Meconium Ileus

60

Alan F. Utria and John H. T. Waldhausen

Meconium ileus is a small bowel obstruction in newborns caused by inspissated meconium. In the vast majority of cases, it is the first manifestation of cystic fibrosis (CF). While routine prenatal ultrasound may raise suspicion for meconium ileus, it is typically diagnosed in neonates who fail to pass meconium. It can present in a simple or complicated form, the latter defined by associated atresia, volvulus, or perforation and occurring in about half of all cases. Nonoperative management with contrast enema can be successful in the simple form, but it is important that the surgeon know the various operative procedures in case of failed nonoperative intervention or complicated meconium ileus. Short-term outcomes from the treatment of meconium ileus are good; however, there are long-term complications related to cystic fibrosis requiring these infants receive lifelong follow-up.

Pathophysiology

Meconium ileus is characterized by intestinal obstruction resulting from the impaction of viscid, desiccated, protein-rich meconium in the bowel lumen. It is typically seen in children with CF, an autosomal recessive disorder that results from mutations in a gene on the long arm of chromosome 7 encoding the cystic fibrosis transmembrane conductance regulator (CFTR), a cell membrane protein. The most common mutation is a homozygous deletion of phenylalanine 508 (ΔF508), which impairs CFTR folding and therefore its function. However, approximately 1900 other mutant alleles resulting in variable impairment of function have been identified. CFTR is a chloride channel, regulating the excretion of both Cl^- and HCO_3^- from the apical cell surface. Defective Cl^- excretion results in a compensatory hyperabsorption of Na^+ through the epithelial sodium channel (ENaC). The combined result of reduced intraluminal Cl^- and Na^+ content leads to increased water resorption and subsequent desiccation and inspissation of the meconium. Additionally, decreased HCO_3^- excretion also contributes to the pathogenesis of meconium ileus. HCO_3^- is important for chelating intraluminal Ca^{2+} around which secreted mucin forms a tight matrix. Chelating the Ca^{2+} allows for expansion and increased solubility of the secreted mucin within the intestinal lumen. Of note, not all infants with cystic fibrosis have meconium ileus. This incomplete penetrance is explained by the various mutations in the CFTR gene, whereby more "severe" mutations have been shown to result in meconium ileus.

Epidemiology

Meconium ileus occurs in 15–20% of infants with cystic fibrosis. However, of patients diagnosed with meconium ileus, 80–90% will have underlying cystic fibrosis. The incidence of cystic fibrosis is quoted as 1 in 2500 live births, but due to prenatal screening and genetic counseling of prospective parents with known carrier status, there are data to suggest the incidence is decreasing. The small proportion of infants without cystic fibrosis who present with meconium ileus tend to be premature and have poor intestinal motility.

Prenatal Diagnosis

Genetic screening of prospective mothers for cystic fibrosis is recommended by the American College of Obstetrics and Gynecology. If the mother is a CF carrier then paternal testing is recommended. Knowing the parents' CF carrier status in combination with the second trimester prenatal ultrasound has allowed for prenatal risk stratification. Second trimester

A. F. Utria
Department of General and Thoracic Surgery, Seattle Children's Hospital, Seattle, WA, USA
e-mail: alan.utria@seattlechildrens.org

J. H. T. Waldhausen (✉)
Department of Surgery, University of Washington School of Medicine, Seattle Children's Hospital, Seattle, WA, USA
e-mail: john.waldhausen@seattlechildrens.org

P. Mattei (ed.), *Fundamentals of Pediatric Surgery*, https://doi.org/10.1007/978-3-031-07524-7_60

ultrasound findings concerning meconium ileus include hyperechoic intra-abdominal masses representing inspissated meconium, dilated bowel, and inability to visualize the gallbladder. These findings are not specific to meconium ileus and should be interpreted along with the parents' carrier status. Unless both parents are found to be CF carriers, the fetus is considered low risk for meconium ileus or cystic fibrosis and can be followed with repeat ultrasound in 6 weeks. If the ultrasound findings persist the parents should be referred to a tertiary center. If both parents are carriers, ultrasound findings suspicious for meconium ileus should be followed up with amniocentesis; pending those results referral for genetic counseling and tertiary care is recommended.

