

LIVER TRANSPLANTS

When Drug Treatment Fails

Updated 2006

During 2005, 569 liver transplants were performed on children under the age of 18 in the United States. Of those, one was performed on a child with hepatitis C and three were performed on children with hepatitis B.

In sharp contrast, hepatitis B and C together were responsible for almost 40 percent of the 5874 adult liver transplants that occurred in the United States that same year.

That correlation between age and number of transplants generally reflects the natural history of hepatitis B and C in children and adults.

Because hepatitis infections are usually silent and seemingly without symptoms in children, it is unusual for children to require transplants. However, as chronically infected children age and reach their 30s and 40s, and their immune systems attempt to repel the infection by attacking infected liver cells, more and more people with chronic viral hepatitis will require transplants to replace their diseased, scarred and cancerous livers.

In the small population of children who do require transplants, viral hepatitis has cut an unusually virulent path and extensively damaged their young livers to the point that their livers fail.

Currently in the United States transplant population:

Hepatitis A, B, C and D account for an estimated 1 to 2 percent of all liver transplants in children each year.

As of September 1, 2006, there were 10 young patients with hepatitis A, B, C or D awaiting liver transplants, according to the United Network for Organ Sharing (UNOS), the organization that oversees the national organ allocation system.

What causes most of the liver transplants in children each year is biliary atresia, a disease that scars the bile ducts and causes liver scarring and cirrhosis. The second most

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common cause of liver failure in children is congenital metabolic problems that prevent the liver from producing crucial enzymes.

In 2005, about 3 percent of adult liver transplant recipients had hepatitis B or were co-infected with B. Many adults with chronic hepatitis B were infected during childhood.

Hepatitis C, alone or in combination with alcohol abuse or coinfection with hepatitis B, was responsible for 29 percent of all adult liver transplants in the United States in 2005. The liver transplant waiting list is expected to increase dramatically in the next decade as more and more people with hepatitis C develop end-stage liver disease.

As of September 1, 2005, at the approximately 122 liver transplant centers in the United States, the following people were awaiting liver transplants:

Four children with hepatitis B or B/D
Five children with hepatitis C
One child with hepatitis A
639 adults with hepatitis B
6,323 adults with hepatitis C
88 adults coinfecting with hepatitis B and C

“The numbers are exceedingly small for liver transplants in children with hepatitis B and C because it usually takes up to 20 to 30 years for children who are chronically infected with hepatitis to develop cirrhosis,” noted Dr. Philip Rosenthal, a hepatologist and medical director of the Pediatric Liver Transplant Program at the University of California, San Francisco. “But not always—there are children who face a more aggressive course of hepatitis B or C and they are the ones who are transplanted at a young age.”

Viral Hepatitis in Children

There are between 60,000 and 150,000 children and teens chronically infected with hepatitis C in the USA and 20 to 30 percent of the 1.25 million Americans chronically infected with hepatitis B acquired their initial infection during childhood.

Hepatitis B and C are slowly evolving diseases that rarely cause serious liver disease in

The current survival rate for children three years after transplantation is about 86 percent.

The percentage of children who survive the operation and are one month post-transplant is 96.7 percent.

In adults, this survival rate is only 78 percent, according to the Scientific Registry of Transplant Recipients.

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children. Hepatitis A infection usually occurs in children during a short-lived and asymptomatic period.

While viral hepatitis is not the catalyst behind most pediatric transplants today, it can lead to liver cancer, tumors and liver failure.

Liver disease occurs more rapidly in children when there is a coinfection, for example, of hepatitis B and HIV.

History of Liver Transplants in Children

In 1963, doctors in the United States attempted the first liver transplant. Dr. Thomas Starzl performed the first successful human liver transplant in Denver in 1967. Between 1970 and 1980, the liver transplant survival rate for children was a dismal 25 percent.

In 1980, with the introduction of medication that inhibits the immune system's innate tendency to reject a transplanted organ, plus better organ preservation techniques, the survival rate climbed to between 70 to 90 percent in children.

Survival rates have improved in recent years because of drugs like cyclosporine and tacrolimus that suppress the immune system and keep it from attacking and damaging the new liver.

