Chapter

Meconium Ileus

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Abstract

Meconium ileus is a type of neonatal intestinal obstruction that occurs when abnormally thick meconium impacts in the ileum causing blockage of intestinal flow. Most infants with meconium ileus have cystic fibrosis, a congenital condition characterized by abnormally thick intestinal secretions and pancreatic insufficiency. The pathogenesis of meconium ileus is due to hyperviscous mucus secreted by abnormal intestinal glands, abnormal concentrating processes in the proximal small intestine, and pancreatic enzyme insufficiency. The clinical presentation of meconium ileus is that of abdominal distention, bilious vomiting, and failure to pass meconium. Cases of meconium ileus are usually evaluated with plain abdominal radiograph and contrast enema. Numerous air-filled loops of bowel on the supine view with characteristic absence of air-fluid levels are commonly seen on the radiograph, but the presence of calcification suggests intestinal perforation. Contrast enema examination is useful in cases with microcolon. Uncomplicated meconium ileus obstruction can be relieved by giving one or more dilute diatrizoate sodium enema (with Nacetylcysteine added) under fluoroscopy. Surgery is indicated when there is progressive distention or signs of clinical deterioration despite multiple enemas, as well as in complicated cases like meconium peritonitis, ileal atresia or stenosis, ileal perforation, and volvulus with or without pseudocyst formation.

Keywords: meconium ileus, cystic fibrosis, ileal obstruction, gastrografin enema, nonoperative treatment, enterotomy, enterostomy, resection and anastomosis

1. Introduction

Meconium ileus is a type of neonatal intestinal obstruction that occurs when abnormally thick and tenacious meconium becomes impacted, thus creating a blockage in a part of the distal small intestine, usually the ileum [1, 2]. It accounts for about 30–33% of cases of neonatal small intestinal obstruction [3]. Meconium ileus is a rare condition affecting only 1 in 25,000 babies [4]. It occurs in either a simple or a complicated form and is said to be the earliest clinical manifestation of cystic fibrosis occurring in approximately 16–20% of patients with cystic fibrosis [4]. Cystic fibrosis is a disease condition characterized by abnormally thick intestinal secretions and pancreatic insufficiency.

While majority of patients with meconium ileus have the disease cystic fibrosis (80–90%), a few of them do not have it; approximately 20% of one series of cases of meconium ileus did not have cystic fibrosis [5]. Preterm infants whose mothers had medications to slow down labor are sometimes associated with meconium ileus.

Meconium is the first series of stools that a newborn pass. It is formed during intrauterine life and consists of shed intestinal epithelial cells, bile, succus entericus, mucus, lanugo, and amniotic fluid ingested in utero. It is a dark olive green viscous and almost odorless substance that comprises the initial stools of the newborn. Meconium contains lactic acid-producing bacteria (e.g., *Lactobacillus*) and the so-called enteric bacteria family (e.g., *Escherichia coli*) [6]. It is usually evacuated within the first 24–48 hours after birth following which the usual yellowish feces are passed by the neonate. However, there might be in utero evacuation of meconium as a result of a vagal response due to perinatal stress to the fetus. Such newborn immediately after delivery may develop signs of respiratory distress from meconium aspiration syndrome.

Meconium ileus may be associated with complications such as meconium peritonitis, ileal atresia or stenosis, ileal perforation, and volvulus with or without pseudocyst formation [7–13]. The infants with cystic fibrosis are more likely to present with complicated meconium ileus [14].

2. Detailed overview of meconium ileus

An overview of meconium ileus in terms of etiology, pathophysiology, clinical features, investigations, and treatment will now be undertaken.

2.1 Etiology

Up to 20% of babies with cystic fibrosis are born with meconium ileus, and almost all babies with meconium ileus have cystic fibrosis [15, 16]. Cystic fibrosis is caused by gene mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) encoding gene [17–19]. The loss of CFTR-mediated Cl– and/or HCO3– transport by the intestinal epithelium and/or from pancreatic dysfunction is postulated as the pathogenesis of meconium ileus [20–24]. Cystic fibrosis is characterized by the triad of chronic obstruction and infection of the respiratory tract, exocrine pancreatic insufficiency, and elevated sweat chloride levels.

