AGA Technical Review on Short Bowel Syndrome and Intestinal Transplantation

This literature review and the recommendations therein were prepared for the American Gastroenterological Association Clinical Practice Committee. This paper was approved by the Committee on August 5, 2002, and by the AGA Governing Board on November 1, 2002.

The normal human small intestine length is generally considered to be between 3 and 8 meters, depending upon whether radiologic, surgical, or autopsy measurements are made.\(^1\) Short bowel syndrome (SBS) occurs when there is <200 cm of bowel remaining. This is an approximate length as most methods of residual intestine measurement (such as radiologic contrast studies, pathology of the resected specimen, and perioperative measurement of unweighted intestine) are not especially accurate. Because absorption is related to the amount of residual intestine, it is more important to document the amount of remaining, viable intestine.

Those patients at greatest nutritional risk generally have a duodenostomy or a jejunoileal anastomosis with <35 cm of residual small intestine, jejunocolic or ileocolic anastomosis with <60 cm of residual small intestine, or an end jejunostomy with <115 cm of residual small intestine.\(^6\)–\(^8\) It has been suggested that intestinal failure is better defined in terms of fecal energy loss rather than residual bowel length.\(^9\) Given the observations that fecal energy loss does not always correlate well with residual bowel length,\(^9\) and the significant individual variability in jejunal absorption efficiency,\(^10\) it is reasonable to consider a more standardized approach to defining intestinal failure and “functional” SBS from a clinical standpoint. However, fecal energy loss is a function of both energy intake and energy absorption. Patients who are unable to increase their oral intake sufficiently or are unable to absorb sufficient energy despite significantly increased intake, are defined as patients with intestinal failure and require parenteral nutrition support. A standardized diet may be useful for clinically defining functional SBS, although there is insufficient data with regard to what the composition of such a diet optimally should be.

Methods

Most available data on the treatment of SBS are based on retrospective analyses of case series (type II-3 or type III data) and are often few in number, because of the rareness of the covered diseases, where randomized, controlled trials were undertaken (type 1 and type IIb data), and the studies are described in detail. Data and reports were obtained from extensive PubMed and Medline searches using several key words, including SBS, various conditions predisposing to SBS, parenteral nutrition, enteral nutrition, relevant specific nutritional deficiencies, intestinal surgery, and intestinal transplantation. In addition, surgical and gastroenterological texts, published national and international scientific meeting abstracts, and the extensive manuscript/abstract files of the authors were reviewed. Expert opinion was sought for the few areas in which no suitable published reports existed (e.g., TPN cycling and preparation of the patient for home TPN).

Human data and reports were reviewed exclusively.

Patients with functional SBS who have severe malabsorptive processes related to refractory sprue, chronic intestinal pseudo-obstruction syndrome, or congenital villus hypoplasia are not the specific focus of this technical review, although most of the medical and nutritional management problems and therapies are similar, if not identical.

Incidence and Prevalence of Short Bowel Syndrome

It is unclear how many individuals in the USA suffer from SBS, but based on the numbers in Europe, the incidence may be ≈2 per million.\(^11\) More recent data from 1993 indicated the incidence and prevalence of home parenteral nutrition, for which SBS was the most prevalent indication, increased slightly to 2–3 per year.
per million inhabitants and 4 per year per million, respectively. The most recent European survey, in 1997, indicated the incidence of home TPN increased slightly to \( \geq 3 \) per million and the prevalence had increased to 4 per million. SBS constituted the largest single group of patients who required home TPN (35%). In comparison, the most recent data for incidence and prevalence in the USA is from 1992. At that time, it was estimated based on extrapolated data from the Oley Foundation Home TPN Registry that \( \approx 40,000 \) patients required TPN each year. Approximately 26% of the patients in the Oley registry had SBS, although some patients with a primary TPN indication of malignancy or radiation enteritis may have had SBS as well. These numbers for either Europe or the USA do not reflect patients with SBS who never required TPN or for whom TPN could be discontinued successfully. Approximately 50%–70% of the short bowel patients who initially require TPN can be weaned off TPN successfully in optimal settings with better outcomes in children. Therefore, the number of patients with SBS may be substantially greater than previously estimated. A registry of short bowel patients, including those who require TPN permanently, transiently, and not at all, should be implemented.

**Pathophysiology of Short Bowel Syndrome**

SBS may be a congenital or acquired condition. Infants born with intestinal atresia (jejunal or ileal) constitute the congenital forms. Otherwise, SBS results from surgical resection of bowel. This is usually related to multiple resections for recurrent Crohn’s disease, massive enterectomy made necessary because of a catastrophic vascular event (such as a mesenteric arterial embolism or venous thrombosis, volvulus, trauma, or tumor resection in adults, and in children, gastrochisis, necrotizing enterocolitis), intestinal atresias, and extensive aganglionosis. Functional SBS may also occur in cases of severe malabsorption where the bowel length is often intact. Such conditions may include chronic intestinal pseudo-obstruction syndrome, refractory sprue, radiation enteritis, or congenital villus atrophy. Severe nutrient and fluid malabsorption occurs following extensive small intestinal resection. Patients with \(<100\) cm of jejunum remaining generally have a net secretory response to food. Patients can be grouped into 2 distinct subgroups: those with intact colon in continuity and those without colon in continuity. In patients with SBS, the colon becomes an important digestive organ. The colon absorbs sodium, water, and energy from short-chain fatty acids (SCFAs) (see below discussion regarding soluble dietary fiber).

**How Does the Remaining Intestine Adapt Following Resection?**

Patients often clinically adapt to the significantly reduced energy absorption associated with SBS through hyperphagia. However, the intestine adapts as well to ensure more efficient absorption per unit length. After massive enterectomy, the intestine hypertrophies and becomes more efficient in nutrient absorption; there is slight lengthening, but more importantly, diameter and villus height increase, effectively increasing the absorptive surface. This process may evolve over 1 or 2 years. Several factors are important determinants in the functional adaptation process and clinical outcome. These include the presence or absence of the colon and ileocecal valve, length of remaining bowel, health of the remaining bowel, patient age, and comorbid conditions. Although the length of remaining bowel necessary to prevent dependence on TPN is \( \approx 100 \) cm in the absence of an intact and functional colon or \( 60 \) cm in the presence of a completely functional colon, the degree of adaptation and TPN dependence may be highly individualized. In infants, adaptation to full enteral nutrition has been reported with as little as \( 10 \) cm of residual intestine. However, Carbonnel et al. found small bowel length, determined radiographically, to be an independent risk factor for loss of nutritional autonomy in 103 patients, of which 24 became TPN dependent. In addition, those with a jejunostomy were at increased risk for TPN dependence and those with a jejunal-ileal anastomosis were at decreased risk. Patients with active Crohn’s disease, radiation enteritis, carcinoma, or pseudo-obstruction involving their remaining bowel will have a blunted adaptation response.

Animal models of SBS have suggested several gut hormones are involved in postresection intestinal adaptation. These include enteroglucagon, glucagon peptide II, epidermal growth factor, growth hormone, cholecystokinin, gastrin, insulin, and neurotensin. There is little data on the role of either endogenous or exogenous hormones on intestinal adaptation in humans. Despite the fact that, normally, most nutrients are absorbed in the proximal jejunum, the residual ileum is able to adapt and to assume the role of macronutrient absorption. However, the specialized cells of the terminal ileum, where vitamin B\(_{12}\) /intrinsic factor receptors are located and where bile salts are reabsorbed, cannot be replaced by jejunal hypertrophy.
Effects of Massive Enterectomy on Gastrointestinal Motility and Transit Time

Following small intestinal resection, dysmotility may develop, which may predispose to bacterial overgrowth in the residual intestine. In addition, resection of the ileocecal valve allows colonic bacteria to enter and populate the small intestine. Bacterial overgrowth may negatively impact on digestion and nutrient assimilation, as bacteria compete for nutrients with the enterocytes. Diagnosis may be more difficult using breath tests because of more rapid intestinal transit in short bowel patients. Endoscopically obtained small bowel aspirate for culture may be required. Treatment can be undertaken with oral metronidazole, tetracycline, or other antibiotics.

Following jejunal resection, gastric emptying of liquids is more rapid, although intestinal transit may still remain normal because of the braking effect of the ileum. Gastric emptying is significantly slower in patients who have residual colon in continuity and is similar to normal controls. The loss of inhibition on gastric emptying and intestinal transit in patients without colon is related to a significant decrease in peptide YY (PYY), glucagon-like peptide I (GLP-I), and neuropeptide Y (PYY). PYY is normally released from L cells in the ileum and colon when stimulated by fat or bile salts. Obviously, these cells are missing in patients who had distal ileal and colonic resection. Those patients with the shortest residual jejunum (<100 cm residual) exhibit the most rapid liquid gastric emptying. Solid emptying may also be more rapid in these patients. Rapid gastric emptying may contribute to fluid losses in patients with SBS.

Medical Therapy of Short Bowel Syndrome

The goal of medical therapy is for the patient to resume work and a normal lifestyle, or as normal of one as possible. This is undertaken via the use of specific measures to gradually decrease the requirement for TPN, and at best, to eliminate its need. The most important aspects of the medical management of the patient with SBS are to provide adequate nutrition, including both macro- and micronutrients (to prevent energy malnutrition and specific nutrient deficiencies), to provide sufficient fluid (to prevent dehydration), and to correct and prevent acid-based disturbances. Most macronutrients, including carbohydrate, nitrogen, and fat, are absorbed within the first 100 cm, and up to 150 cm of jejunum.

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<th>Table 1. Dietary Macronutrient Recommendations for Short Bowel Syndrome</th>
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LCT, long-chain triglyceride; MCT, medium-chain triglyceride.

