

# Pediatric Organ Transplant Patients and Long-Term Care:

## A Review

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### Abstract

We review the role of the academic generalist in the care of the child or adolescent who has undergone an organ transplant. This care is seen within the context of the “medical home” and the special considerations for pediatric patients. These special considerations include growth and development, psychosocial adjustment, cardiac and renal complications, endocrine problems, medication management and regimen adherence, infectious complications, vaccination, post-transplant malignancies, post-transplant lymphoproliferative disorders, acute post-transplant complications, recurrence, contraception and pregnancy for adolescents, and transition to adulthood. Research needs in this complex area are highlighted.

**Key Words:** Organ transplantation, pediatrics.

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### Introduction

IN 2004, 1,816 PEDIATRIC TRANSPLANTS were performed in the United States alone. These patients represented 7% of all transplants performed that year. This number has been steadily increasing over time—a 30% increase over the prior ten years. In addition, the survival rates of pediatric transplant patients continue to improve, with rates comparable to those of the adult transplant population, with the exception of small bowel transplants. Being in a pediatric age group should no longer be considered a risk factor for poor outcomes following transplantation (1). With this in mind, it is important for pediatricians to be aware of the issues that will confront these unique patients. These patients will seek a stable “medical home,”<sup>1</sup> in addition to their transplant centers. Generalists will certainly have the opportunity to care for a patient with a solid organ transplant. One of the most important ways to facilitate this care is for these pe-

diatric generalists to feel comfortable communicating with the transplant specialists about how to best offer patients comprehensive and quality care.

### Background

In a recent overview of the state of pediatric transplantation as of 2004 (1), the most commonly performed organ transplants were renal (cadaveric and living related) and liver (cadaveric and living related), with heart, lung, heart and lung, and small intestine (with or without liver) following. Kidney transplantation survival rates have climbed to 93% for one-year survival and to 76% (living) and 65% (cadaveric) for seven-year survival. For liver transplant patients, the 5-year survival ranges from 79–87%, which exceeds the survival rate for adult recipients. Children now compose 12% of all heart transplants and have an unadjusted one-year sur-

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<sup>1</sup> Medical care of infants, children, adolescents and young adults that is acceptable, continuous, comprehensive, family centered, coordinated, compassionate and culturally effective; care that is delivered or directed by well-trained physicians who provide primary care and help to manage and facilitate all aspects of pediatric care; and led by a physician known to the child and family, working in partnership through mutual responsibility and trust (American Academy of Pediatrics). (*Pediatrics* 2002; 110 (1):184–186.)

vival rate of 70–89%, depending on age at time of transplantation.

### Special Pediatric Considerations

In caring for the medical needs of pediatric transplant patients it is important to be aware of unique problems they may experience and how common problems may be affected by their immunocompromised state. They may also have different presentations or more significant outcomes as compared to adult patients.

#### Growth

Most children have problems with growth prior to receiving the organ transplant, due to their underlying chronic disease/ill health. The use of growth hormone is commonly indicated for patients with significant delay in growth. Many children have significant metabolic bone disease (especially renal and liver patients), and others may have congenital or metabolic syndromes that are associated with short stature/poor growth, which are not completely corrected by the transplant. After the transplant, a rule of 25% is understood: 25% will have persistent growth failure, 25% will become obese, and the remaining 50% will usually show dramatic catch-up growth and normalize their weight percentiles. Poor growth can be seen by the 6-month-to-one-year period after transplant, with catch-up growth occurring within 1–4 years. On average, final height remains lower than that of non-transplanted adults (2). Often the best predictors for linear growth are an age < 2 years at the time of transplant, pre-transplant nutritional status and stature, steroid use and graft function (2).

