The Cleveland Clinic institutional guidelines for the management of intestinal failure, including long-term or home parenteral nutrition and related complications, intestinal rehabilitation, and small bowel transplantation, were reviewed. PubMed was searched for relevant articles. The search was performed in November 2008; keywords used were home parenteral nutrition, short bowel syndrome, intestinal rehabilitation, and small-bowel transplantation. Randomized, prospective, observational, retrospective reviews and case report articles that contained relevant data for long-term parenteral nutrition, intestinal rehabilitation, and intestinal transplantation were selected. Researchers reviewed 67 selected articles that met our inclusion criteria. Our institution data registries for intestinal rehabilitation and home parenteral nutrition were also reviewed for relevant data. The survival of tens of thousands of children and adults with complicated gastrointestinal problems has been possible because of parenteral nutrition. In selected patients, a program of intestinal rehabilitation may avoid the need for long-term parenteral nutrition.

Arch Surg. 2010;145(6):521-527

In the 1960s, parenteral nutrition (PN) became part of medical therapy for patients unable to use enterally provided nutrition when Stanley J. Dudrick, MD, under the direction of Jonathan E. Rhoads, MD, developed and perfected techniques that allowed PN to be infused safely into dogs, newborns, and adults. Parenteral nutrition has been used in infants and adults to manage catastrophic complications of surgical diseases, traumatic fistulae, and inflammatory bowel disease by providing adequate nutrition to allow weight gain and wound healing. Its use was expanded from the hospital to treatment of patients with short bowel syndrome (SBS) at home with the first report of a long-term home parenteral nutrition (HPN) case in 1973.

Home parenteral nutrition was started at the Cleveland Clinic in 1975 and its use has rapidly expanded during the last 33 years. The number of patients who are discharged by the HPN team exceeds 200 per year. Most patients need HPN for less than 6 months either to manage complicated surgical conditions that resolve spontaneously or to restore gastrointestinal continuity and function through staged procedures. In the early years of the program, patients were taught how to prepare their own PN solutions because there were no home infusion companies. The time required to train patients was 2 to 3 weeks, and training occurred in the hospital. The training included catheter care, mixing individual components of nutrient fluids, use of the intravenous infusion pump, metabolic self-monitoring, and ways to perform emergency repairs of the catheter. Patients had to pick up a large amount of supplies at the hospital every month. Home infusion companies were eventually established to prepare solutions, deliver them to patients, and manage insurance issues under Medicare part B.

This article reviews the Cleveland Clinic institutional guidelines for the management of intestinal failure, including long-term or HPN and related complications,
intestinal rehabilitation, and small bowel transplantation. PubMed was searched in November 2008 for relevant articles; keywords used were home parenteral nutrition, short bowel syndrome, intestinal rehabilitation, and small-bowel transplantation. Randomized, prospective, observational, retrospective reviews, and case report articles that contained relevant data for long-term PN, intestinal rehabilitation, and intestinal transplantation were selected. Researchers reviewed 67 selected articles that met our inclusion criteria. Our institution data registries for intestinal rehabilitation and HPN were also reviewed for relevant data.

**INDICATIONS OF HPN**

Home parenteral nutrition is indicated when the gastrointestinal tract is unable to maintain normal nutrition and hydration and the patient is otherwise clinically stable and ready for discharge from the hospital. At the Cleveland Clinic, common underlying diagnoses are inflammatory bowel disease, mesenteric ischemia, enterocutaneous fistulas, small bowel obstruction, and radiation enteritis.10-15

**PREPARATION FOR DISCHARGE WITH HPN**

A multidisciplinary hospital-based team evaluates, initiates, and manages patients with HPN. After the patient is approved to receive HPN by a nutrition support team physician, an appropriate vascular access device (VAD) is placed. Peripherally inserted central catheters are usually used for less than 30 days. Tunneled catheters or medical ports are preferred if HPN is needed for longer durations.16 The tip of the catheter is positioned near the junction of the superior vena cava and the right atrium to minimize the incidence of thrombosis or malfunction (Figure 1).16-18 In a study that evaluated 138 readmitted patients for catheter tip position, 15.9% of catheters were malpositioned, and peripherally inserted central catheters were significantly more likely to be malpositioned than tunneled catheters or ports.19

