ABSTRACT: Intestinal failure (IF) is a condition where there is insufficient functional bowel to allow for adequate nutrient and fluid absorption to sustain adequate growth in children. Several etiologies can predispose to IF, including necrotizing enterocolitis, gastroschisis, and intestinal atresias. Intestinal rehabilitation can be seen as a 3-pronged strategy merging nutrition, pharmacologic, and surgical approaches to achieve the ultimate goal of enteral nutrition. Nutrition approaches should seek to facilitate transition from parenteral nutrition (PN) to enteral nutrition because prolonged use of PN is associated with severe morbidity and mortality. Enteral nutrition, on the other hand, promotes and enhances an adaptive response in the intestine. Medications used in the treatment of IF may help alleviate symptoms of diarrhea, bacterial overgrowth, and gastrointestinal dysmotility. Surgical procedures, such as longitudinal intestinal lengthening and tapering (LILT) or serial transverse enteroplasty (STEP), can increase mucosal surface area and may enhance intestinal adaptation. IF is a difficult disease process with a complex patient population and is best guided through this 3-pronged approach by a multidisciplinary team featuring surgeons, gastroenterologists, dietitians, pharmacists, and nurses.

Intestinal Failure

Various definitions of intestinal failure (IF) have been proposed. Perhaps the simplest is that IF is a condition of malabsorption of fluid and nutrients, necessitating parenteral nutrition (PN) to sustain adequate growth in children. Etiologies of IF are detailed in Table 1. Many of these conditions do not intrinsically cause IF, but their natural histories often mandate surgical resection of bowel.

Nutrition Approaches to IF

PN
Arguably, there has been no greater advancement in managing IF than the use of PN in patients with enteral intolerance. IF patients are susceptible to significant fluid losses and electrolyte imbalances. Emesis, stomal output, and diarrhea are several symptoms that alter fluid balance. Care must be taken to adjust the PN content, and replenish the patient with additional hydration fluid. Typically, PN should be maintained as a standard formula, whereas additional losses are replaced on an individual basis. Measurement of electrolytes in urine and stomal output is helpful in assessing electrolyte supplementation. Acute electrolyte deficiencies can be supplemented in replacement fluids as an adjunct to PN. When the patient’s fluid and electrolyte status has stabilized, these supplements can be incorporated into the PN components.

Management of PN-Associated Liver Disease (PNALD)

Although PN has allowed for the provision of nutrients and calories, pediatric patients are susceptible to PN-associated cholestasis and subsequent liver damage. Ironically, the very therapy that sustains patients with short bowel syndrome (SBS) may also be hepatotoxic. Between 40% and 60% of IF patients who require long-term PN develop liver-associated disease. Infants and children often present with cholestasis, whereas adolescents present with steatosis. Ursodeoxycholic acid and siscalide have been used to prevent or treat PNALD, but with limited effectiveness.\(^1\) Ursodeoxycholic acid is a hydrophilic bile acid that improves bile acid flow and displaces toxic acids. It reduces the clinical signs and symptoms of cholestasis, but does not prevent disease progression. To prevent interactions with cholestyramine, ursodeoxycholic acid should be
taken 1 hour before or 4–6 hours after cholestyramine administration.

It has been demonstrated that lipids are metabolized differently depending on their route of administration. Enteral lipids are absorbed by the enterocyte in the form of a micelle and packaged into chylomicrons for ultimate disposal in the liver. In the bloodstream, these particles rapidly acquire apolipoproteins from circulating high-density lipoproteins and subsequently can be metabolized by the liver. The emulsified particles of commercially made and IV-administered lipid emulsions, such as Intralipid (Kabi Pharmacia, Clayton, NC), mimic the size and structure of chylomicrons but differ in their content. In contrast to chylomicrons, artificial lipid particles primarily contain essential fatty acids, such as ω-6 fatty acids and triglycerides, but are devoid of cholesterol or protein. Recent studies have suggested that these ω-6 fatty acid–containing emulsions are dependent on lipoprotein lipase, apolipoprotein E, and low-density-lipoprotein receptors for clearance, and are metabolized with less lipolysis and release of essential fatty acids than chylomicrons. In fact, it appears that they may be cleared as whole particles by tissues other than the liver. These factors may account for the increased incidence of steatosis associated with IV administration of IV lipid emulsion products.

