Meconium Ileus

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65.1 Introduction

Meconium ileus, the earliest clinical manifestation of CF, occurs in as much as 20% of patients with CF. The clinical features are mainly due to the presence of abnormal, inspissated, and adhesive meconium. In affected neonates, CF causes intestinal obstruction in the midileum to terminal ileum, thus leading to progressive abdominal distension and a failure to pass the meconium. Approximately 40% of patients with meconium ileus have complications of intestinal volvulus, atresia, or bowel necrosis (Escobar et al. 2005). If perforation occurs earlier in utero, then intestinal reabsorption and formation of pseudocysts or abdominal calcifications may be observed. The colon is typically "unused" or "microcolon." Relief of the intestinal obstruction can be achieved through a hyperosmolar contrast enema under fluoroscopic guidance. Failed meconium disimpaction or complex meconium ileus necessitates surgery (Carlyle et al. 2012). When conservative management with enema irrigation fails, operative intervention is necessary. Currently, there is no consensus regarding the ideal surgical strategy for managing meconium ileus. However, the long-term outcomes and survival of patients with meconium ileus and CF have significantly improved over the past few decades and are no worse than those in patients with CF without meconium ileus (Johnson et al. 2010).

65.2 Historical Overview

The first description of an infant with meconium ileum, accompanied by a description of the histological pancreatic changes, was reported by Landsteiner in 1905 (Landsteiner 1905). He suggested that a lack of pancreatic secretion causes the thickening of the meconium, resulting in bowel obstruction. In 1929, Kornblith described meconium ileus with congenital stenosis of the main pancreatic duct (Kornblith and Otani 1929). Dodd suggested that the failure of pancreatic enzymes to reach the gut during perinatal life was at least partially responsible for meconiums ileus (Dodd 1936). The term CF of the pancreas was coined in 1936 by Fanconi, who described the association of chronic pulmonary disease with pancreatic insufficiency in infants (Fanconi et al. 1936). In 1938, Andersen first described the characteristics of CF in the pancreas and correlated the findings with the lung and intestinal disease in newborns with meconium ileus (Andersen 1938). She also suggested that CF is a recessive

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disease and initially used pancreatic enzyme replacement therapy. Farber recognized significant multiple organ involvement with tenacious thick mucus, hence his terminology of mucoviscidosis (Farber et al. 1943). Di Sant'Agnese's description of sweat abnormalities in CF in 1953 led to the development of the diagnostic sweat test. For several decades, meconium ileus and CF remained as pediatric diseases with high mortality rates. The first significant improvement in treatment came in 1948, when Hiatt and Wilson described the intraoperative method of disimpaction of the inspissated meconium with saline via enterostomy tube (Hiatt and Wilson 1948). This was followed in 1969 by Noblett's use of hyperosmolar enema with Gastrografin in the management of uncomplicated meconium ileus (Noblett 1969). Over the years, several operative methods followed. Shwachman encouraged Gross to treat meconium ileus; the Mikulicz side-by-side enterostomy was first reported by Gross in 1953. Distal chimney enterostomy was described by (Bishop and Koop 1957) and was followed by a description of proximal enterostomy by (Santulli and Blanc 1961). In 1970, O'Neill reported successful tube enterostomy with and without bowel resection. In 1989, scientists discovered the CF transmembrane conductance regulator (CFTR) gene and the most prevalent CF-causing mutation (F508del) (Kerem et al. 1989; Riordan et al. 1989; Rommens et al. 1989). The first CFTR-modulating drug entered the market in 2012 (Ramsey et al. 2011).

65.3 Incidence

Meconium ileus is seen in approximately 20% of patients with CF. The incidence rates for CF in Europe are similar to those seen across the United States and Canada; approximately 1 in 2000 to 3000 infants of northern European descendent are diagnosed at birth, with an allele frequency as high as 1 in 29 (Ratjen et al. 2015). CF is less common in other ancestral groups, affecting approximately 1 in 17,000 African Americans, 1 in 13,5000 Hispanic Whites, and 1 in 31,000 Asian Americans (Kopp et al. 2015). The incidence is far lower in India, at only 1 in 40,000–100,000 births. However, CF is thought to be underdiagnosed in Africa and in Asia. In many countries, infants are not tested for CF at birth, and national registries are lacking data. Many countries lack a national CF registry, and studies are conducted by individuals, thus hindering accurate determination of the prevalence.