Before patient discharge, a review of insurance coverage and selection of a home care agency are necessary.20 Every HPN candidate should be reevaluated by a case manager, social worker, nurse, dietitian, and physician before discharge. Before 1997, most patients were completely trained in the hospital for 2 to 3 weeks. However, currently, training is initiated in the hospital and completed at home for 2 to 3 days. Interactive and videotaped educational interventions have been shown to reduce catheter-related bloodstream infections, number of hospitalizations, and reactive depression and are currently being updated.21 The PN solution with additives should be stable and the infusion cycled, usually for 10 to 12 hours at night, before discharge. Assessing the adult patient’s fluid requirements with a high-output stoma or fistula is made easier by assessing his or her enteral fluid balance. Enteral intake should ideally be 1500 mL greater than gastrointestinal tract output to allow for 1000 mL of urine output and 500 mL of insensible fluid loss. If enteral intake is restricted and/or gastrointestinal tract output is great, then intravenous fluids should be given to allow the sum of enteral and intravenous fluids to be 1500 mL greater than gastrointestinal output to ensure adequate hydration.22 Caloric requirements are calculated based on the Harris-Benedict equation,23 with adjustments for body mass index (calculated as weight in kilograms divided by height in meters squared). For body mass index greater than 35, we provide 10 to 15 kcal/kg of dry body weight and 1.5 g/kg of amino acids of ideal body weight.24 Goal body weight should be discussed with the patient before discharge. When patients were sent home to gain weight in preparation for restorative gastrointestinal surgery, it was noted that they required, on a daily basis, 35 to 45 kcal/kg of actual body weight.25 Dextrose provides most of the...
Table 1. Monitoring of Patients While Receiving HPN and During Transition to Oral Intake

<table>
<thead>
<tr>
<th>Component</th>
<th>Baseline at Discharge</th>
<th>Daily</th>
<th>Weekly</th>
<th>Monthly</th>
<th>3-6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intake and output, temperature, and weight</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Urinary and blood glucose measurements if receiving total parenteral nutrition</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Check central line</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Electrolytes, blood urea nitrogen, and creatinine measurements</td>
<td>Yes</td>
<td>Yes, progress to next level if stable</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Calcium, magnesium, and phosphorus measurements</td>
<td>Yes</td>
<td>Yes, progress to next level if stable</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Albumin or prealbumin measurement</td>
<td>Yes</td>
<td>Yes, progress to next level if stable</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Liver enzymes, ALP, aspartate aminotransferase, alanine aminotransferase, and bilirubin measurements</td>
<td>Yes</td>
<td>Yes, progress to next level if stable</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Prothrombin time and international normalized ratio</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Trace elements</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Medications</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Vitamins</td>
<td>As indicated</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Anthropometrics and functional status</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Abbreviations: ALP, alkaline phosphatase; HPN, home parenteral nutrition.

calories, and patients receive fat as 500 mL of a 20% fat emulsion once a week to prevent essential fatty acid deficiency.

HPN MONITORING

Patients are asked to record their weight, fluid intake and output, temperature, and urine-dipstick-for-sugar results daily. Routine laboratory work includes serum complete blood cell count, electrolytes, urea nitrogen, creatinine, glucose, calcium, albumin, liver enzymes, bilirubin, magnesium, and phosphorus. These studies are performed weekly until the results are stable and then monthly. Serum trace elements are checked initially and then every 6 months (Table 1). Patients are followed up in the outpatient clinic 1 month after discharge and then once every 3 to 6 months. At each visit, routine nutritional assessment and evaluation of the catheter are performed. Intake and output records and blood chemical analysis results are reviewed. The patient is also considered for an intestinal rehabilitation clinic visit to attempt to minimize PN dependency. All patients are prospectively enrolled in an HPN computerized registry that has all clinical and laboratory information related to HPN. This registry is updated every clinic visit, or laboratory work or an adjustment is made to the PN formula.