There are several methods that clinicians can use to reduce the risk of PN-associated cholestasis. In neonates and infants, PN caloric intake should be limited to 90–100 kcal/kg to avoid overfeeding. In addition, attempts should be made to cycle PN 2–6 hours a day, which promotes the cyclic release of gastrointestinal (GI) hormones. Patients that exhibit signs and symptoms of infections, bacterial overgrowth, or line sepsis should be aggressively treated. Last, efforts should be made to encourage and advance enteral nutrition.

An exciting and recently published case report discusses the potential role of IV fat emulsion to treat infants receiving prolonged courses of PN complicated by PNALD. Clinicians should consider stopping all conventional lipid emulsions and instead providing 1 g/kg/d as parenteral fish oil. Lower doses of Omegaven may not be effective and may predispose patients to essential fatty acid deficiency, which has also been linked to the development of fatty liver.

**Enteral Nutrition**

Despite the benefits of PN, however, the ultimate goal for all patients should be to achieve enteral tolerance. Enteral feeding, regardless of whether it is oral or via a feeding tube (eg, nasogastric tube or gastrostomy), promotes physiologic responses that may enhance the intestine’s adaptation process. Mucosal hyperplasia, for example, is stimulated through direct contact with epithelial cells; stimulation of gastric, biliary, and pancreatic secretions; and enhanced production of trophic hormones. Early enteral feeding (ie, within 6 weeks after intestinal resection) reduces the duration of PN, as well as the associated risk of PN-associated cholestasis.

Oral feedings of infants can prevent feeding aversion, as a result of learning how to suck and swallow. Continuous enteral feedings achieve total and constant saturation of intestinal transporters, thus using the full extent of the remaining absorptive surface area. Bolus feedings are another method of providing enteral nutrition in older children, but are poorly tolerated in infants.

Multiple administration routes can be used for enteral nutrition. Patients who receive bolus or continuous feedings should also be encouraged to eat orally. Patients should be engaged in oral motor stimulation therapy if needed. Early referral to occupational and speech therapists is important, especially given the difficulty in treating feeding aversion in SBS patients.

Patients may initially require PN support until they tolerate goal enteral nutrition. Enteral feedings should be advanced steadily as clinical status permits. Parenteral calories are simultaneously decreased by rate or number of hours to ensure nutrition status and fluid balance. It is not uncommon to have some GI intolerance as feedings are advanced. Typically, however, fecal samples should have reducing substances <1% and a fecal pH above 5.5. Severe carbohydrate malabsorption is identified if fecal reducing substances are >1% and fecal pH is <5.5.

**Transition to Enteral Nutrition: Factors for Consideration**

Once patients with SBS are successfully transitioned from PN to enteral nutrition, care must be taken to avoid nutrient deficiencies. As previously noted, fat malabsorption predisposes patients to deficiencies in the fat-soluble vitamins, as well as in zinc, calcium, and magnesium. In patients with ileal resection, cyanocobalamin (vitamin B₁₂) deficiency may occur. Some centers will administer pancreatic enzymes with fat malabsorption to improve nutrient absorption.

### Table 1
**Common etiologies of pediatric intestinal failure**

<table>
<thead>
<tr>
<th>Short bowel syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrotizing enterocolitis</td>
</tr>
<tr>
<td>Gastrochisis</td>
</tr>
<tr>
<td>Intestinal atresia</td>
</tr>
<tr>
<td>Midgut volvulus</td>
</tr>
<tr>
<td>Dysmotility disorders</td>
</tr>
<tr>
<td>Hirschsprung’s disease</td>
</tr>
<tr>
<td>Pseudo-obstruction</td>
</tr>
<tr>
<td>Congenital diseases</td>
</tr>
<tr>
<td>Microvillous atrophy</td>
</tr>
</tbody>
</table>
**Dietary Modifications**

Only a small number of evidence-based studies exist regarding diet modifications for IF. These studies do not allow for a consensus regarding the efficacy of peptide-based diets. One study has shown an improvement in nitrogen absorption, whereas others have failed to demonstrate a significant impact. The benefits of an amino acid–based formula over a protein hydrolysate is also unclear. It is true, however, that IF patients are predisposed to intestinal mucosal barrier breakdown, bowel dilatation, and bacterial overgrowth, all of which may increase the risk of food allergies. As a result, amino acid–based formulas may reduce the risk of the development of food allergies.