The pathogenesis of meconium ileus is due to hyperviscous mucus secreted by abnormal intestinal glands, abnormal concentrating processes in the proximal small intestine, and pancreatic enzyme insufficiency.

The histology is characterized by the presence of distended goblet cells in the intestinal mucosa.

2.2 Pathophysiology

The simple form of meconium ileus is characterized by thickened sticky meconium obstructing the ileum with consequent proximal dilatation, bowel wall thickening, and congestion. Immediately beyond the level of the obstructing inspissated meconium in the terminal ileum, there may be a few separate gray-white globular meconium pellets. Further distally, the colon is narrow and empty—the microcolon.

The complicated form may result in volvulus, atresia, necrosis, perforation, meconium peritonitis, and pseudocyst formation. These complications may manifest as incidental findings on abdominal radiographs or with clinical features suggestive of bowel obstruction caused by reactive fibro-adhesive bands due to the meconium in the peritoneal cavity or as clinical features of peritonitis. If a neonate at birth manifests features of peritonitis, it is likely due to meconium peritonitis

secondary to meconium ileus bowel perforation. This may also result in intestinal atresia, intraperitoneal calcifications, or ascites [25]. Meconium pseudocyst is formed when the extruded meconium becomes walled off; it is a cystic mass with rim calcification [26].

In utero, about 50% of meconium ileus cases may be complicated by intestinal perforation, meconium peritonitis, volvulus, and ischemic necrosis of the bowel that results in stenosis or atresia [4].

Meconium ileus patients are at risk for developing cholestasis, especially if they are on total parenteral nutrition. As such, alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels should be monitored weekly in such infants.

2.3 Clinical features

At birth, the neonate may be apparently normal. However, with progression of time and feeding, the infant develops abdominal distention, bilious vomiting, and failure to pass meconium. Sometimes thickened distended bowel loops are observed through the abdominal wall filled with rubbery meconium which when palpated feel characteristically doughy [3]. Bowel sounds tend to be hypoactive, and digital rectal examination may be followed by passage of pale mucosal plugs. Meconium pellets might be palpated in the scrotum of some infants who had in utero bowel perforation. In cases complicated by peritonitis or when postnatal perforation has occurred, the infant presents with respiratory distress, marked abdominal distention with abdominal erythema, significant abdominal tenderness, and ascites.

2.4 Investigations

Cases of meconium ileus are usually evaluated with abdominal radiograph in which meconium might have a mottled appearance or be invisible [27].

Plain abdominal radiographs are routinely the first imaging done for cases of meconium ileus. They show numerous air-filled loops of bowel on the supine view with characteristic absence of air-fluid levels on the upright view due to the tenacious meconium and the abnormal mucous-gland secretion [5]. Although the absence of air-fluid levels strongly suggests meconium ileus, the presence of air-fluid levels does not exclude it as it may occasionally be demonstrated in some cases. In some cases of meconium ileus, the admixture of meconium and bowel gas gives a soap-bubble appearance usually in the right lower quadrant (Neuhauser sign). The presence of calcification, free air, or multiple air-fluid levels suggests intestinal perforation [4].

A contrast enema examination is useful in confirming the diagnosis of meconium ileus in which microcolon is seen; this differentiates it from meconium plug syndrome in which a normal or dilated colon is seen [25]. The microcolon, which represents the underused colon, could also be seen in other congenital conditions causing complete intrauterine obstruction of the distal small bowel such as ileal atresia; however for cases of meconium ileus, the presence of meconium pellets distending the distal ileum is usually identified when the contrast refluxes into the small bowel, and the diagnosis is confirmed (**Figure 1**).