Following are the most recent figures of pediatric liver transplants, based on Organ Procurement and Transplantation Network (OPTN) data as of 15 September, 2006:

	Transplant Year				Total	
	2004		2005			
	N	%	N	%	N	%
TRR LIVER PROCEDURE TYPE						
Whole Liver	380	65.5	344	60.5	724	63.0
Partial Liver, remainder not Tx or Living Transplant	110	19.0	115	20.2	225	19.6
Split Liver	85	14.7	91	16.0	176	15.3
Whole Liver with Pancreas (Technical Reasons)	5	0.9	18	3.2	23	2.0
Partial Liver with Pancreas (Technical Reasons)	0	0	1	0.2	1	0.1
Total	580	100.0	569	100.0	1149	100.0

A new study on children undergoing liver transplants presented in the April 2006 issue of *Liver Transplantation* found that, even with newly-developed transplant techniques, the waiting list times for pediatric transplant candidates have increased compared to the early 1990s. The study also revealed that, although waiting list deaths have decreased for children overall, they have remained basically the same for infants.

Viral hepatitis is one of the most common causes of liver disease in children. Between 10 to 30 percent of children in the United States have antibodies that show past infection with the hepatitis A virus and about 10 percent of high-risk children, including urban poor, have been infected with the hepatitis B virus.

What Is a Liver Transplant?

A liver transplant operation removes all or a portion of a diseased liver and replaces it with a whole liver or a reduced liver or segment.

Historically, people who required liver transplants had to wait for an entire liver from someone who had just died or was “brain dead” with fully functioning internal organs. It was essential that the donor liver be as young as possible and free of disease and damage—a rarity among livers from people who just died.

In years past, children who needed livers fared badly. Adult livers, which made up most of the donations, were literally too large for them. And, children’s immune systems tended to reject the livers more readily than adult organ recipients.

But in recent years, segmental transplants have been performed with increasing frequency. This approach allows an adult liver from a deceased donor to be reduced to fit into the child. In split liver transplants, two transplant patients share one donor liver. The smaller portion goes to a child and the larger portion goes to an adult. This ability to transplant a liver segment is ideal for children, who cannot accommodate an entire adult liver. This allows donor livers to go farther in meeting the need for organs among children who require new livers.

Another recent breakthrough for children has been live donor liver transplantation (LDLT). This is a procedure in which a living person donates a portion of his or her liver to another. The first LDLT operation took place in the United States in 1989 when a child received a segment of his mother’s liver. Parent or grandparent living liver donations are ideal. Today, LDLT for children has enjoyed wide success and many pediatric programs use this technique.

The number of split livers and living donor-related transplantation has markedly increased in the pediatric population. About 35 percent of transplants in children involve split livers and 25 percent are liver segments from living donors.

Liver Transplant Operations

When a deceased donor organ is available, a transplant center receives a liver offer from UNOS for a specified patient. The patient is admitted to the hospital. While the donor team is procuring the donor liver, the recipient team begins to prepare the patient. The diseased liver is removed, and the healthy liver is put in its place.

The operation usually takes between six to eight hours. The initial 48 hours after surgery are critical. Within 24 to 48 hours, doctors can tell if the organ is functioning properly. Complete recovery may take several weeks. After discharge, patients return regularly so doctors can test to see if the patient's immune system is rejecting the organ. The highest risk period for rejection is during the first three months following the transplant.

During a live donor liver transplant, two teams perform the donor and recipient operations simultaneously. As the diseased liver is removed from the recipient by one team, about half of the donor's normal liver is removed by the other surgical team.

In LDLT operations, generally the left lateral segment of the adult's liver is removed. The critical veins and arteries remain untouched in the adult donor. The child's liver is removed and this left lateral donor segment is implanted.

Once the donor operation is completed, both teams complete the transplant by attaching the half-liver into the recipient. The donor operation usually takes about five hours and the recipient operation about 10 hours, according to the University of Southern California Liver Transplant Program patient guide.

The donor is usually in the intensive care unit for about 24 hours and in the hospital for five to seven days. Most patients are up and out of bed by the second or third day following surgery. It usually takes a month or more to recover fully.

One of the biggest risks during this time are opportunistic infections that can occur because of the immunosuppressive drugs a transplant patient must take. These drugs subdue T-cells—immune system cells that fight infection, stand guard against cancer and attack foreign tissue. It is the T-cells' hostility to foreign tissues and organs that poses a challenge for transplantation.