HPN COMPLICATIONS

The most common HPN-related complication necessitating subsequent hospitalization is infection, followed by metabolic and mechanical complications. Infectious complications include tunnel and exit site infections, and sepsis from the catheter or other sources. Gram-positive organisms, coagulase-negative staphylococci, and Staphylococcus aureus are the most common pathogens that cause catheter-related sepsis. Patients with catheter-related bloodstream infections present with fever, chills, leukocytosis, and myalgia usually associated with the infusion of their PN solution. If the patient is hemodynamically unstable, the VAD should be removed immediately. If the patient is stable, appropriate blood cultures (quantitative blood cultures from each lumen of the VAD and from a peripheral vein) are obtained, and empirical intravenous antimicrobial therapy should be given through each catheter lumen on the basis of clinical suspicion, the severity of the patient’s acute illness, the underlying disease, and the potential pathogens involved. In suspected catheter-related bloodstream infections, PN is continued, the infectious disease service is consulted, and a 5% dextrose solution with appropriate electrolytes is started. If the patient has a fungal infection or an infection of the subcutaneous port or tunnel, the catheter should be removed. The catheter should also be removed in cases of septic thrombophlebitis, endocarditis, metastatic abscesses, multiple organisms, granulocytopenia, valvular heart disease, and gram-negative bacilli (Pseudomonas species). If there is no evidence of persistent bloodstream infection, the VAD is treated by administering antibiotics through it. The PN infusion may be resumed once an additional blood culture through the VAD produces negative results.

Mechanical complications include catheter dislodgement, withdrawal occlusion, air embolism, and pump malfunction. Catheter-related venous thrombosis has been reported to occur in 0.3% to 28.3% of patients. Risk factors for venous thrombosis include catheter tip position, catheter material and type, multiple lumens, side of VAD insertion, infusate, underlying illness such as cancer and congestive heart failure, duration the catheter is in place, traumatic catheter insertion, malposition, immobility, dehydration, and hypercoagulability. Thrombotic occlusions can be owing to intraluminal clot, fibrin sleeve formation, mural thrombus, or thrombosis of the blood vessel. Venograms are the criterion standard to establish the diagnosis, but color flow Doppler imaging is now the investigation of choice. Magnetic resonance angiography has also recently been used. Treatment options are primarily anticoagulation or thrombolysis. In cases of intraluminal catheter thrombus pro-
ducting withdrawal occlusion or complete occlusion, a thrombolytic drug can be instilled. Patient teaching begins when the VAD is placed and includes flushing techniques and recognizing signs and symptoms of venous thrombosis and infection.

Long-term complications of HPN include liver failure and metabolic bone disease. A total of 25% to 100% of patients receiving long-term PN develop liver enzyme abnormalities, and end-stage liver disease may develop in 15% to 40% of these patients. Salvino et al cast 162 patients using HPN for more than 2 years; they concluded that, when long-term PN is given with a modest amount of total energy and a minimal amount of intravenous fat, abnormal liver enzyme levels are common, but severe liver dysfunction is unusual. Excess carbohydrates (>50 kcal/kg) and excess fat (>1 g/kg daily) are associated with steatosis and cholestasis. The prevalence of complicated HPN-related liver disease also increases with longer duration of PN. Fish oil–based fat emulsion has recently been demonstrated to be of value in infants with PN-related cholestasis. It was used in 18 infants with SBS and cholestasis compared with 21 infants with cholestasis who received soy-based emulsion. The study showed earlier reversal of cholestasis (9.4 vs 44.1 weeks) and decreased mortality (2 vs 7 deaths) with fish oil–based fat emulsion. However, fish oil–based fat emulsion is not commercially available in the United States.

In cases of mild elevations of liver enzyme levels (defined as <2 times the upper limit of normal), we assess overfeeding, encourage oral intake, review medications for hepatotoxicity, and reduce fat emulsion use. In cases of modest elevations in liver enzyme levels (2-5 times above the upper limit of normal or total bilirubin level >3.0 mg/dL [to convert to micromoles per liter, multiply by 17.104]), the steps mentioned herein should be performed. In addition, ultrasonography of the gallbladder is ordered to rule out biliary tract disease and infectious causes. Referral should be made for an urgent hepatologist consultation. The diagnosis of liver abnormalities can be best assessed by liver biopsy. Less invasive measures include ultrasonography-based elastography and magnetic resonance elastography.