Although protein provides little osmotic load, simple carbohydrates, such as sucrose and fructose, can lead to osmotic diarrhea. GI bacteria break down these simple sugars in osmotically active acids that increase the osmotic load. In contradistinction, complex carbohydrates found in pasta, potatoes, and breads are well tolerated and, if possible, should comprise the majority of energy intake. Fat can be a significant source of energy intake for IF patients. Unfortunately, fat is not well tolerated due to bile salt malabsorption, which leads to decreased micelle formation and fat digestion. Medium-chain triglycerides (MCTs) compared with long-chain triglycerides (LCTs) do not require micelles for absorption and thus are better tolerated in patients with bile acid or pancreatic insufficiency. MCTs, however, also increase the osmotic load in the intestine and provide fewer calories than LCTs. In addition, LCTs may stimulate intestinal adaptation after intestinal resection. In SBS patients with a colon in continuity, it has been shown that a mixture of an MCT and LCT diet can improve energy and fat absorption.

The addition of fiber to the diet can decrease overall intestinal transit time. In patients with a colon in continuity, the metabolism of fiber can serve as an energy source, as well as lead to the production of short-chain fatty acids (SCFAs). SCFAs, such as butyrate, are considered a fuel source for colonocytes and also enhance sodium and water absorption, thereby reducing stool output and sodium losses.

Of the formulas available, Alimentum (Ross, Columbus, OH), Pregestimil, and Nutramigen (Mead Johnson, Evansville, IN) are “semielemental” hypoallergenic formulas with hydrolyzed casein as the protein source, not amino acids. Nutramigen is the most nutritious choice for babies with moderate protein allergies. The most elemental formulas are Elecare (Ross) and Neocate (SHS, Gaithersburg, MD). Both have amino acids as a protein source. Elecare has 33% MCT and Neocate has only about 5% MCT as a fat source. Babies with severe protein allergies or multiple food allergies should be given Elecare or Neocate. In babies with severe fat mal-absorption and SBS, Elecare may be preferable.

**Pharmacologic Approaches to IF**

Patients with SBS often require unique therapies to assist in bowel adaptation (Table 2). Depending on the patient, they may require prokinetic agents or anti-diarrheal agents or a combination of both. Other therapies such as the use of IV fish oil have been used to treat PN-associated liver injury in these patients. Due to the complexities of SBS, dosage recommendations are often quite different from established norms.

**Antimotility Agents**

In SBS, gut motor activity is typified by a normal feeding pattern, along with more frequent interdigestive motor complexes and a marked reduction in phase 2 activity. Loperamide is often used in these patients to reduce transit rate and enhance absorption. By reducing intestinal motility, water and sodium output from an ileostomy is reduced by approximately 20%–30%. It acts to enhance the general muscle tone of the small intestine, thus increasing water and nutrient absorption. The drug works by way of intestinal opioid receptors, acting directly on intestinal muscles to inhibit peristalsis. Loperamide is preferred over opiates such as codeine because it is not a sedative or addictive. Because it undergoes enterohepatic circulation (which is altered in patients with SBS), higher doses are often needed; doses as high as 0.8 mg/kg/d to a maximum of 24 mg/d may be required. It should not be used in patients with slow transit times or those with refractory small bowel bacterial overgrowth. The liquid formulation of loperamide should not be used due to its sorbitol and alcohol content.