Macronutrient Assimilation and Dietary Therapy

Typically, patients who have undergone massive enterectomy require TPN for the first 7–10 days. Nutritional therapy should not be introduced until the patient is hemodynamically stable and fluid management issues are relatively stable. The goal is to provide patients with ≈25–35 kcal/kg per day depending upon whether nutritional support is for maintenance or correction of undernutrition and 1.0–1.5 kg per day of protein (Table 1). Additional energy and protein are required by children, especially infants and neonates. Some debate exists whether the patient’s actual body weight or ideal body weight should be used in this calculation. For the postoperative patient, standard enteral formula is recommended. These should be instituted gradually as tolerated. Once patients are able to eat, they should be encouraged to eat a regular diet, but modified as described below. There is no value in separating liquids from solids in the diet. Such practices have no effect on macronutrient, electrolyte or mineral absorption, fecal volume, or fecal weight.

Proteins and amino acids. Dietary protein is first digested, and then absorbed as dipeptides and triptides. Therefore, it was reasoned that dietary protein provided in a predigested form would be more readily absorbed. However, nitrogen absorption is the macronutrient least affected by the decreased intestinal absorptive surface. Therefore, the utility of peptide-based diets in such patients is generally without merit. McIntyre et al. compared energy, nitrogen, and fat absorption, as well as stool weight in 7 patients, all with end-jejunostomy and <150 cm (range, 60–150 cm) of remaining small intestine. These patients were fed with either a peptide-based or an essentially isocaloric and isonitrogenous polymeric formula. Although the study was small, no differences were observed in energy, nitrogen, fat, carbohydrate, and at best, to eliminate its need.
electrolyte, mineral, or fluid absorption.\(^{32}\) Uncontrolled data from Levy et al. supports these findings.\(^{33}\) However, in a small study of 6 patients, all with 90–150 cm of residual jejunum and end-jejuno-ostomy, data from Cosnes et al. suggests nitrogen absorption may be improved with the use of a peptide-based diet. Energy, other macronutrient, electrolyte, mineral, and fluid absorption was unaffected.\(^{34}\) Therefore, the clinical effect of the modestly increased nitrogen absorption was insignificant. It must be recognized that all the studies described above were very small, the study populations somewhat heterogeneous, the various peptide constituents and their concentrations in these various formulas differed significantly, and there was variation in the type and amount of fat (long-chain triglycerides [LCTs] versus medium-chain triglycerides [MCTs]). It is therefore difficult to make definitive comparisons between studies.

The amino acid glutamine, together with glucose, is the preferred fuel for the small intestinal enterocyte.\(^{35}\) Rodent TPN models suggested that both parenteral or enteral glutamine supplements could effect more rapid and significant bowel adaptation following massive enterectomy.\(^{36,37}\) Therefore, it was thought glutamine supplementation in humans would have a similar effect. Although an early case series of 10 patients suggested that glutamine, combined with growth hormone supplementation and a high complex carbohydrate diet could result in decreased stool output and increased absorption of energy, protein, carbohydrate, sodium, and water,\(^{38}\) 2 subsequent double-blinded, randomized placebo-controlled trials failed to confirm any of these effects.\(^{39,40}\) In addition, Scolapio et al. showed that glutamine and growth hormone supplementation did not lead to morphological changes in the intestine.\(^{39}\) Glutamine-supplemented oral rehydration solution (ORS) (see fluid and electrolyte management) was associated with decreased Na absorption and a trend toward decreased fluid absorption in a small controlled trial in 6 patients.\(^{40,41}\) All of the patients studied by Byrne et al. had colon in continuity;\(^{38}\) it is likely the treatment-associated increase in energy absorption was related solely to the increased complex carbohydrate diet discussed above. Treatment with growth hormone and glutamine in the setting of SBS has been associated with significantly increased extracellular fluid and peripheral edema.\(^{39,42,43}\) Therefore, treatment with glutamine and growth hormone cannot be recommended.

**Lipid.** Luminal digestion of lipid may be impaired because of impaired bile salt reabsorption related to resected ileum (>100 cm).\(^{44}\) Therefore, treatment with ox bile supplements has been attempted in 3 cases to increase the duodenal bile salt concentration to a concentration greater than the level at which micellar solubilization of lipid occurs.\(^{45–47}\) Unfortunately, this therapy has been associated with significantly increased fecal volume, at least in those patients with intact colon. A preliminary, open-labeled study of 4 patients (2 with colon in continuity) indicated treatment with the conjugated bile acid cholylsarcosine (6 g/day) was associated with an increase in fat absorption of 17 ± 3 g/day without any effect on stool wet weight.\(^{48}\) As a conjugated bile acid, cholylsarcosine is resistant to colonic bacterial deconjugation, although 1 of the 4 patients did experience a significant increase in wet stool output and another experienced nausea. Cholestyramine is not useful in patients with >100 cm of ileal resection, and may actually worsen steatorrhea because of the binding of dietary lipid.\(^{49}\)

Although dietary fat restriction may result in increased fecal fat losses, there is no difference in the percentage of fat absorbed between high fat (75% non-protein calories derived from fat)/low carbohydrate and low fat/high carbohydrate, isocaloric and isonitrogenous diets.\(^{50}\) In addition, stool weight did not differ between diets. Because fat is energy-dense (9.0 kcal/g) when compared to carbohydrate (4.0 kcal/g), fat restriction may ultimately deprive the patient of a necessary source of energy. Up to 65% of dietary carbohydrate may be malabsorbed and lost in the feces without degradation by colonic bacteria.\(^{31}\)

The colon also absorbs MCTs (C8-C10), possibly related to the fact that MCTs are water soluble. In a study of 10 short bowel patients with colon in continuity and 9 patients with no residual colon, [randomized in a cross-over design to consume an LCT diet based on ordinary dietary fat, consisting of 20% carbohydrate, 24% protein, and 56% fat versus an MCT-LCT diet, where 50% of the LCT was replaced with MCT (margarine, MCT oil)],\(^{51}\) those patients with intact colon absorbed 96% ± 3% of C8 and 87% ± 6% of C10, versus 63% ± 25% for C8 and 57% ± 28% for C10, respectively, in patients with no residual colon (P = 0.007 for C8 and P = 0.004 for C10) from the mixed LCT-MCT diet. Significantly increased energy absorption (=21 MJ/day; 500 kcal/day) was found in patients with colon, but the LCT-MCT diet did not result in increased energy absorption when compared to the LCT diet in patients with an end-jejuno-ostomy or ileostomy whose fecal output was also increased. MCT contain 8.3 kcal/g. Some, but not all, LCT can be replaced by MCT in the diet. In a short bowel patient eating 10.5 MJ/day (2500 kcal/day), =1.5–3 MJ/day (360–720 kcal/day; 40–80 g) of LCT...
can be replaced with MCT. However, LCTs are still necessary to provide essential fatty acids, and primarily linoleic fatty acid, which is not found in MCTs. In addition, excessive intake of MCT may result in nausea, vomiting, and ketosis.

**Carbohydrates.** Rarely is the proximal jejunum resected in patients who require massive enterectomy. Because most intestinal disaccharidases are present in highest concentration proximally, it would stand to reason such patients would be unlikely to benefit from a lactose-free diet. Marteau et al. studied 14 short bowel patients in whom a lactose-free diet was compared to a diet containing 20 g/day containing ≤4 g milk.32 Lactose absorption, breath hydrogen, subjective symptoms of flatulence, and diarrhea were similar regardless of which diet was consumed. This data confirmed the findings of an earlier controlled study in 17 short bowel patients where it was also reported that lactose absorption was enhanced when provided in yogurt rather than via milk.33 Regardless, in the absence of significant jejunal resection, lactose should not be restricted in the diet of the short bowel patient. The amount of lactose found in a glass of milk (20–25 g) is generally well tolerated even in patients with an end-jejunostomy.35 Because most lactose is found in milk-based foodstuff, which are also the most important source of dietary calcium, dietary lactose restriction will result in insufficient dietary calcium intake.

**The role of soluble fiber.** Soluble nonstarch polysaccharides and some starches54 are not generally absorbed by the small intestine. Soluble fiber is water soluble and found primarily in the following (in descending order of concentration): oatmeal, oat bran, psyllium (Metamucil, Procter and Gamble, Cincinnati, OH; Konsyl, Konsyl Pharmaceuticals, Ft. Worth, TX), barley, artichokes, strawberries, legumes, prunes, grapefruit, and squash. Soluble fiber and starches pass undigested into the colon where colonic bacteria ferment them not only to hydrogen and methane, hence patient “gas” complaints, but also to SCFAs, including butyrate, propionate, and acetate. SCFAs are the preferred fuel for the colonocyte.55 Therefore, in the patient with SBS, the colon becomes an important machine for energy absorption. Approximately 75 mmol of SCFA are produced from 10 g of unabsorbed carbohydrate.56 Patients with SBS, but intact colon in continuity were able to decrease fecal energy loss by 1.3–3.1 MJ/day (310–740 kcal) when they were fed a diet consisting of 60% carbohydrate.57 Colonic metabolism of unabsorbed carbohydrate was indicated by decreased fecal carbohydrate losses in the patients with colon in continuity. It is possible for an intact colon to absorb up to 2.2–4.9 MJ (525–1170 kcal) daily from dietary fiber.8,9,57 Colonic energy absorption may also increase somewhat during the postresection adaptation phase, related to increased colonic bacterial carbohydrate fermentation.10,58 This may be related to increased colonic bacteria in patients with SBS as well as an increase in the concentration or activity of various enzymes, such as B-galactosidase, over time during the adaptation period.58 Because SCFAs stimulate sodium and water absorption,42 patients might be expected to experience decreased fecal fluid and sodium loss, but this has not been observed clinically.57