Postnatal Diagnosis

Infants born with a distended abdomen should immediately raise suspicion for meconium ileus. This distension is the result of inspissated meconium at the terminal ileum resulting in an obstruction. The only other intestinal etiology for a distended abdomen in the newborn prior to ingestion of air is an *in utero* perforation with subsequent meconium cyst resulting in obstruction. This could represent complicated meconium ileus or could be due to other causes of *in utero* perforation such as atresia. If distension is not prominent or is missed, infants will declare themselves with failure to pass meconium, progressive distension, bilious emesis, and feeding intolerance. These findings are non-specific and in addition to simple and complicated meconium ileus, the differential diagnosis should include Hirschsprung disease, intestinal atresia, meconium plug syndrome, small left colon, ano-rectal malformations, malrotation with or without volvulus, and a bowel perforation. Additionally, complicated meconium ileus may also present with erythema of the abdominal wall, abdominal tenderness, and hemodynamic instability. In these cases, urgent resuscitation and operative exploration are indicated.

The work-up should begin with a thorough history and physical examination as well as ensuring the infant is hemodynamically stable and has appropriate intravenous access and nasogastric decompression. Imaging with abdominal radiographs and ultrasound is helpful in narrowing down the differential. Abdominal radiographs demonstrating ground-glass or soap bubble appearance (Neuhauser's sign) is highly suggestive of meconium ileus (Fig. 60.1). Additional non-specific signs of bowel obstruction, such as dilated loops of bowel of varying caliber, typically without air-fluid levels due to the viscosity of the meconium, as well as lack of air in the rectum, might be present. In cases of complicated meconium ileus where there has been an intestinal perforation with subsequent meconium peritonitis, abdominal calcifications may be present. Postnatal US may demonstrate a microcolon, trapping of air bubbles within the meconium at the outer portion of the intestinal lumen, and dilated small bowel loops containing thick, adherent meconium, resulting in pseudo-thickening of the bowel wall and a stratified appearance. Ultrasound can also aid in the diagnosis of complicated meconium ileus by demonstrating free intraperitoneal fluid with echogenic particles, single or multiple pseudocysts with hyperechogenic walls, and curvilinear calcifications, hepatic, splenic, peritoneal, or scrotal calcifications, and a conglomerate of collapsed bowel loops. If the infant is stable and there is low concern for complicated meconium ileus, a contrast enema can be performed, which can be both diagnostic and therapeutic. As a diagnostic tool, the contrast enema will demonstrate a microcolon, and, when contrast is refluxed into the terminal ileum, filling defects indicating meconium pellets will be evident (Fig. 60.2). Further retrograde reflux of contrast into dilated small bowel past the obstruction confirms the diagnosis of meconium ileus and rules out atresia.

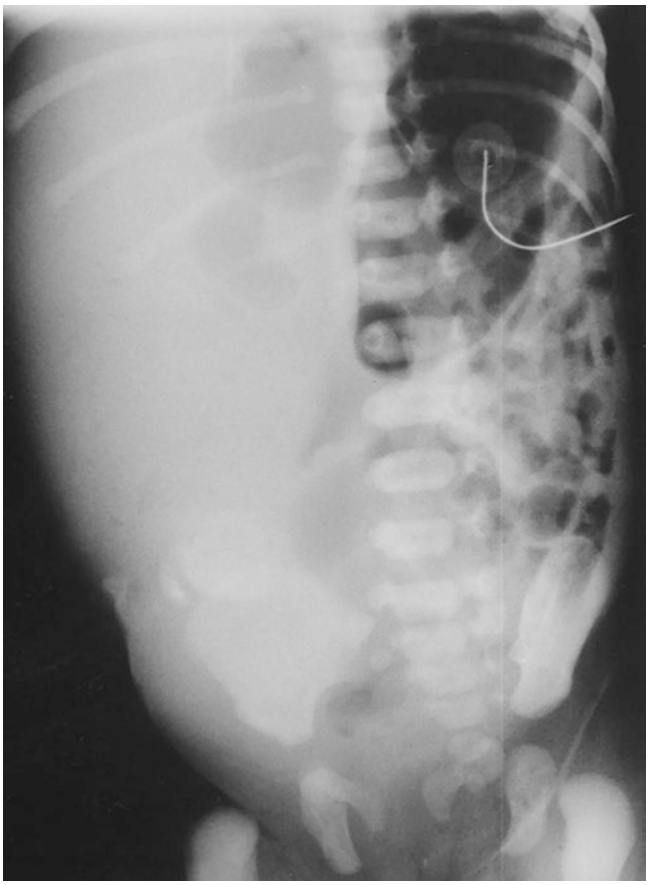

Fig. 60.1 Plain radiograph of a newborn infant with meconium ileus. Note the dilated loops suggestive of obstruction, the paucity of gas, and the ground-glass appearance of meconium in the *right lower quadrant* (Neuhauser's sign)