A patient with two copies of the most common F508del mutation has a 25% risk of presenting with meconium ileus, whereas a patient with a F508del paired with another mutation has a 17% risk. A family history of CF is present in 10–20% of patients with meconium ileus, and the recurrence rate of meconium ileus has been found to be 39% among siblings with CF (Allan et al. 1981; Blackman et al. 2006).

65.4 Etiopathogenesis

The development of meconium ileus is based on an autosomal recessive mutation in both copies of the CFTR gene, located on the long arm of chromosome band 7q31.2. If both parents are carriers of the CFTR gene mutation, there is a one in four chance (25%) that their offspring will develop the disease. More than 2000 different mutations of the CFTR gene have been identified to date, but only approximately 400 are thought to cause disease. The most common is F508del (previously termed ΔF508), a three base-pair deletion on exon 11 that results in the loss of phenylalanine 508; this mutation accounts for ~70% of pathogenic CFTR variants globally. Approximately 90% of patients with CF in the United States have one or two F508del alleles, and the worldwide frequency is 70% (Sharma and Cutting 2020). Most mutations have no known specific effects on the clinical phenotype or function of the protein product. A five-class system was developed for classifying CFTR mutations on the basis of functional consequences, with the aim of grouping patients with similar prognoses. Infants with meconium ileus and pancreatic insufficiency frequently carry severe class I-III CFTR mutations on both alleles (F508del, G542X, W1282X, R553X, and

G551D), thus resulting in absent or nonfunctional CFTR at the cell surface. Patients with milder mutations (class IV or V) on at least one allele maintain some residual ion channel activity with sufficient exocrine pancreatic function. However, this classification is increasingly recognized to be an oversimplification. The development of meconium ileus is unlikely to be associated with environmental factors, because it appears early in life and exclusively in patients with severe CFTR mutations. Studies on twins and siblings have shown that monozygous twins have a higher concordance of meconium ileus than do dizygous twins and siblings, thereby suggesting that non-CFTR modifier genes, such as chromosome 12p13.3, which also contribute to the development of meconium ileus (Blackman et al. 2006). In contrast, genetic modifier effects do not have a role in the development of later presentations of distal intestinal obstruction syndrome (DIOS) in CF (Smith et al. 2009). However, despite multiple modifier genes enhance or reduce the risk of meconium ileus, their clinical significance has remained limited.

65.5 Pathophysiology

The pathophysiology of meconium ileus is associated with defects in the CFTR gene, which encodes a chloride channel located at the apical membrane in epithelial cells. CF is characterized by the build-up of thick, viscous mucus in multiple mucin-producing organs, such as the intestines, lungs, pancreas, and reproductive organs. For this reason, CF has been described as mucoviscidosis, thus suggesting that the polymeric gel-forming mucus and the glycosylation of proteins play critical roles in CF. The CFTR protein regulates the viscoelastic properties of mucus (Ooi and Durie 2016).

Defects in CFTR gene expression lead to deficiencies in cyclic adenosine monophosphate-dependent chloride and bicarbonate transport in the affected epithelia, a process necessary for fluid secretion and extracellular alkalization. Work by Quinton and others has shown that CFTR-dependent secretion of bicarbonate is important for normal mucus release and viscosity and for mucin unfolding in the bowel (Quinton 2008). Defective bicarbonate secretion by the neighboring epithelial cells that surround mucin-secreting goblet cells makes the intraluminal environment more acidic and dry, thus contributing to the pathophysiology of meconium ileus. In addition, defective chelation of Ca^{2+} by bicarbonate compromises further mucus unfolding and crosslinking, thereby making the meconium thick, viscid, and adhesive.