Transplant recipients typically must take a lifelong course of immune-suppressant drugs to reduce the chances of tissue rejection.

After the transplant, the quality of life for patients usually improves dramatically and most lead healthy, normal lives after a three- to four-month recovery period.

The half-livers in both the donor and recipient grow to be full sized within six to eight weeks.

How Are Organs Assigned?

UNOS (www.unos.org), a nonprofit charitable organization, maintains the United States' organ transplant waiting list under contract with the U.S. Department of Health and Human Services' Health Resources and Services Administration.

Under that contract and on behalf of the Organ Procurement and Transplantation Network (OPTN), UNOS develops organ transplantation policies with feedback from medical professionals, transplant recipients and donor families.

Generally, the only way to get on the national waiting list for a liver is to visit a transplant hospital. Usually, if a child or adult is experiencing serious liver disease, he or she is already being treated by a gastroenterologist or hepatologist who is either associated with a medical center that performs transplants or can refer a child to the closest transplant center.

Each hospital has its own criteria for listing patients. However, UNOS has guidelines that most medical centers subscribe to for organ transplants.

What Qualifies Someone for a Liver Transplant?

According to UNOS:

Through the Organ Procurement and Transplantation Network (OPTN), UNOS collects data about every transplant in the United States, it facilitates the organ matching and placement process and organizes medical professionals, transplant recipients and donor families to develop the country's organ transplantation policies that dictate who receives an organ transplant.

The network has developed a formula to determine when an adult or child qualifies for a liver transplant. For children under the age of 12, this scale is called the Pediatric

End-Stage Liver Disease (PELD). A PELD score is based on a patient's risk of dying while waiting for a liver transplant, and is based on objective and verifiable medical data. There is a priority exception to PELD, and that is a category known as Status 1. Status 1 patients have acute (sudden and severe onset) liver failure and a life expectancy of hours to a few days without a transplant. About one percent of transplant candidates are in this category.

PELD uses several criteria to recognize the specific growth and development needs of children. The PELD measures used for children are:

- bilirubin, which measures how effectively the liver excretes bile;
- INR (prothrombin time), which measures the liver's ability to make blood clotting factors;
- albumin, which measures the liver's ability to maintain nutrition;
- growth failure; and
- whether the child is less than one year old.

Patients with higher PELD scores will always be considered before those with lower scores for transplants, even if some patients with lower scores have waited longer. Over time, a patient's score may go up or down depending on the status of his or her disease.

UNOS offers an on-line calculator to use to assess the ranking of a child with liver disease. It can be viewed at:

<http://www.unos.org/resources/MeldPeldCalculator.asp?index=99>.

For patients already on the waiting list, each liver transplant program is responsible for updating the laboratory and clinical values needed to calculate their patients' PELD scores. These values must be entered on a regular basis, based on the patient's current PELD score.

For example, centers must enter in new laboratory data at least once a week for patients on the list with very high PELD scores, but only once per year for patients on the list with very low PELD scores. Thus, patients will have their labs drawn based on this schedule in order to make sure their PELD scores are up-to-date. The center can also update a patient's PELD score if the patient gets sicker.

Once listed, getting a liver transplant depends on several factors, such as:

- Blood type
- The number of other patients listed within the local area

- The illness level of the other patients waiting in the local area
- The number of organs available in the local area or region

UNOS and How it Works

Regions

UNOS has established 11 geographic regions for administrative purposes. Each region is assigned a UNOS staff administrator to assist in coordinating regional activities.

Prioritizing patients for transplantation

Each organ type has its own individual distribution policy, reflecting the unique medical considerations of each type of transplant. However, certain general factors apply to all organ allocation policies:

- Patients who are close biological matches with a particular donor offer (including blood type, body size and/or tissue typing match) are given priority. Closer matching tends to result in better long-term survival after transplantation.
- For heart, liver and intestinal organs, patients whose medical status is most urgent receive priority over those whose medical status is not as urgent.
- When possible, organs are offered first to patients locally, then to a larger region, then nationally. This is done to minimize organ preservation time, which is associated with better transplant survival. However, there are exceptions to this sequence for particularly well-matched organ offers and for the most urgent category of liver patients.
- The policies strive to ensure equivalent access for patients who might be at a disadvantage because of the progression of their disease or their ability to receive suitable organ offers. For example, most policies afford children special priority because of the medical risks they face while awaiting transplant.
- Waiting time is used to break ties between patients who are similar in other respects. Patients who have waited longer at their current medical status receive priority over those who have waited less time.

