Short Bowel Syndrome and Intestinal Lengthening Procedures

Pooja S. Salvi and Robert A. Cowles

Key Points

1. Following small bowel resection, the intestine in patients with short bowel syndrome (SBS) undergoes compensatory adaptive changes to increase functional nutrient and water absorption. Loss of the distal ileum is associated with least favorable adaptation, owing to the presence of specialized epithelial cells in the ileum that are critical for fat absorption, and which secrete hormones involved in intestinal transit and mucosal growth.
2. Intestinal loss and dependence on parenteral nutrition have significant physiologic consequences for patients with SBS. Multidisciplinary intestinal rehabilitation programs coordinate medical and surgical interventions for these patients, to optimize intestinal adaptation, prevent complications of SBS, and accelerate weaning from parenteral nutrition.
3. Small intestinal lengthening procedures and intestinal transplant are surgical interventions that can improve outcomes in patients with SBS. Intestinal lengthening procedures can increase bowel function and surface area, to aid in weaning from parenteral nutrition, whereas intestinal transplant can be considered in patients with parenteral nutrition failure.

1. Background

Pediatric short bowel syndrome (SBS) is a unique surgical problem, in that the etiology is most often surgical, whereas the treatment involves a truly multi-

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disciplinary approach in which surgery is rarely curative. Nonetheless, knowledge of the causes and pathophysiology of this disorder is critical for the pediatric surgeon, in order to facilitate timely intervention that can prevent prolonged patient morbidity.

Starvation from anatomic loss or functional failure of the gastrointestinal (GI) tract has long been a challenge encountered by pediatric surgeons caring for infants. In the 1960s, the advent of parenteral nutrition (PN) introduced the possibility of survival and growth in these patients and opened the door for surgeons to operate on infants with congenital and acquired conditions of the intestine who otherwise would have had no chance of survival.

Pediatric intestinal failure (IF) is defined as the inability to absorb sufficient nutrients and water to support a child's growth and hydration. Short bowel syndrome (SBS) is a chronic or protracted form of IF, characterized by insufficient nutrient absorption after massive small bowel loss, and is the most common cause of IF in the pediatric population. Other causes of IF include GI conditions resulting in malabsorption from mucosal enteropathy and disorders of intestinal motility.

2. Epidemiology: causes and incidence

In most cases, pediatric SBS is caused by congenital or acquired conditions of the newborn that result in massive bowel resection or functional bowel loss. Table 1 lists the most common etiologies. Necrotizing enterocolitis (NEC) is the leading cause of pediatric SBS, with highest incidence in premature infants. Acute management of NEC aims to control abdominal sepsis, sometimes requiring laparotomy and resection of ischemic bowel leading to SBS. Efforts to prevent prematurity, which is the most important risk factor for NEC, and to identify the underlying etiology of this disease process have not been successful in decreasing the incidence. Simultaneous advances in neonatal intensive care have increased survival of infants with NEC and thus resulted in more children requiring management after massive bowel resection.

Indeed, there have been reports that the prevalence of pediatric SBS may be rising based on the increased prevalence of common underlying disorders. Specifically, the mean incidence of NEC has increased from 3–11% between 1997 and 2000 to 5–15% between 2003 and 2007. Gastroschisis, another significant cause of SBS, has increased in incidence by 30% from 1995–2005 to 2006–2012. As a congenital disorder of the abdominal wall, gastroschisis can

Table 1 Common causes of pediatric short bowel syndrome

Necrotizing enterocolitis
Gastroschisis
Intestinal atresia
Midgut volvulus
Total or subtotal intestinal aganglionosis
Vascular thrombosis
Trauma
Inflammatory bowel disease

require bowel resection due to intestinal injury or ischemia. Prolonged intestinal dysmotility can also affect newborns with gastroschisis, further contributing to the challenge of weaning PN, even in the absence of massive bowel resection.