Water-soluble agents are typically used in contrast evaluation of meconium ileus, and several of such contrast agents have been used. The hyperosmolar meglumine (GastrografinRx) diluted at ratio 1:3 to water used to be the mainstay, but some radiologists have stopped using it because of the occurrence of deaths

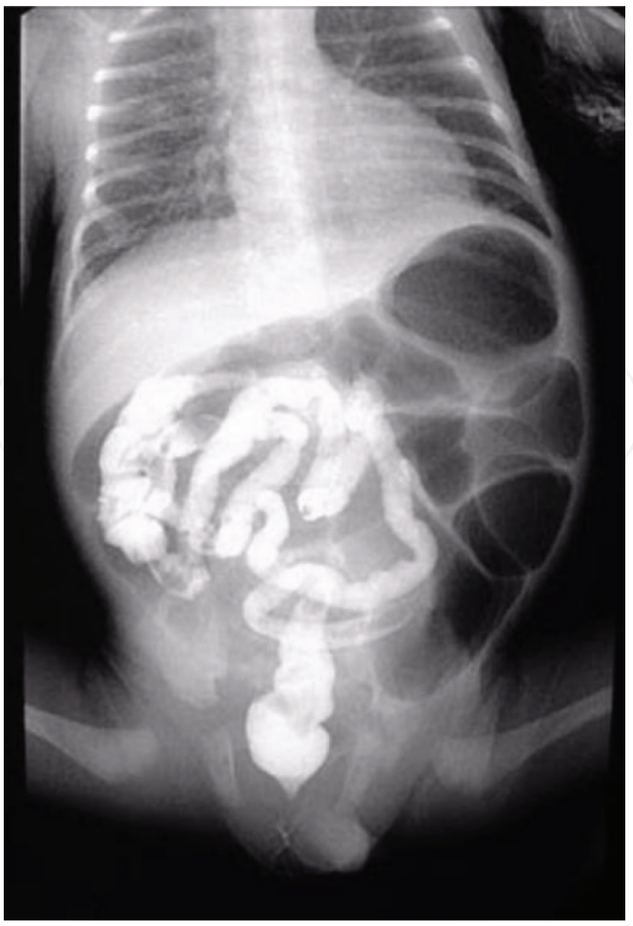


Figure 1.
Contrast enema showing microcolon and meconium pellets in the terminal ileum [courtesy Radiopaedia].

from fulminant colitis and dehydration sometimes reported with its use [28]. Also, the report of the Cystic Fibrosis Foundation Consensus Conference on gastrointestinal disorders concluded that there is no scientific evidence that hyperosmolar Gastrografin enema is any better than an iso-osmolar or hypo-osmolar enema. Nevertheless, many radiologists use it safely by ensuring appropriate dilution ratios. Adequate monitoring of fluid and electrolyte balance before, during, and after the contrast study is essential to avert potential fluid shifts with consequent hypovolemia which is worsened when bowel perforation and contrast leak occur. Nonionic contrast agents like Hypaque and Omnipaque are becoming popular with many radiologists since they have less risk of dehydration or colitis. Because of the tenacious and sticky nature of meconium, mucolytic agents like acetylcysteine are sometimes mixed with the contrast enema solution to aid passage of the meconium.

Meconium peritonitis may be an incidental abdominal radiograph finding in which the extruded meconium may be calcified or the radiograph may only suggest fluid in the abdomen when no calcification is present. When the calcification appears amorphous and curvilinear suggesting cystic loculation of the peritoneum, the term cystic or pseudocystic meconium peritonitis is used [5].

Prenatal ultrasound scan done at 17–18 weeks gestational age may show signs suggestive of meconium ileus; this include enlarged bowel loops or a mass with proximal bowel distention (likely cystic meconium peritonitis) [11, 12]. Also, calcified meconium may be seen if meconium peritonitis has already occurred. Also there might be polyhydramnios.

Postnatal ultrasound scan is seldom necessary for meconium peritonitis, as the findings on plain radiographs are usually diagnostic. However, ultrasonography may be useful when cystic masses are present. The cystic masses often appear circumscribed and heterogeneous with sonolucent areas seen within the cyst suggestive of fluid. They demonstrate increased echogenicity resulting from debris and calcifications, and loops of fluid-filled bowel bound to the matrix of the associated adhesions may be noted. The cyst wall may be thick or thin. Multiple speckled echoes are seen with free-floating meconium in the abdomen, and these result in the snowstorm configuration.

