

## Current Status of Intestinal Failure and Intestinal Transplantation

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Pediatric intestinal failure occurs secondary to short bowel syndrome, motility disorders, or malabsorption. The establishment of an intestinal rehabilitation program and the introduction of innovative surgical and medical treatments, such as the serial transverse enteroplasty procedure and omega-3-containing lipid emulsions, have been major advances in the treatment of intestinal failure. Intestinal transplantation is now established as a therapeutic modality in selected children with irreversible intestinal failure. The improved short to intermediate term survival of intestinal transplant recipients in the last decade can be attributed to immunosuppression with a lymphocyte-depleting agent, control of acute cellular rejection, and comprehensive infection control with careful monitoring of viral pathogens including cytomegalovirus and Epstein-Barr virus. (**Pediatr Gastroenterol Hepatol Nutr 2012; 15: 127~137**)

**Key Words:** Intestinal failure, Short bowel syndrome, Intestinal transplantation, Child, Survival

### INTRODUCTION

Intestinal failure in infants and children is defined as the inability to achieve adequate weight and growth without supplemental parenteral nutrition [1,2]. It occurs when there is a reduction of functional gastrointestinal mass below the minimal amount necessary for adequate digestion and absorption to maintain appropriate protein-energy, fluid, electrolyte, or micronutrient balance. Short bowel syndrome (SBS) is the most common cause of intestinal failure [3]. Intestinal failure may occur in patients with apparent normal intestinal anatomy/length secondary to motility disorders and malabsorption. The first human intestinal trans-

plantation was performed in Boston in 1964. Intestinal transplantation is an established, life-saving modality for patients with intestinal failure who develop significant parenteral nutrition-associated complications.

### INTESTINAL FAILURE

#### Etiology

SBS is a form of intestinal failure resulting from surgical resection, congenital defect, or diseases associated with the loss of absorptive surface area. The incidence of SBS has been estimated to be between 3-5 and 24.5/100,000 births per year [4,5]. Advances in neonatal intensive care, anesthesia, nutrition sup-

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port, and surgical techniques have improved the survival of infants such that the prevalence of SBS has increased in recent years [6]. The common etiologies of SBS include necrotizing enterocolitis (NEC), gastroschisis, intestinal atresia, and midgut volvulus [7]. NEC is the most common disorder resulting in SBS and subsequent intestinal failure in children. Hirschsprung disease involving the small bowel as well as the colon is a cause of SBS. The residual length of short bowel, an intact ileocecal valve, and preservation of the right colon are important factors for survival and adaptation [1].

Intestinal failure may occur in patients with apparent normal intestinal anatomy/length secondary to motility disorders and malabsorption. Chronic intestinal pseudoobstruction is a heterogeneous group of rare disorders, presenting with symptoms and signs of intestinal obstruction, but without a mechanical obstruction. They result from a variety of abnormalities in the enteric nervous system or musculature, and can affect variable segments of the gastrointestinal tract. Congenital diseases of enterocyte development such as microvillus inclusion disease and tufting enteropathy [8] cause intestinal failure. Most children suffering from congenital enteropathy remain permanently dependent on total parenteral nutrition (TPN).

### Adaptation

Adaptation is the spontaneous recovery of intestinal function following massive surgical resection. Intestinal adaptation is marked by an increase in intestinal epithelial absorptive capacity as a compensatory measure for the loss of functional intestinal mass. After surgical resections, adaptation begins almost immediately, but bowel function generally cannot improve over time in patients with microvillus inclusion disease, tufting enteropathy, and chronic idiopathic intestinal pseudo-obstruction.

In the absence of any surgical bowel lengthening and tapering procedure, 35 cm of the neonatal small bowel is associated with a 50% probability of weaning from parenteral nutrition [9]. Generally, premature neonates have a greater capacity for intestinal

growth and, hence, bowel adaptation than full term infants. The presence of an ileocecal valve is a marker for the remaining ileum and this may in fact be the underlying important determinant for weaning from parenteral nutrition, rather than the presence of the valve itself. The loss of colonic length has a relatively modest effect on the necessity for long-term parenteral nutrition. In general, the primary function of the colon is fluid and electrolyte absorption [10].

