered in the other children. Proper attention to the family history must be considered of exceedingly great importance. More care on our part probably would have directed us to a correct evaluation in several instances in which we made mistakes that in retrospect look foolish.

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Preliminary roentgenographic study is always desirable in these cases. A simple roentgenogram of the abdomen without the use of a contrast medium is probably the most valuable aid in diagnosis in such circumstances as those of this study, and may be all the roentgenographic study that is necessary. We believe that the use of barium sulfate is dangerous in such cases, in view of the tremendous difficulties we encountered in removing the barium from the intestinal tract of several infants.

The occurrence of fecal impaction calls for proper evaluation. It is true that in ordinary types of fecal impaction intestinal obstruction is occasionally seen and relief of the impaction mechanically results in relief of symptoms. We saw this effect repeatedly in our series of patients, but it was not always possible to demonstrate the impaction before operation, especially in the younger patients; it would, therefore, seem unwise to depend on this condition for the diagnosis. It is equally unwise, however, to expect permanent relief from removal of the impacted feces in cases such as ours. Apparently, fecal impaction in young infants is indicative of a profound disturbance of intestinal motility and does not have the same significance as fecal impaction encountered in children. In the early acute cases the most useful information can be obtained at operation, and we feel strongly that an early exploratory laparotomy is indicated. Little is to be gained by temporizing procedures in the case of small infants. The surgeon must make a careful analysis of the situation, and if he fails to find mechanical cause for obstruction he must recognize the implications of his negative results and not close the abdomen without considering the need for enterostomy.

The concept of intestinal obstruction resulting from functional disturbance is not new. The best known example is paralytic ileus developing in the course of peritonitis, gallbladder disease, renal colic or severe infections, including pneumonia. It is evident that the condition which we are describing is, at least in its early stages, entirely different from this type of disturbance. The effects of prolonged severe abdominal distention and of a complicating terminal peritonitis, which supervened in several of our cases, need not concern us here.

It is likewise obvious that the obstruction in our cases was not meconium ileus, a condition related to cystic fibrosis of the pancreas and characterized by inspissation of abnormally viscid meconium in the intestinal tract. The character of the feces in our cases was in no way similar to that seen in cases of meconium ileus, and the histologic structure of the pancreas was normal in all cases in which sections could be made.

In the more chronic cases the relation to megacolon will always be a problem. Our thinking has been much influenced by our histo-

pathologic observations, and we regard the disturbance characterized by early acute intestinal obstruction as fundamentally identical with the more protracted, and perhaps milder, forms, in which a picture virtually indistinguishable from that of megacolon may eventually present itself. The development of fixed anatomic enlargement of the colon must be, among other factors, a function of time. The early stages of megacolon are notoriously difficult to recognize whatever the underlying mechanism. Since, in the older infants of our group, enlargement of the colon was demonstrable at autopsy roughly in proportion to the length of survival, one might argue that these cases represented an early stage of megacolon. To this argument, which is based on an anatomic definition of megacolon, we have no objection, but to take the size of the megacolon as the decisive criterion would be begging the question. The real problem is whether cases such as ours can be separated from what we may call, for the sake of convenience, the classic type of megacolon. Absence of the ganglion cells in the myenteric plexus has been reported briefly in several cases classified under the head of megacolon, but attempts to explain the typical megacolon uniformly on such a basis have been unsuccessful. There have been few systematic studies of the distribution of the myenteric plexus throughout the length of the intestinal tract. In our own material, we have made such a study in 10 control cases, those of infants with presumably normal intestinal motility, and, in addition, in 2 cases of typical megacolon. In both groups we observed well developed ganglion cells at every level of the intestine. Tiffin, Chandler and Faber,[1] who reviewed the literature in 1940, suggested that cases in which the motor disturbance of the bowel is associated with absence of the myenteric plexus might form a subgroup of the clinical condition which at present is called idiopathic megacolon; this suggestion seems to be borne out by our observations. Clinical distinction between cases of agenesis of the myenteric plexus with protracted course and those of clinical megacolon is not easy. We are accustomed to see occasional episodes of intestinal obstruction resulting from impaction of feces in cases of megacolon regardless of etiology. Until more case reports become available, there are only a few clues on which to base the tentative clinical distinction. Again, the family history would seem to be an important item. Possibly the results of spinal anesthesia may be significant. Finally, the observation may be significant that in cases of agenesis of the myenteric plexus obstruction develops before there is a real anatomic megacolon. A careful analysis of the past history will usually make it clear that the patient with agenesis of the myenteric plexus has had interference with normal bowel function all his life and that previous acute, but perhaps milder, episodes of intestinal obstruction have occurred.

TREATMENT

We do not feel that our experience is adequate for the outlining of a final therapeutic program. Although temporary relief, even during acute obstructive episodes, may be obtained from conservative measures, we believe that surgical exploration is indicated in all these cases. It is our present impression that functional obstructions of this type should be treated at least temporarily like organic obstructions in which correction of the mechanical factors proves impossible and a rerouting of the fecal stream is therefore necessary. It seems to us that an enterostomy at the lowest level of normal intestinal motility is indicated and that the question of closure of the enterostomy opening can be left for later consideration. In 1 of our cases the final repair and rerouting of the fecal stream through its normal passage with excision of a relatively short segment of colon almost a year after the initial operation was successful; but in another case repeated attempts to close the enterostomy proved unsuccessful, and we have to assume that the restoration of intestinal motility may be impossible. Further experience will be necessary to decide whether resection of part or of all the nonmotile portion of the intestine is a desirable and practical procedure.

SUMMARY

We have described a series of cases with a clinical picture of acute, recurrent or chronic intestinal obstruction in which no mechanical cause was demonstrable. We believe that the functional disturbance in intestinal motility in such cases is related to the congenital absence of nerve cells in the enteric nervous system. The picture in the acute cases was demonstrated to be clinically indistinguishable from that due to the mechanical causes of intestinal obstruction, while the picture of the chronic cases merged with that of idiopathic megacolon. A familial trend was recognized in several cases and seems to us to form one of the most important clues to the cause and diagnosis of the condition, which we propose to call "agenesis of the myenteric plexus." The first step necessary in recognizing cases of this defect, and so avoiding the embarrassment and confusion commonly occurring in management of the patient, is to think of this possibility at the time that a young infant is presented with clinical symptoms of intestinal obstruction. A tentative outline of the management of such patients is presented.

Children's Hospital of Michigan (Dr. Zuelzer).
University Hospital, Ann Arbor, Mich. (Dr. Wilson).