In general, the overall incidence and prevalence of pediatric SBS are difficult to measure. The biggest reason being SBS is a functional state defined by need for PN, rather than an anatomic one. As such, diagnostic criteria for SBS based on duration of PN-dependence are not uniform across institutions or even providers. Second, the provision of PN can occur in a number of different inpatient and outpatient venues, making it difficult to track patients over time. In one study, SBS defined as the need for PN for more than 42 days after bowel resection or a residual small bowel length of less than 25% of that expected for gestational age yielded an incidence of 24.5 cases per 100,000 live births.

3. Pathophysiology of short bowel syndrome

To understand the pathophysiologic processes that contribute to PN-dependence in SBS, it is important to first understand normal intestinal physiology. In the intact GI tract, the small intestine is the primary site of nutrient absorption. Intestinal villi, the finger-like projections of the small intestinal mucosa, are lined with enterocytes that have the capacity to absorb nutrients from luminal contents. The villus configuration of the mucosa contributes to the enormous absorptive surface area of the small intestine, which is greatest in the proximal small bowel and least in the distal ileum. This proximal-to-distal gradient reflects the concentration of nutrients and macromolecules present in the different regions of the intestine. The majority of macronutrients undergo mechanical and chemical digestion in the stomach and proximal intestine, and subsequently undergo more thorough digestion by intestinal brush border enzymes, followed by absorption in the small intestine. Additionally, the small intestine is an essential site of fluid and electrolyte absorption, responsible for absorbing 80% of the fluid that passes through the GI tract.

In pediatric SBS, disruption of the GI tract from small bowel resection can result in one of three anatomic configurations of the remnant intestine: (1) small intestinal resection with a small bowel (typically jejunoileal) anastomosis, (2) small bowel and partial colon resection with an enterocolonic anastomosis, or (3) small bowel resection with a jejunostomy (Fig. 1). Each of these configurations has a unique pathophysiology, with implications for disease severity and management.

A. Small bowel resection with jejunoileal anastomosis

Patients who undergo resection of only the small intestine with subsequent jejunoileal anastomosis rarely experience major changes in nutrient or water absorption, though this depends to some degree on the length of intestine removed. The remnant small intestine and colon have the capacity to undergo compensatory histologic and functional changes over time. After bowel resection, the small intestinal epithelium grows longer intestinal villi and exhibits enhanced nutrient absorptive capacity, and the colon is capable of providing energy by way of microbial production of short-chain fatty

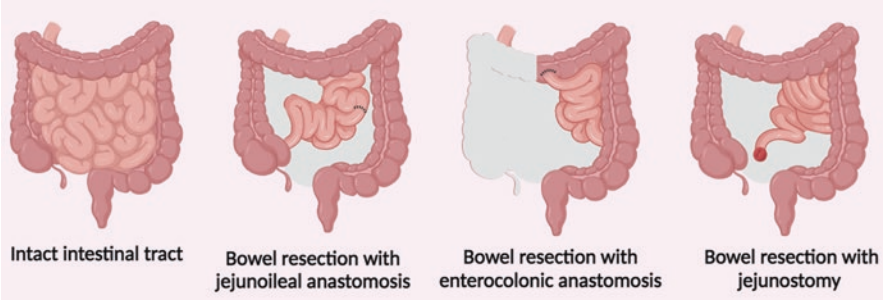

Fig. 1 Anatomic configurations of the intestinal tract in patients with short bowel syndrome after small bowel resection. The most favorable post-bowel resection anatomy is achieved with an intact ileocecal valve and intestinal continuity via a small bowel (e.g., jejunoileal) anastomosis. Resection of the distal ileum and ascending colon with an enterocolonic anastomosis is less favorable, due to loss of specialized epithelial cells in the distal small intestine. An end jejunostomy, in which the distal small intestine and colon are resected or are not contiguous with the proximal intestinal tract, is the least favorable anatomy due to both loss of specialized ileal mucosa and fluid losses from the stoma. (Source: Pooja S. Salvi and Robert A. Cowles)

acids (SCFA), which serve as fuel for colonocytes. Additionally, the colon has a large reserve capacity for fluid absorption, which is utilized under conditions of small bowel loss.