**Prokinetic Agents**

Intolerance to enteral nutrition continues to be a problem with SBS. Nausea, vomiting, and abdominal distention are common signs and symptoms. Prokinetic agents such as metoclopramide, erythromycin, and cisapride have been shown to promote gastric motility in these patients. Side effects, however, limit their usefulness. Metoclopramide, a central and peripheral dopamine type 2 receptor antagonist, has a variety of central nervous system side effects, including dystonic reactions, extrapyramidal side effects, and tardive dyskinesia. Erythromycin has been used as a motilin receptor agonist. All are associated with a wide number of potentially serious drug interactions.

Cisapride, a 5-HT₃ agonist, is associated with serious cardiac arrhythmias and sudden death, limiting its usefulness. Cisapride has been part of an FDA-mandated limited-access protocol in the United States since May 2000 due to concerns of adverse cardiac events. The prescribing physician participating in the limited-access program must be board eligible or certified in 1 or more of the follow-
<table>
<thead>
<tr>
<th>Indication</th>
<th>Medication</th>
<th>Typical dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimotility agents</td>
<td>Loperamide</td>
<td>0.08–0.24 mg/kg/dose PO q 8–12 h; maximum dose 2 mg (0.8 mg/kg/d)</td>
<td>Use tablets, avoid liquid formulations.</td>
</tr>
<tr>
<td>Prokinetics</td>
<td>Cisapride</td>
<td>Neonates: 0.15–0.2 mg/kg/dose 3–4 times/d (maximum dose: 0.8 mg/kg/d)</td>
<td>May cause QT prolongation; numerous drug interactions; only available via compassionate use protocol.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infants and children: 0.15–0.3 mg/kg/dose 3–4 times/d (maximum dose: 10 mg/dose)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>2–3 mg/kg/dose PO or IV q 6–8 h has been used; lactobionate initial dose of 1–3 mg/kg IV infused over 60 min followed by 10–20 mg/kg/d orally in 2–4 divided doses before meals</td>
<td>Involved in many drug interactions; prokinetic at low doses but causes gastric antral spasm and delayed gastric emptying at high doses; oral route preferred; serious cardiac complications including arrest have occurred with IV administration.</td>
</tr>
<tr>
<td></td>
<td>Metoclopramide</td>
<td>Oral, IM, IV: Neonates, infants and children: 0.4–0.8 mg/kg/d in 4 divided doses</td>
<td>High incidence of central nervous system effects.</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Octreotide</td>
<td>Wide dosing variation exists IV, subcutaneous: begin with 1–10 μg/kg every 12 h and increase by 0.3 μg/kg/dose at 3-d intervals</td>
<td>Dose titrated to stool output. May cause hyper- or hypoglycemia. According to animal data, suppression of growth hormone may be of concern when used as long-term therapy in children.</td>
</tr>
<tr>
<td></td>
<td>Ursodeoxycholic acid (urso, ursodiol)</td>
<td>Infants and children: 30 mg/kg/d in 3 divided doses</td>
<td>May cause diarrhea; liquid formulation must be specially compounded.</td>
</tr>
<tr>
<td></td>
<td>Cholestyramine</td>
<td>240 mg/kg/d in 3 divided doses (maximum dose: 4 g 1–2 times per day)</td>
<td>Interacts with ursodeoxycholic acid.</td>
</tr>
</tbody>
</table>

IM, intramuscular; q, every.
ing areas: internal medicine (including gastroenterology and cardiology), family practice, pediatrics (including neonatology), or surgery. As part of this program, institutional review board (IRB) approval completion of a Form FDA 1572 and signed informed consent are required.30

Tegaserod (Zelnorm; Novartis, East Hanover, NJ), a selective 5-HT4 receptor agonist, stimulates peristalsis and accelerates colonic transit.29,31 Originally approved for irritable bowel syndrome (constipation type) in women, doses of up to 12 mg/d have been used to accelerate small bowel and colonic transit. It modulates both normal and altered motility throughout the GI tract. Evidence supporting its use is limited to case series in critically ill adults to advance enteral feedings in the presence of impaired gastric motility.32 Because its main metabolic pathway is presystemic, no clinically relevant drug-drug interactions have been identified. It does not cross the blood-brain barrier, nor does it have cardiac repolarization effects or QTc-interval prolongation.33 In March 2007, however, tegaserod was withdrawn from the market over concerns of increased risks of cardiovascular events, such as heart attacks and strokes.

