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REVIEW ARTICLE

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Surgical therapy for short bowel syndrome

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Abstract Patients with short bowel syndrome (SBS) suffer tremendous morbidity secondary to prolonged hospitalization and chronic parenteral nutrition (TPN). Overall, the majority of infants will adapt and ultimately become independent of TPN, but this process may require many months or years. Reasons for continued TPN dependency include bowel dysmotility, bacterial overgrowth, insufficient adaptation, or very short bowel length. It is this subpopulation of patients who may benefit from surgical procedures that optimize intestinal adaptation and increase the mucosal absorptive surface area. The goal of this review article is to summarize the process of intestinal adaptation and then to outline the surgical principles and techniques available to surgeons who treat this complicated group of patients.

Keywords Short bowel syndrome · Intestinal failure · Intestinal adaptation · Surgery · Pediatrics

Introduction

Short bowel syndrome (SBS) is the spectrum of malabsorption that occurs after resection of a major portion of the small intestine for congenital or acquired lesions [1, 2]. A useful definition is based on the need for intervention. Patients requiring total parenteral nutrition (TPN) support for more than 1–3 months after major resection can be defined as having SBS [3]. Other definitions are based on residual bowel length. For instance, small bowel resection greater than 75% of small bowel length is considered SBS [1]. Variation in the definitions among institutions produces differences in outcome among published series. The Canadian Association of Paediatric Surgeons (CAPS) defines SBS as the need for TPN for more than 42 days after bowel resection, or a residual small bowel length of less than 25% expected for gestational age [4]. This is the definition used at The Hospital for Sick Children in Toronto. Unfortunately, patient characteristics such as gestational age, region of bowel resected, functional capacity of the remaining intestine, and the presence or absence of the ileocecal valve all contribute to the difficulty in determining the critical length of bowel required to avoid SBS [5].

The major features of SBS are dehydration secondary to diarrhea, malabsorption of macro- and micronutrients, malnutrition, and failure to thrive [3, 5]. Resection of certain regions of the intestine can lead to permanent loss of specialized absorptive functions. After resection, the residual small bowel undergoes intestinal adaptation, which is the gut's attempt to optimize its absorptive capacity. The adaptation process may take several months or years to complete. During that time, the infant is either partially or totally dependent on parenteral nutrition. If the intestinal adaptation is adequate, the bowel will eventually absorb sufficient nutrients to allow patient growth. In a number of cases, intestinal adaptation is inadequate, and the child remains at least partially dependent on parenteral nutrition [6].

The most common causes of pediatric short bowel syndrome are neonatal conditions such as necrotizing enterocolitis, extensive aganglionosis, intestinal atresia, midgut volvulus, and abdominal wall defects [3, 7]. In older children and teenagers, Crohn's disease and trauma are more common causes [8]. Accurate estimates of incidence and outcome in SBS children remain difficult because of variation in the definition of SBS among institutions, difficulty of tertiary care referral centers to accurately determine their catchment populations, and problems ensuring complete follow-up of the whole cohort. A recent population-based study at our institution determined the incidence of neonatal SBS to be 24.5 per 100,000 live births, with a much higher incidence in

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babies born before 37 weeks' gestation compared with term newborns (353.7/100,000 live births vs. 3.5/100,000 live births) [9].

Regardless of initial pathology, massive resection and compromised intestinal adaptation lead to a predictable sequence of secondary events. The multitude of complications that ensue with long-term hospitalization and prolonged parenteral nutrition include central-line complications, multiple systemic infections, cholestasis, liver failure, failure to thrive, and the resultant effects on family dynamics [2, 7]. Prompt weaning from parenteral nutrition appears necessary to prevent liver dysfunction and improve outcome. As TPN-induced liver failure progresses to cirrhosis, intestinal and liver transplantation become the only therapeutic option for these infants. Many of these infants do not survive long enough to receive a bowel and/or liver transplant because they are too premature and small to be eligible for the procedure [10]. SBS case fatality rates are quoted as anywhere between 10% and 50%. Population-based mortality estimates such as the cause-specific and proportional mortality rates (for children less than 4 years old) are 2.0/100,000 population/year and 1.4%, respectively [9].

It seems obvious that a relationship would exist between residual intestinal length and the ability to adapt and become independent of parenteral nutrition. The association, however, is not as clear as one would believe. Patient characteristics such as the region of bowel resected, functional capacity of the remaining intestine, presence or absence of the ileocecal valve, length of residual colon, underlying diagnosis, and gestational age probably all contribute to the problem of determining the minimum small bowel length required to avoid SBS [5].

Wilmore [11] correlated a successful outcome following extensive bowel resection (in infants with "normal" birth weight) with at least 15 cm of jejunum or ileum and the ileocecal valve, or 40 cm of small bowel without the ileocecal valve. Consideration of gestational age when reporting residual bowel length is imperative because bowel length increases as the neonate approaches term. Touloukian showed that a 28-week-old neonate has approximately 200 cm of bowel, and this increases to 300 cm at term [12]. The outcome of a premature baby with 40 cm of residual bowel may be different from that of a term baby with 40 cm because of the gut's ability to grow in length as the baby matures. The anticipated increase in bowel length is greatest in premature infants, which may be an important prognostic factor in SBS patients.

The advances in medical management of SBS over the last 30 years, most importantly TPN, have led to improved survival [13, 14]. Parenteral nutrition permits survival after massive small bowel resection and provides the patient time and opportunity to achieve intestinal adaptation. Spontaneous adaptation occurs in approximately 75% of SBS patients and allows them to be weaned from TPN [2]. Reasons for continued TPN dependency include bowel dysmotility, bacterial overgrowth, insufficient adaptation, or very short bowel length. These patients may benefit from surgical procedures that improve intestinal function to optimize adaptation and increase the absorptive surface area [15]. This article summarizes the process of intestinal adaptation, and then outlines the surgical techniques available to surgeons who treat this complicated group of patients.

