

Where are we at with short bowel syndrome and small bowel transplant?

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Abstract

Intestinal failure can be defined as the critical reduction of functional gut mass below the minimal amount necessary for adequate digestion and absorption to satisfy body nutrient and fluid requirements in adults or children. Short bowel syndrome (SBS) is characterized by a state of malabsorption following extensive resection of the small bowel. SBS may occur after resection of more than 50% and is certain after resection of more than 70% of the small intestine, or if less than 100 cm of small bowel is left. Several treatment modalities other than total parenteral nutrition, including hormones (recombinant human growth hormone, glucagon-like peptide-2) and tailoring surgeries (Bianchi procedure, serial transverse enteroplasty), had been proposed, however these were either experimental or inefficient. Small bowel transplant is a rather new approach for SBS. The once feared field of solid organ transplantation is nowadays becoming more and more popular, even in developing countries. This is partially secondary to the developments in immunosuppressive strategy. In this regard, alemtuzumab deserves special attention. There are more complex surgeries, such as multivisceral transplantation, for multi-organ involvement including small bowel. This latter technique is relatively new when compared to small bowel transplant, and is performed in certain centers worldwide. In this review,

an attempt is made to give an insight into small bowel syndrome, small bowel transplantation, and related issues.

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Key words: Short bowel syndrome; Small bowel transplantation; Nutrition; Immunosuppression

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INTRODUCTION

Intestinal failure (IF) can be defined as the critical reduction of functional gut mass below the minimal amount necessary for adequate digestion and absorption to satisfy body nutrient and fluid requirements in adults or children. IF itself is a general term used in combination with short bowel syndrome (SBS)^[1]. SBS is characterized by a state of malabsorption following extensive resection of the small bowel^[2,3]. There is no exact current data regarding the incidence and prevalence of SBS. Data derived from patients receiving home parenteral nutrition (PN) indicate an incidence of severe SBS of 1-2 cases per 100 000 people per year^[4].

Several conditions requiring intestinal resection lead to SBS in adults. In a reported series of 210 cases, these conditions included: 52 postoperative (25%), 51 irradiation/cancer (24%), 46 mesenteric vascular disease (22%), 34 Crohn's disease (16%), and 27 other benign causes (13%)^[5].

Causes of IF in children include: SBS, congenital diseases of enterocyte development, and severe motility disorders (total or subtotal aganglionosis or chronic intestinal pseudo-obstruction syndrome) as shown in Table 1^[6].

SBS may occur after resection of more than 50% and is certain after resection of more than 70% of the small intestine, or if less than 100 cm of small bowel is left. It is particularly severe after resection of the ileocecal region or if the colon has been additionally removed. Function is not dependent on length alone, since 150 cm of diseased bowel might function worse than 75 cm of healthy intestine. For this reason, some definitions of SBS and IF have been based on measurements of the functional capacity of the remaining bowel. A 48-h nutritional balance study in patients dependent on home total PN (TPN) compared with patients who were not, demonstrated that IF could be predicted by an absorption rate below 1.4 kg/d of wet weight and 84% of the calculated basal metabolic rate (1171 kilocalories/d of energy). It is important to note that nutritional balance studies are very difficult to perform accurately in practice, as they require the analysis of food portions and accurate stool collections^[7-10].

After the insult on the gastrointestinal system, intestines show an adaptation process. This intestinal adaptation process in SBS has three phases. The acute phase starts directly after resection and generally lasts less than 4 wk. This serves for the patient's stabilization. The second phase is the adaptation phase, which lasts 1-2 years and represents maximal stimulation of intestinal adaptation achieved by gradually increasing intestinal nutrient exposure. The last phase is the maintenance phase, which requires permanent individualized dietetic treatment^[11].

SURGICAL THERAPY FOR SBS

A small number of patients will acquire intestinal autonomy (i.e., PN weaning) very slowly because of major motility disorders or a small bowel without an ileocecal valve. In such patients, different surgical approaches have been proposed for increasing nutrient and fluid absorption by either slowing intestinal transit or increasing surface area.

Although surgical procedures aimed at slowing intestinal transit have been attempted and extensively reviewed, the clinical results are conflicting. Such procedures include intestinal valves, reversed intestinal segments, colon interposition, and electrical retrograde small bowel stimulation^[12].