Zangheri et al. created the following classification system related to perinatal outcome [29]:

- Grade 0: isolated intra-abdominal calcifications (IAC)
- Grade I: IAC and one of the following: ascites, pseudocyst, or bowel dilatation
- Grade II: IAC and two of the following: ascites, pseudocyst, or bowel dilatation
- Grade III: all of the above (IAC, ascites, pseudocyst, and bowel dilatation)

Patients diagnosed with meconium ileus should be tested for cystic fibrosis; the sweat chloride test should be done [25].

2.5 Treatment

2.5.1 Initial medical management

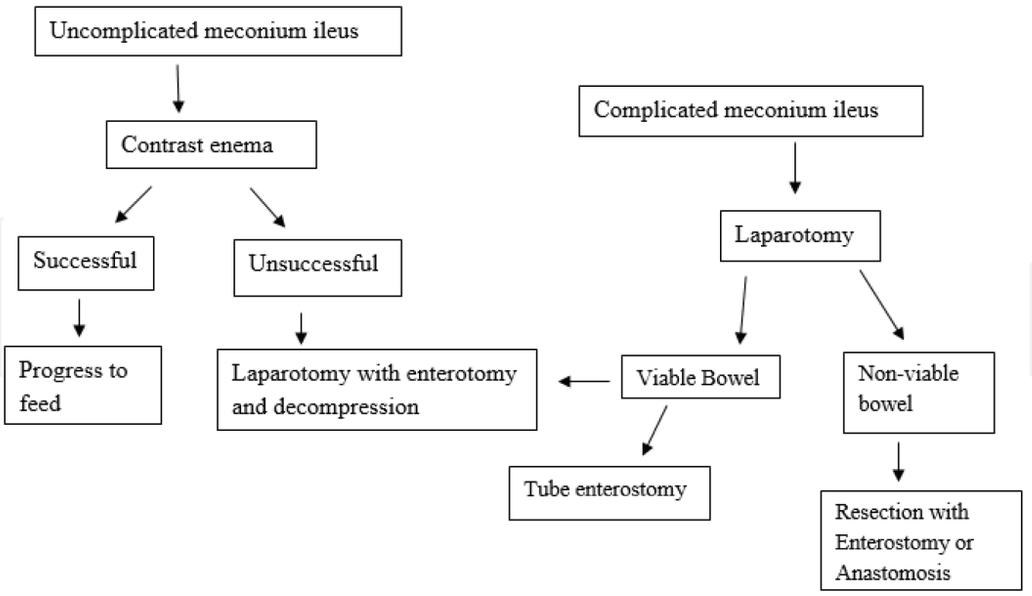
Meconium ileus cases, both simple and complicated, are approached as intestinal obstruction and as such would require urgent initial resuscitative measures. These include intravenous fluid resuscitation, nasogastric decompression, urethral catheterization for hourly urinary monitoring, multiparameter vital sign monitoring, intravenous antibiotic therapy, laboratory evaluation of full blood count, coagulation work-up, and serum electrolytes, urea, and creatinine with necessary corrections instituted. Where necessary, mechanical respiratory support is provided. Once the infant has been optimized, the decision for nonoperative or operative management is taken based on the presentation.

2.5.2 Nonoperative treatment

Nonoperative management can be achieved by diatrizoate meglumine enemas as first described by Noblett in 1969 [30]. Variations on his approach have been established as effective first-line treatment for uncomplicated meconium ileus.

Uncomplicated meconium ileus obstruction can be relieved by giving one or more dilute diatrizoate sodium or diatrizoate (gastrografin) enema (with N-acetylcysteine added) under fluoroscopic guidance. The hyperosmolar nature of this compound increases the influx of fluid into the bowel lumen to liquefy the viscid meconium and thus facilitate its expulsion with consequent large gastrointestinal water losses. While carrying out this procedure, therefore, adequate intravenous fluid administration must be ensured to prevent hypovolemia.