Patients who have been recipients of solid organ transplants have generally had problems with growth and especially with metabolic bone disease—from either chronic liver or chronic kidney disease. It is important to ensure that pediatric transplant patients receive adequate calcium supplementation and vitamin D and avoid immobilization. Post-transplant adult patients continue to have problems with osteopenia and osteoporosis, due to the medications needed to maintain immunosuppression. Much work is being done on using bisphosphonates to improve bone integrity. Interestingly, in pediatric transplant patients, the results have been contradictory. A study done by D'Atiga et al. on children after liver transplant revealed that they showed an initial reduction in bone mineral density (BMD) scores, similar to adults after transplant. But they then showed an increase in BMD 12 months or more after transplan-

tation and reached normal levels in all but one patient. All patients had increased markers of bone turnover and reduced levels of vitamin D (3). In addition, those patients with increased BMD had an increase in linear growth. However, those patients who were already post-pubertal grew less and had less improvement in BMD.

Helenius et al. have done a survey illustrating that post-transplant children were found to have an increased risk of spinal scoliosis compared to the population as a whole. The relative risk of scoliosis needing treatment (a curve >20 degrees) was 17.0 (CI 6.75–42.7) for a transplant patient compared to an age-matched control (4). Thus transplanted patients should continue to be screened for scoliosis, despite a recent U.S. Preventive Services Task Force recommendation against routine screening for scoliosis (5). In addition, transplanted patients tend to have more complicated scoliosis repairs and less complete correction (6). The dental needs of children after transplant must also be assessed, with early referral to a pediatric dentist, consistent with the American Academy of Pediatrics recommendations.

#### Development

When looking at the functional level of post-transplant children, 50% of patients are found to be functioning at least one grade level lower than peers. Twenty-five per cent (25%) of these children are diagnosed with learning problems, and 35% of patients with biliary atresia will have some form of developmental delay. Clinical predictors of worse outcome in the first year after transplant are malnutrition and, not surprisingly, a prolonged in-hospital course (7). While caring for the post-transplant patient, it is important to keep these concerns in mind. The timing of the transplant can impact the development of the patient. Infants may have problems with caregiver attachment that can cause stress on the parent-infant bond, due to frequent hospitalization. Normal development can be assessed by the Bayley scales of infant development, tracking mental and motor development (8). Motor delay tends to persist throughout the first year after transplant and is most pronounced in children less than 6 months old with liver transplant. This may be due in part to the mechanical effect of the transplant-abdominal incision, hepatomegaly and ascites (2). Close monitoring of neurologic development, with referral to early intervention, and complete evaluations for hearing and vision impairment are essential.

Normally, during the toddler years, important motor, language, cognitive and social milestones

are met. For children after-transplant, physical mobility may be diminished, a problem often exacerbated by fewer chances for communication/interaction with same-aged peers. When they are toddlers, disruptive behaviors can appear and must be dealt with to improve patient and parent functioning. Early school age children engage in cognitive and social processes that are essential for normal development (8). Extended school absences with subsequent re-entry can lead to school refusal, separation anxiety and concern regarding appearance. Children at this age are forming social relationships with their peers, and transplantation can sometimes decrease these opportunities. A balance needs to be found between health concerns and adequate activity in school and other extra-curricular opportunities. In a study by Wray et al., 25–40% of heart and heart/lung transplant recipients experienced behavioral and academic problems, which persisted as long as 5 years after transplant (9). In general, post-transplant patients tend to have a normal IQ score within 5 years after transplant. But they also tend to have greater problems with language ability and memory (2). Approximately 30% of liver transplant patients are a grade behind their peers, and 20% of recipients require special education (2).

Adolescents frequently have problems regarding identity, body image, sexuality and emerging independence. As noted by Green and Ray (10), 75% of transplanted children complained about the cosmetic affects of the immunosuppressant medications. These can include hirsutism or alopecia, gingival hyperplasia, weight gain, stretch marks, scars and hernias. These cosmetic effects may affect adherence to medication, particularly during adolescence, the period that presents the highest risk of decreased compliance with immunosuppressant medication and the highest risk of graft loss. Adolescents need to be screened for depression and anxiety, and presented with interventions to help them manage anger and stress, and improve coping skills (8).