Adaptation

Adaptation is a compensatory response that follows an abrupt decrease in mucosal surface area after an extensive small bowel resection [16]. The process includes both anatomic and functional changes that increase the gut's digestive and absorptive capacity; these changes begin within 48 h of surgery but may require up to 2–3 years for completion. If the adaptation process is insufficient, lifelong parenteral nutrition may be necessary.

Structural alterations

Adaptation in the remnant small bowel includes increases in length and caliber, with hyperplasia/hypertrophy of each intestinal layer. The magnitude of the response is greater after resection of the proximal small bowel compared with a distal resection [17]. After proximal small bowel resection, the remnant ileum adopts many of the morphologic features of the jejunum. The patient's age at the time of resection affects the extent of bowel lengthening. The growth rate of the neonatal gut is greater than that of the rest of the body, probably to prepare the infant for enteral nutrition [18]. Neonates are more likely than adults to achieve independence from TPN after extensive resection.

The adapting intestine develops an increased caliber and hypertrophy of the longitudinal and circular smooth muscle layers [17]. These changes occur within 1 month of the operation [17]. The increased intestinal caliber increases the absorptive surface area, but it may also result in ineffective peristalsis. This dysmotility leads to stasis of intestinal content, bacterial overgrowth, sepsis, and malabsorption [16].

Within 48 h of bowel resection, epithelial hyperplasia begins within the intestinal crypts [19]. Hyperplasia of intestinal epithelium increases villus height and crypt depth secondary to increased proliferation and accelerated migration along the villus. This is more pronounced in the ileum than in the jejunum [20]. The number of villi is also increased.

Functional changes

Digestion and absorption

Functional adaptive changes occur to combat the sudden decrease in digestive and absorptive capacity after

resection. Diarrhea is a significant complication of extensive intestinal resection; therefore, increased sodium and water absorption is a very important component of adaptation. The sodium-glucose cotransporter is the major mode of sodium transport in the small bowel, and a 2.5-fold increase in glucose-dependent sodium absorption per centimeter of intestine after a 70% small bowel resection in rats has been found [16].

Studies of disaccharidases and dipeptidases along the brush border of the adapting small bowel show increased activity when measured per villus [21]. This demonstrates enhanced digestive capacity by the enterocytes on the villi.

Intestinal permeability

Intestinal epithelium performs an important barrier function to infection. Septic episodes in SBS may be secondary to a breach of this barrier with translocation of bacteria [16]. The small number of murine studies that have examined the role of postresection adaptation on intestinal permeability have produced conflicting results. This may be due to the different times the ileum was studied after resection and represents the dynamic nature of intestinal adaptation [22, 23].

Bacterial overgrowth secondary to gut dysmotility is common in patients with SBS and can lead to bacterial translocation. Aldazabal et al. measured bacterial translocation to the mesenteric lymph nodes, blood, and spleen in rats receiving TPN after 80% small bowel resection [24]. Ninety-two percent of these animals had positive bacterial cultures, compared with 47% in nonresected animals receiving TPN. The changes in permeability may be secondary to impaired immune system production of biliary and mucosal antibodies (secretory IgA) [25].

Mechanisms of adaptation

Multiple mechanisms and mediators have been proposed for the adaptation response, but no single factor adequately explains all the changes that occur in intestinal structure and function. There is a role for luminal nutrients, gastrointestinal secretions, and humoral factors [26].

Hormones, growth factors, and cytokines have been proposed to be important in adaptation because their levels are increased in the serum and tissues after massive small bowel resection, and exogenous administration of these substances has been demonstrated to enhance various components of the adaptation response (e.g., insulin-like growth factor-1, glucagons, peptide-YY, and epidermal growth factor).

Multiple experimental observations suggest that endogenous gastrointestinal secretions are important for adaptation. There is a decreasing gradient in bowel thickness from the origin of pancreaticobiliary secretions (ampulla of Vater) toward the ileum. Experiments that transpose the ampulla to the more distal gastrointestinal tract result in villus hyperplasia of the distal ileum [27]. Pancreatic secretions seem to be more trophic to mucosa than bile [27]. It is not known what component of the pancreaticobiliary secretions is trophic to the intestinal mucosa.

Perhaps the strongest stimulus for adaptation is the presence of enteral nutrition within the lumen. Animal experiments have demonstrated the lack of adaptation that occurs in dogs receiving only TPN [28]. The mucosa of starving dogs reveals severe atrophy. This process is paralleled in humans, but it requires a longer period of starvation to elicit the same degree of atrophy [29]. Luminal nutrients probably have both a direct and indirect effect on adaptation. Nutrients promote release of various hormones and secretions as well as stimulate peristalsis and splanchnic blood flow.

Nutrition composition is also important, with complex nutrients initiating a stronger adaptation response. Complex nutrients require greater metabolic effort for digestion and absorption; therefore, the compensatory response is maximized. Fats, especially long-chained, unsaturated lipids, are the most trophic of the macronutrients [30].

The facts outlined above demonstrate the importance of timely surgical intervention to optimize adaptation potential in individual patients. In the United States, an estimated 20,000 patients with intestinal disease receive home parenteral nutrition at an annual cost of approximately $150,000 U.S. per patient [31]. This translates into $3 billion U.S. annually. As O'Brien et al. stated, if therapy designed to enhance adaptation allows discontinuation of TPN in just 10% of patients with SBS, a minimum of $300,000,000 U.S. could be saved annually [16].

The role of surgery in short bowel syndrome

The surgeon has an important role in the natural history of all patients with SBS. The surgeon is present at the beginning of every case, when his or her perioperative and operative decisions have a direct impact on whether a patient will develop SBS. Often the surgeon is making the best of a poor situation. The surgeon is also intimately involved during the subsequent adaptation process to perform adjunctive operative procedures, as necessary, to optimize a patient's chance for TPN independence. Ultimately, if adaptation is insufficient and the patient develops end-stage liver disease, the surgeon will perform an intestinal or liver transplant.