B. Distal small bowel resection with enterocolonic anastomosis

Patients who undergo ileal and ileocolonic resections fare worse than patients undergoing more proximal bowel resections. This is in part due to the relatively diminished capacity for functional adaptation in the proximal small intestine, relative to the ileum. Additionally, ileal resection can result in loss of bile salt resorption and aberrations in GI hormone secretion since bile salt transporters and specific hormone-secreting cells are specifically expressed in the mucosa of this intestinal region. Consequently, insufficient enterohepatic bile circulation can result in fat malabsorption and steatorrhea. Loss of the ileocecal valve at the distal end of the small bowel may also impair GI function and the ability to wean a child from PN.

C. Jejunostomy

As expected, patients who require a jejunostomy after bowel resection have worse outcomes than the previous two anatomic configurations, owing to the loss of functional adaptation and physiologic reserve exhibited by the distal small intestine and colon. In patients with less than 100 cm of small bowel proximal to the jejunostomy, dehydration is a major concern, due to net fluid losses from the ostomy that cannot be adequately resorbed. Furthermore, changes in intestinal hormone secretion following jejunostomy result in accelerated gastric emptying and intestinal transit. In addition to potentially worsening high-volume stomal losses, acceleration of intestinal transit allows for less contact time between luminal contents and the mucosa for absorption. Refeeding of a distal mucous fistula can help achieve

increased enteral nutrition and fluid absorption as well as preventing villous atrophy of the defunctionalized segment.

D. Extra-intestinal consequences of SBS

Altered intestinal anatomy and physiology in children with SBS can lead to pathology outside the GI tract, often resulting from abnormal nutrient absorption. Metabolic bone disease is common in this population, owing to increased calcium excretion, toxicity from PN, and overall malnutrition. Additionally, bile salt deficiency due to loss of bile salt transporters in the ileum predisposes patients to sequelae of inadequate fat absorption including formation of calcium oxalate kidney stones and gallstones. In SBS, fatty acids present in the distal intestine due to fat malabsorption preferentially bind intraluminal calcium, which under normal conditions is bound by oxalate. As a result, oxalate is freely absorbed into the bloodstream in the colon and subsequently undergoes renal excretion, thus increasing the risk of calcium oxalate nephrolithiasis. Similarly, patients with diminished bile acids are unable to effectively solubilize cholesterol, which increases the likelihood of cholesterol gallstone formation due to supersaturation of cholesterol in bile. Other physiologic alterations in SBS can also increase risk for cholelithiasis, including altered bilirubin metabolism and altered GI hormone secretion leading to reduced gallbladder contractility.

Importantly, loss of specialized cells in the distal intestine that produce regulatory GI hormones, such as cholecystokinin and secretin, can disrupt hormonal feedback mechanisms that modulate GI motility and intestinal gastrin production. Hypergastrinemia and associated hyperacidity may necessitate treatment with proton pump inhibitors or histamine receptor blockers, though these signs are typically transient, lasting for weeks to months after intestinal resection.

GI dysmotility after intestinal surgery and achlorhydria from pharmacologic acid suppression contribute to small intestinal bacterial overgrowth (SIBO) in children with SBS. This condition, characterized by changes in the normal enteric microbiome, can lead to mucosal damage from excessive epithelial inflammation and diminished mucosal nutrient absorption. D-lactic acidosis is a specific metabolic abnormality associated with intestinal bacterial dysbiosis that occurs when the presence of abnormal gut flora overwhelms normal bacterial metabolism of D-lactate, a product of carbohydrate metabolism, in the colon. Accumulation of D-lactate in the bloodstream can manifest in children as neurologic symptoms ranging from lethargy and poor school performance to coma.