Psychiatric studies of psychosocial adjustment found that fewer children had adjustment problems if their transplant occurred before the age of 8 years. These children were more likely to consider themselves similar to their peers. After this age, there was an increased incidence of adjustment problems (11). In addition, a recent article by Shemesh et al. demonstrated that depression is frequently underrecognized by caregivers and physicians caring for transplanted patients. At least 10% of patients have experienced some depression, anxiety and post-traumatic stress disorder (12).

## **Cardiac Hypertension and Cardiomyopathy**

It is well known that the drugs used to induce immunosuppression have been associated with hypertension in post-transplant patients. Hypertension occurs in approximately 30% of children following liver transplant, approximately 10% of whom will require hypertensive medication (2). Patients should be monitored at least annually at a minimum and after every adjustment to their immunosuppressant regimen. The choice of hypertensive regimen should be dictated based on the patients other co-morbid conditions (asthma, diabetes, hyperlipidemia, gout) and side effect profile (e.g., hyperkalemia). It is important to note that if calcium channel blockers in the non-hydropyridine class are used they can interfere with the level of immunosuppression. It is best to avoid verapamil or diltiazem if possible. If they must be used, drug levels of cyclosporine/tacrolimus must be followed after each dosage change. Inadequately controlled hypertension is certainly a risk factor for future cardiovascular disease and should be carefully monitored and controlled.

## **Endocrine/Diabetes**

The drugs used to induce immunosuppression in the transplant patient put the patient at increased risk of developing diabetes. Some pediatric patients will develop diabetes while on both high-dose steroids and high-dose tacrolimus in the immediate post-transplant period. It is important to realize that their risk of diabetes does not completely disappear once they are weaned off high-dose steroids. Calcineurin inhibitors and especially tacrolimus, interfere with insulin secretion. In a review done by Avitzur et al. (13), 10% of pediatric patients were found to have diabetes at ten or more years after transplant. For this reason, the post-transplant patient should have yearly screening for diabetes with fasting glucose and/or hemoglobin A1C. The practitioner should have an increased index of suspicion if a patient develops polyuria and/or polydipsia. In addition, the patient should be counseled to maintain a healthy weight based on body mass index measurements and to maintain an active lifestyle.

## **Hyperlipidemia**

Both steroids and calcineurin inhibitors increase patients' risk of elevated cholesterol and increase their long-term risk for atherosclerotic disease. The risk is especially high for the cardiac transplant patient (90%), moderate for the renal

patient (70%), and lowest for the liver patient (10%). Most heart transplant patients are automatically started on statin therapy after transplant. Preliminary studies appear to indicate that statins can be used safely long term. Annual screening of lipid panel should be done in all transplant patients.

### Renal

The most important long-term concern for transplant patients is the effect of the calcineurin inhibitors on renal function. These drugs cause renal insufficiency due to arteriolar nephrosclerosis and interstitial fibrosis. Patients can have an immediate decrease in glomerular filtration rate (GFR) after transplant due to vasoconstriction, and the GFR progressively decreases over time. In addition, renal insufficiency in the immediate post-transplant period is fairly common (14). A recent study also reported that hepatitis C associated glomerulonephritis is probably underdiagnosed in the immediate transplant period (15). The incidence of chronic renal insufficiency (i.e., creatinine > 2.5) is approximately 8% in the adult transplant population. The incidence of end-stage renal failure is reported to be as high as 9.5 in some transplant series (16). In the review by Avitzur et al. looking at pediatric liver transplant patients 10 years after transplant, 50% had a decreased GFR with moderate renal insufficiency and 4% had severe renal failure (13). It is recommended that a bun/creatinine evaluation and urinalysis be conducted annually. Care should be taken to avoid nephrotoxic agents, and dose adjustments of all medications should be based on the patient's changing renal function.