If the diagnosis of meconium ileus is confirmed, biochemical analysis with the sweat chloride test and genetic

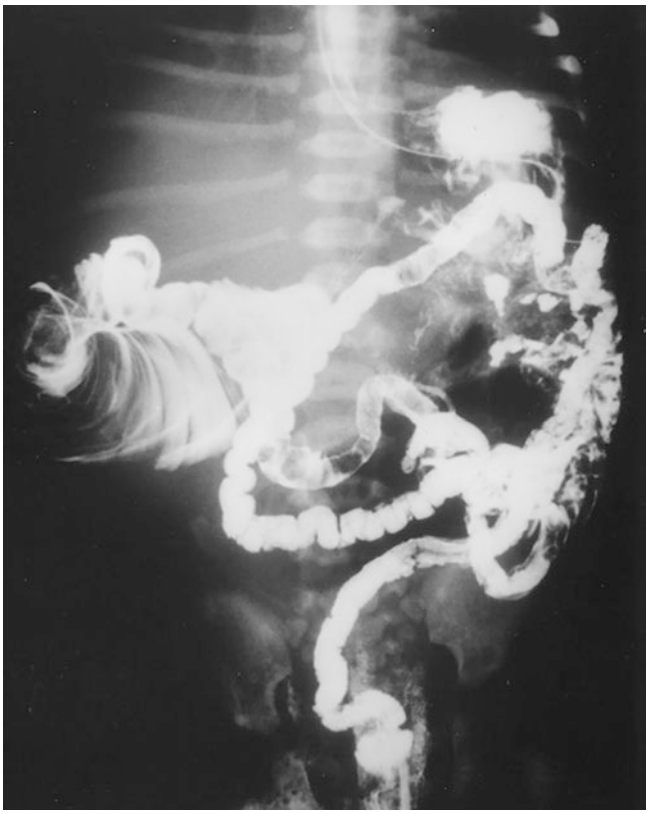

Fig. 60.2 Contrast enema in an infant with meconium ileus. Note the small caliber of the unused microcolon, the filling defects in the ileum (meconium pellets), and the hugely dilated bowel proximal to the obstruction

analysis of the CFTR gene should be performed to determine CF diagnosis. Pilocarpine iontophoresis remains the gold standard as genetic testing may miss up to 10% of mutations depending on the specific test. However, pilocarpine iontophoresis testing accuracy necessitates that the infant be 2–4 weeks old. Historically, testing of the meconium for levels of albumin and trypsin was also performed with high albumin and low trypsin levels considered indicative of CF. However, a positive result is dependent on the status of pancreatic function and therefore may miss up to 25% of patients with CF and no pancreatic insufficiency. Serum immunoreactive trypsinogen measurements can also be performed and if elevated are sensitive but not specific for CF.

Nonoperative Treatment

In stable patients with simple meconium ileus, a contrast enema may be therapeutic. A hypertonic, water-soluble, radiopaque solution, such as Gastrografin (meglumine diatrizoate that contains 0.1% polysorbate 80 and 37% organically bound iodine), is delivered through a rectal catheter under fluoroscopic guidance by a pediatric radiologist. Alternatives to Gastrografin include Optitray (ioversol), Omnipaque (iohexol), and Cysto-Conray II (iothalamate meglumine). It is imperative that the infant is well hydrated and has appropriate access prior to attempted treatment as the enema can lead to significant fluid shifts due to its hyperosmolarity. The enema acts through osmosis, drawing water into the bowel lumen, softening the meconium and resulting in the rapid passage of semiliquid meconium. In order for this treatment to be successful, it is necessary to reflux the contrast into the terminal ileum and the dilated bowel. If the radiologist is unable to reflux contrast into dilated bowel on the first attempt, it is reasonable to attempt additional enemas every 12–24 h so long as each subsequent enema appears to make further proximal progress and the infant is adequately fluid resuscitated and hemodynamically stable and the abdominal exam does not become concerning for peritonitis. Upon completion of each enema, an abdominal radiograph should be performed to rule out perforation and repeated every 12 h as late perforation may occur. Bowel perforation may occur secondary to catheter trauma or distension from the osmotically driven fluid shift into the bowel lumen. Contrast enemas can be supplemented with beside irrigations using warm saline enemas or by instilling 5–10% N-acetylcysteine into the GI tract through a nasogastric tube, which is mostly avoided due to the risk of pneumonitis from reflux and aspiration into the lungs. If the contrast enema is unsuccessful at relieving the obstruction, surgical intervention is indicated. Success rates for non-operative management range from 30% to 80%. The experience of the pediatric radiologist with this procedure affects the likelihood of success.