2.5.3 Treatment algorithm



Diatrizoate meglumine (GastrografinRx) is a hyperosmolar, water-soluble, radiopaque solution containing 0.1% polysorbate 80 (Tween 80) and 37% organically bound iodine with osmolarity of 1900 mOsm/L. Success rate of 63–83% have been reported for gastrografin enemas for patients with uncomplicated meconium ileus [31].

Noblett's criteria for nonoperative gastrografin enema therapy [30]:

- Other causes of neonatal distal intestinal obstruction must first be excluded.
- There should be no clinical or radiologic signs of complications like volvulus, gangrene, perforation, peritonitis, and atresia of the small bowel.
- Ensure adequate fluid and electrolyte replacement and correction of hypothermia as preparatory measures before the enema.
- Provision for adequate resuscitation and hydration in anticipation of transient osmotic fluid losses associated with the hyperosmolar enema.
- The enema must be carried out under fluoroscopic guidance.
- Intravenous antibiotics should be administered to the infant.
- Assurance of close surgical supervision from the initial evaluation through the hospital course.

To carry out the enema, a two-way Foley's catheter is inserted into the rectum through which a 25–50% solution of gastrografin is slowly infused at low hydrostatic pressure under fluoroscopic control. The balloon of the catheter should not be inflated to minimize the risk of rectal perforation. Upon instillation, fluid is drawn into the intestinal lumen by osmosis, and this hydrates and softens the meconium mass. For very inspissated meconium, 1% N-acetylcysteine may be added to the enema solution for better deconcentration. The procedure is usually followed by rapid passage of loose meconium (liquefied to some extent), and this continues for the next 24–48 hours.

Although the perforation that occurs during enema administration can usually be seen on fluoroscopy, it is important to obtain an immediate abdominal radiograph after completion of the gastrografin enema to rule out bowel perforation and a late abdominal radiograph (8–12 hours later or as clinically indicated) to confirm evacuation of the obstruction and to exclude late perforation [31].

Sometimes a second gastrografin enema or serial gastrografin enemas can be performed at 6–24 hour intervals if evacuation is incomplete or if the first attempt at gastrografin evacuation does not reflux contrast into dilated bowel. Administration of a 10% N-acetylcysteine solution (5 mL q6h) through a nasogastric tube to liquefy upper gastrointestinal secretions as suggested by Noblett is also useful in such cases [30]. The potential complications associated with the gastrografin enema procedure include perforation, hypovolemic shock, and ischemia.

The risk of perforation during the procedure increases with repeated enemas. Late perforations, usually occurring 12–48 hours after the enema, may be due to direct injury to the bowel mucosa by the contrast medium, severe bowel distention by fluid osmotically drawn into the intestine, or extensive bowel necrosis.

Nonoperative treatment can be done for infants with peritoneal (or scrotal) calcifications on radiography who are presumed to have had meconium peritonitis in utero but who show no signs of obstruction and are passing meconium without difficulty [32].

In nonoperative management, if the enema was successful and the features of bowel obstruction have resolved, usually within 48 hours, the infant is commenced on feeds with pancreatic enzyme supplements added for infants with confirmed cystic fibrosis.

2.5.4 Surgical treatment

In uncomplicated meconium ileus, surgical exploration is indicated when there is progressive distention or signs of clinical deterioration or peritonitis despite multiple enemas. Whereas in complicated cases (e.g., meconium peritonitis, ileal atresia or stenosis, ileal perforation, and volvulus with or without pseudocyst formation), surgery is always indicated.

Indications for surgical management in meconium ileus [31]:

- Persistent or worsening abdominal distension
- Persistent bowel obstruction
- Enlarging abdominal mass
- Intestinal atresia
- Volvulus
- Perforation
- Meconium cyst formation with peritonitis
- Bowel necrosis
- Conditions associated with cystic fibrosis and meconium Ileus

In the operative management of simple uncomplicated meconium ileus, the aim is to evacuate meconium from the intestine without resecting any bowel segment; however, this might be inevitable in certain instances. On the other hand, complicated meconium ileus requires resection more often and may necessitate the use of temporary stomas.