All patients using long-term HPN are at risk for metabolic bone disease (osteoporosis and osteomalacia) and should have a dual-energy x-ray absorptiometry scan performed in their first year. Patients with abnormal dual-energy x-ray absorptiometry scan results should be referred to an endocrinologist for possible treatment with calcium, vitamin D, bisphosphonates, and teriparatide. Patients with normal dual-energy x-ray absorptiometry scan results should have an additional dual-energy x-ray absorptiometry scan every 2 years. Monthly calcium, phosphorus, and magnesium measurements should be obtained, and a 24-hour urine sample should be taken for calcium and magnesium measurements every 6 months. For patients at risk for metabolic bone disease, PN solution should be adjusted by minimizing the protein load if possible to 0.8 to 1.0 g/kg daily, providing at least 15 mEq of calcium, 15 mEq of magnesium, and 20 mmol of phosphorus daily. Normal levels of serum calcium, magnesium, and phosphorus are maintained and metabolic acidosis is avoided by adjusting chlo-

NUTRITION THERAPY

Diet therapy for patients with SBS depends in large part on whether the patient has the colon or part of it in continuity with the small bowel (Table 2). After recovery from massive small bowel resection, patients who have difficulty maintaining fluid balance should be instructed on the liberal use of salt and 1 to 2 L of oral rehydration solution sipped between meals (Table 3). If negative fluid balance persists, the patient should continue to receive intravenous hydration and nil by mouth for 24 hours. During the next 48 to 72 hours, the patient should be slowly

INTESTINAL REHABILITATION

The Intestinal Rehabilitation Program at the Cleveland Clinic was founded in 2001 to care for patients with intestinal failure. The main goal of the program is to safely reduce or avoid the need for long-term PN through dietary and medical therapy with referral for surgical reconstruction or small bowel transplantation if indicated. Starting with 3 patients in 2001, the program expanded to evaluate and care for 150 new patients in 2007 and more than 180 new patients in 2008. Short bowel syndrome can result in extensive nutrient and fluid losses. Common sequelae of SBS are gastric acid hypersecretion, inactivation of endogenous pancreatic enzymes, bile acid wasting, rapid intestinal transit, reduced absorptive surface area, and small bowel bacterial overgrowth. Assessment of bowel anatomy through operative reports, pathology reports, intestinal imaging, and plasma citrulline level is performed to determine bowel structure and function.

It is always desirable to wean patients off PN or avoid using it because of the complications associated with its long-term use. Factors that influence or predict the success of PN weaning in patients with SBS include length of the remnant small bowel; presence of colon, ileum, and ileocecal valve; absence of residual disease in the remnant bowel; age of the patient; duration of time receiving PN; and nutritional status before weaning. In general, patients with a remaining small bowel length greater than 100 cm and part of the colon, or a length of greater than 150 cm without an intact and a functional colon, can usually adapt and be weaned off PN successfully. Criteria that should be met before reducing PN include maintaining adequate hydration and nutrition status in the absence of symptoms that limit oral intake. In patients being weaned off PN, clinical monitoring includes daily urine outputs, daily weight, and presence of thirst. Laboratory monitoring includes weekly measurement of electrolytes along with calcium, phosphorus, magnesium, serum urea nitrogen, and creatinine (Table 1). A thorough evaluation of the patient’s gastrointestinal anatomy, nutrition and hydration status, enteral and parenteral intake, urine and gastrointestinal losses, and the use of antidiarrheal and other medications is performed on initial Intestinal Rehabilitation Program referral and at subsequent intervals.
weaned off intravenous fluids, as small portions of appropriate foods and fluids are reintroduced with the goal of maintaining urine output of greater than 800 mL/d.59 Within 4 to 6 weeks after resection, patients with an enterostomy should gradually resume eating fibrous foods and begin soluble fiber supplementation as tolerated to add bulk and prolong transit time through the remaining bowel. Patients unable to consume adequate nutrition orally may benefit from enteral nutrition infused at a slow rate into the gastrointestinal tract through a nasogastric feeding tube or a percutaneous endoscopic gastrostomy tube.60 A recent report61 has documented enhanced nutrient absorption in patients with SBS receiving continuous enteral nutrition via a feeding tube.