**Vitamins.** Micronutrients often require supplementation (Table 2). Because water-soluble vitamins are absorbed in the proximal jejunum, it is unusual for deficiencies to develop in short bowel patients (except in those who have high jejunoostomies or duodenostomies), although these patients generally require TPN. Thiamine deficiency has been reported and became an important issue during a recent parenteral vitamin shortage.59 Patients have presented with Wernicke’s encephalopathy, beriberi, and severe metabolic alkalosis.60 If thiamine deficiency is suspected, whole blood thiamine concentration is not helpful; this reflects recent nutritional intake. Erythrocyte transketolase activity should be determined and empiric therapy begun with 100 mg of parenteral thiamine daily. Biotin deficiency has rarely been reported in patients with SBS.61 It is manifested in a scaly dermatitis, alopecia, lethargy, hypotonia, and lactic acidosis. Therapy consists of parenteral biotin supplementation of 0.3–1 mg daily, although this is not currently commercially available. Vitamin B12 supplementation is required (500 μg/month SQ) in patients

| Table 2. Vitamin and Mineral Supplements for Patients With Short Bowel Syndrome |
|----------------------------------|---------------------------------|
| Vitamin A                        | 10000–50000 units daily^a       |
| Vitamin B12                      | 300 μg subcutaneously monthly for those w/ terminal ileal resections or disease |
| Vitamin C                        | 200–500 mg                      |
| Vitamin D                        | 1600 units DHT daily; may require 25-OH- or 1,23 (OH2)-D3 |
| Vitamin E                        | 30 IU daily                     |
| Vitamin K                        | 10 mg weekly                    |
| Calcium                          | See text                        |
| Magnesium                        | See text                        |
| Iron                             | As needed                       |
| Selenium                         | 60–100 μg daily                 |
| Zinc                             | 220–440 mg daily (sulfate form)  |
| Bicarbonate                      | As needed                       |

NOTE. The table lists rough guidelines only. Vitamin and mineral supplementation must be monitored routinely and tailored to the individual patient, because relative absorption and requirements may vary. ^aUse cautiously in patients with cholestatic liver disease.
who have had a significant portion of their terminal ileum resected (>60 cm). Folic acid is provided as a constituent of parenteral multivitamins. However, in patients with proximal jejunal resections, folate deficiency may develop. Such patients should receive 1 mg/day supplement.

Fat-soluble vitamin deficiency (A, D, and E) is more common because of the steatorrhea that occurs in SBS and the subsequent decrease in micellar formation and fat digestion. The use of cholestyramine may also result in fat-soluble vitamin deficiency. Night blindness and xerophthalmia has been described in SBS. As vitamin A deficiency progresses, corneal ulceration and permanent visual loss may ensue, and short bowel patients who do not receive parenteral multivitamins should have their serum vitamin A concentration monitored. If a low-serum vitamin A concentration is detected, therapy is 10,000–50,000 units daily, and may be administered either orally or parenterally.

Vitamin D deficiency manifests in osteomalacia. Usually dietary intake is a relatively unimportant source of vitamin D because the majority is endogenously synthesized from 7-dehydrocholesterol via ultraviolet light. However, because enterohemepatic circulation is disrupted in patients who have undergone significant ileal resections, deficiency may result.

Vitamin E deficiency in patients with SBS may manifest in hemolysis and various neurological deficits. Because serum vitamin E concentration reflects serum total lipid concentration, which may be low in short bowel patients, a low serum vitamin E concentration alone may not be indicative of a deficient state; the ratio of serum vitamin E to total lipid should be calculated.

Vitamin K is synthesized by colonic bacteria (60%), although dietary intake accounts for about 40% of requirements; deficiency is therefore uncommon in patients with intact colon. However, vitamin K deficiency is frequent in patients who have no residual colon or have been given recent broad-spectrum antibiotics. Requirement is ≈1 mg daily. Vitamin K only recently has been a constituent in adult multivitamins for TPN, although pediatric multivitamin formulations all contain vitamin K.

Trace metals. Patients with SBS lose a significant amount of zinc and selenium in their feces. A significant amount of zinc is lost in small bowel effluent (12 mg/L small intestinal fluid and 16 mg/L stool). Zinc deficiency has been associated with growth abnormalities, delayed wound healing, and cellular immunity dysfunction. Patients in whom zinc deficiency is suspected should be treated empirically with oral zinc sulfate (220–440 mg daily) or parenteral zinc if the patient requires TPN. Serum and leukocyte measurements of zinc concentration, although helpful, may be unreliable. Selenium deficiency has been associated with cardiomyopathy, peripheral neuropathy, proximal muscle weakness and pain, whitening of the hair, and macrocytosis. Serum selenium is a reliable indicator of selenium status, and if low, oral or parenteral supplementation should be provided. Although there are 3 reported possible cases of chromium deficiency in patients requiring long-term TPN, deficiency has not been reported in short bowel patients who do not require TPN; therefore, routine supplementation is not recommended. Chromium is a necessary cofactor for insulin’s effects in peripheral tissue. Even as TPN is a concern, available evidence suggests there is sufficient chromium present in the TPN solutions as a contaminant, and supplemental chromium may invite the possibility of nephrotoxicity. Copper deficiency is very rare in the patient with SBS. Deficiency may result in microcytic anemia, neuropathy, and decreased fertility.

Medication Absorption

The provision of medications to the patient with SBS can represent a challenge to the practicing clinician. Just as fluid and nutrient absorption is impaired, medication absorption is often impaired as well. As with nutrient absorption, significant interpatient variability may be observed. Given that the risk for catheter sepsis is greater the more times the line is manipulated, it is important to use the oral or enteral route for medication delivery whenever possible. The degree to which a medication is malabsorbed is dependent upon several variables. These include the surface area and health of the residual intestinal surface area, morphologic and physiologic factors, including the presence or absence of the terminal ileum (B12 and bile salt absorption—necessary for cyclosporin absorption), or the presence of an acidic or alkaline environment (related to the use of H2 blockers in TPN or use of proton pump inhibitors). Many, but not all, medications are absorbed in the jejunum; so, for many medications, absorption will be minimally impacted in the absence of decreased intestinal transit time, which will decrease mucosal contact time. Most of the available data on oral medication absorption in patients with SBS is in the form of isolated case reports.

Fluid and Electrolyte Management

Massive enterectomy is associated with transient gastric hypersecretion. Basal acid secretion is significantly increased up to the first few months following resection. Massive small bowel resection is associated
with hypergastrinemia during the initial first 6 months after surgery.90 The H₂ antagonists and proton pump inhibitors are useful in reducing gastric fluid secretion, and therefore will also reduce fluid losses during this period.17,91–94 However, absorption of orally dosed medications may be impaired, and either large doses, oral medication, or intravenous delivery may be required. Although fluid losses are decreased, macronutrient and electrolyte absorption are not affected by H₂ antagonists and proton pump inhibitors.

Fluid losses usually require chronic control with antimitoty agents, such as loperamide hydrochloride or diphenoxylate. Typical doses are 4–16 mg/day. If these are ineffective, especially in patients with no colon in continuity or those who are left with a minimum of residual jejunum or duodenum, codeine sulfate or tincture of opium may be necessary. The usual dose for codeine sulfate is 15–60 mg two to three times a day. Rarely, patients will require treatment with octreotide. The mechanism of action is unclear, but octreotide may be useful to slow intestinal transit time and increase water and sodium absorption.95,96 In one open-labeled study of 9 patients with end-jejunostomies, daily jejunostomy volume was reduced from 8.1 ± 1.6 to 4.8 ± 0.7 L/day using a dose of 100 µg SQ, three times daily 30 minutes before meals.97 Because use of octreotide does not lead to the discontinuation of TPN, its use should be reserved for patients with high output jejunostomies in whom fluid and electrolyte management is problematic. Octreotide reduces splanchnic protein synthesis, thereby reducing mucosal protein incorporation and villus growth rate, and may impair postresectional intestinal adaptation.98 There is also an increased risk for cholelithiasis98,99 in a patient group already predisposed to this problem.100

Glucose–polymer-based ORS should be instituted to decrease dehydration and to decrease TPN fluid requirements in patients with residual jejunum ending in a jejunostomy. Patients with <100 cm of residual jejunum are at significant risk for dehydration because they secrete more Na and fluid than consumed orally.91 Because the jejunum is permeable to Na and chloride (Cl), passively absorbed solutions with high NaCl concentration are readily absorbed. Glucose promotes salt and water absorption by solvent drag.101 However, Na and water are not absorbed from hypotonic or isotonic solutions in the jejunum. Several commercially available ORS formulas are available, although probably the best, and certainly the least expensive, is the one recommended by the World Health Organization (WHO).102 This can be formulated by dissolving the following in 1 L tap water: NaCl (2.5 g), KCl (1.5 g), Na₂CO₃ (2.5 g), and glucose (table sugar, 20 g). Only the KCl requires a physician prescription. Most, if not all, of the commercially available ORS have substantially less Na (range, 45–50 mmol/L). NaCl may be added; the optimal Na concentration should be at least 90 mmol/L, which is the usual concentration of small bowel effluent.19 Solutions with lower Na concentrations lead to increased Na losses. Therefore, patients with SBS should be cautioned against consumption of plain water and should be encouraged to drink ORS whenever they are thirsty. More recent evidence has shown that hypotonic (160 mOsmol/kg) ORS leads to decreased intraluminal duodenoejunal fluid flow rate in normal volunteers, although the effect on gastro-intestinal fluid losses or patient hydration status in short bowel patients has not been evaluated.105

For patients with residual colon in continuity, ORS may still be of value, but, provided sufficient Na is present in the diet, the amount of Na in the ORS may not be as critical since the colon readily absorbs Na and water against a steep electrochemical gradient.104 For patients with no remaining jejunum, but who have residual ileum, the presence of glucose in the ORS is not critical because ileal water absorption is not affected by the presence of glucose.105

In addition to Na losses, significant quantities of Mg are lost in jejunal or ileal effluent as well.106 Patients may develop Mg deficiency despite a normal serum concentration; therefore, it is prudent to measure 24-hour urine Mg loss.107 The median 24-hour urine Mg in normal volunteers in the study was 127 mg (vs. 19 mg for Mg deficient short bowel patients).