### Medication

It is important for the pediatrician to have a basic understanding of the commonly used immunosuppressants and their major side effects. Most transplant regimens will contain a calcineurin inhibitor (CSA, tacrolimus) or an mTOR inhibitor (rapamycin or sirolimus) plus either a steroid or a "steroid sparing" agent (azathioprine or mycophenolate). The possibility of drug interactions must always be avoided. Either choose an alternative drug or, if unavoidable, recheck the CSA or tacrolimus level to assess for need to adjust up or down. Coordination with the patient's transplant center is of course essential. In choosing antimicrobial agents, it is important to recall that some induce calcineurin inhibitors (isoniazid, rifampin, nafcillin), thus lowering therapeutic lev-

els and increasing risk of rejection. Others inhibit the patient's metabolism and thus increase the risk of toxic levels (macrolides, anti-fungals), and finally some antibiotics cause renal toxicity, which can be dose related, idiopathic or synergistic. Again, most important, checking and following calcineurin inhibitor levels will be the key to successful management.

### Compliance

Compliance is a major concern for any physician caring for patients with chronic medical conditions and should be assessed periodically. Special attention should be paid to fluctuating levels of immunosuppressant, ideally before there is any impact on graft function. Potential risk factors that impact family compliance are history of substance abuse, school dropout, child abuse, single parent, and economic stresses. Adolescence is a particularly difficult period for many patients with chronic disease and may be partly responsible for lower graft survival rates in this age group (17).

### Infection

As noted by Marty and Rubin (18), one of the factors that have allowed transplantation to progress has been the advances in controlling infectious disease in the transplant patient. "Prevention of infection whenever possible with prophylactic or preemptive antimicrobial therapy and prompt diagnosis and aggressive treatment of invasion when prevention fails are key pillars." In their review, they demonstrate a timetable for approach to infections in the post-transplant patient. The key periods are the first month after transplant, 1–6 months, and then six months or more. Interestingly, in the first month after transplant, the patient is at high risk not for opportunistic infections, but rather those infections stemming from complications of the surgical procedures (wound infection, catheter infection, etc.) or unrecognized infection in the patient before transplant. The second time period is characterized by lingering infections secondary to anatomic or technical abnormalities, onset of viral infections (especially cytomegalovirus [CMV], Epstein-Barr virus [EBV], human herpesvirus 6, Hep B, Hep C and HIV) and then the beginning of opportunistic infections by *Pneumocystis* and *Aspergillus*. These infections occur as a result of sustained immunosuppression and the effects of the co-infecting viruses (18). Prevention requires prophylaxis with trimethoprim and sulfamethoxazole (TMP/SMZ) and control of CMV and EBV replication and invasion. In the

final time period, 6 months or more after transplant, infections fall into 3 types: patients with normal functioning grafts (80%) are at risk for community-acquired respiratory infections; 10% have a recurrence of hepatitis B or C; and those few with poorly functioning grafts (10%) are at highest risk for opportunistic infection (18).

When treating infections in the post-transplant patient, it is often necessary to use empiric therapy—a best guess approach. These regimens depend on the clinical syndrome (pneumonia, urinary tract infection, bacteremia), the timing after transplant and local factors of the site in which the patient is being treated (i.e., resistance patterns) (18). One should first assess if the patient has a therapeutic emergency, with emphasis on resuscitation of the patient, immediate assessment and culturing, and broad-spectrum bactericidal therapy (18). Once the patient is stable and improving, reassessment and narrowing of regimens can be done 3–5 days later.

### Vaccinations (Routine)

It is actually most valuable if pediatric patients can receive most of their primary vaccination series before transplant, due to decreased efficacy in the immunosuppressed patient. That being said, many patients have not been able to receive these vaccinations due to ill health and uncertainty in the timing of the transplant. Ideally, live vaccines are not given within 2–4 weeks of the transplant, and it is not always clear when a pediatric patient will actually receive an organ. Campbell and Herold recently published recommendations for the solid organ transplant candidate, including starting many of the vaccines before the usual age and at an accelerated rate (19).