Antisecretory Drugs

Patients with SBS, especially children, often develop gastroesophageal reflux. Contributing factors include altered gut secretions, dysmotility, and bacterial overgrowth. Gastric acid hypersecretion may occur during the early weeks after a small bowel resection. H2 antagonists and proton-pump inhibitors have both been used for this purpose because acid blockade can reduce jejunostomy output. Parenteral administration may be preferred, especially in those patients with extremely short bowel, where drug absorption is less than optimal. Octreotide, a somatostatin analog, has been shown to have an inhibitory effect on gut motility.34 It has been shown that long-acting octreotide may be useful in prolonging small bowel transit time in adults with SBS.35 It reduces ileostomy output and large-volume jejunostomy output. Experience with these drugs in children is limited.

Table 3
Comparison of agents used for treatment of bacterial overgrowth (typical course 7–10 days; all meds are to be given orally)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pediatric dose</th>
<th>Comments</th>
<th>% Orally absorbed</th>
<th>% Renally excreted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin</td>
<td>&lt;5 years: 100 mg bid</td>
<td>Injection given orally</td>
<td>9%</td>
<td>40% (2%–5% active)</td>
</tr>
<tr>
<td>Augmentin</td>
<td>10 mg/kg/dose bid</td>
<td>Complete (amoxicillin)</td>
<td>30%–40%</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacina</td>
<td>20–40 mg/kg/d bid</td>
<td>50%–80%</td>
<td>30%–50%</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>10–30 mg/kg/day</td>
<td>90%</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Colistin</td>
<td>&lt;5 years: 25 mg</td>
<td>Injection given orally</td>
<td>Insignificant</td>
<td>75% in 24 hours</td>
</tr>
<tr>
<td></td>
<td>2–4 times/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5–12 years: 50 mg 2–4 times/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>&gt;8 yrs: 100 mg bid</td>
<td>Injection given orally</td>
<td>100%</td>
<td>23%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>2 mg/kg/dose bid</td>
<td>Injection given orally</td>
<td>None</td>
<td>100%</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>10 mg/kg/dose bid</td>
<td>Available as tablets only</td>
<td>90%</td>
<td>10%</td>
</tr>
<tr>
<td>Neomycin</td>
<td>50 mg/kg/day</td>
<td>Divided every 6 hours</td>
<td>3%</td>
<td>0.9%–1.5%</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>&gt;8 years: 25–50 mg/kg/day in divided doses every 6 hours</td>
<td>Injection given orally</td>
<td>75%</td>
<td>60%</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>&lt;5 years: 10 mg 2–4 times/day</td>
<td>Injection given orally</td>
<td>Poor</td>
<td>90%–95%</td>
</tr>
<tr>
<td>Rifaxamin</td>
<td>Not established</td>
<td>Non formulary at Children’s Hospital of Boston</td>
<td>&lt;0.4%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>125 mg every 6 hours (10 mg/kg/dose qid)</td>
<td>Poor</td>
<td>Oral doses primarily via feces</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Max total daily dose 2 g/day</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

bid, twice daily; qid, four times daily; tid, three times daily.
Antimicrobials (Table 3)

Intestinal bacterial translocation often predisposes patients with SBS to sepsis. Reflux of bacteria from the colon up into the small intestine, in tandem with poor motility, which prevents flushing of gut bacteria in an antegrade fashion, bowel dilation, and stasis of the small bowel all promote bacterial overgrowth. This results in inflammation of the mucosal surface and impairs both adaptation and transport of nutrients. Bacterial overgrowth may also cause deconjugation of bile acids, resulting in bile acid deficiency. Symptoms include abdominal distention, cramping, diarrhea, and weight loss. Mental status changes can occur due to accumulation of β-lactate.

Short courses of oral antimicrobials are the mainstay of therapy in the management of bacterial overgrowth. Most protocols include metronidazole with or without trimethoprim/sulfamethoxazole, aminoglycosides, extended-spectrum penicillins/cephalosporins, or vancomycin. Some centers also include a week of antifungals such as amphotericin B. Due to product design limitations, oral administration of injectable products may be necessary. Typically, antimicrobials are given for 1 week per month, although some patients may require continuous administration. Concerns about the development of resistance may require rotating the agents in the protocol.