Several mouse models of CF have been created, including the most common mutations, F508del and G551D (Rosen et al. 2018). One model involves a replacement strategy that interrupts the CFTR gene and generates a complete "knockout" that does not produce normal CFTR protein products. In the so-called residual function models, an insertional strategy results in the production of a low amount of CFTR mRNA. Although the intestinal CF pathology resembles that of meconium ileus, it develops postnatally and therefore clearly differs from the human meconium ileus seen at birth. Meconium ileus is fatal in pig and ferret models, with a penetrance of 50–100% and 100%, respectively—values much higher than those in humans (Meyerholz et al. 2010). The various animal models are characterized by sticky meconium, severe neonatal intestinal obstruction, microcolon, goblet cell hyperplasia, and crypt dilatation—symptoms similar to those in the human manifestation. However, no single animal model completely replicates the complexity of human CF. Gene-targeted animal models have aided in the understanding of the gastrointestinal manifestations of CF and are essential in redirecting efforts using new paradigms to develop novel therapeutic strategies.

65.6 Pathology

In meconium ileus, the dilated loops of the small bowel are filled with inspissated tenacious, sticky, green meconium, which may also be tarry or gritty. The dilated proximal ileum is filled with semiliquid meconium and its walls thicker.

Distally, the meconium becomes thicker, adhesive, dark green, putty-like, and firmly adherent to the bowel walls. The distal ileum is filled with small inspissated "rabbit pellets" of meconium, which are stained gray and have a beaded appearance. Little or no meconium is passed into the colon. Typically, the colon is of small caliber and is "unused" or "microcolon." In complicated cases of meconium ileus, intestinal perforation and secondary meconium peritonitis and calcification can occur. Spontaneous healing of ileal perforation in utero can lead to resorption of the involved portion of the bowel and intestinal atresia. When the peristalsis is vigorous, the twisting of the ileal tract full of dense meconium may result in volvulus, with a high risk of perforation.

Perforation of the small bowel in utero results in a meconium leak and produces a sterile chemical peritonitis, which results in calcification than is visible radiographically, and intestinal adhesion by dense fibrosis. Collections of meconium may be walled off, forming meconium pseudocysts. The passage of spilled meconium into the inguinal canal can cause meconium periorchitis. Perinatal meconium peritonitis manifests as a green exudate overlying the serosal surface of the adjacent bowel and peritoneal cavity.

Histological findings in the bowel reveal dilated crypts with accumulation of secretions, prominent goblet cells in the mucosa, the presence of a thick mucus layer, and accumulation of meconium adherent to the mucosal surface. Intestinal specimens from infants with complicated meconium ileus also show submucosal inflammation and fibrosis, as seen more prominently in DIOS ilea (Smith et al. 2009). Thus, the transmural inflammation present at birth in patients with CF may be a factor contributing to intestinal dysmotility and the later development of DIOS.

65.7 Diagnosis

The diagnosis of meconium ileus is made on the basis of clinical history and physical examination, as well as imaging. Nearly 25% of patients with meconium ileus have a family history of CF. Prenatally, a fetus is tested if it is considered to be at high risk of CF, such as when both parents are known to be carriers of at least one pathogenic CFTR variant. This testing can be performed on chorionic villus specimens at 10–12 weeks and on amniocentesis samples at 16–18 weeks. Clinical practice is currently shifting toward noninvasive prenatal testing using cell-free fetal DNA from maternal peripheral blood. When both parents are carriers of the CF gene mutation, there is a 1 in 4 chance (25%) of CF in the child, a risk 625 times greater than that in the general population (0.04%). Newborn screening methods differ among countries.

Prenatal sonographic characteristics associated with meconium ileus are hyperechoic masses, dilated bowel loops and non-visualization of the gallbladder. Approximately 0.8–13.3% of fetuses with echogenic bowel are estimated to have CF (Scotet et al. 2010; De Oronzo 2011). The positive predictive value of hyperechoic bowel CF is 52% in fetuses with high CF risk, but only 6.4% in fetuses with low CF risk (Bahado-Singh et al. 1994). Hyperechogenic bowel in the second and third trimesters is considered a normal variant, and as much as 65% of cases resolve on sonographic follow-up and do not have CF or meconium ileus (Ruiz et al. 2009). Echogenic bowel has been associated with a variety of other conditions such as trisomy, prematurity, fetal demise, and maternal infections. Dilated bowel loops on prenatal ultrasound have been reported even less frequently in association with CF than hyperechoic bowel. Additional findings associated with meconium ileus are fetal ascites and the presence of intraabdominal cysts. Maternal polyhydramnios are frequently observed in prenatal diagnosis of complicated forms of meconium ileus, presumably as a result of the bowel obstruction.