Diagnosis of SIBO in SBS is challenging due to the nonspecific constellation of symptoms and the difficulty of accurately and non-invasively assessing the bacterial composition of the small intestine. Direct culture of small bowel fluid and hydrogen breath tests are among the currently utilized methods to diagnose SIBO, though variation in the microbial species present in individual patients can obscure interpretation of findings.

E. Enteral autonomy

As mentioned previously, proof that the metabolic and growth demands of children could be sustained with parenteral nutrition in the 1960s opened up possibilities for surgeons to intervene on conditions that would have previously left a child with a non-survivable amount of intestine. Though PN formulations and delivery have improved substantially over the past 50 years, the goal of treatment in pediatric SBS remains achieving enteral autonomy or weaning from PN.

A number of anatomic and physiologic factors contribute to the likelihood of achieving enteral autonomy. Residual bowel length relative to expected bowel length is the primary determinant of outcome. However, since potential for gut growth is closely correlated to an infant's stage of development, it is important to consider a child's gestational age when calculating expected bowel length. At the beginning of the third trimester, infant small bowel is approximately 125 cm in length, whereas a term infant has approximately 200 cm of small bowel and 40–50 cm of colon. To account for gestational age, it is common practice to present residual small bowel as a percentage of the total bowel length expected for a patient based on their age. Multiple studies have demonstrated that small bowel length greater than 10% of expected is a predictor for enteral autonomy and survival in infants with SBS.

Location of resected bowel is another significant predictor of weaning from PN. Preservation of the ileocecal valve is a predictor of enteral autonomy. Though this was previously attributed to possible transit-slowing mechanisms of the valve, this advantage is more likely related to properties of the ileal mucosa itself. For example, specialized function and hormone secretion from the ileum, such as secretion of glucagon-like peptides 1 and 2, may enhance intestinal adaptation, and the distal intestine exhibits a greater capacity for adaptive growth than proximal bowel regions.

4. Treatment

A. Multidisciplinary intestinal rehabilitation programs

Intestinal adaptation, including the functional absorptive changes in the remnant intestine, begins shortly after bowel resection and is typically complete within 24–60 months. Intestinal rehabilitation (IR) refers to the supportive medical and surgical interventions that can maximize this adaptive response and thus accelerate an infant's time to enteral autonomy. IR is a multidisciplinary approach that includes both proactive and prophylactic management strategies and is the mainstay for pediatric SBS treatment. Optimization of enteral and parenteral nutrition formulations is a central element of IR, in order to maintain a patient's growth, while promoting intestinal adaptation. Medical management is further necessary to prevent and promptly address highly morbid complications of PN, such as central-line-associated bloodstream infections (CLABSI) and PN-associated liver disease.

PN-associated liver disease (PNALD) is a strong predictor of mortality in children with SBS, and protocols to aggressively prevent progression of

PNALD have been successful in improving patient survival. The pathogenesis of PNALD is likely multifactorial. Decreased enteral nutrient intake can compromise the intestinal epithelial barrier and allow passage of enteric bacteria into the hepatic circulation, where subsequent endotoxin release, inflammatory cytokine production, and sepsis result in liver damage. Additionally, there is evidence that PN itself is hepatotoxic. Intravenous lipid emulsions (ILE) in PN formulations contain proinflammatory components, such as omega-6 fatty acids, which induce hepatocyte apoptosis and cause cholestasis. Furthermore, there is evidence that ILE are associated with loss of specialized biliary transport proteins, which are responsible for transporting components of bile from hepatocytes into bile ducts. Downregulation of these transport proteins is associated with inflammation and fibrosis of the biliary system and liver parenchyma.