For selected patients with dilated bowel segments, longitudinal intestinal lengthening and tailoring (Bianchi procedure) was first proposed in 1980. The Bianchi procedure has the advantage of tapering the dilated segment and using the divided intestine to increase total small bowel length. Anatomic criteria have been suggested for patient selection for this procedure: (1) intestinal diameter > 3 cm; (2) length of residual small bowel > 40 cm; and (3) length of dilated bowel > 20 cm. This procedure allows improvement in more than 50% of patients in terms of

Table 1 Causes of intestinal failure in children

Atresia	Necrotizing enterocolitis
Midgut volvulus	Arterial thrombosis
Abdominal wall defects	Venous Thrombosis
Gastrochisis	Intussusception
Ompalocele	Inflammatory bowel disease
Hirschsprung's disease	Post traumatic resection

intestinal transit, stool frequency, intestinal absorption rate, weight gain, and PN weaning^[13].

The Bianchi procedure does not create any additional surface area for absorption, but has been demonstrated to increase the function of the remnant small bowel. Specific improvements have been shown in fat absorption, carbohydrate absorption, and the slowing of transit time through the intestine in children at 4 centers. Outcome is influenced by age and clinical status, especially liver status, of the patient at the time of surgery. It is yet not recommended to perform the Bianchi procedure in patients with severe liver disease or cirrhosis. However, this procedure may be successfully achieved after isolated liver transplantation for SBS^[14].

A new procedure called serial transverse enteroplasty (STEP) was introduced in 2003 for infants and children with SBS. Experience with this procedure still remains too limited to make any confident recommendation^[15,16].

A study comparing the outcomes of Bianchi type longitudinal lengthening to STEP lengthening stated that surgical lengthening with both Bianchi and STEP procedures results in an improvement in enteral nutrition, reverses complications of TPN, and avoids intestinal transplantation (ITx) in the majority, with few surgical complications. ITx can salvage most patients who later develop life-threatening complications or fail to wean TPN.

Surgical lengthening may therefore be useful in selected patients without complications of portal hypertension as a bridge to ITx, primarily in the youngest and jaundiced infants who are below 8 or 10 kg in body weight and unlikely to find an appropriate organ donor. Patients with advanced liver disease are poor candidates for lengthening and should instead be referred for ITx^[17].

HORMONAL THERAPY FOR SBS

Recombinant human growth hormone (rhGH) was used in adult patients with SBS in both open and randomized clinical trials^[18]. Scolapio *et al.*^[19] did not show benefits from the use of rhGH in short bowel adult patients, whereas Seguy *et al.*^[20] recently showed a significant improvement of the absorption rates, with a decrease in PN requirements of adult patients with SBS. In another study, growth hormone administration (0.5 IU/kg per day or 0.024 mg/kg per day) alone for 8 wk had no effect on the absorptive capacity of energy, protein, or fluid in 10 patients^[21]. The use of rhGH treatment in adults remains controversial, whereas the incidence rate of secondary ef-

fects is high. To date, few studies have been reported in children with SBS^[22-24]. An open-label clinical trial was performed in infants who received 0.3 IU/kg per day rhGH for a 10 d period of treatment^[22]. A significant weight gain during treatment was reported, whereas no information was given about PN weaning. An open-label trial involving 8 PN-dependent children with neonatal SBS receiving > 50% of their protein energy requirements from PN was also performed^[23]. They received 0.6 IU/kg per day rhGH for 3 mo. All were weaned from PN during the treatment period. However, only 2 children remained free of PN 1 year later. More recently, PN-dependent children with neonatal SBS received 0.14 mg/kg per day and glutamine for 3 mo^[24]. Preliminary results suggested a beneficial effect of rhGH by decreasing the need for PN, but with mild effects on body composition and gut mucosa. More prolonged, and perhaps earlier, use of rhGH in SBS infants or children might be helpful for future management.

Glucagon-like peptide-2 (GLP-2), a 33 amino acid peptide-encoded carboxy-terminal to the sequence of GLP-1 in the proglucagon gene, is produced by L cells in the ileum in response to luminal nutrients^[25]. The effect of GLP-2 on gastrointestinal function was assessed in patients without a terminal ileum or colon who had functional SBS with severe malabsorption and no postprandial secretion of GLP-2^[26]. Balance studies were performed before and after treatment with GLP-2; 400 µg subcutaneously twice a day for 35 d. Treatment with GLP-2 improved the intestinal absorption of energy and increased body weight. Thus, GLP-2 improves intestinal absorption and nutritional status in short-bowel patients with impaired postprandial GLP-2 secretion in whom the terminal ileum and the colon have been resected, based on the hypothesis that distal small bowel and caecal resection would decrease GLP-2 levels and reduce adaptation^[27]. GLP-2 might be the most logical medical approach for early management of short bowel patients, especially those with ileal resection. Genetically engineered GLP-2 analogs should be commercially available in the near future for clinical use.