The search for a biomarker to predict the adaptive ability of the intestine is critical with regard to prognosis and the decision to transplant or continue rehabilitative efforts. Plasma citrulline, a nonessential amino acid produced almost exclusively by enterocytes, appears to be an excellent biomarker. Intestinal failure patients with a serum citrulline level < 12 mmol/L are usually unable to wean from parenteral nutrition [11].

### Nutritional deficiency

Maintenance of proper electrolyte balance is important. Children with SBS and an enterostomy or poor colonic function lose much more sodium than potassium in their stool and may have enormous parenteral sodium needs. Total body electrolyte levels (e.g., potassium, sodium, magnesium) may be reduced in the face of normal serum levels. Therefore, urinary levels may be a more accurate reflection of the total body condition. Sodium should be administered in TPN in a quantity adequate to maintain urinary sodium > 30 mEq/L and sodium to potassium ratios approximating 1 : 1. Prolonged sodium losses lead to growth failure [12]. Low serum bicarbonate may be managed by increasing acetate in the parenteral nutrition.

Hypocalcemia can be a consequence of fat malabsorption. Fatty acids bind calcium, leading to the absorption of free oxalate and loss of calcium in the stool. Free urinary oxalate in large amounts bind in the renal tubules with calcium to form calcium oxalate stones and decrease the amount of absorbed calcium [13].

Trace element depletion is common among patients with SBS if parenteral administration is

inadequate. Adequate parenteral zinc supplementation is particularly important among patients who have undergone extensive intestinal resection because zinc losses are as high as 17 mg/L in ileostomy fluid [14]. Severe zinc deficiency results in acrodermatitis enteropathica, characterized by a rash of the face, hands, feet, and genitalia. It is common for children with SBS to require 300-500  $\mu$ g/kg/d of zinc. Serum zinc levels tend to be decreased when a patient is systemically zinc deficient, but serum levels correlate relatively badly with the deficiency. As zinc is a cofactor for alkaline phosphatase synthesis, a surrogate marker for zinc deficiency is the serum alkaline phosphatase level, which is likely to be decreased in patients with the clinical manifestations of zinc deficiency.

Copper deficiency is a trace element deficiency that is often iatrogenically induced [15]. It is a common dogma that among children with parenteral nutrition-associated liver disease (PNLD), hepatic copper retention places an excessive oxidative burden upon the liver. The common practice is to reduce or eliminate parenteral copper in patients with PNLD. This may result in copper deficiency resulting in neutropenia, thrombocytopenia, or pancytopenia. If these findings are present in children on copper-deficient TPN, copper and ceruloplasmin levels should be measured, and copper replaced, if evidence for copper deficiency exists.

Vitamin B<sub>12</sub> levels are of particular concern in patients with an ileal resection. Vitamin B<sub>12</sub> assays can be unreliable, therefore additional screening of urine methylmalonic acid, which accumulates in B<sub>12</sub> deficiency, is advisable [16]. Vitamin B<sub>12</sub> malabsorption requires life-long vitamin B<sub>12</sub> supplementation, usually accomplished with monthly intramuscular injections.

Provision of enteral water-soluble vitamins is unnecessary while patients are on parenteral vitamin supplements. But, if adaptation occurs and patients are weaned off TPN, enteral provision of most water-soluble vitamins is recommended. Fat-soluble vitamin supplementation is delivered via parenteral vitamins and parenteral lipid, generally preventing

deficiency. But, after weaning of TPN, enteral supplementation is advisable. After transition to full enteral nutrition, the most common micronutrient deficiencies are vitamin D, zinc, and iron [17].