Initial resection

Primary prevention of SBS should be a high priority. Thompson outlined how it may be possible to avoid extensive bowel resection if surgeons intervene early in cases of intestinal ischemia, mesenteric emboli, or clots,

and in cases of complete bowel obstruction [32]. Intraoperative determination of intestinal viability and the use of second-look laparotomies can potentially preserve what appeared to be bowel of questionable viability. A conservative attitude regarding resection in Crohn's disease and the use of stricturoplasties may minimize the chance of SBS in these patients.

When faced with a patient who requires massive intestinal resection, one of the most difficult intraoperative decisions for a surgeon to make is whether to proceed with a resection that will result in SBS. In general, we have a fairly aggressive approach to resection, but the overall mortality of SBS does remain high. The family's wishes and the existence of comorbidities such as prematurity, bronchopulmonary dysplasia, or other structural anomalies are all important considerations that will influence one's decision [32, 33].

Once the decision is made to proceed with massive bowel resection, the goal should be to preserve all bowel length possible, including the ileocecal valve. The use of internal stents for patients with multiple intestinal atresias or patchy necrotizing enterocolitis requiring multiple resections is helpful [33]. It is important to document the length of residual small and large bowel remaining with the patient. Stomas are frequently required because of intraabdominal contamination, inflammation, or hemodynamic instability. Placing the end stoma beside the mucous fistula, at the same stoma site, is a simple way of making subsequent stoma closure more straightforward. Bowel continuity can be reestablished without the need for a full laparotomy and lysis of adhesions. In my experience, patients tolerate this approach better and have faster resolution of their ileus.

The early treatment of SBS is focused on the acute surgical emergency. Generally, adjunctive SBS procedures should not be performed at the time of the initial resection. Intestinal adaptation will often be adequate to preclude the need for surgical therapy [32].

Reoperation

During the adaptation phase, surgical intervention is reserved for managing significant surgical complications or for providing central venous or enteral access (e.g., gastrostomy) to allow adaptation to continue [34].

It is difficult to know the precise point at which adjunctive surgical procedures should be performed in SBS patients. Patients who plateau and fail to make progress with TPN weaning should be considered for surgery. Also, patients who develop complications such as TPN cholestasis, recurrent line sepsis, or bacterial overgrowth may be candidates. Three factors guide the decision of which operation to perform: the underlying intestinal function, the length of the residual bowel, and the caliber of the intestinal remnant [34].

Before surgery occurs, patients require a complete assessment of their general medical condition and comorbid diseases. It is important to know whether the patient has end-stage liver disease, as this would be a contraindication for surgery, and a referral for intestinal and liver transplantation may be more appropriate. All previous operative notes should be reviewed, and a small bowel follow-through should be obtained to assess motility, bowel length, and caliber.

At the time of the adjunctive surgical procedure, a liver biopsy should be performed to determine the extent of TPN cholestasis. Prophylactic cholecystectomy should also be considered at the time of reoperation. Patients with a history of ileal resection and long-term parenteral nutrition are at risk for cholelithiasis. Twenty percent of infants on long-term parenteral nutrition develop gallstones secondary to lack of enteral feeding and gallbladder stasis [20]. Patients with SBS are three times more likely to develop gallstones because the loss of bile salts from ileal resection permits cholesterol in bile to precipitate [29]. The incidence of complications from cholelithiasis is not known in children; however, it has been suggested that patients with cholelithiasis at the time of reoperation have a cholecystectomy, as it can usually be performed quickly and safely [35].

The primary objective of surgery for SBS is to improve intestinal function, optimize bowel motility, and increase the mucosal absorptive surface area.

Techniques to improve intestinal function

Lysis of adhesions, stricturoplasty, and segmental intestinal resection

Children with a history of gastrointestinal pathology are at risk of developing mechanical bowel obstruction. The etiology may be stenosis secondary to the late effects of bowel ischemia or inflammation, as seen in patients with necrotizing enterocolitis or Crohn's disease. In addition, previous intraabdominal surgery or inflammation produces adhesions that may be the source of obstruction. Bowel obstruction causes proximal bowel dilatation, dysmotility, and bacterial overgrowth. Dilated bowel from primary or secondary dysmotility conditions, such as adaptation with bacterial overgrowth, can be very difficult to distinguish from mechanically obstructed bowel with proximal dilatation. Mechanical obstruction may be corrected by lysis of adhesive bands, stricturoplasty if bowel length is short, or segmental resection for patients with adequate bowel length [36].

Reestablishing intestinal continuity

Diverting stomas are often necessary at the time of laparotomy for children suffering acute, life-threatening conditions. The presence of peritoneal contamination, extensive inflammation, hemodynamic instability, or other systemic factors that might effect anastomotic healing (e.g., malnutrition or immunosuppression) often preclude the desire to perform a primary anastomosis.

There are several advantages to reversing stomas and reestablishing gastrointestinal continuity. The primary benefit of stoma closure is that it increases the mucosal surface area available for nutrient absorption. Nutrient absorption is improved because the longer intestinal length increases transit time and permits nutrients more time for contact with the absorptive mucosa. If the colon is present, the patient benefits because the colon is the major site of water reabsorption and therefore affects the volume of stool output. It also enhances carbohydrate absorption as bacteria ferment unabsorbed carbohydrates into short-chain fatty acids, acetate, butyrate, and proprionate, which are then absorbed by colonocytes. These substances are then used as caloric substrate. This salvage mechanism may provide up to 5–10% of calories [29].

Diverted intestine undergoes mucosal atrophy; therefore, reestablishing intestinal continuity facilitates the adaptive response in the distal bowel [37]. Multiple mechanisms and mediators have been proposed for the adaptation response, but no single factor adequately explains all the changes that occur in intestinal structure and function. There is a role for luminal nutrients, gastrointestinal secretions, and humoral factors, and delivery of these substances to the previously diverted segment enhances adaptation [26].