Operative Treatment

In cases of simple meconium ileus where non-operative management has failed, a simple enterotomy and intraoperative irrigation can be effective in treating the obstruction (Fig. 60.3). The surgeon performs an antimesenteric enterotomy on the dilated ileum through which inspissated meconium can be removed and irrigations through the enterotomy are administered via a 10- or 12-Fr red rubber catheter (Fig. 60.4). An alternative to creating an enterotomy is performing irrigations via the appendix; however, this technique is less successful in cases with excessive inspissated meconium present in the small bowel as removing the inspissated meconium through the appendix can be challenging. Either normal saline or a 5–10% acetylcysteine solution can be used for the irrigations. The enterotomy is closed in a transverse fashion to prevent narrowing of the lumen. An appendectomy should be performed, and the appendix sent to pathology for examination for ganglion cells to evaluate for long-segment Hirschsprung disease. It is important to be aware, however, that the lack of ganglion cells in the appendix

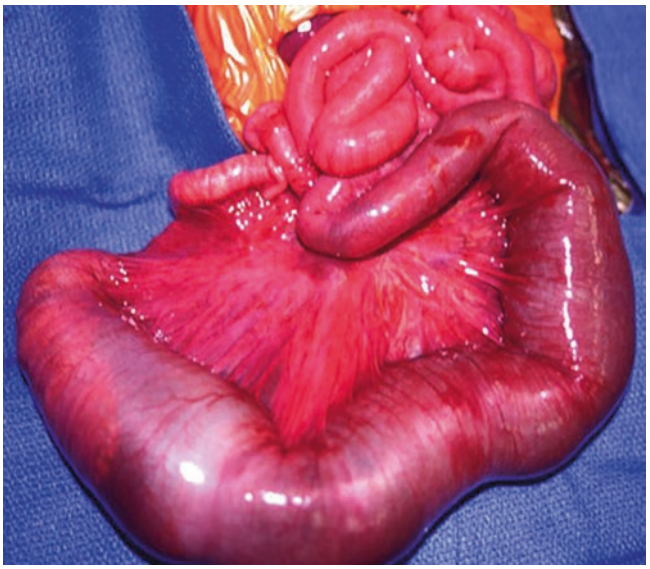

Fig. 60.3 Operative findings in a patient with meconium ileus. There is gradual tapering of the ileum, which is filled with inspissated meconium

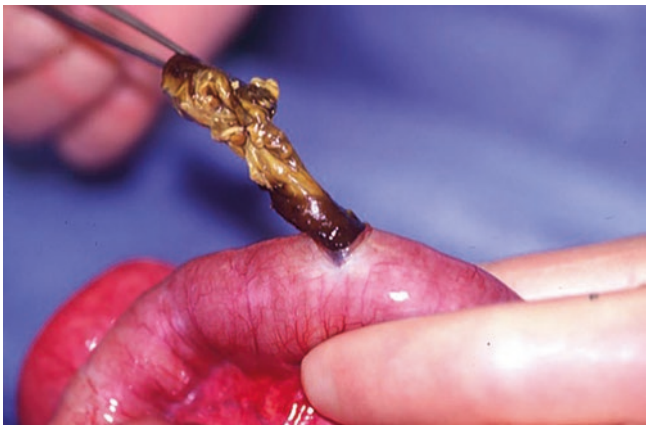

Fig. 60.4 The meconium has the consistency of tar and can be pulled out through the enterostomy in large pieces

may be a false indicator of long-segment Hirschsprung disease. Increased mucous production and goblet cell hyperplasia within the appendix is suggestive of CF.

If the surgeon feels that antegrade postoperative irrigations might be necessary, access to the bowel lumen can be created in several ways: (1) the Bishop-Koop ileostomy, in which the distal limb is brought out as an end stoma and the proximal bowel is anastomosed end-to-side just proximal to the ostomy; (2) the Santulli operation, similar to the Bishop-Koop but with the limbs of bowel reversed, creating a proximal stoma with the distal bowel sewn to it end-to-side; (3) the Mikulicz operation, the creation of a double-barrel stoma in which the two ends are sutured or classically annealed together with a crushing clamp side-to-side proximal to the end of the stoma; (4) tube ileostomy, in which a small-caliber Malecot or T-tube is placed through an enterotomy and held in place with a purse-string suture, while the limb of bowel is secured to the fascia; and (5) Appendicostomy, whereby the appendix is brought up through the umbilicus or abdominal wall and secured in place.