The diagnosis of CF relies on both the clinical presentation, as well as evidence of CFTR dysfunction. Newborn screening is based on elevated levels of trypsinogen (IRT) detected on dry blood spots on the Guthrie card. IRT, a pancreatic enzyme precursor released into the blood stream after pancreatic damage, is used as a CF screen-

ing method in newborns. However, patients should have their diagnosis of CF confirmed or refuted, either by a sweat test or the presence of a CFTR mutation, according to approved procedural guidelines in established international protocols such as the Clinical and Laboratory Standards Institute Guidelines (Farrell et al. 2017). CFTR dysfunction, such as abnormal sweat chloride, is diagnosed at a concentration of greater than 60 mmol/L, whereas 39–59 mmol/L is considered to indicate intermediate cases that should be followed up in specialist CF centers. Newborns with corrected gestational age above 36 weeks, whose body weights are greater than 2 kg, and who have positive CF newborn screens or positive prenatal gene tests should receive sweat chloride testing as soon as possible after 10 days of age, ideally before 4 weeks of age. Genotyping has become a key element of the diagnostic workup, particularly since the introduction of CFTR-modulating therapies that are specific to certain mutations.

A unique clinical characteristic of meconium ileus is that neonates present immediately after birth with abdominal distension, which is produced before the patients swallow air. The bowel loops are doughy with visible peristaltic waves and finger pressure over a loop causes indentations—the so-called putty sign (Fig. 65.1a). Bowel obstruction also results in delayed passage of meconium and bilious vomiting or bile-stained gastric fluid. Complicated meconium ileus presents in utero with bowel obstruction or signs of bowel perforation and/or necrosis, such as intraabdominal calcifications, or signs of peritonitis such as a discolored or edematous abdominal wall and abdominal tenderness. Meconium pseudocysts and signs of peritoneal irritation may be present. Bowel perforation and peritonitis can cause hypovolemia and/or sepsis. After birth, an abdominal radiograph of uncomplicated meconium ileus shows a similar appearance in erect or supine position without air-fluid levels, despite the obstructed bowel, because the air cannot layer above the thick and viscous meconium. Radiographs may also show multiple dilated bowel loops of various sizes, owing to the configuration of different segments of the bowel. A "ground-glass" appearance ("Neuhauser's sign") or fine, granular "soap bubbles" ("Singleton's sign") are often seen in the right half of the abdomen, owing to trapped air in the sticky meconium.

When the meconium ileus is complicated, the abdominal radiograph may show calcification as a result of meconium peritonitis due to fetal bowel perforation. A double bubble image or air-fluid levels can be seen in association with ileal atresia after a volvulus with ischemic damage. If the intestinal perforation occurs early in the antenatal period, the X-ray appearance of a round rim of calcification indicates a meconium pseudocyst. In complicated meconium ileus, calcified meconium pseudocysts or complications, such as