The main disadvantage to stoma closure is diarrhea and the resulting perineal irritation. Elevated stool volume and frequency result from inadequate absorption in the proximal bowel, but also from colonic mucosal inflammation caused by the irritating effects of bile acid delivery to the large bowel, producing secretory diarrhea and steatorrhea [15]. Aggressive application of barrier products to the perineum can usually protect the skin, but it is important to begin applying these immediately after surgery, as it can be difficult, and more painful for the patient, to treat a rash that is already well established.

Patients with a colon in continuity are at risk of calcium oxalate nephrolithiasis. Oxalate is absorbed because the delivery of bile acids to the colon prevents oxalate excretion in the stool. The circulating oxalate can then precipitate with calcium and cause renal calculi [3].

Determining the optimal time for stoma closure can be difficult. These patients often have significant comorbid conditions in addition to their gastrointestinal disorders. Predicting which patients will tolerate stoma closure without significant diarrhea and perineal complications is often not possible. Even though high stoma output often initially gets converted to large stool volumes, most patients usually benefit from the longer intestinal surface area. This author believes the goal should be to reverse stomas early, once the patient is deemed able to tolerate it from a technical and physiological perspective. Maximizing the percentage of calories received from the enteral route helps decrease the risk of parenteral nutrition-associated cholestasis [19]. Experience from the Intestinal Care Center in Pittsburgh suggests that patients who have had more than 30% of their colon resected and who have stoma output totaling more than 40 cc/kg/day are more likely to suffer significant perineal complications [34].

Techniques to improve intestinal motility

Intestinal tapering and plication

Increased intestinal caliber is the normal physiologic response to extensive bowel resection. Bowel dilatation slows intestinal transit and increases mucosal absorptive area. At a point, however, this normal adaptive mechanism becomes pathologic. The dilated segments become dysmotile, and fecal stasis, bacterial overgrowth, and malabsorption ensue. Oral antibiotic therapy can help suppress overgrowth, but some patients develop refractory bacterial overgrowth and require surgical intervention.

Dysmotile segments of bowel must be distinguished from mechanically obstructed bowel with proximal dilatation. Mechanical obstruction can be corrected by release of adhesive bands, stricturoplasty, or resection of the obstructing segment. Functionally dysmotile segments should be streamlined by tapering or plication to improve peristalsis and decrease bacterial overgrowth. Streamlining has the advantage of preserving bowel length compared with resection of dilated segments [36].

Tapering enteroplasty involves partial resection of the antimesenteric border of the dilated segment to reduce the diameter of the intestinal loop (Fig. 1). The blood supply arising from the mesenteric side is not disturbed. The disadvantage is that some absorptive surface area is lost, which is already limited in these patients. There is also a risk of postoperative leak from the suture line, but this is not significant. To ensure an adequate and uniform lumen, an appropriately-sized Foley catheter or chest tube can be inserted into the bowel lumen through a small enterotomy at the beginning of the dilated segment. It can be gently held in position along the mesenteric border of the bowel with a Babcock clamp, and then the excess bowel can be excised with a stapler or free-hand.

Plication also streamlines the bowel, but no bowel wall is resected. The dilated bowel wall is inverted into the lumen, and the serosal surfaces are imbricated (Fig. 2). Therefore, mucosal surface area for absorption is maintained and motility improved [38]. Unfortunately, the inverted bowel may cause bowel obstruction because it blocks the bowel lumen. Also, the suture line may fail, resulting in repeat dilatation and dysmotility [15]. The serosa can be removed along the antimesenteric bowel wall at the site of the imbrication in an attempt to prevent suture line failure.

Antiperistaltic small intestinal segments

Reversed small bowel segments to slow intestinal transit and increase absorption have been used mostly in adults.

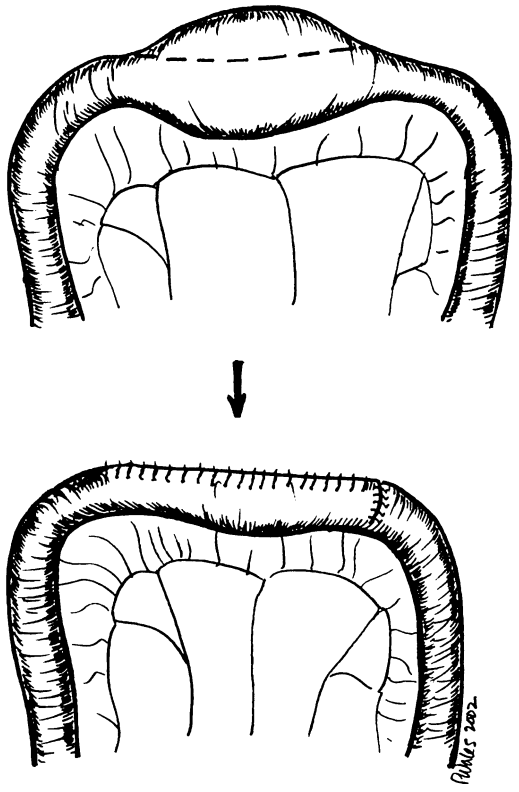

Fig. 1 Tapering enteroplasty. The antimesenteric portion of the dilated segment of bowel is removed, and a portion of the absorptive surface is lost. Reprinted with permission from Wales P (2004) Intestinal failure: aspects of surgery. In: Walker WA, Goulet OJ, Kleinman RE, et al. (eds) Pediatric gastrointestinal disease, 4th edn. BC Decker, Hamilton, Ontario

A segment of small bowel is placed in the opposite direction of normal intestinal flow or peristalsis. The reversed peristalsis in the interposed segment slows the movement of intestinal contents. The difficulty is determining how long the reversed segment should be, because long segments can stop intestinal flow altogether, producing intestinal obstruction.