Patients with SBS may develop gastric hypersecretion [18]. Because most gastrin catabolism takes place in the small intestine, these patients become hypergastrinemic and produce excessive gastric acid and gastric volume. The volume produced may contribute to fluid and electrolyte losses, and the hyperacidity may result in peptic ulceration. Acid hypersecretion may be associated with deactivation of pancreatic enzymes and bile acid precipitation with subsequent ineffective micelle formation. For patients with excessive enteral fluid losses soon after small bowel resection, a trial of acid suppressing medications is suggested. The gastric hypersecretion typically resolves during the first few months after surgery.

### Bacterial overgrowth

Bacterial overgrowth of the small intestine is an important pathophysiologic change in SBS [19]. Adverse effects include deconjugation of bile acids, which render them incapable of forming micelles, competitive metabolism and use of enteral nutrients and vitamins, synthesis of toxic byproducts such as d-lactate, and bacterial translocation to produce septicemia. Small bowel bacterial overgrowth is usually associated with anorexia, vomiting, diarrhea, cramps, abdominal distention, D-lactic acidosis, and failure to thrive. In addition, bacterial overgrowth exacerbates hepatotoxicity related to parenteral nutrition. A rational antibacterial strategy is to give cycled 10-14-day courses of antibiotics specific for their anaerobic spectrum. These could be followed by 14-20-day rest periods. Antibiotics of choice include metronidazole and rifaximin [20].

### Catheter-related infections

A central venous catheter (CVC) is essential for children for whom long-term TPN is anticipated. Strict protocols for line care, for accessing CVCs, and for dressing changes are customarily employed to de-

crease the frequency of line-associated complications. One of the factors resulting in repeated line infections may be the propensity of bacteria to form biofilms adherent to the walls of CVCs that provide nutrients to viable, but aggregated bacteria, as well as protection from systemic antibiotics. Bacteria are periodically shed from these films and produce systemic infections.

Any suspicion for catheter-related infections needs to be thoroughly assessed. A child with SBS and symptoms of fever, lethargy, irritability, or abdominal distension may have catheter-related infections. The most important investigation to confirm catheter related infections is a blood culture through the central line. If the patient's clinical presentation is congruent with catheter-related infections, broad spectrum intravenous antibiotics are started through the central line.

A promising therapy in the prevention of catheter related infections is the use of ethanol locks. Ethanol can penetrate biofilms that form on central lines, and no bacteria or fungi have been reported to be resistant to ethanol. The ethanol lock therapy for the prevention of catheter related infections in pediatric intestinal failure patients significantly decreases bloodstream infection rates [21,22].

### **PNLD**

One of the most devastating disorders in patients on long-term TPN is PNLD. Patients on TPN are at risk for fatty liver, hepatic fibrosis, and cholestasis. The pathogenesis is multifactorial and is related to prematurity, low birth weight, duration of TPN, SBS requiring multiple laparotomies, and recurrent sepsis. Other important mechanisms include lack of enteral feeding that leads to reduced gut hormone secretion, reduction of bile flow and biliary stasis that leads to the development of cholestasis, and biliary sludge and gallstones that exacerbate hepatic dysfunction, especially in premature neonates with immature hepatic function [23]. The use of lipid emulsions, particularly soy bean emulsions, have been associated with cholestasis in children [24]. Management strategies for the prevention of PNLD include early enteral feeding,

a multidisciplinary approach to the management of parenteral nutrition with a specialized nutritional care team, and aseptic catheter techniques to reduce sepsis. Fish oil is rich in omega-3 fatty acids that have potential anti-inflammatory effects upon the liver. The use of fish oil containing lipid emulsions (e.g., soy bean/medium chain triglyceride/olive oil/fish oil) improves established cholestasis and may prevent the onset in premature infants and children [25,26]. Efforts to cycle TPN in an attempt to better mimic intestinal physiologic and hormonal regulation have been employed to enhance adaptation as well as improve cholestasis [27]. Oral administration of ursodeoxycholic acid may improve bile flow and reduce gall bladder stasis, although there is little data to suggest that prophylactic use prevents the onset of PNLD [28].