The fibrous wall of the pseudocyst is debrided without sacrificing viable intestine. Extensive adhesiolysis is required for adhesive obstruction due to meconium peritonitis; these adhesions are typically dense and very vascular. It is not necessary to perform a radical debridement of all meconium calcified plaque encountered, as long as the obstruction is relieved [32].

The surgical approach for treatment of uncomplicated meconium ileus should be individualized for each infant, although many procedures have been proposed over the years with variable success rates achieved. In all cases, uncomplicated or complicated, the following procedures are commonly done:

- Enterotomy and decompression
- Enterostomy (with or without tube) with subsequent irrigation
- Resection and enterostomy
- Resection and anastomosis

2.5.5 Enterotomy and decompression

An enterotomy is made on the antimesenteric border of the dilated ileum for instillation of irrigation solution (dilute acetylcysteine or saline solution) which help to loosen the inspissated meconium and liquefy it for effective evacuation through the enterotomy. The irrigation solution is introduced using a size 10 French catheter, and both the proximal and distal loops of bowel are irrigated. After complete decompression of inspissated meconium, the enterotomy is closed transversely. An appendectomy is performed with the specimen sent for histologic examination to detect the presence of ganglion cells, as well as possible presence of mucous plugging of the crypts and exuberant intraluminal mucinous material, which are suggestive of cystic fibrosis. Postoperatively, a gentle anal dilatation and rectal irrigation may sometimes be required for further evacuation of large amount of meconium passed distally into the colon during intraoperative irrigation. Enterotomy and decompression are usually indicated for simple uncomplicated meconium ileus. A supraumbilical transverse incision or transverse right lower abdominal incision can be used for the procedure.

2.5.6 Enterostomy with subsequent irrigation

In cases where the irrigation done after an enterotomy cannot effectively evacuate the inspissated meconium despite a patient approach, an indwelling ostomy tube (e.g., T-tube) can be inserted for postoperative bowel irrigation decompression. The irrigations are started on the first postoperative day and continued for 7–14 days. After successfully evacuating the inspissated meconium, the tube is removed, and the enterocutaneous fistula thus formed is allowed to close spontaneously. T-tube enterostomy was first described by Harberg et al. in 1981 [33]. Enterostomy for postoperative irrigation can also be done without using tube; in which case the ileal opening is sutured to skin and the bowel tacked to the fascia in standard fashion.

2.5.7 Resection with enterostomy or anastomosis

Bowel resection is indicated when meconium ileus is associated with a nonviable bowel, bowel perforation, atresia, volvulus, and the like. Resection is usually combined with enterostomy procedure, but primary anastomosis may be done if the intraoperative findings and the patient's general condition are favorable. The disadvantages of the procedures involving resection and stoma(s) or anastomosis are potential postoperative fluid losses through high-volume stomas, bowel shortening by resection, and the need for a second procedure to reestablish intestinal continuity [25, 31]. Hence, they are rarely used today.

Various stoma operations have been described with the most widespread being the Bishop-Koop-type anastomosis. This is a Roux-en-Y construct in which the distal limb is brought out as an end stoma and the proximal bowel is anastomosed end-to-side approximately 4 cm from the opening of the distal segment (**Figure 2**). Normal gastrointestinal transit is permitted by this technique, and should distal obstruction occur, it provides a means for management through the ileostomy [25, 31].

The reverse of the Bishop-Koop enterostomy is the proximal enterostomy, described by Santulli and Blanc in 1961 [25, 31]. In this technique, the end of the distal limb is anastomosed to the side of the proximal limb after resection, while the end of the proximal limb is brought out as the enterostomy (**Figure 2**). This arrangement enhances proximal irrigation and decompression, thus making intraoperative evacuation of the dilated proximal bowel loop unnecessary. A catheter can be inserted into the distal limb through the stoma for irrigation of the distal bowel. The proximal stoma created in this technique predisposes to high-output losses with inherent risk of dehydration.