Mg deficiency may precipitate Ca deficiency because hypomagnesemia impairs the release of parathyroid hormone.108 In addition, the majority of patients with SBS who do not require TPN are in negative Ca balance.109 Therefore, in the absence of TPN, oral Ca supplementation is routinely recommended (800–1200 mg per day). Mg replacement is problematic. Attempts with oral MgO or oral consumption of injectable Mg have generally not been successful and have been associated with increased fecal loss because of their cathartic effect.110 Although Mg gluconate is water soluble, Mg has generally not been a constituent of ORS. Therefore, some patients may require periodic parenteral Mg despite the absence of a TPN or intravenous fluid requirement. Iron is absorbed in the duodenum; therefore, in the absence of hemorrhage it is not routinely required as a supplement. Phosphorous deficiency is not well described in SBS, and therefore supplementation is rarely, if ever, required.
Pharmacologic Enhancement of Intestinal Adaptation

The GLP-II is another hormone secreted from L cells (as well as from pancreatic A cells). Postprandial serum GLP-II concentration is not unexpectedly depressed in patients who have had extensive small bowel resection, especially including ileum. It has been postulated that the relative lack of jejunal hypertrophy following ileal resection may be at least partly related to the resection of GLP-II-producing L cells, although these investigations were undertaken in patients over 2 years following their resection without a baseline comparison. GLP-II (400 μg SQ, twice a day for 35 days) was administered in a small, pilot, open-labeled trial to 4 patients with SBS without residual colon who required TPN and in 4 patients with sufficient residual jejunum where TPN was not required. Jejunal villus length and crypt depth tended to increase (although not significantly), energy absorption tended to increase (non-significantly), and fecal weight decreased, indicating increased fluid absorption. Although GLP-II is not commercially available, investigational studies of a longer-acting, genetically engineered analogue of GLP-II are underway. Growth hormone administration (0.5 IU/kg per day or 0.024 mg/kg per day) alone for 8 weeks had no effect on absorptive capacity of energy, protein, or fluid in 10 patients (4 with colon in continuity).

Dietary Restriction

Normally, oxalate in the diet binds to dietary calcium and is excreted in the stool. However, in the presence of significant fat malabsorption, dietary calcium preferentially binds to free fatty acids, rendering the oxalate free to pass into the colon. Dietary oxalate is absorbed to a minimal extent in the small intestine, but can be absorbed more readily in the colon. Absorption may also be enhanced because colonic permeability increases secondary to injury from malabsorbed bile salts also passing into the colon. Dietary oxalate is absorbed to a minimal extent in the small intestine, but can be absorbed more readily in the colon. Absorption may also be enhanced because colonic permeability increases secondary to injury from malabsorbed bile salts also passing into the colon. Once absorbed into the colon, oxalate is renally filtered, where it binds to calcium, resulting in hyperoxaluria and calcium oxalate nephrocalcinosis and nephrolithiasis. Therefore, in patients with SBS who have colon in continuity, oxalate should be restricted in the diet. Table 3 lists the relative oxalate content of many foods. Oral Ca supplements may also be of value for the prevention of Ca-oxalate nephrolithiasis. Hyperoxaluria may also develop in patients without colon who are TPN-dependent. This is most likely related to metabolism of vitamin C in the TPN solution, in the presence of light, to oxalate. Therefore, it may be beneficial to shield TPN to which vitamin C has been added either as a multivitamin solution or individually, but it remains unclear if dietary oxalate should be restricted in all patients with an end jejunostomy who require TPN.

Providing Parenteral Nutrition

Macronutrients. Most patients will require TPN, at least initially. For the normally nourished patient, TPN should be supplied at 25–30 kcal/kg per day based on ideal body weight for adults, with greater levels of support for infants and children depending upon age. Dextrose is a monohydrate, providing 3.4 kcal/ml. The maximum dextrose infusion rate should be 5–7 mg/min. Blood glucose should be monitored at least daily, and optimally 4 times a day, and should be <180–200 mg/dL; the addition of regular insulin to the TPN solution may be required. If insulin is required, it should be added to the TPN bag at an initial dose of 0.1 U/g of dextrose, with subsequent adjustments made as necessary. Intravenous lipids are generally used to provide 20%–30% of infused calories, although a greater percentage of lipid may be used in the patient with significant glucose intolerance or fluid management issues; 20% lipid emulsion is more calorically dense than dextrose. Generally, the percentage of lipid calories should be increased and the percentage of dextrose calories decreased if the amount of supplemental insulin required exceeds 0.2 U/g of dextrose, although the serum triglyceride concentration should be kept under 700–800 mg/dL, and optimally, <400 mg/dL. Protein is supplied in the form of amino acids, and should be supplied at 1.0–1.5 g · kg⁻¹ · day⁻¹, based on ideal body weight for adults, with greater levels of support for infants and children depending upon age.

Getting the Patient Ready for Home TPN

Initially, TPN is infused continuously while postoperative complications are addressed and metabolic issues stabilized. Attempts should be made, when appropriate, to wean patients who have sufficient absorptive capacity (as discussed above), being mindful that maximal adaptation may take as long as 1–2 years (as alluded to above). For patients who will require TPN at home, the TPN infusion should be compressed to nighttime infusion. Typically, this would be over a 10-hour period with an additional 30–60-minute taper period; some patients with fluid management issues from renal failure or congestive heart failure will be unable to tolerate this infusion rate. Because pancreatic insulin secretion requires some period to adapt to the significant dextrose infusion, cycling should be a gradual process. Once the goal infusion volume has been determined (e.g., 1.5, 2.0,
### Table 3. Oxalate Content of Foods