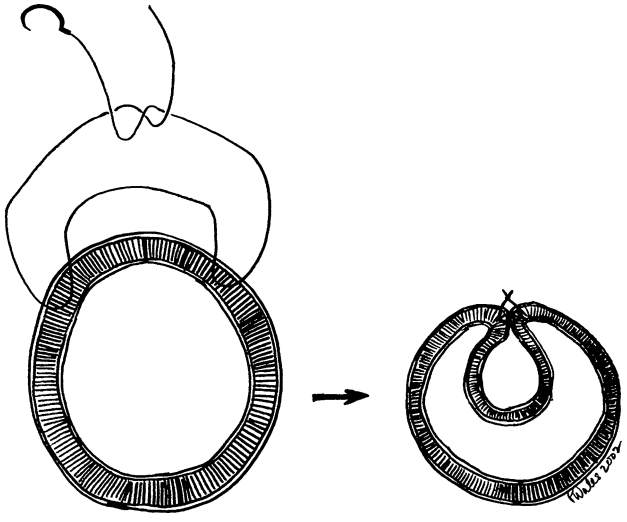

Fig. 2 Intestinal plication. A portion of the dilated bowel wall is inverted into the bowel lumen and secured by seromuscular sutures. Reprinted with permission from Wales P (2004) Intestinal failure: aspects of surgery. In: Walker WA, Goulet OJ, Kleinman RE, et al. (eds) Pediatric gastrointestinal disease, 4th edn. BC Decker, Hamilton, Ontario

Experience with reversed small bowel segments occurred in the 1970s when they were employed to slow peristalsis in patients with postvagotomy diarrhea [39]. The indication for reversed intestinal segments was expanded to include patients with SBS. In a canine model of beagle puppies with extensive small bowel resection, there was a short-term improvement in water, lipid, and nitrogen absorption [40]. Panis et al. described reversed small bowel segments in a case series of eight adult patients [41]. A median length of 12 cm was used for the reversed segment. Complications occurred in six of eight (75%) patients, and one patient died. Four patients (50%) weaned off parenteral nutrition, and the other four had decreased TPN requirements. Adult series have in general shown a favorable response to reversed segments in approximately 70% of patients, but the experience in children has shown a lack of sustained benefit [39, 42].

Neonates and infants are less favorable candidates for reversed small bowel segments because of their potential for intestinal growth (lengthening). Growth of a reversed segment may ultimately produce complete bowel obstruction [42]. In adults, the ideal length of the reversed segment is approximately 10–15 cm, and in infants it is 3 cm [34]. This procedure has limited use as a definitive procedure for patients with SBS.

Colonic interposition

The frequency of colonic peristaltic contractions is lower than that in small bowel. Proximal placement of an isoperistaltic segment of colon between two ends of small bowel may prolong intestinal transit and permit more effective absorption of nutrients and electrolytes. Animal studies performed in the 1970s in both rats and canines were successful in showing delayed intestinal transit and improved growth [43, 44].

As with reversed small bowel segments, pediatric data show some favorable outcomes, with the ability to wean from parenteral nutrition, but the results are variable [45, 46]. The proposed advantage of isoperistaltic colonic interposition is fewer obstructive complications than witnessed in reversed small bowel segments, but the overall human experience is low [39].

Creation of intestinal valves

The ileocecal valve (ICV) has two functions: It slows transit of small bowel content into the colon, and it prevents reflux of colonic bacteria into the ileum. Colonic bacteria in the small bowel induce mucosal inflammation and malabsorption. Wilmore published his landmark paper in 1972 in which he demonstrated

the relationship between residual intestinal length, the presence or absence of the ICV, and gut adaptation and parenteral nutrition independence [11]. As a result, numerous procedures have been developed over the years to create intestinal valves that will slow intestinal transit and minimize colonic reflux in SBS patients. In most cases, the valve represents a short intussusception created by "telescoping" a proximal segment of bowel into the distal segment and suturing the seromuscular layers together [47] (Fig. 3). Serosal stripping can be performed between the two walls of intestine being sutured to try to reduce the chance of valve failure.

An intestinal valve produces a partial obstruction, with proximal dilatation of the small bowel. The partial obstruction increases absorption time, but more importantly it induces the adaptation and dilatation that could permit a subsequent lengthening procedure. Georgeson et al. presented a series of six patients who received valve construction followed by an intestinal lengthening procedure 3–9 months later [48]. There were no complications associated with the valve. Three patients were weaned from parenteral nutrition. Other reported cases of intestinal valves in children have had mixed results [15].

The major limitation is to determine the optimal valve length to slow intestinal transit without inadvertently causing a mechanical bowel obstruction. The variability between patients makes standard recommendations difficult. It has been reported that valve length in children should be less than 3 cm [34]. Creation of a valve requires approximately 8 cm of bowel; therefore, this procedure may not be feasible for many patients with SBS [42].

Reversed electrical intestinal pacing

Hyperperistalsis is common in SBS. The premise of reversed electrical intestinal pacing is based on the cardiology experience in which the heart is paced to treat arrhythmias. Overriding the intrinsic intestinal pacemaker could slow intestinal transit in SBS patients with hyperperistalsis to optimize water and nutrient absorption.

The normal intestinal pacemaker is located in the foregut within the duodenum. The electrical wave is propagated toward the ileum to generate peristalsis. Canine experiments have demonstrated better absorption of water and electrolytes, but manipulation of the duodenal pacemaker requires duodenal transsection [49, 50]. Hence, no humans have received this approach because of the perceived high morbidity.

More recently, entrainment of intestinal slow waves in dogs has been achieved by Lin et al. [51]. Four pairs of intraluminal intestinal electrodes placed within the jejunum permitted intestinal pacing by entraining the intestinal slow waves. This treatment has not been evaluated in human trials, but it may be helpful in both SBS patients and in patients with primary motility disorders.