The Mikulicz enterostomy, first reported by Gross in 1953, consists of a double-barrel stoma in which the two ends are sutured together side to side for some length

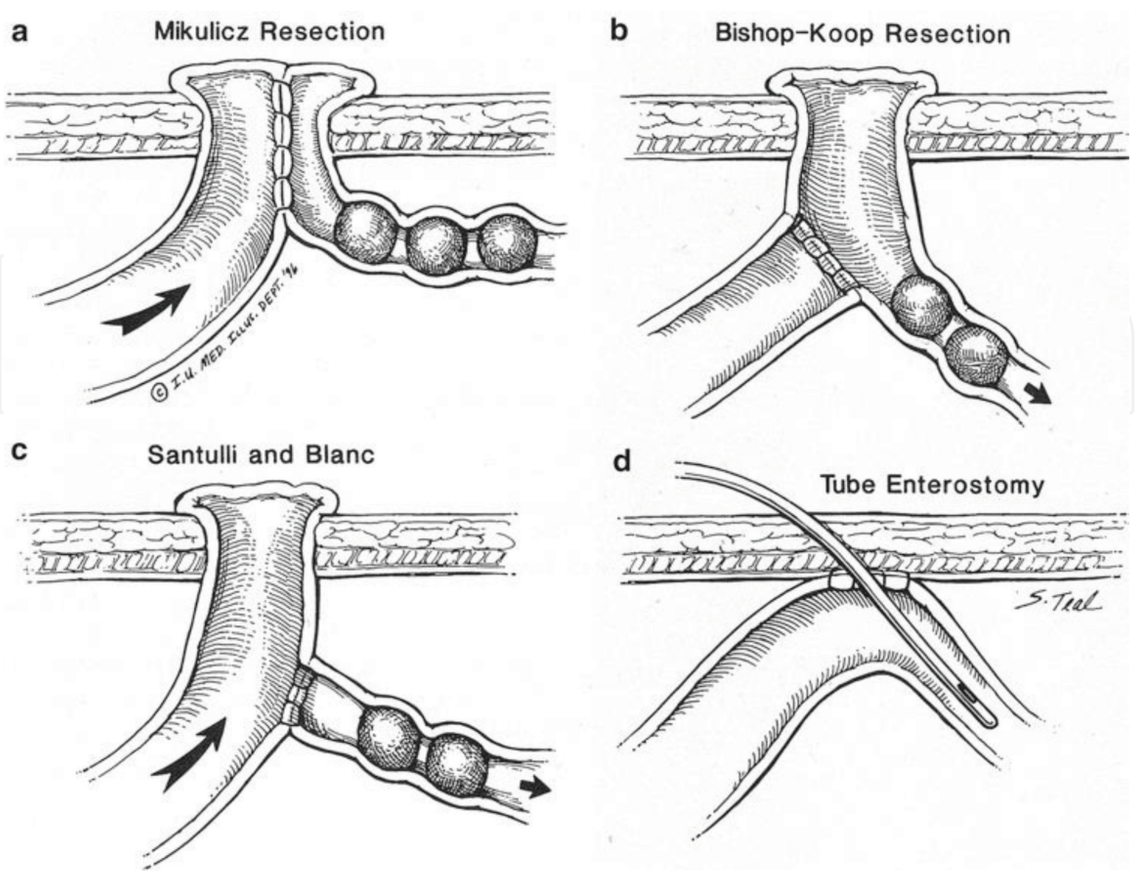


Figure 2.
Schematic description of some enterostomies as copied from Ref. [36].

proximal to the end of the stoma (**Figure 2**) [25, 31]. It was designed for bedside stoma closure in which the common wall was crushed and obliterated with a specially designed clamp and the bowel ends were closed over the top. It has the following distinct advantages:

- The procedures reduce operating and anesthetic times because complete evacuation of inspissated meconium is unnecessary.
- The procedures avoid intra-abdominal anastomosis, which eliminates the risk of anastomotic leakage.
- The bowel can be opened after complete closure of the abdominal wound; this reduces the risk of intraperitoneal contamination.

Swenson was the first to suggest resection with primary anastomosis in 1962 [25, 31]. Anastomotic leakage was initially a major issue with such operation; however some authors have reported improved results with adequate resection of the compromised bowel, complete evacuation of proximal and distal meconium, and preserving an adequate blood supply to the anastomosis [34, 35].