ENTERAL NUTRITION IN SBS

Enteral nutrition is the most significant single factor in promoting intestinal adaptation, and may play a part in reducing the frequency of IF-associated liver disease. Detailed evidence on the management of SBS has recently been published^[28]. Breast milk may be the best choice in the first few months, because of the presence of trophic factors such as epidermal growth factor. Amino acid based formulas may be beneficial in weaning children from PN, perhaps due to a smaller antigenic load^[29].

Continuous nasogastric (NG) feeding initially, followed by overnight NG feeding and bolus feeding during the day, is recommended in order to utilize existing small bowel function and encourage oral feeding. Maintaining a urinary sodium/potassium ratio of at least 2:1 with an absolute urinary sodium concentration of over

10-20 mmol/L is important in children with ongoing fluid and electrolyte losses^[30].

Currently, insufficient evidence exists in the literature to support the routine use of pectin, glutamine, growth hormone, insulin like growth factor 1, or *Saccharomyces boulardii* as trophic factors in the process of adaptation^[31].

PN IN SBS

The North American Home Parenteral and Enteral Nutrition patient registry indicates a 4-year survival on a home PN of 80% for SBS patients and 70% for motility disorders^[32]. The quality of life (QOL) of home PN patients of all ages is reported to not be significantly different from the scores in a reference population of healthy children and adolescents^[33,34]. The main complications commonly associated with long term use of PN are: (1) Central venous catheter (CVC) related infections; (2) Thrombosis of the vessels leading to impaired venous access; and (3) IF-associated liver disease.

Episodes of line infection can cause a greater than 30% rise in bilirubin level, and cholestasis may develop in 90% of infants after first line infection^[35,36]. The reduction in the overall incidence of CVC infection is crucial to sustained good health. Failure to prevent CVC infection greatly contributes to progression of liver disease. Involvement of a multidisciplinary nutritional care team and early discharge on home PN has been shown to reduce the incidence of CVC infection^[37,38].

The repeated episodes of line infections with multiple surgical procedures to remove and replace new catheters may predispose to thrombosis of the major vessels, leading to impaired venous access (defined as the loss of two vascular sites in the neck to thrombosis)^[39,40]. Despite meticulous care and aggressive strategies to prevent line infections, some children may develop end stage loss of venous access and need referral for ITx^[41].

Pulmonary thromboembolism is another potentially fatal complication of long term venous access, occurring in 39% of children^[42]. In asymptomatic children, yearly echocardiography and ventilation-perfusion scanning are recommended, unless there is clinical suspicion or the child is exhibiting symptoms suggestive of pulmonary embolism.

TPN failure was defined by Medicare as any one of the following: (1) impending or overt liver failure (jaundice, elevated liver enzymes, cirrhosis, portal hypertension); (2) thrombosis of central veins (at least two); (3) frequent central-line sepsis (more than two per year, fungemia, shock, acute respiratory distress syndrome); and (4) frequent severe dehydration. Prospective analyses of home TPN patients have shown that an ultra-short bowel of less than 20-30 cm is associated with a high risk of liver failure and poor survival in children and adults. Similarly, infants with total intestinal agangliosis or microvillus inclusion disease have low life expectancy. Transplantation in this situation has been termed "pre-emptive", and is being increasingly applied in the major

centers. “Preemptive” indications are (1) the high risk of death attributable to the underlying disease resulting from desmoid tumors associated with familial adenomatous polyposis; (2) congenital mucosal disorders such as microvillous inclusion disease; and (3) ultra-SBS with residual small intestine < 10 cm in infants and < 20 cm in adults^[43].

SMALL BOWEL TRANSPLANTATION

The successful emergence of small bowel transplantation as a curative alternative has provided many patients with bowel failure to have an improved QOL, better nutrition, and a reduction in PN-associated complications. Since the initial small bowel transplants first performed in the 1980s^[44,45], there have been technical improvements, novel immunosuppressive agents, better understanding of immune and gastrointestinal physiology, and increased clinical program experience. All of these factors have contributed to a remarkable improvement in bowel transplant, 1-year graft, and patient survival (estimated 80% and 80%, respectively), compared with only several years ago^[46-48].