<table>
<thead>
<tr>
<th>Food group</th>
<th>For low oxalate diet, restricted to 40–50 mg daily</th>
<th>Moderate oxalate content</th>
<th>High oxalate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Little or no oxalate (&lt;3 mg/serving)</td>
<td>2–10 mg/serving</td>
<td>&gt;10 mg/serving</td>
</tr>
<tr>
<td></td>
<td>Eat as desired</td>
<td>Limit: 2 (1/2 cup) servings/day</td>
<td>Avoid completely</td>
</tr>
<tr>
<td><strong>Beverages</strong></td>
<td>Apple or pineapple juice</td>
<td>Cranberry juice (4 oz)</td>
<td>Draft beer</td>
</tr>
<tr>
<td></td>
<td>Bottled beer</td>
<td>Grape juice (4 oz)</td>
<td>Juices containing berries</td>
</tr>
<tr>
<td></td>
<td>Colas (12 oz limit/day)</td>
<td>Nescafe powder</td>
<td>Ovaltine and other beverage mixes</td>
</tr>
<tr>
<td></td>
<td>Distilled alcohol</td>
<td></td>
<td>Tea, cocoa</td>
</tr>
<tr>
<td></td>
<td>Grapefruit juice</td>
<td></td>
<td>Lemonade or limeaid</td>
</tr>
<tr>
<td></td>
<td>Orange juice (4 oz)</td>
<td></td>
<td>Tomato juice (4 oz)</td>
</tr>
<tr>
<td></td>
<td>Wine, red, rose</td>
<td></td>
<td>Instant coffee</td>
</tr>
<tr>
<td></td>
<td>Tap water</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Milk, yogurt</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Coffee</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Meats</strong></td>
<td>Eggs</td>
<td>Sardines</td>
<td>Peanut butter</td>
</tr>
<tr>
<td></td>
<td>Cheese, cheddar</td>
<td></td>
<td>Soybean curd (tofu)</td>
</tr>
<tr>
<td></td>
<td>Lean lamb, beef, or pork</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poultry</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seafood</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fruits and vegetables</strong></td>
<td>Asparagus</td>
<td>Broccoli</td>
<td>Beans</td>
</tr>
<tr>
<td></td>
<td>Avocado</td>
<td>Cauliflower</td>
<td>Beets</td>
</tr>
<tr>
<td></td>
<td>Brussels sprouts</td>
<td>Cucumber</td>
<td>Carrots</td>
</tr>
<tr>
<td></td>
<td>Cauliflower</td>
<td>Green peas</td>
<td>Celery</td>
</tr>
<tr>
<td></td>
<td>Cabbage</td>
<td>Lettuce</td>
<td>Swiss chard</td>
</tr>
<tr>
<td></td>
<td>Mushrooms</td>
<td>Lima beans</td>
<td>Chives</td>
</tr>
<tr>
<td></td>
<td>Onions</td>
<td>Tomato, 1 small</td>
<td>Collards</td>
</tr>
<tr>
<td></td>
<td>Potatoes</td>
<td>Turnips</td>
<td>Dandelion greens</td>
</tr>
<tr>
<td></td>
<td>Radishes</td>
<td>Egg plant</td>
<td>Endive</td>
</tr>
<tr>
<td></td>
<td>Sweet corn</td>
<td>Apples</td>
<td>Escarole</td>
</tr>
<tr>
<td></td>
<td>Bananas</td>
<td>Apricots</td>
<td>French fries</td>
</tr>
<tr>
<td></td>
<td>Cherries, Bing</td>
<td>Black Currents</td>
<td>Kale</td>
</tr>
<tr>
<td></td>
<td>Grapefruits</td>
<td>Cherries, red sour</td>
<td>Leeks</td>
</tr>
<tr>
<td></td>
<td>Grapes, white</td>
<td>Fruit cocktail</td>
<td>Okra</td>
</tr>
<tr>
<td></td>
<td>Mangoes</td>
<td>Orange</td>
<td>Berries</td>
</tr>
<tr>
<td></td>
<td>Melons</td>
<td>Peaches</td>
<td>Concord grapes</td>
</tr>
<tr>
<td></td>
<td>Nectarines</td>
<td>Plums, red</td>
<td>Red currants</td>
</tr>
<tr>
<td></td>
<td>Pears</td>
<td>Prunes</td>
<td>Parsnips</td>
</tr>
<tr>
<td></td>
<td>Pineapple</td>
<td>Squash</td>
<td>Sweet potato</td>
</tr>
<tr>
<td></td>
<td>Plums, green/golden</td>
<td>Vegetable soup</td>
<td>Tangerines</td>
</tr>
<tr>
<td><strong>Breads, pasta, cereal</strong></td>
<td>Macaroni</td>
<td>Cornflakes</td>
<td>Grits, white corn</td>
</tr>
<tr>
<td></td>
<td>Noodles</td>
<td>Sponge cake</td>
<td>Soybean crackers</td>
</tr>
<tr>
<td></td>
<td>Oatmeal</td>
<td>Spaghetti, canned in tomato sauce</td>
<td>Wheat germ</td>
</tr>
<tr>
<td></td>
<td>Rice</td>
<td></td>
<td>Bran cereal</td>
</tr>
<tr>
<td></td>
<td>Spaghetti</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>White bread</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td>Mayonnaise</td>
<td>Chicken noodle soup, dehydrated fruitcake</td>
<td>Nuts</td>
</tr>
<tr>
<td></td>
<td>Salad dressing</td>
<td></td>
<td>Pretzels</td>
</tr>
<tr>
<td></td>
<td>Vegetable oils</td>
<td></td>
<td>Chocolate</td>
</tr>
<tr>
<td></td>
<td>Jelly or preserves (made w/allowed fruits)</td>
<td></td>
<td>Pepper (&gt;1 tsp/day)</td>
</tr>
<tr>
<td></td>
<td>Butter</td>
<td></td>
<td>Vegetable soup</td>
</tr>
<tr>
<td></td>
<td>Soups made w/allowed ingredients</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sugar</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2.5, or 3.0 liters for adults; with less volume for infants and children), the total volume should be infused over gradually decreasing time periods (e.g., compress by increments of 2–4 hours daily). TPN should be infused ideally via a single lumen catheter with its tip positioned in either the superior vena cava (SVC) or inferior vena cava (IVC) to decrease the risk of infection and thrombosis.121,122 Tunneled catheters, including Hickman, Broviac, or Groshong catheters, implantable ports, or percutaneously inserted central catheters should be used at home, although the experience with percutaneously inserted central catheters for >1 year at home is minimal. To qualify for Medicare reimbursement, home TPN must be required for at least 3 months, fat malabsorption must be documented, and enteral feeding must have failed.

The patient’s home environment should be evaluated. A room, preferably the bedroom—definitely not a “dirty” room, such as the kitchen or bathroom—should be identified for TPN to be set up prior to use. The patient should be instructed to purchase a small refrigerator, which will be used solely for the storage of TPN solutions. A local support group under the umbrella of the Oley Foundation (1-800-776-OLEY or oley.org) should be contacted. The Oley Foundation is an independent, nonprofit organization of patients and professionals that provides information, outreach services, emotional support, and conference activities to patients who require home TPN as well as their families and health care professionals involved in their care. The transition from hospital to home may be smoother if the patient has another patient contact who has previously undergone the same process. It is generally advised that the patient should undergo some education about TPN prior to hospital discharge. This should include the indications for TPN, basic instruction on getting their solutions ready for use (they will need to add their vitamins, insulin, H2 blockers if prescribed, and flush catheter), catheter care, dressing changes, and information on their intravenous pump. It is often useful for the patient to meet their home care nurse (who will continue the education process at home until the patient or caregiver is self-sufficient), prior to discharge. The treating physician should have some familiarity with appropriate catheter care and the identification of complications associated with long-term TPN, including catheter-related infections, occlusions, and metabolic complications. These are beyond the scope of this review, but have recently been reviewed elsewhere.123,124 (Catheter-related infections and thrombosis are discussed in greater detail under complications of parenteral nutrition that may make intestinal transplantation necessary.) Algorithms 1 and 2 describe the evaluation and treatment of fever in the home TPN patient and algorithm 3 describes the evaluation and treatment of catheter occlusion in the home TPN patient, which may be either thrombotic or non-thrombotic in origin.

Patients should not be discharged home until their fluid and electrolyte requirements have stabilized. Once home, office visits and laboratory monitoring will initially be more frequent, although the stable patient who has minimal difficulty generally can visit the office and have routine laboratory testing done as infrequently as 3 times a year. The goal is to return patients to society. Home TPN should not prevent a patient from working or traveling.

Patients in whom TPN is being weaned, and who acquire <75% of the nutritional needs parenterally, should have vitamin (usually the fat-soluble vitamins) and trace metal (Zn, Cu, Se) analyses performed 2 or 3 times yearly, and whenever possible deficiencies have been clinically recognized. Vitamin K is not a constituent of all parenteral multivitamin solutions, although vitamin K is present in the intravenous lipid emulsion. Therefore, the prothrombin time should be regularly monitored, especially in those patients who lack residual colon. During the clinic visit, the catheter exit site or skin overlying an implanted infusion port should be examined for warmth, erythema, and tenderness, and the catheter dressing should be examined for purulent exudate, which may signal infection. A properly maintained catheter may remain in place indefinitely.125

Quality of Life and Survival of Short Bowel Patients

No quality of life data exists for patients with SBS who do not require TPN. In addition, Oley Foundation surveys and similar surveys from home TPN programs in Europe include all home TPN patients. Patients with SBS were not analyzed separately in these surveys. In a study of 124 consecutive adult short bowel patients with nonmalignant diseases at 2 centers in France, survival was 86% at 2 years and 75% at 5 years.7 TPN-dependence was 49% at 2 years and 45% at 5 years. Those patients with end-enterostomy or <50 cm had significantly lower survival rates. TPN dependence was related to remaining bowel length and/or absence of ileocolic anastomosis. A review of the 225 patients treated in the Mayo Clinic home TPN program showed similar survival.126

Complications of Long-term TPN

Hepatic complications. Liver abnormalities are a recognized complication in long-term TPN patients and
can present as a broad spectrum of pathologic entities, including steatosis, cholestasis, steatohepatitis, fibrosis, and cirrhosis. A recent report from the USA suggested that 15% of patients receiving TPN for >1 year will develop end-stage liver disease (ESLD), which is associated with 100% mortality within 2 years of onset. Another recent report from France suggested that >50% of adult patients on TPN for >5 years will develop complicated liver disease (e.g., severe fibrosis [grade 2], cirrhosis, or one of the following: bilirubin >3.5 mg/dL for >1 month, ascites, portal hypertension, hepatic encephalopathy, portal hypertension, or liver failure with Factor V <50%), although this study also included patients with chronic hepatitis B and C. In France, all home TPN patients are managed and monitored by government authorized regional home TPN centers. Therefore, these results may be more representative of what occurs in an entire population of home TPN patients than other center specific studies.

Liver complications appear to be especially prevalent in pediatric patients on long-term TPN. Those patients with the shortest residual intestine are at greatest risk for development of eventual ESLD. Recent investigations have suggested the liver disease associated with long-term TPN is most likely caused by malab-
sections and SBS are usually calcium bilirubinate, and form at a rate 3 times greater than in patients without previous resection.\textsuperscript{144,145} The pathogenesis of calcium-bilirubinate gallstones in patients with SBS is unclear. Postmeal stimulated serum cholecystokinin (CCK) concentration is depressed in some patients with SBS,\textsuperscript{146} although this has not been shown in all studies.\textsuperscript{147} CCK injections have been used experimentally in an attempt to induce gallbladder contraction and thereby prevent gallstone formation,\textsuperscript{147} but this has not been universally successful.\textsuperscript{148} In addition, CCK injections have been commonly associated with nausea, vomiting, and abdominal pain.\textsuperscript{147,148}

**Catheter-related infections.** The Oley Foundation registry data indicates that on average, TPN patients were hospitalized for infectious complications approximately once per year.\textsuperscript{15} Unfortunately the registry did not identify what percentage of these admissions were for catheter-related infections, nor did they indicate how many catheter-related infections were managed without hospital admission. Messing et al. found intestinal failure patients on permanent TPN to have a high mortality rate (>50\% with median follow-up of 64 months), with 31\% of deaths attributable to sepsis.\textsuperscript{6} In this series, the central venous catheter (CVC) was clearly identified as the source of sepsis in 50\% of septic deaths. Other centers have reported that with experience and proper line care technique, the rate of catheter-related infections in patients receiving HPN for gastrointestinal disorders can be as low as 0.8 infections per 1000 catheter days (including catheter sepsis, exit site, and tunnel infections) during 1154 patient years of follow-up and 1.4 infections per 1000 catheter days for children in 241 years of patient follow-up.\textsuperscript{121} (Refer to algorithm 2 for management of catheter-related infections.)