Most centers begin to resume the vaccination of the post-transplant patient 6 months after transplant. Usually the patient has been tapered off high-dose steroids and has reached a more stable level of immunosuppression by this time. A complete review has been done by Burroughs and Moscona (20). It is not usually necessary to restart any vaccine series that have already begun before transplant. In general, killed and component vaccines are safe to give to the transplant patient. These vaccines include formulations of the diphtheria, tetanus and acellular pertussis vaccine, *Haemophilus influenzae* type B, hepatitis B vaccine, hepatitis A vaccine, inactivated polio vaccine (IPV), pneumococcal vaccine (both 23 valent Pneumovax and 7 valent conjugated Prevnar) and both forms of the meningococcal vaccine (quadrivalent Menomune and conjugated Menactra).

Although vaccines have been shown to be less immunogenic in patients with lowered immune systems—whether it be immunosuppression from steroids or from AIDS—it is not customary to assess for immunity after vaccination for most vaccines, with the exception of hepatitis B and hepatitis A vaccines. Evidence and recommendations for checking and re-boosting patients for the hepatitis B vaccine come mostly from the hemodialysis literature. Patients found to have waning protective antibody levels to hepatitis B SAb have benefited from booster vaccination.

It is important, however, to remember not to give live vaccines to the post-transplant patient. These include vaccines for measles, mumps and rubella (whether singly or as the MMR vaccine), varicella, the oral polio vaccine (which is no longer routinely given in the U.S.), the live attenuated influenza vaccine (via the nasal route), and the new rotavirus vaccine being developed. Although there has been some investigation into using live vaccines, the studies have been small and limited. There has been a single report of giving the varicella vaccine to patients following solid organ transplants (21). In addition, there have been small studies evaluating measles vaccine in both renal transplant and liver transplant patients (22). However, the current recommendations do not recommend offering these vaccines until larger studies have shown a favorable risk-to-benefit ratio.

Patients' family members should receive all live virus vaccines if they are not already immune, with the exception of the live oral polio vaccine, which can be shed. It is reasonable to check transplant patients' titers to see what they might still be susceptible to and thus avoid exposure. This is done universally before transplant at centers in the U.S.; this information can often be obtained from the transplant specialist. If this information is not available, it is reasonable to check these titers to know what the patient is vulnerable to and offer immediate post-exposure prophylaxis as indicated. Letters of medical waiver should be given to schools or camps, as appropriate.

Respiratory syncytial virus (RSV) vaccine is not available yet, but RSV prophylaxis should be considered, as appropriate. There have been no reported studies yet looking specifically at solid organ transplant patients. It has been recommended to target high-risk candidates for treatment: children < 1 year old, those with significant lung disease and children being transplanted during the RSV season.

There is a recent study on recommendations for “travel vaccinations” for the post-solid-organ transplant patient (23). It is not uncommon to need

to decide if your patient should be offered malaria prophylaxis and other protection prior to traveling outside the U.S. Recommendations can be checked at the [cdc.gov](http://cdc.gov) website for travelers, based on the country of travel. It is usually strongly recommended that patients receive hepatitis A vaccine, if they haven't already received it. They may also receive the yellow fever, Japanese encephalitis, rabies, and parenteral typhoid and cholera vaccines, if indicated. They should not, however, receive oral typhoid vaccine or oral cholera vaccines, which are live vaccines. And under no circumstances should a patient receive the bacille Calmette-Guérin vaccine (BCG) vaccine. Letters of medical waiver should be given to the patient. In addition it is helpful to give your patients a summary letter of their medical condition and a list of medications. It is, unfortunately, not uncommon for travelers to lose their medication abroad, and a summary letter can sometimes facilitate their emergent replacement. Live vaccines, as noted above, are contraindicated, but killed vaccines, such as those for meningococcal, rabies, and Japanese encephalitis virus, are occasionally recommended for travel and may be given.