The UNOS computer system is programmed to consider each of these issues automatically when matching donor organs to patients awaiting a transplant. Therefore, the patients ranked highest will be those who have both the greatest need and greatest likelihood for a successful transplant.

Matching organs with patients in need: The organ offer process

When a deceased organ donor is identified, a transplant coordinator from an organ procurement organization enters medical information about the donor into the UNOS computer system.

The system then matches the donor's medical characteristics with the medical information of candidates awaiting a transplant. The computer generates a ranked list of patients for each organ recovered from the donor. The transplant team of the first person on the match run is offered the organ needed. Often the top-ranked patient may not get the organ for one of several reasons, including the following:

- he or she cannot be located or cannot reach the hospital in time for a transplant
- he or she is temporarily too sick to receive a transplant
- the medical team believes the organ would not benefit the candidate due to the donor's age or medical condition
- medical tests performed after the initial offer show that the candidate's immune system would likely reject the organ

If an offer is turned down for one transplant candidate, the organ is offered to the next candidate on the match run. These offers continue until the organ is placed or until no potential recipient can be located in time for a successful transplant.

Addressing the donor shortage: Increasing organ availability

Transplantation has saved and enhanced the lives of more than 300,000 people in the United States. It is the leading form of treatment for many forms of end-stage organ failure. With this success, however, has come increasing demand for donated organs. Today more than 82,000 people are awaiting transplants nationwide. Sadly, about 17 patients die every day while awaiting an organ—one person every 85 minutes.

Living donation (transplanting all or part of an organ from a living person) has increased dramatically in the last few years, helping increase the number of transplants performed. In addition, UNOS has enacted a number of policies to encourage more efficient use of available organs, such as "splitting" livers from deceased donors to allow two recipients to be transplanted.

How the Transplant System Works: Matching Donors and Recipients

Under contract with the U.S. Department of Health and Human Services' Health Services & Resources Administration (HRSA), the United Network for Organ Sharing

(UNOS) maintains a centralized computer network linking all organ procurement organizations (OPO—an organization designated by the Centers for Medicare and Medicaid Services (CMS) and responsible for the procurement of organs for transplantation and the promotion of organ donation) and transplant centers. This computer network is accessible 24 hours a day, seven days a week, with organ placement specialists in the UNOS Organ Center always available to answer questions.

After being referred by a doctor, a transplant center evaluates the possible transplant. The transplant center runs a number of tests and considers the patient's mental and physical health, as well as his or her social support system. If the center determines that the patient is a transplant candidate, they will add the patient's medical profile to the national patient waiting list for organ transplant. The patient is not placed on a ranked list at that time. Rather, the patient's name is added to the "pool" of patients waiting.

When a deceased organ donor is identified, a transplant coordinator from an OPO accesses the UNOS computer. Each patient in the "pool" is matched by the computer against the donor characteristics. The computer then generates a ranked list of patients for each organ that is procured from that donor in ranked order according to organ allocation policies. Factors affecting ranking may include:

- tissue match
- blood type
- length of time on the waiting list
- immune status
- distance between the potential recipient and the donor

For heart, liver, and intestines, the potential recipient's degree of medical urgency is also considered. Therefore, the computer generates a differently ranked list of patients for each donor organ matched.

The organ is offered to the transplant team of the first person on the list. Often, the top patient will not get the organ for one of several reasons. When a patient is selected, he or she must be available, healthy enough to undergo major surgery, and willing to be transplanted immediately. Also, a laboratory test to measure compatibility between the donor and recipient may be necessary. For example, patients with high antibody levels often prove incompatible to the donor organ and cannot receive the organ because the patient's immune system would reject it.

Once a patient is selected and contacted and all testing is complete, surgery is scheduled and the transplant takes place.

Living Organ Donation

The United Network for Organ Sharing (UNOS) maintains the national list of patients waiting for deceased organ donor transplants. UNOS' computer matches patients to donor organs according to objective criteria such as blood and tissue type, immune status, medical urgency and time spent on the waiting list. The ranking system determines which patient is offered the available organ.