**D-Lactic acidosis.** Lactobacilli and other bacteria, including *Clostridium perfringens* and *Streptococcus bovis*, when present, ferment non-absorbed carbohydrate to D-lactic acid, which cannot be metabolized by D-lactate dehydrogenase. These organisms may proliferate in an acidic environment that may be promoted by the metabolism of unabsorbed carbohydrate to SCFAs. A severe metabolic acidosis, encephalopathy, headache, ataxia, and dysarthria may develop in the absence of hepatic dysfunction if significant absorption of D-lactic acid occurs.\textsuperscript{29} Thiamine deficiency should be excluded.\textsuperscript{149,150} D-lactate concentrations will be increased in blood and urine (L-lactate concentration, which is usually measured when serum lactate concentration is ordered, is normal). The mechanism for the neurological symptoms is unknown. Fortunately, this complication is very rare. Treatments described in case reports have included nothing (with spontaneous resolution), oral metronidazole, neomycin, vancomycin, (for 10–14 days), and avoidance of “refined” carbohydrates.\textsuperscript{151,152}

**Catheter occlusion.** The long-standing requirement for a CVC in intestinal failure patients predisposes to thrombus and/or fibrin formation and ultimately occlusion of central veins. Catheter occlusion may also result from TPN solution incompatibilities. Refer to algorithm 2 for evaluation and treatment of patients with CVC occlusions. The Oley Foundation registry did not provide data for all central vein occlusions, but did indicate that the SVC thrombosis resulted in <0.3 hospital admissions per patient year. Moukarzel et al. found that in long-term pediatric TPN patients, the mean life span of a CVC was 22.4 ± 14.7 months (range, 1.5–178 months) and 25\% of catheter removals were for thrombotic complications.\textsuperscript{155} In many long-term TPN patients, the central veins being utilized will eventually occlude and as new veins are used, multiple central venous occlusions can occur. The incidence of catheter thrombosis is ≈0.2 episodes per 1000 catheter days in 1154 years of patient follow-up.\textsuperscript{154} Prior catheter thrombosis is a risk factor for development of SVC/IVC syndrome in the future; therefore, warfarin anticoagulation should be undertaken in patients with prior catheter thrombosis in the absence of catheter malposition as the cause.\textsuperscript{154} Typically, TPN catheters are first placed in the SVC by accessing either the internal jugular, brachial, or subclavian veins. If these veins are no longer accessible, the catheters are usually placed in the IVC via the femoral or saphenous veins. Other life-threatening complications can be associated with the progressive loss of venous access, including SVC syndrome, pulmonary embolus, and septic thrombi.\textsuperscript{122,154–157} True loss of catheter insertion sites is extremely rare; clinicians often prematurely determine that a patient has no suitable venous access. When all the usual central veins have been exhausted, alternatives include translumbar or transhepatic access to the IVC, and thoracotomy with direct placement of an intra-atrial catheter among others.\textsuperscript{158–160} In the 1154 patient years experience previously described at a single institution, no patient ever lost CVC access and only 2 required right atrial catheter placement during that time period.\textsuperscript{154}

**Other complications.** Renal dysfunction,\textsuperscript{161} metabolic bone disease,\textsuperscript{162} memory deficits,\textsuperscript{163} and neurological problems have also been described in patients who require long-term TPN.\textsuperscript{164}
Role of Surgery

Nontransplant Surgery

The primary emphasis of nontransplant surgery in SBS is to increase nutrient and fluid absorption by either slowing intestinal transit or increasing intestinal surface area. The goal is similar to that of medical therapy, which is to reduce the requirement for TPN. Medical and surgical therapy often exhibit a symbiotic relationship. Various surgical procedures have been described in case reports and series only (Table 4). There are no studies comparing surgical and medical approaches.

Restoration of intestinal continuity, such as re-anastomosis of small intestine with colon, should be done whenever possible, since it can be performed with relatively low morbidity and mortality (often with good success of discontinuation of parenteral nutrition). This allows for colonic fermentation of unabsorbed carbohydrate from the small intestine and an important source of energy assimilation (see role of soluble fiber). The other forms of surgery for SBS are more technically challenging and should only be considered in select patients. In general, the results are not particularly encouraging, although individual patients with specific criteria (as described below) may benefit.

Operations to slow transit include segmental reversal of the small bowel, colonic interposition, construction of valves, and electrical pacing of the small intestine. Approximately 40 cases of segmental reversed small bowel (SRSB) have been reported. Unfortunately, most cases are antidotal, without long-term patient follow-up. The surgical technique works on the premise of decreasing intestinal transit by creating a short antiperistaltic segment of small intestine. There is general agreement by most authors that SRSB should not be performed at the time of the initial resection, but at a later time (e.g., during surgery for restoring intestinal continuity). This allows time for intestinal adaptation to occur, which may eliminate the need for surgery. The length of intestine reversed should be ≈10 cm. Shorter segments may be insufficient in slowing transit and longer segments may result in intestinal obstruction. In addition, the reversed segment should be located in the most distal part of the small intestine to eliminate the possibility of obstructive symptoms. A limitation of SRSB is that patients may have only a very short segment of residual small bowel, which may not allow resection of a 10-cm segment for reversal. In a report of 8 short bowel patients (mean age, 58 years) treated with SRSB, 4 of 8 patients were able to discontinue parenteral nutrition. Discontinuation of parenteral nutrition was not immediate, with a median of 8 months after surgery. There were no postoperative deaths directly related to the surgery. Three of the patients experienced transient intestinal obstruction.

Colon interposition can be interposed between small intestine in either an isoperistaltic or antiperistaltic direction. Both methods have been reported to slow intestinal transit and increase absorption in animal models. The use of colon interposition has been reported in 12 patients (11 isoperistaltic segments); all but 1 were infants <1 year of age. Lengths of colon have ranged between 8 and 24 cm. Four of the infants and 1 adult were reported to have good outcomes in terms of discontinuing parenteral nutrition 4 months after surgery. Colon interposition was not associated with any perioperative mortality or morbidity. The antiperistaltic placed colon does not appear as successful as an isoperistaltic segment. Clinical and experimental experience with colonic interposition remains limited.
Construction of intestinal valves is another surgical method to slow intestinal transit in SBS. Clinical experience with intestinal valves is much less than for reversed small intestine segments. The valves create a partial mechanical obstruction and disrupt the normal motility of the small intestine, and prevent retrograde reflux of intestinal contents. Experimental studies have reported delayed transit, dilation of proximal intestine, and increased absorption. Nipple valves have been placed in 6 infants to increase intestinal lengthening. Intussuscepted valves have been reported in 5 adults and 1 infant with short bowel. Four of the patients had significant improvement and the others required removal of the valve because of mechanical obstruction. Durability of valves to serve as sphincters has been questioned.

Recirculating loops and retrograde intestinal pacing have been met with limited success. Objective evidence of increased absorption with both has not been confirmed. Obstruction and stasis contribute to the failure of recirculating intestinal loops.

Intestinal surface area may be increased by the longitudinal intestinal lengthening and tailoring (LILT) procedure. Bianchi first described the technique of LILT in 1980. Since then, ≈100 such surgeries have been reported in the literature, predominately in children with short bowel. It is most useful in children with significantly dilated residual intestine in whom dysmotility is present, often with secondary bacterial overgrowth. This surgery includes isolation of the dual blood supply to the small intestine by separation of the mesenteric borders, followed by longitudinal division of the bowel with isoperistaltic end-to-end anastomosis, thereby effectively doubling the length of bowel. The indication for performing LILT is to prevent the need for long-term TPN and its associated complications, including ESLD. Patient selection for LILT surgery include: (1) intestinal diameter > 3 cm; (2) length of residual small bowel > 40 cm; (3) length of dilated bowel > 20 cm; (4) parenteral nutrition dependent; and (5) absence of liver failure. A recent study of 16 infants and children reported significant improvement in stool volume, intestinal transit time, and D-xylose and fat absorption after lengthening the small intestine by ≈42%. Of these 16 patients, 14 could be weaned off parenteral nutrition. Bianchi reported similar results. Some patients have remained off parenteral nutrition as long as 10 years following LILT. Anastomotic stenosis is the most common complication reported with this operation, reported in ≈10% of patients. There is very limited experience with this procedure in adults.

Intestinal Transplantation

Intestinal transplantation is a therapeutic option for patients with intestinal failure. While clinical experience was limited to few case reports prior to the 1990s, the world experience now includes ≈500 intestinal transplants (2/3 in pediatric patients), with the number performed per year increasing every year since 1994. So far, intestinal transplants have been performed only in situations where no other therapeutic alternatives were thought to be available. Therefore, there are no randomized controlled studies (Type I data) comparing intestinal transplantation to other therapies, and very few retrospective case-control studies that would qualify as type II data. Most available data is based on retrospective analyses of national and international registries, individual center experiences, and individual case reports.

**Indications for transplantation.** Thus far, intestinal transplants have only been performed in patients who have developed life-threatening complications attributable to their intestinal failure and/or long-term TPN therapy. Until recently, there had been no official
policy by a third-party payer regarding intestinal transplantation; Medicare has now approved payment for intestinal transplants in patients who fail TPN therapy (Medicare Coverage Policy Decisions—Intestinal and Multivisceral Transplantation [CAG-00036], Oct. 4, 2000). The Health Care Finance Administration (HCFA) based their decision on a review of 3 independent evaluations of the medical literature: (a) data submitted by the unnamed requestor, (b) a 1999 technology assessment performed by the Blue Cross Blue Shield Association’s Technology Evaluation Center, and (c) a separate technology assessment performed by the Center for Practice and Technology Assessment at the Agency for Health Care Research and Quality (AHRQ). Medicare has defined “Failure of TPN therapy” by the development of 1 or more of the following complications:

1. Impending or overt liver failure (elevated serum bilirubin and/or liver enzymes, splenomegaly, thrombocytopenia, gastroesophageal varices, coagulopathy, stomal bleeding, hepatic fibrosis, or cirrhosis).