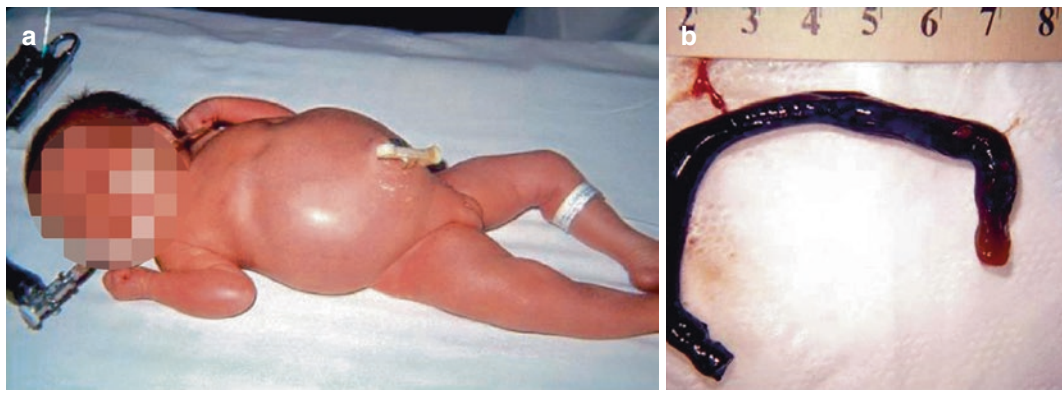

Fig. 65.1 (**a**) A newborn with intestinal obstruction and a family history of cystic fibrosis. A Gastrografin enema failed, and the patient underwent laparotomy for meconium ileus. (**b**) Passage of a large meconium plug in a newborn with meconium plug syndrome

volvulus, atresia, necrosis, or perforation, can be seen. Plain radiography is the initial imaging method used; however, there is a need for further evaluation though a contrast study, as it can also be therapeutic. The radiological features of meconium ileus on contrast enema are well described, including a typically "unused" colon or "microcolon" of normal length that may be empty or may contain several pellets of inspissated meconium—a feature of uterine underutilization. A reflux of contrast material into the terminal ileum will show meconium pellets and more proximally dilated loops of the small bowel.

65.8 Differential Diagnosis

Clinical and radiological features are important in diagnosing meconium ileus but are not pathognomonic. Other differential diagnoses of neonatal bowel obstructions are jejunoileal atresia, Hirschsprung's disease, neonatal small left colon, and meconium plug syndrome. Meconium ileus accounts for as much as 25% of cases of intestinal obstruction in neonates. Ileal atresia shows air-fluid levels and may be associated with meconium ileus. Hirschsprung's disease, particularly total colonic aganglionosis, can also mimic meconium ileus. Colonic Hirschsprung's disease shows a transitional zone, and, in patients with total colonic aganglionosis, the contrast medium refluxes into the terminal ileum and demonstrates air-fluid levels. Ultimately, the histopathological findings of a rectal biopsy can confirm aganglionosis. Neonatal small left colon syndrome, a functional disease with signs of bowel obstruction, can also be included in the differential diagnosis of meconium ileus. The transient dysmotility of the descending colon produces radiological features of a small descending colon with an abrupt transition zone at the splenic flexure. A contrast enema can be therapeutic with the passage of a meconium plug. Although its pathogenesis is unknown, neonatal small left colon syndrome is often associated with maternal diabetes, hyperthyroidism, drug abuse, or eclampsia. Meconium plug syndrome is often a benign cause of intestinal obstruction that clears after rectal stimulation or a contrast enema. However, this syndrome may be associated with Hirschsprung's disease, with an incidence of 13%, when the plug is found on contrast enema. The clinical presentation of meconium plug syndrome (Fig. 65.1b) is similar to meconium ileus, and it has been reported to be associated with CF (Olsen et al. 1982; Keckler et al. 2008). Patients with meconium plug syndrome should be tested for CF, and a rectal biopsy should be performed to exclude Hirschsprung's disease, particularly when normal bowel function does not occur after the passage of the plug. Other conditions may mimic bowel obstruction, such as delayed peristalsis associated with prematurity, hypothyroidism, and transient ileus in sepsis. Meconium ileus may occur even in the absence of CF (Fakhoury et al. 1992; Gorter et al. 2010).