The spectrum of underlying diseases causing SBS in patients who have been transplanted is extensive and variable between pediatric and adult populations (Table 2). Generally, nonmalignant conditions are the norm for recipients, although occasional tumors such as desmoids^[49] have been successfully treated with ITx.

Contraindications to small bowel transplantation include non-resectable or disseminated malignancy, unreconstructable vascular anatomy, diseases that are likely to recur after transplantation, profound disabilities that will not be corrected by transplantation, a loss of vascular access sufficient to allow transplantation, or an inability or unwillingness to comply with the post-transplant management plan (Table 3)^[50].

Transplantation of the intestine can be performed as an isolated graft or in combination with other abdominal organs, since patients with IF often experience other complex abdominal pathologies that require organ replacement. As a result, there have been several variants of intestinal transplants, all derivatives of the “cluster” concept originally proposed by Starzl *et al*^[51].

Isolated ITx is transplantation of the small intestine with or without the large intestine, and is more commonly performed in adults, whereas combined liver-intestinal transplant (LITx), performed *en bloc* or separately, is more commonly performed in children. The latter scenario occurs when there is concomitant liver failure (typically PN induced). With ITx, the entire jejunum and ileum is transplanted in the majority of cases and, when taken from a living donor and in cases in which reduction of the size of the graft is required, a 200-cm segment^[52] is usually transplanted. In this regard, it is important to match size because of the need for closure of the abdomen. There is maintenance of as much native bowel as possible, particularly with recent data suggesting that increased

Table 2 Indications for bowel transplantation in children and adults

Children	Adults
Gastroschisis	Ischemia
Volvulus	Crohn's disease
Necrotizing enterocolitis	Trauma
Pseudoobstruction	Volvulus
Intestinal atresia	Motility disorders
Aganglionosis/Hirschsprung	Desmoids
Retransplant	Retransplant
Microvillous inclusion	Miscellaneous
Malabsorption	Gardner's syndrome
Tumors	

Table 3 Contraindications to small bowel transplant

Absolute contraindications
Neurological disabilities
Life threatening disease unrelated to the digestive system
Non-resectable malignancy
Relative contraindications
Severe immunological deficiencies
Multi-system autoimmune diseases
Inadequate vascular anatomy to warrant long term patency
Prematurity with lung disease

residual or allograft bowel provides some protection from PN-associated injury. This is particularly relevant because there may be some supplementation of transplanted patients with PN for a period of time. When ITx is performed *en bloc*, the duodenum with a segment (or the entire pancreas) (Omaha technique) may be included to avoid the need for biliary reconstruction. Upper gastrointestinal continuity is maintained through the native stomach and pancreaticoduodenal complex, which are retained. In LITx, intestinal transplant is combined with the liver. These organs are transplanted *en bloc* or separately. When the liver and intestine are transplanted separately, the two organs can be transplanted at the same session or sequentially from the same or a different donor. The great majority of the donors for these two forms of ITx are from cadaveric donors, although living donors are also an option^[53].

Multivisceral transplantation (MVTx) is the removal and replacement of both native foregut and midgut^[54], in which the native abdominal viscera are resected and the composite graft, which includes the stomach, pancreaticoduodenal complex, and small intestine, are transplanted *en bloc* and form the new gastrointestinal tract. The liver, kidneys, and large intestine of the donor may or may not be included depending on the clinical scenario. Removal of the native organs is facilitated by early dearterialization, achieved by mass clamping of the celiac and superior mesenteric arteries. This can be achieved through a cephalad approach after division of the esophagus or proximal stomach, or a caudal approach between the inferior surface of the pancreas and left renal vein. Since 2000, the use of MVTx is increasing, and despite the fact

that the donors for MVTx are exclusively cadaveric, the 1-year graft and patient survival is at least as good as the other forms of ITx. As of mid-2005, an isolated intestinal graft has been performed in 44% of cases, an intestine transplant in combination with the liver in 38%, and a multivisceral transplant in 18%^[55].

The decision to use one form of ITx *vs* another is typically determined by the individual patient's particular needs (type of underlying disorder, surgical history of the patient, type, and size of the donor). The emergence of promising data suggesting improved survival data and long-term sequelae, as well as possible immunologic advantage for MVTx, is allowing the clinical team more options as it determines which form of transplantation should be recommended.