2. Thrombosis of major central venous channels (2 thromboses in subclavian, jugular, or femoral veins). However, it is extremely rare for complete venous access to be lost. This has not been documented in the available literature.154

3. Frequent central line related sepsis (2 episodes of systemic sepsis secondary to line infection per year, 1 episode of line-related fungemia, septic shock, or acute respiratory distress syndrome). However, considering (a) the low mortality rate,149 (b) observations that catheter sepsis is most commonly related to poor catheter care technique,194 and (c) the high incidence of bacteremia-related complications in intestinal transplant recipients.195 The data to support this indication is weak.

4. Frequent severe dehydration.

**Outcomes of patients waiting for intestine transplants.** Intestinal transplant candidates in need of a cadaver donor are placed on the United Network of Organ Sharing (UNOS) waiting list. The UNOS database maintains waiting list data for all solid organs.196 UNOS data reveals that although the waiting list for intestinal transplants is still fairly small (151 patients on the last day of 2000), it has continued to grow every year since 1993. Average patient waiting times for intestine transplants range from 201 to 343 days depending on their ABO blood group. For patients on the intestinal transplant waiting list, 77% must wait longer than 3 months and 44% longer than 1 year to receive a transplant. While these waiting times compare favorably to those for most other organs,197 the death rate on the waiting list for intestinal transplants is significantly higher than that seen on any other solid organ transplant waiting list (Table 5).196,197 Of the 192 deaths that have occurred since 1993 in patients waiting for intestinal transplants, all but 12 have been in patients who also needed livers (Table 6). Therefore, while patients waiting for an isolated intestine do well on the waiting list, those who also need a liver often do poorly.

A brief explanation of the factors that influence the intestine/liver transplant waiting list logistics is essential to further analyze this high waiting list mortality. Patients who require an isolated intestine transplant are placed on the intestine waiting list. If they require both a liver and an intestine transplant, they are also placed on the liver waiting list, and the intestine will be automatically included when they are allocated the liver (based

---

**Table 5. Comparison of Liver Transplant Waiting List Death Rates Between Liver Only Candidates and Intestine/Liver Candidates**

<table>
<thead>
<tr>
<th></th>
<th>Liver</th>
<th>Intestine/liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>145</td>
<td>434</td>
</tr>
<tr>
<td>1998</td>
<td>135</td>
<td>447</td>
</tr>
<tr>
<td>1999</td>
<td>138</td>
<td>326</td>
</tr>
</tbody>
</table>

1999 death rates on liver waiting list (deaths per 1000 patient years waiting) by UNOS status at time of death

<table>
<thead>
<tr>
<th>UNOS status</th>
<th>Liver</th>
<th>Intestine/liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3111</td>
<td>654</td>
</tr>
<tr>
<td>2A</td>
<td>358</td>
<td>855</td>
</tr>
<tr>
<td>2B</td>
<td>175</td>
<td>796</td>
</tr>
<tr>
<td>3</td>
<td>66</td>
<td>176</td>
</tr>
<tr>
<td>7</td>
<td>196</td>
<td>292</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Overall</td>
<td>138</td>
<td>326</td>
</tr>
</tbody>
</table>

1999 death rates on liver waiting list (deaths per 1000 patient years waiting) by age

<table>
<thead>
<tr>
<th>Age group</th>
<th>Liver</th>
<th>Intestine/liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>234</td>
<td>573</td>
</tr>
<tr>
<td>1–5</td>
<td>92</td>
<td>115</td>
</tr>
<tr>
<td>6–10</td>
<td>48</td>
<td>178</td>
</tr>
<tr>
<td>11–17</td>
<td>80</td>
<td>234</td>
</tr>
<tr>
<td>18–34</td>
<td>119</td>
<td>231</td>
</tr>
<tr>
<td>35–39</td>
<td>113</td>
<td>353</td>
</tr>
<tr>
<td>Overall</td>
<td>138</td>
<td>326</td>
</tr>
</tbody>
</table>
on their status on the liver waiting list). However, if they are offered an intestine based on their status on the intestine waiting list, they will not be automatically assigned a liver. Therefore, in patients who need both organs, it is their status on the liver waiting list, rather than their status on the intestine waiting list, that determines organ availability. Similarly, when multiple organs, including the liver and the intestine, are required, allocation of the additional organs is driven by the liver allocation process.

Priority on the liver waiting list is primarily determined by the UNOS status. A patient’s UNOS status is determined by the perceived medical urgency and is based on their risk of dying on the wait list. Until recently, this was based on their Child-Turcotte-Pugh (CTP) score and specific coexistent complications of ESLD (uncontrolled variceal bleeding, hepatorenal syndrome, intractable ascites or hydrothorax, intractable hepatic encephalopathy, spontaneous bacterial peritonitis). This scoring system has been replaced by the Model for End-stage Liver Disease (MELD) system. Retrospective analysis of UNOS liver waiting list mortality data indicates that the prior CTP score-based UNOS status system did not effectively prioritize intestine/liver candidates (see below). Sufficient data is not yet available to demonstrate if the MELD system is superior as a mortality predictor for wait-listed intestine/liver candidates.

The waiting time for liver transplant candidates varies significantly, but has a direct correlation to their UNOS status. In 2000, the median waiting time for liver transplantations was 7 days for Status 1 (the sickest, highest priority patients) and 36 days for Status 2A (second highest priority). Patients in all UNOS statuses except Status 1, who needed both an intestine and a liver, have had a higher waiting list mortality than patients listed for a liver only. The higher waiting list mortality applied to all age groups (Table 5). Despite their higher mortality, liver transplant candidates with coexistent SBS and/or TPN failure who also need intestine transplants do not currently receive special priority on the liver waiting list. In 1998 and 1999, the vast majority (85%) of waiting list deaths in candidates needing both intestines and livers occurred in patients who were prioritized as Status 2B or less on the liver waiting list (Table 5). More recent UNOS data specifically pertaining to liver/intestine candidates is not yet available.

Other issues that may impede expeditious transplantation in all intestinal transplant candidates include donor/recipient size incompatibility and cytomegalovirus (CMV) status. Most candidates for intestinal transplant have had massive bowel resections, and consequently there is a significant reduction in the capacity of their peritoneal cavity. Therefore, they often require donors who are 50%–75% smaller, thereby limiting the field of potential donors. This is extremely problematic in infants, as emphasized by the fact that in 1998 and 1999, the majority of the deaths on the intestine/liver waiting list (66%) occurred in candidates <6 years old. In some situations, the donor/recipient size issue can be managed by surgical resection of segments of bowel and/or liver from grafts that would otherwise be too large. Because CMV enteritis is a significant problem posttransplant, many centers avoid using CMV positive donors in CMV negative recipients, which can also exclude many potential donors.

### Outcomes of Patients Undergoing Intestinal Transplantation

The world experience. There are no randomized trials comparing intestinal transplantation to long-term TPN or alternative forms of therapy. Data on the results of intestinal transplants are available from 3 sources: (1) The International Intestinal Transplant Registry (ITR), (2) UNOS database, and (3) reports from individual centers (Table 4). UNOS has collected both recipient and donor data for intestinal transplants performed since 1990. This data was compiled and published for the first time in 2001, and represents the United States’ experience up to September 5, 2000 (Table 7). Data submission to the UNOS registry is mandatory for all accredited transplant centers. Based on UNOS data, the number of isolated intestine transplants performed in the United States has increased steadily since 1996. In 1999, there were 36 isolated intestine, 20 intestine/liver, and 12 multivisceral (with intestine included) transplants performed. The primary diagnoses in these recipients

### Table 6. Deaths of Patients on Liver Transplant Waiting List in Candidates Requiring Combined Intestine/Liver Transplants, Based on UNOS Medical Urgency Status at Time of Death

<table>
<thead>
<tr>
<th>Year</th>
<th>Status 1</th>
<th>Status 2A</th>
<th>Status 2B</th>
<th>Status 3</th>
<th>Status 7 (temporarily inactive)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>21</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>1998</td>
<td>1</td>
<td>7</td>
<td>2</td>
<td>20</td>
<td>6</td>
<td>11</td>
</tr>
</tbody>
</table>
were SBS in 64%, functional bowel problems in 26%,
graft failure (retransplant) in 6%, and other in 4%.

Data summarizing the world experience with intesti-
nal transplantation is maintained in an international
registry based in London, Canada, that is updated every 2
years. A summary of this data has previously been pub-
lished twice (most recently in 1999).201 This report can
be reviewed on the ITR Web site (www.lhsc.on.ca/itr).

Because intestinal transplants are performed in relatively
small numbers at very few academic transplant centers
around the world, it is likely that this registry data
represents most, if not all, of the intestinal transplants
performed worldwide since 1985. At the time of its last
update in 1999, 474 intestinal transplants had been
performed on 446 patients at 46 different centers in 16
different countries. This total includes intestine only
transplants (216, 45%), combined intestine/liver trans-
plants (186, 40%), and multivisceral (intestine, liver,
pancreas, stomach, etc.) transplants (72, 15%). The ma-
jority of transplants have been performed in patients
<16 years old (62%) (Table 7).