Previously, intravenous lipid restriction was considered as an approach to minimize PNALD. Though successful in slowing the progression to PNALD, which is defined as serum conjugated bilirubin greater than 2 mg/dL, lipid restriction predisposed children to complications associated with essential fatty acid deficiency. As such, more recent approaches to addressing the deleterious effects of ILE involve substitution of traditional soybean-based lipid emulsions, which appear to be particularly hepatotoxic, with novel fish oil-based emulsions or mixed (composite) lipid sources. Fish oil-based emulsions lack phytosterols, a plant-derived cholesterol-like molecule found in soybean-derived lipids that have been associated with progression of PN-associated cholestasis and PNALD.

Current consensus guidelines on pediatric parenteral nutrition recommend the use of fish oil-containing lipid emulsions due to the advantages it demonstrates over soybean-derived lipids, namely, reduced risk of cholestasis and reduced liver inflammation, while maintaining adequate provision of essential fatty acids for neurodevelopment and metabolism. This includes composite lipid emulsions containing soybean oil, medium chain fatty acids, olive oil, and fish oil (SMOF). In general, SMOF should be considered as first-line treatment in children with SBS who have cholestasis or other signs of PNALD.

Treatment of other comorbidities of SBS, such as kidney stones and small intestinal bacterial overgrowth, are components of IR that minimize insults to quality of life, morbidity, and barriers to enteral autonomy. Longitudinal studies of SBS patients have demonstrated that integration into a multidisciplinary IR program was associated with increased survival, although not with increased attainment of enteral autonomy.

B. Surgical intervention

The pediatric surgeon is an essential member of the multidisciplinary IR team. Surgical interventions that can accelerate intestinal adaptation and weaning from PN include establishment of enteral feeding access (e.g., gastrostomy tube placement), closure of enterostomies to minimize fluid losses, establishment of central venous access for infusion of PN, and intestinal lengthening procedures.

Two surgical procedures to increase function and/or surface area of the remnant small intestine in SBS are most often considered. In 1980, Bianchi described the longitudinal intestinal lengthening and tapering (LILT) procedure. Although this approach does not increase functional absorptive surface area, it has been demonstrated to improve intestinal transit by correcting the gross intestinal dilation that can occur after bowel resection. In 2003, the serial transverse enteroplasty (STEP) procedure was introduced as an alternative to the LILT. As its name suggests, the STEP procedure involves making a series of alternating transverse or angulated partial transections across a segment of dilated intestine, thus lengthening the effective intestinal channel and increasing functional absorptive surface area (Fig. 2).

Patient survival after the LILT procedure and STEP procedure is estimated to be 81% and 89%, respectively. Infants with greater than 50 cm of remnant intestine and no signs of clinical jaundice at the time of surgery are most likely to survive. Comparison of outcomes between patients who underwent an intestinal lengthening procedure or did not is generally difficult to make, due to less severe illness in children who are candidates for surgical intervention.