### PHARMACOLOGIC THERAPY

Pharmacologic treatment of short bowel includes antidiarrheal (eg, loperamide hydrochloride, diphenoxylate and atropine, codeine, paregoric, and tincture of opium) and antisecretory agents (eg, histamine2-blockers, proton pump inhibitors, octreotide acetate, and clonidine). Bile acid–binding therapy, such as cholestyramine resin, is usually only indicated for limited distal ileal resection. Antimicrobials (eg, metronidazole, ciprofloxacin, and rifaximin) are all of value in treating patients with bacterial overgrowth. Growth factors such as recombinant human growth hormone and glucagonlike peptide 2 have been shown to enhance intestinal adaptation during short periods, but their long-term efficacy has not as yet been documented.55-57,58 Probiotics may also be of help to patients with SBS (Figure 2). In general, if diarrhea is not improved symptomatically within 14 days at maximum dosage, improvement is unlikely with further use of probiotics.55 Intestinal adaptation in SBS may take 1 to 3 years after resection, so persistent trials of combination therapeutic approaches may be required for prolonged periods.

### SURGICAL THERAPY

There are multiple strategies for surgical therapy for SBS. They may be divided into strategies restoring intestinal continuity (takedown enterostomy), relieving obstruction and dysmotility (strictureplasty or bowel tapering for dilated bowel segments), lengthening the remaining dilated intestine (Bianchi procedure or serial transverse enteroplasty technique), prolonging transit time (reversed intestinal segments, colonic interposition, or creation of artificial sphincters), or transplanting new intestine.62

### SMALL-BOWEL TRANSPLANTATION

The indications for intestinal transplantation approved by the US Center for Medicare and Medicaid Services and from the position paper of the American Society of Transplantation are as follows48,63:

1. Failure of HPN (US Center for Medicare and Medicaid Services)
   - Impending or overt liver failure
   - Central venous catheter–related thrombosis of 2 or more central veins
   - Frequent central line sepsis
   - Frequent episodes of severe dehydration
2. High risk of death attributable to the underlying disease (American Society of Transplantation)
3. Intestinal failure with high morbidity or low acceptance of HPN (American Society of Transplantation)
Although referring physicians may be reluctant to refer patients for intestinal transplantation, survival of HPN patients who fulfill the Medicare guidelines and undergo transplantation is significantly greater than it is for the HPN patients who meet the Medicare guidelines and do not undergo intestinal transplantation. However, patients with HPN failure should be referred for transplantation in a timely fashion so that liver transplantation is avoided. In a study that examined the effect of PN-associated liver disease on intestinal transplantation waiting list dynamics, only 65.5% of the patients who were waiting for an intestine transplant received the transplant and 8.8% died while waiting. In addition, 51.9% of the patients who were waiting to receive liver and intestine transplants received the transplant and 29.8% died while waiting. Early transplantation should be considered in the face of progressive liver disease.

CONCLUSIONS

The artificial intestinal tract was a monumental advance in medicine. The survival of tens of thousands of children and adults with complicated gastrointestinal problems has been possible because of the pioneering work started by Dudrick as a surgical resident at the Hospital of the University of Pennsylvania. His determination, hard work, and ingenuity have given us a valuable tool to help our patients through critical gastrointestinal crises. The favorable outcomes associated with its use in treating patients with intestinal failure during many decades at the Cleveland Clinic is a tribute to Dudrick's pioneering work.

Accepted for Publication: October 27, 2009.
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Author Contributions: Drs Shatnawei and Steiger had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Shatnawei, Parekh, Rhoda, Stafford, Quintini, Kirby, and Steiger. Acquisition of data: Shatnawei and Dasari. Analysis and interpretation of data: Speerhas. Drafting of the manuscript: Shatnawei, Dasari, and Steiger. Critical revision of the manuscript for important intellectual content: Shatnawei, Parekh, Rhoda, Speerhas, Stafford, Quintini, Kirby, and Steiger. Administrative, technical, and material support: Rhoda and Steiger. Study supervision: Parekh, Quintini, Kirby, and Steiger.

Financial Disclosure: None reported.

Previous Presentation: This study was presented at the Dudrick Symposium at Yale University; March 28, 2009; New Haven, Connecticut.

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