There is no one procedure that is superior to the others, and ultimately the decision comes down to surgeon preference or the situation encountered. If creating an anastomosis is not a safe option, a conventional loop- or end-ileostomy can be created. Factors affecting the decision to perform an anastomosis without a diverting ostomy are the overall condition of the patient, the appearance of the bowel, and the likelihood of distal obstruction. While the Bishop-Koop and Santulli are often considered somewhat dated operations, they are still useful and have the advantage over other potential solutions in that subsequent closure of the ostomy is usually a relatively simpler operation that does not require a full laparotomy.

While these operative techniques might also be employed in the treatment of complicated meconium ileus, each case of complicated meconium ileus can present with unique problems that need to be addressed. These include perforations, large pseudocysts, atresias, necrotic bowel, and dense, vascular adhesions. Perforations may sometimes be amenable to repair via resection of the perforated segment and primary anastomosis. If bowel resection is necessary, or an atresia is present, a judgment must be made regarding the safety of an anastomosis versus creating an end-ostomy. Meconium pseudocysts can make understanding the anatomy quite challenging. After entering the abdomen via a transverse incision, one will typically find they have entered the cyst cavity. The posterior fibrous wall of the meconium pseudocyst is usually composed of bowel that is matted together such that individual loops of bowel cannot be discerned and cannot be safely lysed apart or debrided. At times, the actual perforation may be visible, appearing as a stoma in the posterior wall of the cyst. In order to find discernable loops of bowel, it may be possible to dissect laterally toward the abdominal wall and get behind the posterior cyst wall, in which case more normal loops of intestine will be encountered. If this can be accomplished, it may be possible to lyse the adhesions between the bowel loops that form the posterior cyst wall and then create an end ostomy in the abdominal wall. If that cannot be done, it is best to avoid extensive dissection and leave a drain within the cyst rather than risk injuring the bowel. In time, the cyst will collapse and the dense adhesions will resolve, allowing later exploration with anastomosis or ostomy creation as appropriate. Depending on the patient, central venous access for nutrition may be needed. A gastrostomy tube may be necessary at the initial operation or at a later date.

Postoperative Care

In the immediate postoperative period, it is important to closely manage the infant's fluid status as they may continue to have fluid shifts, especially if ongoing irrigations with hypertonic solutions are being performed. The patient should be kept NPO until meconium is spontaneously evacuated and the infant establishes a normal stooling pattern. Parenteral nutrition will be necessary during this time. Infants with an end-ostomy or substantial bowel resection may tolerate continuous feedings better than bolus feedings. The infant must be closely monitored for signs of feeding intolerance. Some surgeons will instill 5–10% N-acetylcysteine into the GI tract through a nasogastric tube; however, this places the infant at risk for pneumonitis should they have reflux with aspiration. A fecal elastase test should also be performed to evaluate pancreatic function and guide the need for potential pancreatic enzyme replacement. If an ostomy was created, it may be closed in 4–6 weeks provided the infant meets the standard criteria for ostomy closure.

Long-Term Complications

Infants with meconium ileus are susceptible to long-term complications related to their underlying cystic fibrosis as well as any operative interventions they may have undergone. Long-term gastrointestinal complications of cystic fibrosis include distal intestinal obstruction syndrome, fibrosing colonopathy, rectal prolapse, constipation, intussusception, atypical presentation of appendicitis, and *Clostridium difficile* colitis. Additionally, bowel obstruction secondary to adhesions is common in patients who had complicated meconium ileus with meconium peritonitis. These long-term complications highlight the need for lifelong multidisciplinary follow-up and the high likelihood of surgical consultation when these patients present acutely with abdominal symptoms. In the case of acute presentation with abdominal symptoms, work-up should proceed as with any patient with abdominal complaints; but the surgeon needs to be aware of the additional complexities of patients with cystic fibrosis.