In addition to deceased (person declared brain dead) donor transplants, patients may also receive organs from living donors. Living donation offers an alternative for individuals awaiting transplantation and increases the existing organ supply.

Facts About Living Donation: History

The first successful living donor transplant was performed between 23-year-old identical twins in 1954. Doctor Joseph E. Murray at Peter Bent Brigham Hospital in Boston, MA, transplanted a healthy kidney from Ronald Herrick into his twin brother, Richard, who had chronic kidney failure. Richard Herrick went on to live an active, normal life, dying eight years later from causes unrelated to the transplant.

Organ Types for Living Donation

Living donor transplants are a viable alternative for patients in need of new organs. Many different types of organs can be delivered by living donors, including:

- **Kidney**—This is the most frequent type of living organ donation. For the donor, there is little risk in living with one kidney because the remaining kidney compensates to do the work of both kidneys.
- **Liver**—Individuals can donate segments of the liver, which has the ability to regenerate the segment that was donated and regain full function.
- **Lung**—Although lung lobes do not regenerate, individuals can donate a lobe of one lung.
- **Pancreas**—Individuals can also donate a portion of the pancreas. Like the lung, the pancreas does not regenerate, but donors usually have no problems with reduced function.
- **Intestine**—Although very rare, it is possible to donate a portion of your intestine.
- **Heart**—A domino transplant makes some heart-lung recipients living heart donors. When a patient receives a heart-lung “bloc” from a deceased donor, his or her healthy heart may be given to an individual waiting for a heart transplant. This procedure is used when physicians determine that the deceased donor lungs will function best if they are used in conjunction with the deceased donor heart.

Qualifications for Living Donors

In order to qualify as a living donor, an individual must be physically fit, in good general health, and free from high blood pressure, diabetes, cancer, kidney disease, and heart disease. Individuals considered for living donation are usually between 18-60 years of age. Gender and race are not factors in determining a successful match. The living donor must first undergo a blood test to determine blood type compatibility with the recipient.

Blood Type Compatibility Chart

Recipient's Blood Type	Donor's Blood Type
O	O
A	A or O
B	B or O
AB	A,B, AB or O

If the donor and recipient have compatible blood types, the donor undergoes a medical history review and a complete physical examination. The following tests may be performed:

- **Tissue Typing:** the donor's blood is drawn for tissue typing of the white blood cells.
- **Crossmatching:** a blood test is done before the transplant to see if the potential recipient will react to the donor organ. If the crossmatch is "positive," then the donor and patient are incompatible. If the crossmatch is "negative," then the transplant may proceed. Crossmatching is routinely performed for kidney and pancreas transplants.
- **Antibody Screen:** an antibody is a protein substance made by the body's immune system in response to an antigen (a foreign substance; for example, a transplanted organ, blood transfusion, virus, or pregnancy). Because the antibodies attack the transplanted organ, the antibody screen tests for panel reactive antibody (PRA). The white blood cells of the donor and the serum of the recipient are mixed to see if there are antibodies in the recipient that react with the antigens of the donor.
- **Urine Tests:** In the case of a kidney donation, urine samples are collected for 24 hours to assess the donor's kidney function.
- **X-rays:** A chest X-ray and an electrocardiogram (EKG) are performed to screen the donor for heart and lung disease.
- **Arteriogram:** This final set of tests involves injecting a liquid that is visible under X-ray into the blood vessels to view the organ to be donated. This procedure is

usually done on an outpatient basis, but in some cases it may require an overnight hospital stay.

- Psychiatric and/or psychological evaluation: The donor and the recipient may undergo a psychiatric and/or psychological evaluation.

The decision to become a living donor is a voluntary one, and the donor may change his or her mind at any time during the process. The donor's decision and reasons are kept confidential.

Risks Involved in Living Donation

All patients experience some pain and discomfort after an operation. And as with any major operation, there are risks involved. It is possible for kidney donors to develop infections or bleeding, and when a portion of the liver or pancreas is donated, the liver or spleen may be injured.

Living donation may also have long-term risks that may not be apparent in the short term. It is therefore important that the benefits to both donor and recipient outweigh the risks associated with the donation and transplantation of the living donor organ. In addition to potential individual health concerns, it is possible for negative psychological consequences to result from living donation.