In patients with ESLD related to TPN, a combined
intestine/liver transplant may be the only option for
continued survival. In patients who will require TPN
permanently, transplantation of the liver alone has gen-
erally resulted in recurrence of ESLD and a poor out-
come. However, in carefully selected ESLD patients with
significant residual intestine who are very likely to be
weaned from TPN soon after transplant, successful trans-
plantation of the liver alone can be achieved.203 Con-
versely, in the setting of ESLD, an isolated intestinal
transplant is likely to yield poor results, although out-
comes data stratifying isolated intestine transplant recip-
ients based on their pretransplant liver abnormalities do
not exist. It is not yet clear when the hepatic pathological
process has become irreversible, or if more benign he-
ptic changes can be distinguished from those that will
ultimately progress to ESLD. While it is generally ac-
nowledged that a combined intestine/liver transplant is
necessary if cirrhosis or portal hypertension are present,
with potentially reversible lesions, such as cholestasis, an
isolated intestinal transplant has been successful in some
circumstances.204 Intestinal failure patients who progress
to ESLD and are placed on the waiting list for a com-
bined intestine/liver transplant have an extremely high
mortality that exceeds that seen on all other solid organ
transplant waiting lists, including liver only transplants
(see below).

**Patient and graft survival.** In the most recent
UNOS cohort evaluated (1997 to 1998), the 1 year
patient and graft survivals were 79% and 64%, respec-
tively for intestine only transplants, and 50% and 49%
in intestine/liver recipients, respectively. With long-
term analysis, patient and graft survivals after intestine
only transplants were 62% and 49% at 3 years, and 50% and
38% at 5 years, respectively. Long-term patient and
graft survivals after combined intestine/liver transplants
were 43% and 41% at 3 years, and 37% and 36% at 5
years, respectively.196

Overall patient and graft survivals in patients trans-
planted after 1995 were 65% and 57% at 1 year, and
50% and 40% at 4 years. These results indicate a statisti-
cally significant improvement in graft ($P = 0.02$), but
not patient ($P = 0.46$), survival from earlier cohorts. In

### Table 7. Intestinal Transplant Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Type of transplant</th>
<th>No. of transplants</th>
<th>Patient survival 1 yr</th>
<th>Graft survival 1 yr</th>
<th>Acute rejection 1 yr</th>
<th>CMV 1 y</th>
<th>PTLD 1 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant201</td>
<td>1999</td>
<td>All</td>
<td>273</td>
<td>59%</td>
<td>35%</td>
<td>73%</td>
<td>23%</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SB only</td>
<td>113</td>
<td>69%</td>
<td>43%</td>
<td>63%</td>
<td>71%</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SB/liver</td>
<td>130</td>
<td>66%</td>
<td>36%</td>
<td>63%</td>
<td>56%</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MV</td>
<td>30</td>
<td>63%</td>
<td>40%</td>
<td>64%</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>UNOS196</td>
<td>2000</td>
<td>All</td>
<td>45</td>
<td>79%</td>
<td>50%</td>
<td>64%</td>
<td>40%</td>
<td>36%</td>
</tr>
<tr>
<td>Abu-Elmagd et al.206</td>
<td></td>
<td>All</td>
<td>104</td>
<td>72%</td>
<td>48%</td>
<td>71%</td>
<td>100%</td>
<td>115%</td>
</tr>
<tr>
<td>Sudan et al.204</td>
<td>1999</td>
<td>SB only</td>
<td>28</td>
<td>93%</td>
<td>48%</td>
<td>64%</td>
<td>40%</td>
<td>93%</td>
</tr>
<tr>
<td>Goulet et al.208</td>
<td></td>
<td>SB only</td>
<td>10</td>
<td>70%</td>
<td>20%</td>
<td>71%</td>
<td>100%</td>
<td>115%</td>
</tr>
<tr>
<td>Pinna et al.205</td>
<td>2000</td>
<td>All</td>
<td>33</td>
<td>56%</td>
<td>2 y</td>
<td>81%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SB only</td>
<td>10</td>
<td>90%</td>
<td>2 y</td>
<td>80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SB/liver</td>
<td>9</td>
<td>58%</td>
<td>2 y</td>
<td>80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>MV</td>
<td>14</td>
<td>70%</td>
<td>2 y</td>
<td>60%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Acute rejection, % of transplant recipients experiencing an acute rejection episode; CMV, % of transplant recipients experiencing a cytomega-
lovirus infection; PTLD, % of transplant recipients experiencing a post-transplant lymphoproliferative disorder; SB, small bowel only transplant; SB/liver, combined small bowel and liver transplant; MV, multivisceral transplant.
all cohorts, the highest patient mortality occurs in the first 6 months posttransplant. This high incidence of early mortality was also noted in individual reports from the most experienced centers.\textsuperscript{205–208} Patient (P = 0.001) and graft (P = 0.002) survival at 1 and 5 years were superior at centers that had performed >10 transplants in the ITR data, although this was not supported by the UNOS registry data.\textsuperscript{196} Overall, these results suggest that the increasing experience with intestinal transplants contributes to improved results. Patient (P = 0.02), but not graft (P = 0.32), survival was significantly better in intestine only transplants compared with transplants involving additional organs (Table 8). This likely reflects the higher pretransplant acuity of the patients who also need livers, the greater magnitude of the surgery they undergo, and the inability to remove their transplanted organs as a life-saving maneuver if there is uncontrolled rejection or sepsis posttransplant.

Living donors have been utilized in a small number of intestinal transplants performed to date. Living donors enhance the opportunity to minimize ischemic time and optimize donor recipient HLA matching. Furthermore, living donors eliminate the need to wait, which can be associated with high mortality in intestinal transplant candidates. The ITR data found no differences in graft survival between recipients of cadaver and living donor intestinal grafts. Although early evidence suggests that use of HLA-matched living donors may be associated with less rejection and fewer infectious complications,\textsuperscript{204} more data will be needed before this approach achieves wide acceptance.

### Posttransplant Complications

Posttransplant complications associated with intestinal transplantation include acute rejection, chronic rejection, CMV infection, and posttransplant lymphoproliferative disease (PTLD).\textsuperscript{201} For intestine only, intestine/liver, and multivisceral transplants, acute rejection occurred in 79%, 71%, and 56%, respectively; chronic rejection in 13%, 3%, and 0%, respectively, CMV infection in 24%, 18%, and 40%, respectively; and PTLD in 7%, 11%, and 13%, respectively. While not yet statistically significant, this data suggests that transplanting additional organs reduces rejection, but increases viral-associated complications.

Patient deaths were attributed to sepsis or multiorgan failure (69%), lymphoma (14%), ischemia/bleeding (13%), and rejection (12%). In surviving patients, 78% had full graft function, 10% had partial function, and 12% had their grafts removed. The most common indication for graft removal was rejection (57%), followed by ischemia/bleeding (23%), sepsis (6%), multiorgan failure (2%), lymphoma (1%), and other (10%).

### Quality of Life in Home TPN Patients and Intestinal Transplant Recipients

The quality of life associated with long-term TPN use has been evaluated by different investigators who have reached different conclusions.\textsuperscript{209,210} However, these investigators did not perform subgroup analysis of those patients with SBS. There are very few quality of life comparisons between intestinal failure patients who remain on TPN and those who undergo intestinal transplantation. Retrospective comparisons between small groups of intestinal transplant patients and long-term TPN patients matched for age and duration of illness suggest that quality of life is the same or slightly better with transplantation.\textsuperscript{211}

### Financial Concerns of Home Parenteral Nutrition and Intestinal Transplantation

Financial issues must also be considered in managing intestinal failure patients. Today, provision of basic home parenteral nutrition (HPN) is associated with charges of between $250 and $500 per day for a given patient, although actual costs for TPN, including the pharmacist’s time for compounding, are on the order of $18–$22 per day, excluding the additional charges of home care services, monitoring, and management of complications. Therefore, if administered 5 days/week, HPN charges often exceed $150,000/year, although costs are significantly less. The costs for transplant evaluation, the transplant and postoperative care, and posttransplant follow-up are not currently available for comparison.

Patients with SBS can lead a productive, lengthy, happy, and a useful life if educated and managed appropriately. It is possible to reduce or even eliminate TPN requirements over time in many of these patients using the evidence-based techniques of dietary and fluid management described in this report. Hormonal therapy may

### Table 8. Intestinal Transplant Registry Data Indicating Influence of Multiple Organ Transplants on Graft and Patient Survival in Intestinal Transplant Recipients

<table>
<thead>
<tr>
<th>Transplant type</th>
<th>% Survival</th>
<th>1 yr</th>
<th>5 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestine only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft\textsuperscript{a}</td>
<td>60%</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>Patient\textsuperscript{b}</td>
<td>71%</td>
<td>45%</td>
<td></td>
</tr>
<tr>
<td>Intestine/liver</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft</td>
<td>55%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Patient</td>
<td>62%</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>Multivisceral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft</td>
<td>48%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Patient</td>
<td>45%</td>
<td>40%</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}P = 0.32.

\textsuperscript{b}P = 0.02.
eventually be available to augment the intestinal adaptation process as this becomes better understood. For patients that do require TPN, it is essential the therapy be prescribed appropriately. In addition, TPN is associated with several potentially serious complications, many of which can be prevented when both the patient and the caring professional have the appropriate expertise.

There are limited indications for small intestinal transplantation. Eminent liver failure is currently the most appropriate indication, although as survival of both patient and graft continue to improve, these indications may be broadened. The management of these patients is complex and is undergoing constant evolution.

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The Clinical Practice Committee acknowledges the following individuals whose critiques of this review paper provided valuable guidance to the authors: Jeffrey L. Barnett, M.D., Eli D. Ehrenpreis, M.D., Sohrab Mobarhan, M.D., Karen Eun-Young Kim, M.D., Gary R. Lichtenstein, M.D.