All patients using long-term parenteral nutrition 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 [29].

### **Enteral nutrition**

Prompt transition to enteral nutrition is the most important intervention in infants with intestinal failure as it obviates PNLD and catheter-related infection. Maintenance of enteral nutrition is a crucial step in guaranteeing that the maximal adaptive response will occur following a resection. An optimal formula for the provision of calories in pediatric intestinal failure has not clearly been established. Both breast milk and commercially available elemental formulas are associated with a reduction in the time of parenteral nutrition dependence in infants with SBS [9]. There is little consensus as to the timing of initiation of feedings, but evidence suggests that following surgery for NEC, early feeding is associated with no greater recurrence rate but a shorter time to reach full feedings [20]. As soon as 12 hours after abdominal surgery, neonates can tolerate small volumes of breast milk [30]. Feedings can be initiated as bolus feedings or continuous feedings via a gastrostomy or nasogastric tube. Although bolus feedings

recapitulate oral feeding through hormonal stimulation, continuous feedings may provide better absorption.

Limitations to advancing enteral feeding are stool/stoma output, abdominal distention, and vomiting. Stool/stoma output is traditionally limited to 40-50 mL/kg per day, although higher volumes are often tolerated as long as hydration and electrolyte stability can be maintained [31].

### Medical and surgical management

Through adaptation, small intestinal surface area and absorptive function may improve over time to facilitate weaning from parenteral nutrition. Beyond provision of enteral nutrition, ancillary therapies such as judicious use of acid suppression, prokinetics and antidiarrheal agents seem to accelerate the rate of adaptation in young children. Clinical studies have demonstrated improved gastric motility and post-operative intestinal dysmotility with low-dose erythromycin. Oral erythromycin is associated with a shorter time to full enteral feeds, a decrease in the duration of parenteral nutrition requirements, and a reduction in the incidence of parenteral nutrition-associated cholestasis [32]. Antidiarrheal drugs such as loperamide decrease stool output from an ileostomy [33]. Recommended dosage for loperamide is 0.08-0.24 mg/kg/day divided two or three times. Cholestyramine often improves diarrhea associated with bile salt malabsorption.

In parenteral nutrition dependent patients with SBS, the use of recombinant human growth hormone has led to variable results [34,35]. More recently, the focus has shifted to glucagon-like peptide 2 and its analogues (Teduglutide) as a strategy to regulate maintenance and adaptive growth of the small intestinal mucosa. Phase III studies have indicated the potential of Teduglutide in reducing the need for parenteral nutrition in adult patients with SBS [36]. No studies involving Teduglutide have been investigated in the pediatric population.

A combined medical and surgical treatment is a key factor in successful intestinal adaptation. Surgical interventions include early stoma closure

and lengthening procedures that can improve the absorptive capacity of the failing gut and shorten the duration of parenteral nutrition. Serial transverse enteroplasty (STEP) creates transverse divisions from alternating directions resulting in an accordion type lengthening of the dilated segment. STEP improves enteral tolerance and results in significant catch-up growth [37].

### Intestinal rehabilitation program

Although relatively few children suffer from intestinal failure, the morbidity and mortality associated with it is high, which can have a profound impact upon both healthcare costs and resources. These financial implications as well as the recognized complexity of patient needs including medical, nutritional, psychosocial, surgical, behavioral, and other aspects of care have led to the development of intestinal rehabilitation programs designed to support a multidisciplinary approach to capture individual expertise in these areas. The goals of each intestinal rehabilitation program are to achieve enteral, if not oral autonomy, freeing of the child from CVC and enteral feeding devices; to reduce morbidity and mortality associated with intestinal failure and its management; and to identify those children who will likely not survive without intestinal transplantation [38].

## INTESTINAL TRANSPLANTATION

### Indication and type

Despite appropriate multidisciplinary treatment of intestinal failure, 20-40% of children with intestinal failure remain parenteral nutrition-dependent and those who developed parenteral nutrition complications, including line sepsis and PNLD, are considered for an intestinal transplantation [39].

