# Liver and intestinal transplantation in children

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**Abstract**

The aim of this article is to provide essential information for pediatricians, regarding liver and intestinal transplantation. Indications for transplantation will be reviewed, as well as the process of evaluation and listing for transplantation. The continuum from pre-transplant to post transplant is covered, including waiting list challenges, types of transplant, immunosuppression, complications, long-term follow up, and outcomes.

**Keywords** gastroenterology; immunosuppression; intestine; liver; pediatrics; transplantation; transplants

## Introduction

Transplantation is a mature technology that is utilized for the management of end-stage organ failure including that of liver and intestine. Liver transplant has been undertaken in substantial numbers since the introduction of Cyclosporin A (CsA) in 1983. Intestinal transplantation has been performed in increasing numbers since the early 1990's, however due to the complexity, outcomes, and limited indications it remains a highly specialized undertaking in few patients at even fewer transplant centers. Currently over 500 pediatric liver transplants, and approximately 100 pediatric intestinal transplants are performed per year in the United States. Survival rates have increased due to improved pre- and post-operative care, surgical techniques, as well as advances in immunosuppression.

## Indications for liver and intestine transplantation (see Tables 1 and 2)

### Liver

Liver transplantation (LT) is indicated in liver failure, both acute and chronic, unresectable liver tumors and several liver-based inborn errors of metabolism. The number of pediatric patients on the transplant waiting list has remained relatively stable for the last decade, however children represent a diminishing proportion of the total waiting list in the United States (4% in 2005 compared to 8% in 1996) because of the overall growth of the adult waiting list.

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Patients with acute liver failure (ALF) should be referred promptly to a center that can provide stabilization of the liver failure and concurrently evaluate and list for LT in an expedited manner. The management of a patient with ALF should address the prognosis with or without LT, in addition to preventing complications while awaiting transplantation. Transplantation should be offered either when the liver failure is not expected to recover or when the complications of acute hepatic dysfunction such as is cerebral edema, are likely to cause the death of the patient prior to recovery of liver function. Prognosis scoring systems, such as the King's College and the Clichy criteria, have been used to estimate the likelihood of survival without LT, however none are totally reliable and experienced clinical judgment is necessary.

There are no minimal listing criteria but in general liver transplant evaluations are undertaken when either the expected length of pre-transplant survival or quality of life without transplant is deemed unacceptable. However, progression of chronic liver failure is variable, and may be difficult to predict. Therefore when considering the need for transplantation, in addition to following disease severity indicators such as worsening nutritional status, level of cholestasis and hepatic synthetic dysfunction manifested as hypoalbuminemia and coagulopathy, there are complications such as encephalopathy, ascites, portal hypertension, and intractable pruritis that are also important. Hepatopulmonary syndrome, a triad of cirrhosis, intrapulmonary vascular dilatation, and hypoxemia; and hepatorenal syndrome, functional renal failure associated with liver disease, may also be indications for transplantation.

### Intestine

Intestinal transplantation is an accepted treatment modality for irreversible intestinal failure accompanied by life-threatening complications. The number of pediatric candidates on the intestine waiting list has increased over the last decade from 53 in 1997, to 140 in 2006. Children account for 77% of the total intestinal transplant waiting list. Intestinal transplant may be indicated for patients with intestinal failure who develop or are at high risk of developing complications such as progressive liver disease, severe or recurrent blood stream infections, or loss of several central venous access sites.

Contraindications to transplant involve medical conditions that would make recovery from transplantation unlikely or conditions where quality of life would not be improved by transplantation. However, these are not contraindications to referring a patient for evaluation, but could ultimately prohibit transplantation and include uncontrolled malignancies, active infection outside the hepatobiliary system, severe cardiac, pulmonary, or central nervous system (CNS) disease, or other life limiting illness. A relative contraindication to intestine transplantation, particularly if a concomitant liver transplant is required, is the loss of all conventional central venous access sites.