In addition to antimicrobials, other therapies have been used to reduce bacterial overgrowth. Periodic flushes with oral polyethylene glycol electrolyte solutions or other cathartics have been used. Probiotics, such as Lactobacillus rhamnosus GG, have been used, although additional studies are needed.

Mineral Supplementation

Magnesium deficiency is often seen in patients with a jejunoileal anastomosis or those with jejunostomies as a result of hyperaldosteronism secondary to dehydration and sodium depletion. Once water and sodium depletion is corrected, magnesium supplementation is often necessary. Most oral magnesium products have poor bioavailability in this patient population, making IV administration the preferred route of delivery. If oral products must be used, magnesium oxide salts are preferred.

Vitamin Deficiencies

Children with IF, especially those with hepatic disease, are at risk for developing a variety of fat-soluble vitamin deficiencies because of fat malabsorption and inadequate dietary intake. Table 4 contains dosing recommendations for children with malabsorption syndrome, as well as cholestasis. Even with supplementation, children with mild to moderate cholestatic liver disease are at risk for developing phyloquinone (vitamin K) deficiency. Traditional assessment of vitamin K status (ie, prothrombin time) may be inadequate, and recently, it has been suggested that elevations in PIVKA-II (protein induced by vitamin K absence-II) concentrations may be a more sensitive marker of vitamin K stores. Vitamin K concentrations are directly correlated with the severity of liver disease. Traditional doses of supplemental oral vitamin K (2.5–5 mg, 2–7 times a week) seem to be inadequate to meet the needs in >50% of the children studied.

Similarly, low vitamin A concentrations are present in children with cholestatic liver disease receiving routine vitamin supplementation. Altered hepatic synthetic function, however, may also decrease retinol binding protein synthesis, suggesting that unbound vitamin A concentrations could actually be elevated in liver failure. Interestingly, vitamin E levels remain normal in this population, although unsupplemented infants and children continue to demonstrate deficiencies.

Nutritional Supplements: Growth Hormone and Glutamine

Enhancement of intestinal adaptation continues to be an attractive alternative in the management of patients with SBS. Rodent studies have described improved intestinal adaptation with the use of growth hormone (GH) or insulin-like growth factor-1 (IGF-1). IGF-1 has been shown to decrease PN-associated mucosal atrophy and in combination with glutamine has increased villous growth and intestinal DNA. GH, through IGF-1 signaling, has been proposed as a potential treatment option for patients with IF. In animals receiving PN, mucosal atrophy with glutamine deficiency can occur, and glutamine supplementation reverses the loss of mucosal thickness. Further, glutamine may improve gut immunity because it has been shown to prevent PN-associated depletion of immunoglobulin A, which produces gut lamina propria plasma cells.

To date, there is insufficient evidence to support the use of GH, glutamine, or a combination of the 2 as standard therapy in IF patients. There have been several small studies that evaluated the use of GH, or a combination of GH and glutamine, that have demonstrated an improved nutrient absorption and ability to wean off PN. Increased lean body mass was shown in 2 studies, using GH and glutamine. Other studies, however, have failed to demonstrate clinical improvement in fecal volume or intestinal absorption. None of these studies, including those with positive findings, have shown statistically significant increases in fat absorption.