There are three major types of grafts: isolated intestine; liver-intestine, which usually includes the duodenum and head of pancreas to avoid the need for a biliary anastomosis; and multivisceral, which contains intestine with stomach, duodenum, pancreas and possibly colon, with liver (full multivisceral) or without liver (modified multivisceral). Isolated in-

testine grafting is indicated for patients with limited venous access, recurrent line infections, reversible liver failure as a result of parenteral nutrition, and unmanageable fluid and electrolyte problems associated with parenteral nutrition. The liver should be added to an intestine graft when the recipient has irreversible liver damage as a result of parenteral nutrition, usually manifested by severe fibrosis with or without portal hypertension and liver dysfunction. Multivisceral transplants are indicated for children with severe motility disorders such as chronic intestinal pseudo-obstruction or patients with extensive abdominal pathology that cannot be safely removed without an evisceration or reconstruction with multiple organs (e.g., children with multiple previous operations and severe portal hypertension) [40]. Isolated intestinal transplantation has been more frequently performed in adults (55% of all intestinal transplants) than children (37%), in whom liver-intestine transplants are required more frequently (50%) due to the greater incidence of PNLD in children.

Living donor intestinal transplantation has several potential advantages including elimination of waiting time, elective nature of the procedure, better human leukocyte antigen (HLA) matching, and short cold ischemia time. In particular, the best indication is probably living donor liver-intestine transplantation in pediatric patients with intestinal and hepatic failure. In this setting, the virtual elimination of waiting time may avoid the high mortality experienced by candidates on the deceased waiting list [41].

A gastrostomy or jejunostomy feeding tube is placed to facilitate early posttransplant enteral nutrition and rehabilitation, and enteral feeding is started at postoperative day 5 to 7 following resolution of the postsurgical ileus. A temporary ileostomy (loop or chimney) provides easy access to the intestinal mucosa for routine surveillance biopsies to monitor rejection and infection [42].

### Immunosuppression

Modification of immunosuppression over the past

three decades has likely contributed to improved graft and patient survival. The recent strategy in many centers is to use a recipient preconditioning protocol with a lymphocyte-depleting agent, such as rabbit anti-thymocyte globulin (thymoglobulin) or alemtuzumab (Campath), a monoclonal anti-CD52 antibody, and to dramatically reduce acute rejection [42]. This has enabled a reduction in posttransplant tacrolimus, and often withdrawal of steroids, with subsequent minimization of long-term side-effects of immunosuppression. Antithymocyte globulin is given as a single dose of 5 mg/kg administered over 4-6 hours and completed prior to reperfusion of the allograft. Alemtuzumab, which has now largely replaced thymoglobulin in most centers, is infused as a single intravenous dose of 0.5 mg/kg up to a maximum of 30 mg, infused over 2 hours on induction of anesthesia. Using this strategy, many patients have been stabilized on low-dose tacrolimus monotherapy.

### Graft rejection

Acute cellular rejection occurs in 60% of children with intestinal transplantation, is severe in over a third, and limits long-term survival [43]. The highly immunogenic small bowel allograft contains a large amount of gut-associated lymphoid tissue, of which donor dendritic cells elicit the most potent immune response from the recipient.

Acute cellular rejection is usually characterized by diarrhea and disruption of the gut mucosal barrier, which may lead to bacterial sepsis and fever. A majority of the episodes occur during the first 90 days, when most recipients still have indwelling central venous lines for fluid management, as the transplanted allograft is adapting to its new environment. Therefore, bacteremia and fever should not be labeled catheter-related infections alone, but should be considered as manifestations of acute cellular rejection and should lead to endoscopic biopsies to exclude rejection [44]. Early detection and prompt treatment of graft rejection and infections have contributed to the improved results of intestinal transplantation. Protocol ileoscopies with intestinal