Editor's Comments

When radiographic treatment fails, simple meconium ileus is probably best treated by enterotomy and irrigation. An ileostomy should rarely be needed and only if there is a large residual volume of meconium or the bowel is, for some reason, of questionable integrity. A simple ileostomy and mucous fistula, each brought out separately through opposite ends of the same small right lower quadrant laparotomy incision is probably just as effective and easy to close as any of the somewhat baroque options left to us by some of our most illustrious surgical predecessors. The Bishop-Koop, Santulli-Blanc, and Mikulicz operations were presumably designed to serve some special function in babies with meconium ileus but mostly were designed to be closed simply, without having to subject the infant to a second laparotomy or even another general anesthetic. In this day and age, except perhaps in extraordinary circumstances, there seems little reason to consider them useful.

A longitudinal enterotomy is made on the antimesenteric border of the dilated portion of the ileum for instillation of irrigation solution and evacuation of the meconium. Although normal saline is used by some with good results, many still prefer to use acetylcysteine, which comes in 10 or 20% solution and can be diluted with saline or water at the operative field to a final concentration of 4–5%. A 10- or 12-Fr catheter is used to instill the irrigation solution, which usually allows the tar-like meconium to be removed more easily from the bowel lumen through the enterotomy. The acetylcysteine also should be instilled distally to allow further evacuation of meconium from the colon. After removal of the inspissated meconium, the enterotomy is closed transversely and an appendectomy is performed.

Laparotomy for complicated meconium ileus can be quite challenging, mostly due to the dense adhesions and the anatomic perplexities one can find. The goal should be to perform a thorough lysis of adhesions and bowel resection, if necessary, but without excessive loss of bowel length or further complications. Multiple operations, sometimes with temporary drains or multiple stomas, may be necessary. Somehow, the infant still typically manages to do relatively well eventually but becomes one's patient for life. The key aspects of the approach are patience, diligently trying to avoid secondary harm, and knowing when to quit and fight another day if the operative findings are simply impossible to solve at that moment.

Postoperative care is all about nutrition, helping to prevent further inspissation with meconium by the judicious administration of enteral acetylcysteine and pancreatic enzymes, and application of evidence-based measures for the treatment of the patient's presumed diagnosis of cystic fibrosis. This is a multidisciplinary affair and requires exquisite sensitivity in helping the parents cope with what is often a surprising and devastating diagnosis for them to hear.

Further Reading

Boczar M, Sawicka E, Zybert K. Meconium ileus in newborns with cystic fibrosis - results of treatment in the group of patients operated on in the years 2000-2014. Dev Period Med. 2015;19(1):32–40.

Carlyle BE, Borowitz DS, Glick PL. A review of pathophysiology and management of fetuses and neonates with meconium ileus for the pediatric surgeon. J Pediatr Surg. 2012;47(4):772–81.

Farrelly PJ, Charlesworth C, Lee S, Southern KW, Baillie CT. Gastrointestinal surgery in cystic fibrosis: a 20-year review. J Pediatr Surg. 2014;49(2):280–3.

Galante G, Freeman AJ. Gastrointestinal, pancreatic, and hepatic manifestations of cystic fibrosis in the newborn. NeoReviews. 2019;20(1):12–24.

Gorter RR, Karimi A, Sleeboom C, Kneepkens CM, Heij HA. Clinical and genetic characteristics of meconium ileus in newborns with and without cystic fibrosis. J Pediatr Gastroenterol Nutr. 2010;50(5):569–72.

Moore PJ, Tarran R. The epithelial sodium channel (ENaC) as a therapeutic target for cystic fibrosis lung disease. Expert Opin Ther Targets. 2018;22(8):687–701.

Sathe M, Houwen R. Meconium ileus in cystic fibrosis. J Cyst Fibros. 2017;16:32–9.

Scotet V, Dugueperoux I, Saliou P, Rault G, Roussey M, Audrezet MP, et al. Evidence for decline in the incidence of cystic fibrosis: a 35-year observational study in Brittany, France. Orphanet J Rare Dis. 2012;7:14.

Tan SMJ, Coffey MJ, Ooi CY. Differences in clinical outcomes of paediatric cystic fibrosis patients with and without meconium ileus. J Cyst Fibros. 2019;18(6):857–62.

Veyrac C, Baud C, Prodhomme O, Saguintaah M, Couture A. US assessment of neonatal bowel (necrotizing enterocolitis excluded). Pediatr Radiol. 2012;42(Suppl 1):S107–14.

Waldhausen JHT, Richards M. Meconium ileus. Clin Colon Rectal Surg. 2018;31(2):121–6.