65.9 Management

The management of meconium ileus consists of nonoperative and operative management of simple and complicated disease. The first steps of the treatment include nasogastric tube decompression, antibiotic prophylaxis, and correction of dehydration, electrolytes, and hypothermia. After the initial assessment, a plain radiograph should exclude the diagnosis of perforation and peritonitis. An initial contrast enema with a water-soluble agent can exclude other causes of distal bowel obstruction and complications such as atresia. Nonoperative management of simple meconium ileus involves hypertonic enemas such as Gastrografin performed under fluoroscopic guidance. Gastrografin is a hyperosmolar (1900 mOsm/L) water-soluble, radiopaque solution that contains 0.1% polysorbate 80 and 37% organically bound iodine. The high osmolar properties pull fluid into the bowel lumen, and the solvent properties help release the viscous meconium. After administration, osmotic diarrhea and osmotic diuresis occur; therefore, patients must undergo aggressive fluid resuscitation via an IV line to avoid fluid hypovolemia, electrolyte imbalance, and cardiovascular collapse. Since its first successful use in neonates

with uncomplicated meconium ileus by (Noblett 1969), hypertonic contrast enema has become the standard of nonoperative care. Importantly the enema should be performed under fluoroscopy, and the contrast agent must reach the meconium impacted ileum to relieve the obstruction. Spontaneous passage of the meconium should follow. An abdominal radiograph should be performed 8–12 h later to monitor the obstruction; the enema can be repeated in the event of incomplete evacuation. A pediatric surgeon should be present during the procedure. Serial Gastrografin enemas can be repeated at 12–24-h intervals. Although other agents have been used, Gastrografin remains the most common. If the contrast agent does not reflux into the dilated bowel or no evacuation occurs after successful refluxing into the obstructed ileum, a surgical intervention should be planned. The success rate for neonates with uncomplicated meconium ileus conservatively managed with enemas is reported to be as high as 83%, but recently the rate decreased to as low as 36% (Copeland et al. 2009). These findings may be attributable to the use of agents with a lower osmotic activity or less aggressive attempts.

65.9.1 Operative Management

Indications for operative interventions are complications of meconium ileus, such as ileal atresia, volvulus, perforation, meconium cysts, peritonitis, bowel necrosis, or a combination of various conditions. In the remaining patients, surgery becomes necessary when nonoperative treatments with enema solubilizing agents fail or are incomplete. The goals of operative management are to decompress the bowel and relieve obstruction by eliminating the meconium, establish intestinal continuity, preserve maximal bowel length, and allow for prompt enteral nutrition.

Several surgical procedures are available for the management of patients with meconium ileus. However, their application remains contentious, and there is no consensus in the literature regarding the ideal surgical strategy for meconium ileus. Enterotomy, with or without resection, was described by O'Neill in 1970 and has been used extensively in the past (Mak et al. 2000). The bowel irrigations are injected through an enterotomy, and the meconium is milked distally into the colon or removed through the enterotomy. A similar method is a T-tube enterostomy, in which the enterostomy is attached to the abdominal wall, thus creating a fistula allowing for tube irrigation with normal saline or *n*-acetylcysteine, and instillation of pancreatic enzymes. The enterostomy can be closed directly at laparotomy or may heal spontaneously after removal. Resection and primary anastomosis, as suggested by Swenson in 1962, is the procedure of choice for many surgeons. Advocates for this procedure argue that it allows for a faster recovery and avoids high-output stoma losses, poor nutritional status associated with better extraintestinal prognosis, and a second laparotomy for stoma closure. This approach comes with a risk of anastomotic leakage and peritonitis or strictures that may require a second laparotomy, particularly in patients in unstable condition with poor bowel perfusion. The complication rate has been reported to be approximately 20–31%, including adhesive bowel obstruction (Farrelly et al. 2014; Jawaheer et al. 2007; Karimi et al. 2011). The adhesions encountered at relaparotomy have been reported to be more common after surgery for MI than in other neonatal surgical conditions, thus suggesting a different underlying inflammatory response after MI (Choudhry and Grant 2006). Another option is to create a stoma that can be closed later, thereby giving patients time to recover. Several stoma types have been advocated for over the years. The formation of a temporary relieving stoma in the form of a Mikulicz double-barreled enterostomy was promoted by Gross (Fig. 65.2). In that case, there is no risk of an intraabdominal anastomotic leak, and complete evacuation of the inspissated meconium is not required. The bowel can be opened after closure of the abdominal wall, thus avoiding intraabdominal contamination.