## Referral for evaluation for transplantation

Generally, a patient cannot be referred too early to an experienced center for evaluation. Even if transplantation is not immediately indicated valuable management advice may benefit

### Diagnoses that may require pediatric liver transplantation

1. Acute liver failure
   a. Infective (e.g. viral hepatitis A or B)
   b. Drugs and Toxins (e.g. acetaminophen, herbals, mushrooms)
   c. Metabolic (e.g. Wilson disease)
   d. Idiopathic
2. Cholestatic liver disease
   a. Biliary Atresia
   b. Paucity of intrahepatic bile ducts (e.g. Alagille syndrome)
   c. Sclerosing cholangitis
   d. Familial cholestasis syndromes (e.g. PFIC 1, BSEP deficiency
3. Chronic hepatitis
   a. Autoimmune hepatitis
   b. Neonatal hepatitis
   c. Chronic hepatitis B or C
4. Neoplasm
   a. Hepatoblastoma
   b. Hepatocellular carcinoma
5. Metabolic Disorders
   a. Structural damage
      i. Alpha 1-antitrypsin deficiency
      ii. Tyrosinemia type 1
      iii. Cystic Fibrosis
   b. Liver based metabolic defects injuring other organ systems
      i. Crigler-Najjar syndrome
      ii. Urea cycle defects
      iii. Primary hyperoxaluria type 1
      iv. Familial hypercholesterolemia

**Table 1**

the patient in terms of avoiding transplantation at a later date or maintaining optimal health until transplantation is necessary. The converse of early referral is an emergent evaluation in a critically ill patient who may die before suitable organs are available.

### Diagnoses that may require pediatric intestinal transplant

A. Anatomical Causes- short bowel syndrome
   1. Necrotizing enterocolitis (NEC)
   2. Congenital intestinal anomalies (e.g. atresias, gastroschisis)
   3. Trauma
   4. Intestinal volvulus
B. Motility disorders:
   1. Total intestinal aganglionosis
   2. Chronic intestinal pseudo-obstruction (CIPO)
C. Mucosal disorders:
   1. Congenital enteropathies (e.g. Microvillus inclusion disease)

**Table 2**

## Evaluation and listing

The purpose of a transplant evaluation is to ensure that transplantation is the best option for the child and family. In addition, the evaluation process examines additional medical or surgical options, and identifies any contraindications. The family must be educated about the transplant process, and prepared psychologically. The evaluation itself involves laboratory testing, radiological exams, education about the transplantation process, and consultations with transplant surgeons, hepatologists, anesthesiologists, social work, and other medical specialties as indicated by the patient's medical status. Once the testing is complete, a multidisciplinary transplant selection committee reviews the results. If transplant is not indicated at the time of the evaluation, the patient will be managed medically and re-evaluated if their status deteriorates. If transplant is medically indicated, then the patient will be placed on the waiting list.

Rules for the allocation of donated organs for transplantation vary around the world, however in the United States patients are prioritized on the liver transplant waiting list by 90 day waiting list mortality risk as estimated by the Model for End-stage Liver Disease (MELD) and Pediatric End-stage Liver Disease (PELD) scores. The MELD score is used for patients aged 12 and older, while the PELD score is used for patients who are less than 12 years of age.

The intestine transplant waitlist is prioritized by status (status 1—Urgent; status 2 Non-urgent) and waiting time on the list. Only isolated intestinal allografts are allocated according to the intestinal list. For patients requiring combined intestine and LT the liver transplant waiting list is utilized but MELD/PELD adjustment factors have been added in an attempt to compensate for the increased waiting list mortality risks carried by patients, especially the very young children, with both liver and intestinal failure.

## Pre-transplant management

Management of complications is an essential piece of the pre-transplant period. It is well known that medical and nutritional status prior to transplantation influences post-surgical mortality and morbidity. To maintain transplant candidates in optimal condition requires careful nutritional oversight and intervention as well as prevention and prompt management of complications such as infection, gastrointestinal bleeding and ascites. While patients are on the transplant waiting list, effective communication between the local provider and the transplant center is essential.

In children awaiting transplantation particular consideration should be given to immunizations. A detailed plan regarding optimizing vaccines should be implemented prior to transplant listing. This may require initiating vaccinations earlier than the usual recommended ages, or decreasing the intervals between vaccines. Timing of vaccination is important, and it may be appropriate to suspend a patient's listing for two to four weeks after the administration of a live vaccine. If primary immunizations are incomplete before transplantation, they can be resumed usually by six months after transplantation, however the American Academy of Pediatrics recommends avoiding live vaccines in transplant recipients. Siblings of transplant recipients should