### Cancer

The immunocompromised patient is at increased risk of developing cancer. Post-transplantation lymphoproliferative disorder (PTLD) is the most common form of cancer in children, while skin cancer is the most common in adults. Transplant patients are at increased risk for non-melanoma skin cancer, especially squamous cell and basal cell cancer. A population-based study done on all transplanted patients in Ireland between 1994 and 2001 revealed a significant increase in the incidence of cancer compared to age-matched controls. It showed that the incidence of non-melanoma skin cancer (NMSC) had two peaks: the first peak after two years following transplant for patients older than 50 years, but more important, a second peak after 6 years for patients younger than 50 years. But this second group had a relative risk 200 times that of age-matched controls (24). The usual higher prevalence of basal cell vs. squamous cell carcinoma (SCC) is reversed in transplant patients. In this study, the risk of invasive SCC was 82 times higher than that of the non-transplant population. This and other studies have highlighted the importance of educating patients regarding the significant increased risk of developing cancer and urging them to avoid unnecessary sun exposure. In addition, they need to receive systematic examinations for early detection of skin lesions.

PTLD is probably the most feared complication of solid organ transplant in the pediatric population, but strategies have been developed for surveillance of EBV titers and adjustment of immunosuppression with detection of elevated titers. Most pediatric transplant centers now have standardized protocols. As a result of these advances, the incidence of PTLD has decreased from 15% to 5–10% of children. Survival has also been improving thanks to treatment involving both decreased immunosuppression, antiviral therapy and monoclonal antibody rituximab (22). Risk factors for the development of PTLD are the following: age <5 yr at time of transplant, primary EBV infection after transplant, and an EBV positive donor graft. Prolonged use of high-dose immunosuppression and anti-lymphocyte antibody are also risk factors (2). What is important for the academic generalist to recognize is that PTLD can present in subtle ways. Presentation can be with onset of unexplained fever, weight loss, failure to thrive or diarrhea, new onset seizures, pneumonia or airway obstruction with progressive lymph node enlargement. It is important to discuss these symptoms with the transplant centers to consider evaluation for PTLD, in addition to usual childhood illnesses. The adenoids, tonsils and gastrointestinal tract are the most common locations for presentation of PTLD, according to a study by Avitzur (13). Academic generalists who manage patients both in the inpatient and outpatient settings need to be alert to subtle and more typical presentations of PTLD.

Other cancers that are more prevalent in solid-organ-transplant patients include cervical cancer, lung cancer (especially bronchogenic carcinoma in lung and heart transplant patients), renal cancer, and lymphoma.

### Transplant Complications

Most complications will occur within the first 6 months of the transplant, whether they are surgical problems, acute rejection or significant infection. However, rejection and infection are problems that can occur even years after the transplant.

### Recurrence of Primary Disease

The recurrence of the primary disease is more often a problem for adult patients who have been transplanted secondary to chronic viral hepatitis B and C. However, patients with autoimmune hepatitis and patients with systemic lupus erythematosus can have a recurrence of disease in the transplanted organ.

## Puberty and Contraception

Following liver transplantation, it can take up to five years for young girls to attain normal puberty, and most girls will experience menarche one to two years later than average. Those who have already reached menarche will have normal menstrual cycles return soon after transplantation (2). It is important to note that fertility may resume as early as 3 weeks after transplant, so discussions of appropriate contraceptive methods should occur prior to transplantation. Hormonal contraception can be offered to the patient, with progesterone only being the drug of first choice. Depo progesterone can be used but its effect on decreasing bone density and increasing weight gain must be considered. Combined estrogen/progesterone (E/P) tablets are another option for a teenage patient. Although combined E/P tablets can induce or exacerbate jaundice or biliary tree problems (2), they are less dependent on precise timing of administration and more “forgiving” in a teenaged population. If combined agents are used, the lowest dose of estrogen in a monophasic pill is preferred, to avoid fluctuating levels of calcineurin inhibitors. The medication should ideally be used continuously, to avoid drug-free intervals, which would affect calcineurin levels. Use of condoms is always recommended, to avoid exposure to sexually transmitted infections. Intra-uterine devices are more likely to fail in patients taking immunosuppressive agents and are not recommended. Other barrier methods are available but have been shown to be used less effectively by adolescents. Emergency contraception can be used by the transplant population.