OUTCOMES OF LIVING DONOR ITx

The technical aspects of living donor intestinal transplantation (LDIT) were standardized by Gruessner *et al*^[56] in 1997. The donor operation consists of harvesting 200 cm (150 cm for pediatric recipients) of distal ileum, preserving at least 20 cm of terminal ileum and ileocecal valve. The vascular pedicle of the graft is formed by the distal branches of the superior mesenteric artery and vein, and is anastomosed to the infrarenal aorta and cava of the recipient. LDIT has several potential advantages, such as elimination of waiting time, the elective nature of the procedure, better human leukocyte antigen (HLA) matching, and a short cold ischemia time. LDIT tends to be performed with well HLA-matched grafts. The significance of HLA matching in ITx is still to be determined. In fact, experienced programs have obtained good outcomes and low rates of rejection with poorly-matched deceased ITx^[57,58]. A significant risk of antibody-mediated graft injury in settings of positive cross-match has been demonstrated^[59].

In normal physiologic conditions, a significant amount of the energy produced in the enterocytes is used to maintain the integrity of the mucosa. Obviously, during period of ischemia, decreased energy production will affect the mucosal resistance, leading to an increased chance for bacterial translocation and septic complications in the post-transplant period^[60,61]. The direct correlation between the duration of ischemia and the degree of mucosal injury is well known^[62]. As shown in animal models, the process of mucosal damage starts even before organ harvesting, during the brain-dead state^[63]. Irreversible damage has been seen after 5 h of cold ischemia and the rate of bacterial translocation increases significantly after 9 h^[60]. A significant reduction of ischemia time has been achieved in the settings of LDIT.

NON-HEART BEATING DONOR INTESTINAL TRANSPLANT

Intestinal mucosa is sensitive to ischemic injury. When the intestinal graft is harvested from non-heart beating

donors (NHBDs), the infectious-related mortality was higher and the absorptive function lower. Histological examination confirmed a higher grade of ischemic injury in the NHBD grafts that correlated with the clinical data. An experimental study suggested that non-heart-beating donation may not be indicated for small bowel transplantation^[64].

IMMUNOSUPPRESSION IN ITx

Many therapies and combinations of immunosuppression (IS) have been used for ITx, but what remain undefined are the optimal IS regimens to achieve the required goals while preserving graft function and not predisposing the recipient to increased infections or malignancy.

Tacrolimus is a drug that allowed the development of a consistently successful intestinal transplant series and, to date, is the maintenance IS drug of choice^[65]. One of the most significant changes to occur with ITx is the near ubiquitous use of induction IS therapy, with an estimated 90% of cases now using this as part of the overall regimen. The most common induction IS agent is anti-IL2-receptor antibody therapy followed by anti-lymphocyte globulin and Campath-1^[66,67]. Their use has been associated with a reduction in the incidence and severity of rejection episodes, and an improvement of survival results, which have allowed maintenance with lower levels of tacrolimus. This latter issue has become important because there is now increasing evidence of calcineurin-inhibitor toxicities in patients receiving non-renal transplants^[68]. Conversion to non-calcineurin-inhibitor drugs (such as rapamycin), use of steroid-sparing protocols, and a determination as to which IS therapy best maintains graft acceptance still need explanation.

COMPLICATIONS OF ITx

Besides general complications seen in small bowel surgeries (like anastomotic leaks), several common complications are worth mentioning in small bowel transplantation.

Acute cellular rejection

The diagnosis of intestinal acute cellular rejection (ACR) requires close correlation of clinical, endoscopic, and pathologic findings. The clinical symptoms of intestinal ACR include fever, nausea, vomiting, increased stomal output, abdominal pain, and distension. In severe cases, acute rejection may manifest as septic shock, with metabolic acidosis, hypotension, and adult respiratory distress syndrome, which likely results from loss of mucosal integrity and bacterial translocation across the intestinal wall.

The endoscopic appearances of intestinal ACR range from edema and hyperemia in mild cases, to granularity, loss of the fine mucosal vascular pattern, diminished peristalsis, and mucosal ulceration in more severe cases. The final diagnosis depends on histologic analysis of

Table 4 Histological characteristics of acute rejection of intestinal graft

Mild	> 6 apoptotic bodies/10 crypts, no mucosal ulceration, mild epithelial injury
Moderate	Diffuse crypt epithelial injury, focal confluent apoptosis, intimal arteritis
Severe	Mucosal ulceration, transmural arteritis

endoscopy-guided mucosal biopsy specimens. A grading system was used to retrospectively evaluate 3268 small bowel allograft biopsies from 52 adult patients who underwent ITx between 1990 and 1999 at the Thomas E Starzl Transplant Institute, University of Pittsburgh Medical Center (Table 4).