Another well-described surgical option is bowel resection and the formation of a "distal chimney enterostomy," with an end-to-side ileal

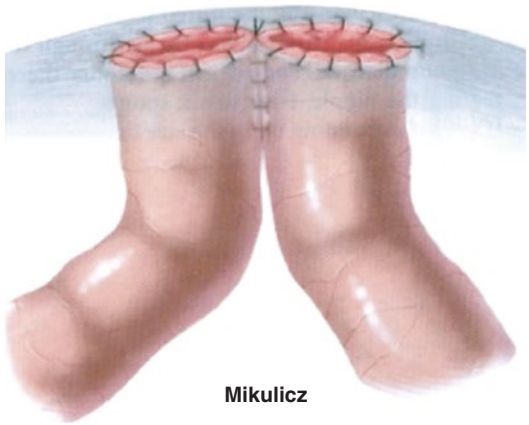

Fig. 65.2 The Mikulicz double-barreled ileostomy

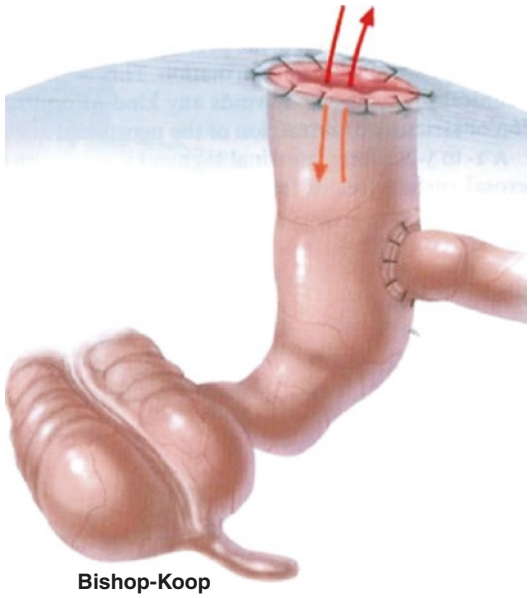

Fig. 65.3 The Bishop-Koop ileostomy

anastomosis, the so-called Bishop-Koop enterostomy (Fig. 65.3).

A variation in this technique has been described, wherein the proximal segment is anastomosed obliquely to the distal stump (Fig. 65.4). The Bishop-Koop method remains preferred by many, because the bowel contents pass into the distal bowel, thus allowing for more fluid and nutrient absorption. Santulli has described a distal chimney enterostomy, which is essentially the reverse of the distal chimney enterostomy (Fig. 65.5). The distal ileal end is anastomosed in