Other Considerations

Because many drugs tend to be incompletely absorbed by patients with SBS, high doses may be required. Drugs such as digoxin and levothyroxine may be given parenterally to ensure consistent ther-
<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Deficiency state</th>
<th>Recommended preparations</th>
<th>Recommended dose in malabsorption syndrome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>Night blindness, xerophthalmia, keratomalacia, Bitot's spots</td>
<td>Retinol (water soluble) palmitate injection: 50,000 units/mL (15 mg retinol/mL)</td>
<td>Prophylaxis: children &gt;8 years and adults, 10,000–15,000 units/d water-miscible product orally; suggested dose for infants with cholestasis receiving enteral feedings is 3000 units/d (provided in 2 mL of infant multivitamin drops)</td>
<td>Adjust dose according to levels, check levels regularly in prolonged therapy. Patients receiving doses &gt;25,000 units/kg should be closely monitored for toxicity. Injectable form may be given orally. 1 USP vitamin A unit = 0.3 μg all-trans isomer of retinol, 1 RE = 1 μg of all-trans retinol. It is recommended that vitamin A be administered with bile salts to patients with malabsorption caused by inadequate bile secretion.</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Rickets, osteomalacia, dental caries, hypocalcemia, hypophosphatemia, phosphaturia, aminoaciduria</td>
<td>Ergocalciferol (vitamin D₂, calciferol, Drisdol)</td>
<td>Suggested dose for infants with cholestasis receiving enteral feedings is 1200 units/d (provided by 2 mL of infant multivitamin drops plus 400 units additional)</td>
<td>1.25 mg ergocalciferol provides 50,000 units of vitamin D activity.</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Anemia, hemolysis, neurologic deficits (wide-based gait, decreased DTRs)</td>
<td>α-Tocopherol polyethylene glycol succinate (water soluble)</td>
<td>Full-term neonates: 5 units/L of formula PO; chronic cholestasis (oral): 50 units/kg/d, and increase in 50 unit/kg/d increments to 150–300 units/d; alternative dosage for infants with cholestasis receiving enteral feedings is 50 units PO daily</td>
<td>1 unit vitamin E = 1 mg δ-α-tocopherol acetate. Necrotizing enterocolitis is reported with oral administration of large dosages (&gt;200 units/d) of hyperosmolar vitamin E preparations in low-birth-weight infants. Adjust dose according to blood levels. Severe reactions resembling anaphylaxis/hypersensitivity were reported during or immediately after IV administration. Chronically ill children receiving long-term antibiotics may require larger doses.</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>Coagulopathy, prolonged PT, abnormal bone matrix synthesis</td>
<td>Phytonadione, vitamin K₁</td>
<td>Suggested dose for infants with cholestasis receiving enteral feedings is 2.5 mg PO QOD or 1 mg SQ q/week</td>
<td></td>
</tr>
</tbody>
</table>
apeutic blood concentrations. Similarly, medications and vitamins that undergo enterohepatic recirculation such as loperamide and vitamin A may require higher than normal doses. Because patients with SBS are prone to dumping syndrome, practitioners should also be careful to avoid hypertonic liquid medications or those products containing sorbitol.

Emerging Therapies

Glucagon-like peptide 2 (GLP-2) has generated recent attention as a potential agent in the management of patients with IF. There have been several studies describing the various gastrointestinal properties of GLP-2, such as enhanced epithelial and mucosal proliferation,60,61 improved gastric motility,62 and decreased gastric secretion.63 The initial studies using GLP-2, or its protease-resistant analog Teduglutide, have demonstrated improvements in intestinal absorption and decreases in fecal volumes.64,65 Studies with large sample sizes are ongoing.

Pharmaceutical care of the patient with SBS is complex and ever changing as intestinal function improves or complications develop. Pharmacologic therapy is directed at controlling gut motility, enhancing intestinal adaptation, minimizing small bowel overgrowth, and preventing nutrient deficiencies and hepatic complications. No single approach is effective for all patients with SBS, and care must be directed toward specific patient conditions, using an integrated team approach.

Surgical Approaches to IF

In addition to medical and pharmacologic treatments for IF, some patients may require surgical management. Surgical indications for IF can be divided into 2 categories: (1) procedures aimed at correcting the etiology of IF, and (2) procedures addressing the numerous complications from IF.