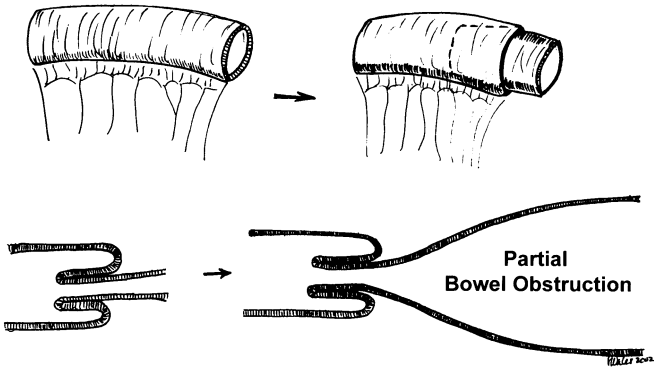

Fig. 3 Creation of intestinal valves. A segment of bowel is telescoped into the distal bowel and secured with sutures. This will slow transit and induce a partial bowel obstruction. The proximal bowel dilates, and an intestinal lengthening procedure becomes possible. Reprinted with permission from Wales P (2004) Intestinal failure: aspects of surgery. In: Walker WA, Goulet OJ, Kleinman RE, et al. (eds) Pediatric gastrointestinal disease, 4th edn. BC Decker, Hamilton, Ontario

Techniques to increase absorptive surface area

As previously mentioned, the underlying problem in SBS is inadequate mucosal surface area for absorption. In addition, the adaptive response or partial mechanical obstruction from strictures produces proximal bowel dilatation, stasis, and bacterial overgrowth. The common thread among all intestinal lengthening procedures is the exploitation of the dilated segment of bowel to gain gut length. More importantly, however, the bowel is tapered, which improves peristalsis and prevents the sequelae of recurrent bacterial overgrowth [42].

Longitudinal intestinal lengthening procedure (Bianchi)

Bianchi first described the longitudinal intestinal lengthening procedure (LILP) in 1980 using a porcine model [52]. The procedure is based on the small bowel's dual blood supply that enters the bowel wall within the two layers of the mesentery. The bifurcated blood supply enters each hemicircumference of the bowel wall. The two leaves of the mesentery that contain the blood vessels are separated on the mesenteric surface of the bowel. The bowel is divided longitudinally between the two layers so that each parallel lumen has its own single source of blood supply [42]. The two newly-created bowel segments are then anastomosed end-to-end, creating one intestinal segment that is twice as long and half the diameter of the original (Fig. 4). The absorptive surface area may increase as the newly-created loops slowly dilate over time. LILP is indicated for TPN-dependent patients with very short and dilated bowel.

Bianchi reported outcomes in 20 patients who received LILP [53]. At 6 years follow-up, nine patients were alive, and seven of nine survivors were independent

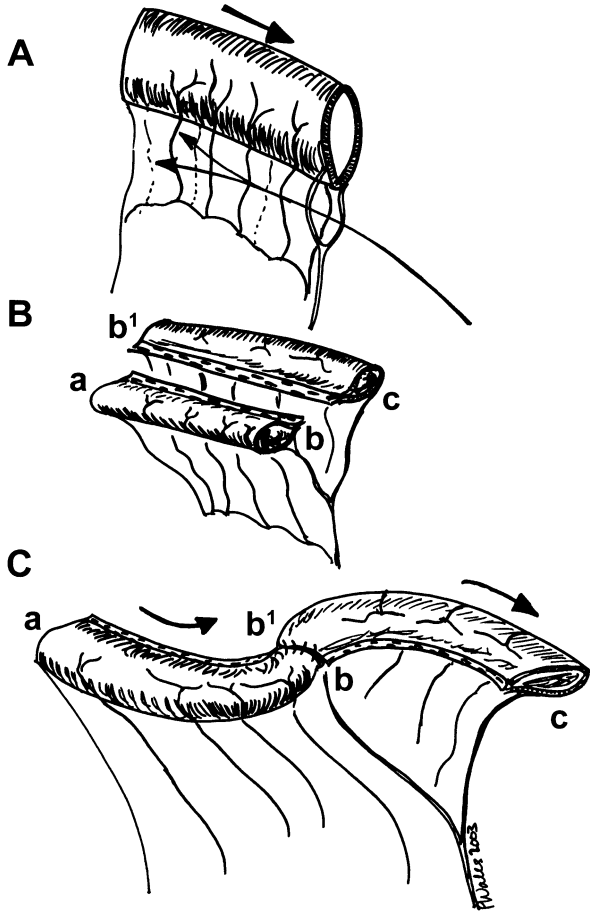

Fig. 4 **A** The mesenteric blood vessels within the two leaves of the mesentery are separated under the dilated bowel segment. **B** The dilated bowel is divided longitudinally within the mesenteric leaves to create two parallel loops of bowel half the diameter of the original loop. **C** The two bowel segments are anastomosed end-to-end to create a bowel segment double the length of the original. The bowel mesentery needs to be amenable to mobilization for this to be feasible. The bowel at *a* is the most proximal portion, and the bowel at *c* is the most distal. The end of the reduced loop at *b1* is anastomosed to the proximal end of the other loop at *b* to create an isoperistaltic segment of tapered and lengthened bowel. Reprinted with permission from Wales P (2004) Intestinal failure: aspects of surgery. In: Walker WA, Goulet OJ, Kleinman RE, et al. (eds) Pediatric gastrointestinal disease, 4th edn. BC Decker, Hamilton, Ontario

of parenteral nutrition. Survival was influenced by a small bowel length greater than 40 cm and no liver dysfunction at the time of the procedure. Weber reported 16 children who received a Bianchi procedure [54]. Eighty-eight percent were TPN-independent; however, some of the children in that series had good residual small bowel length to begin with. Therefore, it is possible that some of the patients would have adapted spontaneously and weaned off TPN without a lengthening procedure. Thirty-one percent required reoperation for complications. Thompson et al. published a series on long-term outcome after LILP in 16 patients with residual small bowel lengths ranging from 23 to120 cm. Forty percent of the patients were independent of parenteral nutrition at both 1 and 5 years postsurgery [55].