2.6 Postoperative care

Immediately postoperatively, management involves ongoing resuscitation with special attention given to replacement of the fluid losses caused by surgery and preoperative hyperosmolar enemas (if attempted), as well as correction of ongoing losses (i.e., losses from nasogastric suction and ileostomy) [31]. Also, the infant is initially on bowel rest with general supportive care provided after any major laparotomy. The oral gastric tube is maintained until bowel function returns, and further acetylcysteine irrigations can be done via the tube as described for nonoperative management. Combining this with rectal irrigations may further aid passage of retained meconium in the distal loop as well. Most infants will need central venous access for parenteral nutrition during this period. If cystic fibrosis has not been confirmed preoperatively, the sweat chloride test should be done to confirm or rule it out. Close attention has to be given to pulmonary care in infants with cystic fibrosis. Multiple pediatric subspecialists including gastroenterologists, geneticists, pulmonologists, and pediatric surgeons are required for a good outcome of management in infants with meconium ileus, more so when they have cystic fibrosis. Once they have established a normal stooling pattern (usually within 1–2 weeks postoperative), they are commenced on graded oral feedings with pancreatic enzyme supplementation. Infants with uncomplicated meconium ileus and cystic fibrosis may receive breast milk or routine infant formula, enzymes, and vitamins, while complicated cases would benefit from predigested infant formulas (e.g., Alimentum and Pregestimil), for enteral feeding [31]. For those with stomas, administering of ostomy-drip feeds of glutamine-enriched formula at low volumes enhances bowel growth and helps prevent bacterial translocation [31]. After 4–6 weeks, when symptoms would have resolved and the infant attained an adequate weight gain, the stomas can be taken down. It is advisable to perform a distal contrast study to rule out obstruction before embarking on this procedure of reanastomosis.

2.7 Postoperative complications

Short-term complications are uncommon in infants with simple meconium ileus.

Infants who have had significant (i.e., >33%) bowel resection may develop short bowel syndrome, especially if the ileocecal valve has been resected.

Short bowel syndrome predisposes to acidic intestinal environment that inactivates pancreatic enzymes and prevents dissolution of enteric-coated microcapsules. As such, histamine 2 receptor blockers are useful adjunct to pancreatic enzyme therapy in patients with significant bowel resections.

There are excessive fluid and sodium losses in those with stomas.

Mucus plugging and atelectasis can occur postoperatively, hence the need to initiate vigorous prophylactic pulmonary care with chest physiotherapy.

High-dose pancreatic enzyme supplementation has been associated with the development of colonic strictures and distal intestinal obstruction syndrome.

Long-term complications are mostly common to patients with cystic fibrosis.

Some infants, especially those who had meconium peritonitis may present years later with bowel obstruction due to adhesions or segmental volvulus.

Some older patients have been known to develop bowel obstruction from inspissated stools in the ileum and colon; this condition is known as "meconium ileus equivalent" [32].

3. Conclusion

Meconium ileus is a cause of neonatal small intestinal obstruction which mainly affects the ileum and common in infants with cystic fibrosis. Contrast (gastrografin) enema is usually diagnostic and may sometimes be therapeutic. Infants who have unsuccessful management with enemas and those with complications related to the obstruction, including volvulus, perforation, or atresia, require operative intervention.

At laparotomy, a small enterotomy is done for those with simple meconium ileus to irrigate the bowel lumen with acetylcysteine solution and thus promote effective evacuation of the highly viscous meconium. Patients with complicated meconium ileus may require bowel resection with anastomosis or tube enterostomy or creation of a stoma. Various types of stomas have been described over the years for management of the disease, but the Bishop-Koop enterostomy seems to be widespread.

Most patients respond well to therapy in the short-term but need to be followed closely for long-term complications like bowel obstruction, which has many potential causes in these patients. Advances in perinatal diagnosis and management of meconium ileus and cystic fibrosis have vastly improved the outlook for affected infants.

Conflict of interest

There is no "conflict of interest."

Notes/thanks/other declarations

None.

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