The results demonstrated that a grade indicating a more severe rejection episode was associated with a greater probability of an unfavorable outcome. Significantly increased levels of eosinophils with coexistent activated lymphocytes and crypt apoptosis suggest acute rejection. Peyer's patches are commonly sampled in mucosal biopsies, especially from the ileum. Although localized Peyer's patches without significant lymphoid activation do not indicate acute rejection, Peyer's patches with lymphoid activation (characterized by lymphoid cells with open chromatin, diffuse infiltration into the surrounding mucosa, or mixtures with eosinophils and neutrophils) are frequently associated with acute rejection.

The significance of lymphocytic cryptitis (increased numbers of lymphocytes in the crypt epithelium) is unclear. Although cryptitis is present in some cases of acute rejection, it is also observed in biopsy tissues without ACR. Because the distribution of acute rejection may be patchy, multiple biopsies (three to five) are often required. Biopsies from either the ileum or the jejunum are sufficient for histologic evaluation in most cases, although sampling from both the ileum and the jejunum may be required in some cases with ambiguous diagnoses. Most of the histologically diagnosed mild-acute rejection episodes are treated with increased IS. Various pathologic conditions must be differentiated from acute rejection, the most common of which include: nonspecific enteritis, cytomegalovirus infection, Epstein-Barr virus (EBV) infection, and post-transplant lymphoproliferative disorder (PTLD)^[69].

Graft vs host disease

Graft vs host disease (GVHD) has the highest occurrence after small intestine transplantation (5.6%)^[70], followed by liver transplantation (1%-2%)^[71,72], with the mortality rate of solid organ transplant-associated acute GVHD ranging from 30% to more than 75%^[73-75]. The amount of lymphoid tissue in the small bowel is much higher compared with other solid organ transplants, and this may explain the fact that the rate of GVHD in the recipients of small bowel transplants is increased (5.6%)^[70]. Therapy consists mainly of increasing IS, support of hematopoiesis with cytokines, and discontinuation of antibiotics or

any drugs that might be myelosuppressive. However, it is difficult to determine whether this is effective, as mortality normally exceeds more than 75%. Approximately 86 cases have been reported in the literature since 1987, and among them only 18 patients survived^[74]. In 13 of the survivors, IS had been increased, while in 5 other cases, IS had been withdrawn. It could be argued that reducing IS and allowing the patient's immune system to have the opportunity to reject the engrafting donor lymphocytes, as well as helping the patient to respond to infections, could be an effective method of treatment^[75-77]. Any treatment is more likely to work if it is begun before the onset of severe pancytopenia.

PTLD

The vast majority of PTLDs are EBV driven and arise either as a consequence of the reactivation of latent infection or, more commonly, infection of the host by latent virus from donor B cells^[78]. The particularly high incidence of PTLD reported after ITx is a consequence of the high levels of IS traditionally used to prevent GVHD and rejection, along with the fact that a large load of donor lymphocytes is transplanted with the graft^[79]. The gastrointestinal tract is frequently affected and it is important to distinguish between PTLD and other causes of graft infiltration, including rejection. *In situ* hybridization of tumor tissue for EBV RNA is a quick and sensitive way of confirming the diagnosis. It is crucial to distinguish PTLD from rejection because many patients will respond to a reduction in IS alone. If this fails, second-line treatment includes antivirals, chemotherapy, or interferon- α .

Experimental treatment using adoptive immunotherapy with donor leukocytes or specific anti-EBV specific cytotoxic T lymphocytes may be effective in aggressive cases.

CONCLUSION

Despite advances in medicine and surgery, SBS still remains a burden on the healthcare system and the economy. Along with novel medical therapies, various surgical techniques had been developed to overcome the consequences of a short bowel. Some of these approaches are still experimental, and the rest have limited success.

This limited success lead to the invention of ITx, which further branched into living donor ITx and MVTx. With the help of novel immunosuppressive regimens, the outcomes of ITx improved. The once feared field of solid organ transplantation is nowadays becoming more and more popular, even in developing countries, in the form of living donor transplantation.

In developing countries the cost of maintenance therapies for SBS and transferring patients for further treatment to developed countries far exceeds the cost of ITx performed on site. Thus ITx must be encouraged and take its place in abdominal organ transplantation departments worldwide.

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