biopsies are recommended to monitor the intestine graft after transplant. The surveillance biopsy schedule is biweekly in the first month, weekly during the second month, and bimonthly during the third month. The endoscopic findings of acute rejection include blunted and short villi, edematous and friable mucosa, superficial or deep ulcers, and diffuse mucosal exfoliation; these findings can be mimicked by infection. The histopathological features of acute cellular rejection include a mixed but mostly mononuclear infiltrate with activated lymphocytes, villus blunting and crypt epithelial cell apoptosis [45]. The rejection is graded as indeterminate, mild, moderate or severe depending upon the extent of the mucosal injury and the degree of inflammatory infiltrate and apoptosis. With severe acute rejection, the changes mentioned earlier are accompanied by diffuse mucosal ulceration and erosion up to a complete loss of the bowel morphology and mucosal sloughing. Treatment of mild acute rejection involves methylprednisolone pulse therapy, with a temporary increase in the tacrolimus dose. Anti-thymocyte globulin or alemtuzumab is reserved for severe or corticosteroid unresponsive rejection, and is given for 7-14 days [42].

Acute humoral rejection occurs in a smaller proportion, particularly in strongly positive lymphocytotoxic, cross-match transplants [43]. Histopathological features include endothelial swelling, fibrin thrombi in capillaries, ulceration of the mucosa, and the presence of diffuse C4d deposits adjacent to capillary endothelial cells. These findings correlate with the presence of donor specific, anti-HLA antibodies (DSA) [44]. Acute humoral rejection is treated with anti-lymphocyte antibody preparations. DSA is also found in two thirds of acute cellular rejection, and declines as rejection episodes resolve [46]. A multivariate analysis of 106 intestinal transplantations identified a strong association between DSA and graft loss [47].

Chronic rejection is observed in about 15% of recipients, and is the predominant cause of delayed allograft failure and enterectomy [43]. The presentations include chronic diarrhea, abdominal pain, chronic

bleeding, and graft malfunction with weight loss. The pathology of chronic rejection is intimal hyperplasia and obliterative arteriopathy in the submucosal layers. Endoscopic biopsies may show mucosal and submucosal fibrosis and atrophy, distorted villi, crypt damage, and occasionally arteriopathy of small arterioles [48]. However, a full thickness biopsy is needed to confirm this diagnosis, which is manifested by atherosclerotic-type lesions with eccentric intimal hyperplasia and concentric fibrous intimal thickening in the large and medium-size arteries. Rates of chronic rejection are significantly lower in patients with liver containing allografts (liver-intestine and full multivisceral) than liver-free allografts, confirming a protective immunomodulating effect of the liver [49]. Patients with recurrent, early, and severe acute rejection are more susceptible for chronic rejection and should be carefully monitored to ensure optimal immunosuppressive treatment and avoid further episodes of acute rejection. Unlike acute rejection, recipient pretreatment does not appear to protect against chronic rejection. There is no definite treatment of chronic rejection because of poor understanding of the mechanism of this type of rejection, and retransplantation is usually the only solution.

### **Infection and posttransplant lymphoproliferative disorder**

Infections remain common after transplantation. It is important to distinguish viral or bacterial enteritis from rejection. Most bacterial infection can be controlled with appropriate antibiotic treatment but sepsis remains a leading cause of death and accounts for approximately 50% of the causes of death [40]. In the immediate posttransplant period, prophylactic systemic antimicrobial and antifungal therapy are administered to all recipients.

A major advance in the reduction of graft failure and patient mortality has been improved diagnosis, prophylaxis, and therapy of viral infections and their complications. Cytomegalovirus (CMV) prophylaxis and treatment with intravenous ganciclovir and CMV-specific hyperimmune globulin (cytogam), and routine use of polymerase chain reaction (PCR) assay

for early detection, have greatly reduced the adverse influence of this virus. Monitoring Epstein-Barr virus (EBV) by PCR, which might be a prelude posttransplant lymphoproliferative disorder (PTLD), enables reduction of immunosuppression or, in advanced cases, the use of the anti-CD20 monoclonal antibody, rituximab [42]. The presence of rising EBV titers on routine surveillance often provides a trigger to reduce the dose of maintenance immunosuppression by 25-50%. As a result of the use of optimal maintenance immunosuppression, and careful monitoring and preemptive treatment for EBV, the current incidence of PTLD is decreasing to 10% among recipients.