Complications from this procedure include adhesive small bowel obstruction, anastomotic strictures or leak, and recurrent bowel dilatation. Patients who develop recurrent dilatation are candidates for the Kimura procedure or, preferably, the serial transverse enteroplasty [42, 56]. The Bianchi procedure requires mobility in the mesentery in order for the two tapered segments to be anastomosed end-to-end. If a patient has a short, tethered, or thickened mesentery, a Bianchi procedure may not be technically feasible [55, 57].

Kimura procedure (isolated bowel segments)

The Kimura procedure is an alternative bowel lengthening technique that may be used when the mesentery is very short, tethered, or absent [58]. It is a two-staged approach that consists of the initial coaptation of the antimesenteric surface of a dilated bowel segment to host organs (abdominal wall or liver), then secondary longitudinal division of the bowel to create two bowel loops, one from the mesenteric half and one from the antimesenteric half [57].

The serosal surface of the antimesenteric bowel wall is deseromyotomized to expose the submucosa. It is then sutured to the abdominal wall or liver that has had its peritoneum removed. Over a period of months, collateral blood supply develops from the host organs into the antimesenteric surface of the bowel. The bowel is then amenable to horizontal division into two parallel structures The two bowel segments are then anastomosed end-to-end, creating a lengthened, tapered intestinal segment analogous to the Bianchi procedure.

No large reports of the Kimura procedure in humans have been published. This operation is not considered a first-line procedure for bowel lengthening. One major concern with it is the limited access to the abdominal cavity due to the nonanatomic placement of the bowel. Repeat laparotomy is frequent in this patient population; therefore, bowel parasitized to the abdominal wall makes these operations more difficult. Another criticism of the Kimura procedure is the lack of nutrient blood flow through the portal system, but in patients who have received this procedure, no problem has been noted.

Serial transverse enteroplasty (STEP)

The serial transverse enteroplasty (STEP) has been the most exciting addition to the surgical management of SBS in several years. The results from porcine experiments were first published in March 2003, and the first case report in a human was published in June 2003 [56, 59]. The STEP procedure satisfies the objectives of other bowel lengthening procedures such as lengthening and tapering, but it has the advantages of being easy to perform, not requiring bowel anastomoses, being able to

theoretically more than double the intestinal length, and being able to be applied as a primary or secondary procedure, such as after a Bianchi operation.

The procedure is performed by first dividing all abdominal adhesions to have full bowel mobility (Fig. 5A). The antimesenteric border of the dilated bowel is marked with a surgical pen to prevent twisting of the bowel during placement of the surgical stapler (Fig. 5B). A reusable GIA stapler is applied sequentially, from alternating and opposite directions through small mesenteric windows at the site of each staple line (Fig. 5C). The stapler is placed from the 90° and 270° positions (with 0° being the mesenteric border). The sequential stapler firings create a zig-zag-like channel (Fig. 6) [56]. The diameter of the channel is determined by the surgeon and is commonly about 2 cm. The presence of normal caliber bowel can be used as an internal guide to channel size.

The blood supply to the intestine enters from the mesenteric side and travels along the bowel wall perpendicular to the long axis of the intestine; therefore, if the staple lines remain perpendicular to the long axis, the bowel segments should remain well vascularized [56]. As opposed to the Bianchi procedure, the mesentery is never in danger and the bowel is never opened.

The Bianchi and Kimura procedures reduce the caliber of the bowel by 50%. With the STEP procedure, the extent of the tapering is dependent on the surgeon. The potential increase in bowel length depends on the extent of the bowel dilatation and the chosen size of the channel created. If the bowel segment is massively dilated, one could theoretically more than double the segmental length [56].

The preliminary reports by Kim et al. [56, 59] establish the feasibility of the STEP procedure for bowel lengthening. It could potentially be applied to other situations in which intestinal tapering is desired, but one wants to avoid the loss of mucosal surface area, such as in small bowel atresias with a very dilated proximal loop. The proximal end usually needs to be tapered or partially resected to deal with the size discrepancy between the proximal and distal bowel ends that are to be anastomosed. The STEP procedure deals with the size discrepancy and preserves surface area.

As with any new treatment modality, enthusiasm needs to be controlled until longer-term patient outcomes become known. We have performed seven STEP procedures to date at The Hospital for Sick Children. Follow-up ranges from 2 weeks to 10 months. Five children ranging from 4 months to 6 years of age with a history of necrotizing enterocolitis (two patients), type 4 jejunal atresia (one patient), total colon Hirschsprung's disease (one patient), and gastroschisis (one patient) received the STEP procedure after suffering complications of bacterial overgrowth, malabsorption, and TPN cholestasis. Two neonatal patients with proximal jejunal atresia received the STEP procedure as primary therapy in an attempt to preserve mucosal surface area and deal with the size discrepancy between the proximal and distal segments. To date, the results have been promising. Our first patient unfortunately died 2 months postoperatively after developing line sepsis that exacerbated her underlying hepatic dysfunction. The other six patients have shown improvement in stool consistency and tolerance of enteral feeds. We continue to monitor their progress.

Sequential intestinal lengthening procedures

In 1994, Georgeson et al. reported their approach to nine infants and children with refractory SBS [48]. The authors employed a combination of several short bowel operations described above, applied sequentially in patients with intestinal failure. For six patients who had a remnant bowel of normal caliber, an intestinal valve was