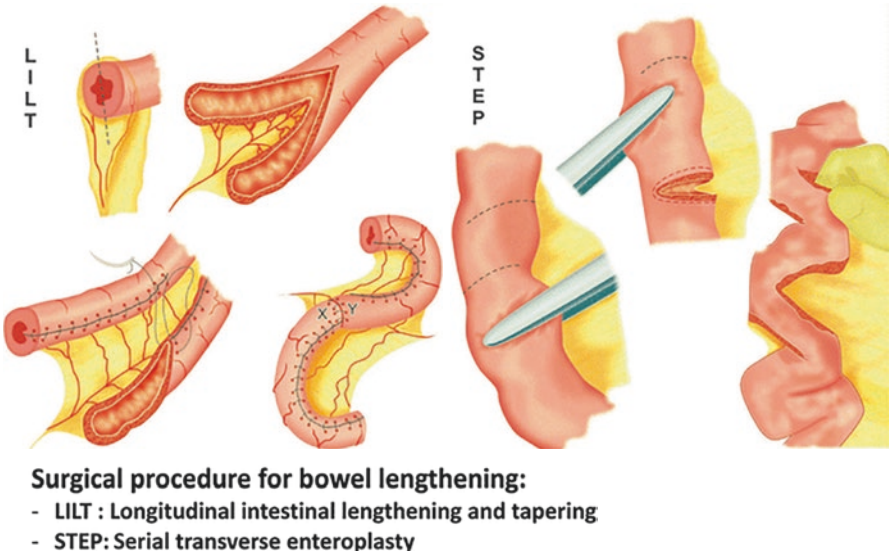

Fig. 2 Intestinal lengthening procedures such as the longitudinal intestinal lengthening procedure (LILT) and the serial transverse enteroplasty procedure (STEP) are surgical interventions that can aid in optimizing intestinal adaptation after small bowel resection, by increasing intestinal function and absorptive surface area of the remnant small intestine. (Source: Goulet O, Lacaille F, Lambe C. Intestinal failure: etiologies and outcomes and decision-making between rehabilitation and transplantation. In: Dunn S, Horslen S, editors, Solid organ transplantation in infants and children. Organ and tissue transplantation. Springer, Cham, 2017. Used under RightsLink License No. 5193281062030, 20 Nov 2021)

An estimated 53% of children achieve enteral autonomy after an intestinal lengthening procedure, and the average time to enteral autonomy after the STEP procedure was 21 months. These figures are important to consider in selecting infants who may benefit from surgical intestinal lengthening. Specifically, patients should have adequate liver function, no evidence of portal hypertension, shortened bowel length, and sufficient physiologic reserve to survive long enough to achieve enteral autonomy. Furthermore, infants with short segments of highly dilated bowel may reap the benefit of improved intestinal motility after the LILT or STEP procedures.

A notable risk of both of these procedures is recurrent bowel dilation. In such cases, a repeat STEP or STEP after LILT can occasionally be performed. Other possible complications include staple line leak, obstruction, bleeding, and enteric fistula formation.

C. Intestinal transplant

In the late 1980s, multiple pioneering surgeons began having success in the field of visceral transplant. Goulet reported the first isolated small intestinal transplant with long-term survival in 1987, followed by the first successful combined liver–small intestinal transplant by Grant in 1989.

Small bowel transplant is currently offered to individuals with SBS who experience PN failure. In children, this includes failure to maintain growth, development, and hydration while receiving PN. PN failure also refers to the development of PN-related complications, such as recurrent catheter-related infections, thrombosis of two of the six major central venous access sites, and the progression of PN-associated liver disease. Multivisceral transplantation, which involves complete replacement of all organs in the abdominal cavity, may be indicated in the setting of porto-mesenteric thrombus or complex enteric fistula, as well as in the more common case of liver failure with portal hypertension. In children, combined liver–small intestinal transplant is performed most commonly (50%), followed by isolated small intestinal transplant (37%) and multivisceral transplant (13%).

With advances in immunosuppression, surgical technique, and monitoring for post-transplant rejection over the last two decades, survival following isolated intestinal transplant and multivisceral transplant has dramatically improved. In 2007, the 1- and 5-year graft survival rates for pediatric intestinal transplant were 74.2 and 483%. However, the potential morbidity of the operation and of long-term immunosuppression in children with poor physiologic reserve from GI malfunction cannot be understated. Organ rejection is a feared complication, which portends poor outcomes. In a report of 108 pediatric patients undergoing intestinal or combined liver–intestinal transplantation at a single institution, approximately 19% of children experienced severe rejection, among which one-third did not survive and 43% required graft removal and re-transplantation.

Following transplantation, IR remains a critical part of long-term recovery. The anatomic reconfiguration of the viscera, in addition to rejection episodes, ischemia-reperfusion, and altered lymphatic drainage can compromise tolerance of enteral feeding. Studies have shown that some degree of enteral malabsorption remains after intestinal transplant in children, but compensatory hyperphagia and increased caloric intake can allow for normal growth and development.