## Pregnancy

Ideally, conception should be postponed for one year, until the majority of post-surgery complications/rejections have been passed. As noted in the review by McKay and Josephson, at this time the risk of rejection is low, the dose of immunosuppressive medication is at its nadir, viral prophylaxis has been completed and the patient is generally stable (26). The consensus of the Women’s Health Committee of the American Society for Transplantation was that pregnancy is safe after the first year, provided that allograft function is stable and that no rejection episodes have occurred in the year before conception. By this point, pregnancies are usually successful, but often complicated by hypertension, pre-term delivery and low-birth-weight infants (26). All solid organ transplants should be followed by a “high-risk” obstetrician, in close coordination with the transplant specialist.

## Prognosis

Adolescence is one of the biggest challenges in any chronic disease population. It has been discouraging that the adolescent population still has the lowest survival rates for any of the transplant populations. The actual reason for this is unclear, but it is speculated that a major problem is compliance with the complicated medication regimen and the need for frequent follow-up and testing. It is also possible that some of the changes occurring during puberty may affect the metabolism of the medications. It is important to try to provide the patients in this age group with additional support and time. There is also an urgent need to focus on educating both the parents and the teen and later the young adult dealing with a chronic disease.

## Compliance

Five complex factors play a significant role in increased noncompliance. They are: prevalence of side effects of the medication, reduced social support, pre-transplant noncompliance, low socioeconomic status, and certain psychological/personality traits (anxiety, depression, cognitive disorder or avoidant coping strategies). A 2002–2003 study in one center found that male sex, high stress from adverse effects, fair self-rated health, and fair social support were the most predictive of noncompliance (27).

In children, the most common individual characteristics of nonadherence are adolescent age, low self-esteem, depression/anxiety, poor communication/socialization skills and lack of acceptance of diagnosis. Familial characteristics include single parent, family instability, lack of social/emotional support, low socioeconomic group, and poor intra-family communication (28). Kalb and Loeber have defined pediatric nonadherence as those instances when a child either actively or passively, but purposely, does not perform a behavior that has been requested by a parent or other adult authority. Willful nonadherence is the intention to defy established limits. To achieve a successful transition from childhood to adolescence and then adulthood, adolescents must develop a number of important skills. These include cognitive development, abstract thinking, and the ability to see and assume the short- and long-term consequences of their own behaviors. Adolescents must develop the capacity to visualize the future consequences of their current actions, something difficult in a healthy teen, let alone one who is chronically ill and perhaps emotionally delayed (29).

## Transition

Health-related quality of life (HRQL) generic childhood screening has been done in various transplant populations. There are no tools specific to transplant patients. HRQL after liver transplantation is lower than in the general population and in comparison to other children with chronic diseases (2). Research is beginning to focus on how best to help this population of patients; one strategy involves looking at models used for patients with problems such as congenital heart disease, cystic fibrosis or sickle cell disease. The important task is to assist these patients in finding a medical home as they go through this transition period. They will need to deal with finding new medical providers at the same time that they are grappling with emotional issues, advanced education, employment and financial issues. It will be important for the pediatrician or adolescent specialist to help them find a new medical home. Research will be needed to help formulate chronic care models in support of the complex needs of transplant patients to achieve desired health outcomes.

## Acknowledgement

We want to thank Maan Dela-Cruz, M.P.H., for her meticulous literature review and edits.

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