Viral pathogens that usually induce self-limited diarrhea in an immunocompetent child can lead to severe and prolonged diarrhea in intestinal transplant recipients. Clinical symptoms and endoscopic findings of viral infection and acute rejection overlap. Thus, differentiation is often challenging. In addition to hematoxylin and eosin stains, immunohistochemistry and use of the PCR may facilitate the identification of the viruses. Besides common and known viral pathogens such as CMV, EBV, and rotavirus, other less common enteric viral infection such as adenovirus and norovirus have emerged in the last decade as important pathogens in intestinal transplant recipients [50,51]. Routine surveillance of CMV, EBV, and adenovirus in blood and intestinal biopsies is recommended to ensure early and timely detection of infection.

### Chronic renal failure (CRF)

CRF is common after solid-organ transplantation and is a leading cause of posttransplant morbidity and mortality. In one study, 8.6% of recipients were on dialysis or requiring kidney transplantation for CRF [52]. Risk factors for CRF include a low preoperative glomerular filtration rate, preoperative intensive care admission, and high tacrolimus level [53].

### Outcome

Patient and graft survival are now at very least equivalent to what would be expected if the patients were to remain on home parenteral nutrition (HPN).

This was demonstrated by the results of a 5-year prospective study emerging from the European HPN database, which documented a 5-year survival in potential transplant candidates who remained on HPN of 73%, decreasing to 56% if they had life-threatening conditions, such as impending liver failure or desmoids tumors [54].

Experiences with more than 2,500 cases were reviewed in the Intestinal Transplant Registry 2011 Report (<http://intestinaltransplant.org>). Between 1985 and 2011, 1,277 pediatric intestinal transplants have been performed with more than 600 survivors. Anti-thymocyte globulin or alemtuzumab pretreatment-based strategy was associated with significant improvement in outcome with 1- and 5-year survival of 92% and 70%. Despite improvements in short-term outcomes, patient survival at 10 and 15 years was only 42% and 35%, respectively [43].

In one study, the 1-, 3- and 5-year patient survival of 199 children who were transplanted in Pittsburgh in the new era is 95%, 84%, and 77%, respectively. Graft survival was 88%, 74%, and 58%, respectively [55]. Poor prognostic markers included children younger than 1 year of age, no induction therapy with interleukin-2 blockers, and waiting in hospital before transplant [56]. Graft failures have led to retransplantation in 7% of pediatric transplants [44].

Patients can successfully be weaned off TPN within a month of intestinal transplantation and maintain their serum protein parameters and Z-scores for weight in a normal range. However, many have ongoing nutritional deficiencies and demonstrate poor catch-up growth [57]. Most intestinal transplant recipients have a good or normal quality of life after transplantation, and their quality of life might be better than when they were on parenteral nutrition.

## CONCLUSION

Intestinal failure occurs when the functional gastrointestinal mass is reduced. A number of management strategies are utilized to achieve successful intestinal rehabilitation and maintain adequate nutrition. These strategies include minimizing the ef-

fect of PNLD, limiting catheter complications, and treating bacterial overgrowth in the remaining small intestine. Intestinal transplantation is now established as a therapeutic and cost-effective modality in selected patients with irreversible intestinal failure. As a result of recent surgical advances, control of acute cellular rejection, and a decrease in lethal infections, survival of intestinal transplant recipients has improved in the last decade. At experienced centers, 5-year patient and graft survival rates approach 80% and 60%, respectively. However, achieving improved long-term (> 10 years) graft survival remains a clinical priority.

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