Additional Notes

Pediatric SBS is the most common cause of pediatric intestinal failure, typically occurring after massive small bowel resection in the newborn period. With increases in neonatal intensive care and prenatal diagnosis, the incidence of SBS has increased and will likely continue to rise. Achieving complete enteral nutrition while maintaining adequate growth and hydration is the goal of treatment for all infants with SBS. Extent and location of bowel loss are significant predictors for whether a child will be able to achieve enteral autonomy, with resection of the ileum being least favorable. The use of multidisciplinary IR programs is essential to providing coordinated care and interventions that maximize intestinal adaptation following resection. Surgical intervention, including intestinal lengthening procedures, can increase intestinal surface area and function in select patients that develop dilated bowel. In children with PN failure, intestinal transplant can be considered, though graft rejection carries with it a poor prognosis.

Study Questions

Question 1. A 6-week-old infant girl is being cared for in the neonatal intensive care unit. She was born at 31 weeks gestation, and developed necrotizing enterocolitis on day of life 7, requiring a laparotomy and resection of ischemic bowel. Which of the following statements is true?

a. Central venous access is not necessary in this patient.
b. Prematurity is not a risk factor for necrotizing enterocolitis.
c. Small intestinal transplant should be the next surgical intervention for this patient.
d. Bowel resection puts this patient at risk for developing gallstones and kidney stones.

Answer: (d). Bowel resection puts this patient at risk for developing gallstones and kidney stones. Bowel resection, particularly distal bowel resection, will result

in loss of specialized cells of the ileum that contain bile salt transporters. Diminished bile acids can lead to reduced solubilization of cholesterol and formation of cholesterol stones in the gall bladder. Furthermore, fat malabsorption will result in calcium binding free fatty acids in the intestine, rather than binding oxalate. As a result, oxalate will be absorbed in the colon and undergo renal excretion, where it can cause oxalate nephrolithiasis.

Question 2. Which of the following anatomic configurations will be least favorable for subsequent functional intestinal adaptation and enteral nutrition tolerance?

a. Resection of the distal small intestine and colon with an enterocolonic anastomosis, leaving the child with 40% of expected bowel length for age.
b. Resection of the proximal jejunum with a small bowel anastomosis, leaving the child with 40% of expected bowel length for age.
c. Resection of multiple small proximal and distal small bowel segments with multiple small bowel anastomoses, leaving the child with 70% of expected bowel length for age.
d. Resection of the distal small intestine and colon and creation of an end jejunostomy, leaving the child with 40% of expected bowel length for age.

Correct answer: (d). Resection of the distal small intestine and colon and creation of an end jejunostomy, leaving the child with 40% of expected bowel length for age. (Is least favorable) The distal small intestine has greater adaptive capacity than the proximal intestine, and thus loss of the ileum is least favorable for functional intestinal adaptation. Additionally, creation of a jejunostomy can pose a challenge for hydration, since the absorptive capacity of the colon is lost.

Question 3. A 4-year-old boy with a history of gastroschisis and bowel resection in infancy presents to the emergency room with abdominal pain and fevers. He receives at home parenteral nutrition through a vascular access catheter. Which of the following statements is false?

a. Catheter-associated blood stream infections are a significant cause of morbidity and mortality in patients with SBS.
b. Patients with distal small bowel loss are predisposed to developing cholesterol gallstones, due to diminished bile salt absorption.
c. Hematuria in this patient would raise suspicion for uric acid stone nephrolithiasis.
d. Long-term parenteral nutrition can lead to cholestatic injury of the liver.

Correct answer: (c). Hematuria in this patient would raise suspicion for uric acid stone nephrolithiasis. (Is false) Patients with short bowel syndrome may be predisposed to formation of calcium oxalate kidney stones, not uric acid stone nephrolithiasis.

Further Reading

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