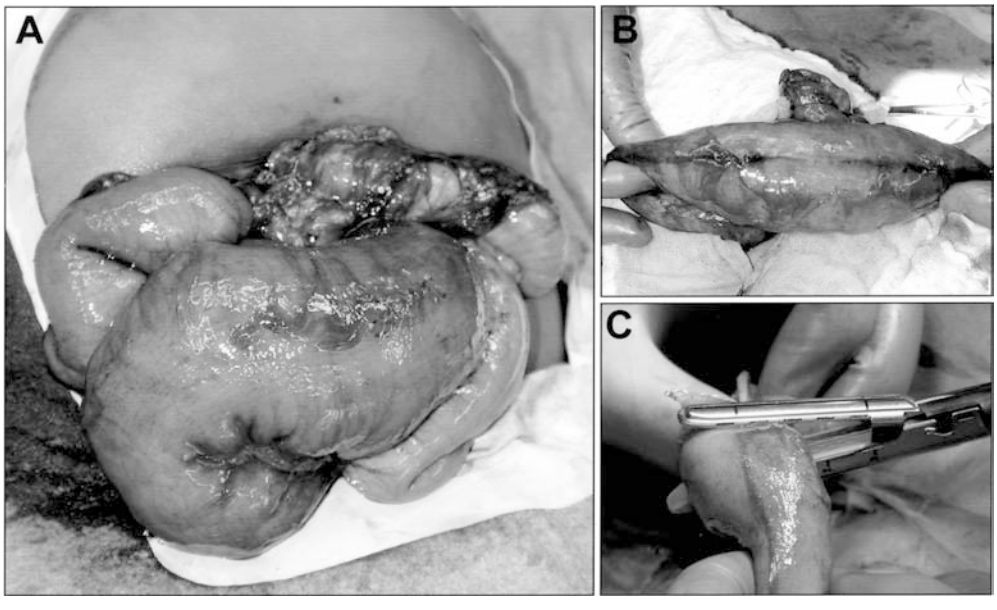

Fig. 5 **A** Patient with SBS and recurrent bacterial overgrowth. Note the very dilated loop of bowel that will be tapered and lengthened. **B** Marking of the antimesenteric border of the dilated bowel with a surgical pen. This helps prevent twisting of bowel during application of the stapler. **C** The surgical stapler is applied to alternating sides of the bowel at 90º and 270º from the mesentery. Reprinted with permission from Wales P (2004) Intestinal failure: aspects of surgery. In: Walker WA, Goulet OJ, Kleinman RE, et al. (eds) Pediatric gastrointestinal disease, 4th edn. BC Decker, Hamilton, Ontario

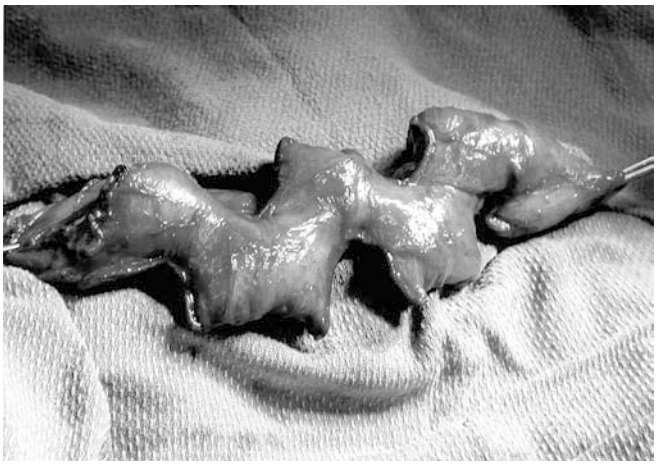

Fig. 6 STEP procedure. Zig-zag pattern of bowel created after sequential and opposite firings of the GIA stapler across the dilated bowel loop. The channel size is determined by the surgeon. The normal loops of bowel can be used as an internal guide. A gastrointestinal contrast study is performed on the 7th postoperative day prior to initiation of enteral feeds. Reprinted with permission from Wales P (2004) Intestinal failure: aspects of surgery. In: Walker WA, Goulet OJ, Kleinman RE, et al. (eds) Pediatric gastrointestinal disease, 4th edn. BC Decker, Hamilton, Ontario

created to induce partial bowel obstruction and proximal dilatation. After several months, a Bianchi procedure was performed. One patient had a Bianchi procedure initially, followed by a Kimura procedure for recurrent bowel dilatation. The outcome in the seven survivors was good after a range of 5–49 months of follow-up. Patients were tolerating a higher percentage of their calories enterally, and two patients were completely weaned from parenteral nutrition.

This publication was a significant contribution because it emphasized the need for perseverance, flexibility, and creative solutions for this very complicated population of patients.

Future considerations

Tissue-engineered intestine is on the horizon as a possible treatment for SBS. Bioengineered small bowel has been initiated using biomaterials such as small intestinal submucosa (SIS) and polyglycolic acid. These materials act as a scaffold to organize cells into tissues. The objective is to encourage ingrowth of intestinal cells and generation of new small intestinal tissue. Rat studies have been performed and show promise [60, 61]. Experiments show that structurally, all layers of the bowel wall can be created. Tissue-engineered intestine was lined by columnar epithelium, goblet, and Paneth cells; however, the unit's ability to absorb water and nutrients was poor. To date, no evidence of innervation of the neointestine has been demonstrated. It is possible that innervation does not occur or that it requires a much longer period of follow-up than previous animal studies have permitted. If tissue-engineered small bowel becomes feasible, it could provide a new treatment option for this very complex group of infants with SBS.

Conclusions

Short bowel syndrome is a complex condition with significant morbidity and mortality. These patients require the expertise of a multidisciplinary team. The advent of TPN provided these acutely ill patients a chance at survival, but TPN is also the cause of life-threatening complications. Fortunately, most children with SBS will adapt spontaneously over time. Children who remain TPN-dependent are candidates for one of several adjunctive operations that promote adaptation by optimizing intestinal function, motility, and surface area. The choice of procedure must be individualized. Patients with a short and dilated bowel should receive an intestinal lengthening and tapering procedure such as the Bianchi or STEP. If the bowel is not dilated, then a colonic interposition is an option. Alternatively, creation of an intestinal valve to induce dilatation followed by a lengthening procedure could be beneficial. If bowel length is adequate but the bowel is dilated, then a simple tapering enteroplasty or plication would suffice.

Objective assessments of outcomes from the various surgical techniques are lacking because of the relatively small number of patients at individual institutions and the lack of a consistent definition of SBS. All these procedures, however, do provide options of less magnitude than intestinal transplantation.

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