Initial surgeries focus on the correction of anatomic or mechanical abnormalities that threaten the patient's bowel or life. Diseases such as necrotizing enterocolitis, gastrochisis, volvulus, and intestinal atresias all can result in the resection of a large percentage of small and large bowel. The major principles of management are bowel conservation (especially small intestine) and the prompt reestablishment of bowel continuity.8

Surgical management of IF should not be viewed as a last resort but rather an integral aspect of intestinal rehabilitation. Although not fully understood, the small intestine undergoes an adaptation process that may consist of histologic and enzymatic changes, enhancing nutrient absorption and improving bowel motility. Surgeons have used various techniques to manage the symptoms of IF. In 1980, a method of longitudinal intestinal lengthening and tailoring (LILT) was developed.66 This method takes advantage of the 2 leaves of the

mesenteric blood supply to the intestines by dividing the bowel longitudinally, at the 12 o'clock position (with the mesentery at the 6 o'clock position). Next, these hemiloops are anastomosed isoperistaltically, resulting in bowel that is smaller in diameter and longer in length. Isolated bowel segments, in which there is an imported blood supply to the antimesenteric border of a dilated bowel loop by attachment to the abdominal wall, have also been attempted.67 A useful adjunct to bowel-lengthening procedures is the creation of a nipple valve.68 This valve, tailored to cause proximal bowel dilation without obstruction, can facilitate a bowel-lengthening operation.

Outcomes With LILT

Reported survival after LILT ranges from 30% to 100%.69,70 Survivors that were successfully weaned off PN ranged from 28% to 100%.69,70 The wide disparity in mortality and reduction of PN dependence can likely be attributed to multiple variables among institutions, including preoperative bowel length and degree of liver failure. Furthermore, many of the reported series have been limited by small sample sizes, with the largest including 49 patients.70 Bowel necrosis with LILT has also been reported.70

Serial Transverse Enteroplasty

The technique of serial transverse enteroplasty (STEP) was described more recently.71,72 In this operation, a stapler is applied across the dilated bowel in an alternating fashion, leaving a zigzag-shaped bowel (Figure 1). This approach both length-
ens and tapers the dilated bowel without damaging the mesenteric blood supply or diminishing mucosal surface area.

A salient advantage of the STEP procedure is that it is simple to perform. Because of the adaptation process, there can be reflation of the bowel after a LILT operation. Further, bowel segments of variable dilation can be lengthened with the maintenance of a uniform channel. Multiple STEP procedures are feasible by repeating the operation after the process of adaptation and dilation has occurred.\(^{73,74}\) The STEP procedure is also suitable for patients with neonatal atresias and limited bowel length, as well as patients with refractory \(\alpha\)-lactic acidosis.\(^{71,75–77}\) Initial studies demonstrated that after the STEP procedure, there are improvements in enteral tolerance, nutrition indices, and ability to wean off PN.\(^{74,75,79}\)

### Outcomes With STEP

Recent data from the International STEP Registry, examining a total of 38 patients, demonstrated a substantial increase in intestinal length and improvement of enteral tolerance.\(^{74}\) In the SBS cohort, nearly 50% of patients were successfully weaned off PN.

### Transplantation

Commonly cited indications for transplantation include failure to wean off of PN, PN-associated liver disease, recurrent central catheter sepsis, and loss of vascular access to provide PN.\(^{80}\) Similar to the LILT and STEP procedures, intestinal transplantation should be viewed as an adjunct to intestinal rehabilitation.

Historically, intestinal transplantation was complicated by significant morbidity and mortality. With recent advances in immunosuppression, specifically the use of tacrolimus, outcomes such as mortality, cost-effectiveness, and quality of life have improved over the last decade.\(^{81}\) Currently, patients undergoing intestinal transplants experience 1-year graft survivals of 80% and survival of 80%.\(^{82}\)

Three different types of transplants can be offered to patients depending on the nature and extent of their IF: isolated intestinal, liver-intestinal, and multivisceral (eg, stomach, duodenum, pancreas, intestine, and liver). Recent data show that of pediatric intestinal transplantations, 50% are liver-intestinal, 37% are isolated, and 13% are multivisceral.\(^{82}\) The decision regarding the type of transplantation should be based on each patient’s specific disease and condition.

### Conclusion

Intestinal rehabilitation for pediatric patients with IF is best approached in a multidisciplinary fashion. With specialized nutritionists, pharmacists, gastroenterologists, nurses, and surgeons, patients can be provided with complex medical care tailored to their specific needs. The overriding goal remains the use of the GI tract for oral/enteral nutrition.

### References