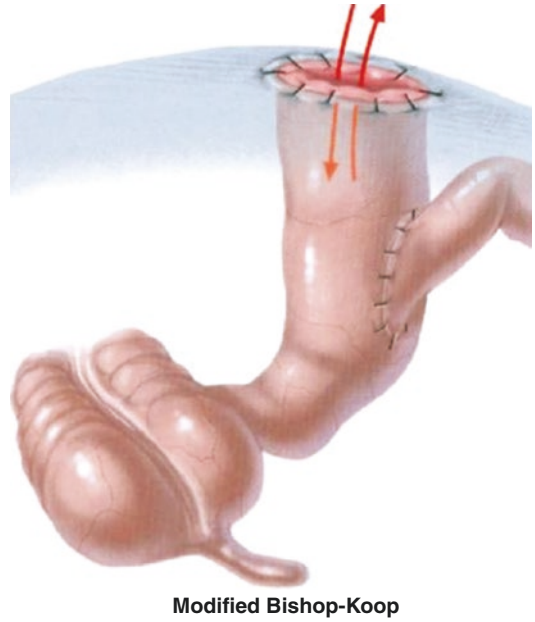

Fig. 65.4 The modified Bishop-Koop ileostomy

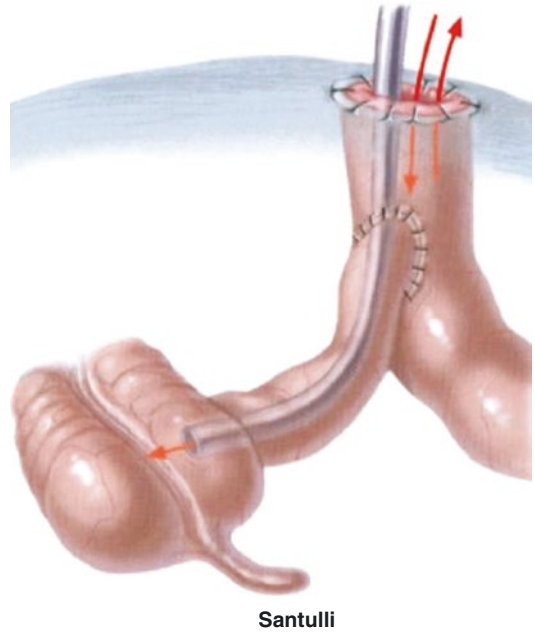

Fig. 65.5 The Santulli enterostomy

an end-to-side fashion to the proximal ileum at a level close to the subfascial plane, whereas the proximal ileum forms the enterostomy. This procedure allows for easier postoperative proximal bowel decompression and irrigation. An intraop-

eratively placed distal tube can be used for later instillation of solubilizing agents. The Santulli stoma is a high-output enterotomy and should be closed relatively sooner to avoid unnecessary electrolyte imbalances, dehydration, and nutritional losses.

Complicated meconium ileus almost always requires a laparotomy, except for in utero perforations that have spontaneously healed without postnatal sequelae. During laparotomy, the entire bowel should be inspected, because other surgical conditions can be encountered, such as atresia, volvulus, peritonitis, necrotic bowel, or meconium cysts. During surgery, critical bowel resection and documenting the remaining bowel length are mandatory. After surgery, the residual intraluminal meconium must be evacuated with the instillation of 2% or 4% acetylcysteine via a nasogastric tube or directly into the intestine via a stoma or enterostomy. Stomas should be closed as soon as possible to avoid electrolyte imbalances and unnecessary nutritional losses. In the postoperative period, particularly after stoma formation, parenteral nutrition is necessary until oral or enteral tube feeding is fully established, and weight gain is satisfactory. To minimize the risk associated with long-term parenteral nutrition, such as cholestasis and liver failure, the selection of appropriated lipids with low osmolarity medium-chain triglycerides and concentrated hydrolyzed protein should be used. Parenteral nutrition can be prolonged and must include the maintenance of salt, electrolytes, and vitamins. The short-term use of ursodeoxycholic acid can improve bile flow and prevent cholestasis. Patients with CF are susceptible to sodium losses, which can be particularly high through stoma outputs and low-dietary intake from breast milk, and may be associated with poor growth. Sodium deficiency should be assessed on an individual basis through the measurement of the urinary sodium:creatinine ratio. The early introduction of oral or enteral feeding is beneficial. Breastfeeding or feeding of expressed breast milk should be encouraged. Pancreatic enzyme replacement therapy should be started when enteral feeding is commenced. Pancreatic insufficiency is confirmed by obtaining a fecal elastase from a rectally collected sample and not from an enterostomy. Postoperatively, the diagnosis of CF must be confirmed as the cause of meconium ileus. Over time, the outcomes of patients with meconium ileus and CF have improved, with a survival rate approaching 100% for both operative and nonoperative management. Historically, patients with CF and meconium ileus have had poorer outcomes than those without meconium ileus. However, advances in surgical and medical management have improved the outcomes of the former, and their survival rates are currently similar to those of CF patients without meconium ileus.

65.10 Conclusion

Pediatric surgeons play a critical role in the initial management of patients with meconium ileus and CF. Although patient care must be individualized, relieving the bowel obstruction, preserving bowel length, and supporting the infant's physiology and nutritional status are essential. Every patient with meconium ileus must be evaluated for CF regardless of newborn screening or ancestry. Neonates presenting with meconium ileus, particularly those undergoing surgery with resection and/or stomas, are at greater risk of nutritional deficits later in life. These patients should receive multidisciplinary management in a specialist center for CF and neonatal surgery to improve long-term outcomes.

Continued success in the management of patients with meconium ileus and CF-related gastrointestinal problems will depend on continuing advances in the understanding of the underlying disease mechanism.

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