Living donors may feel pressured by their families into donating an organ and guilty if they are reluctant to go through with the procedure. Feelings of resentment may also occur if the recipient rejects the donated organ. Living donors must be made aware of the physical and psychological risks involved before they consent to donate an organ. They should discuss their feelings, questions and concerns with a transplant professional and/or social worker.

Positive Aspects of Living Donation

Living donation has several advantages:

- Living donation eliminates the recipient's need for placement on the national waiting list. Transplant surgery can be scheduled at a mutually-agreed upon time rather than performed as an emergency operation. Because the operation can be scheduled in advance, the recipient may begin taking immunosuppressant drugs two days before the operation. This decreases the risk of organ rejection.
- Transplants from living donors are often more successful, because there is a better tissue match between the living donor and the recipient. This higher rate of compatibility also decreases the risk of organ rejection.

- Perhaps the most important aspect of living donation is the psychological benefit. The recipient can experience positive feelings knowing that the gift came from a loved one or a caring stranger. The donor experiences the satisfaction of knowing that he or she has contributed to the improved health of the recipient.

Costs Related to Living Donation

Health insurance coverage varies for living donation. If the recipient is covered by a private insurance plan, most insurance companies pay 100 percent of the donor's expenses. If the recipient is covered by Medicare's end-stage renal disease program, Medicare Part A pays all of the donor's medical expenses, including preliminary testing, the transplant operation, and post-operative recovery costs. Medicare Part B pays for physician services during the hospital stay. Medicare covers follow-up care if complications arise following the donation.

Split Liver Transplant Policies Benefit Children

In 2001, UNOS' governing board voted in favor of a national split liver transplant policy in an effort to reduce the number of children awaiting liver transplants. It recommended that all medical centers that perform liver transplants split each deceased donor liver between a child and an adult. Because these organs regenerate themselves within a month, a split liver transplant would provide two liver transplants from one organ. This policy won't lessen organ demands among adults, according to UNOS, but it will provide more organs for children.

For more information about organ transplants, call UNOS at 804-782-4800 and ask for Patient Services, or call 888-894-6361 for an organ-specific information kit.

Impact of Liver Transplants in People with Hepatitis

Adults requiring a liver transplant due to hepatitis B or C face unique challenges. Although the virus replicates only in liver cells, removing the infected liver and replacing it with a hepatitis-free one may not necessarily remove all traces of the virus.

Researchers are finding that hepatitis viruses hide out in the bile duct and other neighboring organs and often reappear after a liver transplant operation. The return or reactivation of the virus is problematic.

Because transplant patients receive drugs that suppress some or all of their immune systems, that immunosuppression may enhance the viral replication in the new liver. As a result, hepatitis can reassert itself quickly in patients with weakened immune systems. Researchers are focusing on ways to suppress the immune system's tendency to reject the liver without making the patient overly vulnerable to reactivated hepatitis. In cases of hepatitis B, doctors are increasingly using hepatitis B immune globulin (HBIG), which contains hepatitis B antibodies, in an effort to subdue or eradicate viral replication in transplanted patients. Unfortunately, no similar medication is available to subdue hepatitis C viruses.

Hepatitis C and Liver Transplantation

A small but potentially significant study published in the February 2006 issue of *Liver Transplantation* states that “End-stage liver disease due to hepatitis C virus (HCV) infection is the most common indication for liver transplantation in the United States. While many patients initially appear to do well following transplantation, graft reinfection as measured by detectable serum HCV ribonucleic acid (RNA) is universal.

“Serum HCV RNA decreases rapidly during and immediately after the removal of the infected liver and the implantation of the new, uninfected one. This is followed by a steady increase in viral concentrations within days. Once the new liver becomes infected—presumably by circulating virions that remain or from extrahepatic compartments—hepatic viral replication resumes, causing serum HCV RNA levels to rise.”

The AASLD reported in 2002 that “physicians involved in the care of liver transplant patients must have a clear understanding of the pathogenesis of recurrent hepatitis C, and the impact of immunosuppressive therapy on the course of these patients. Antiviral therapy has been used to prevent or treat recurrent hepatitis C, but tolerance is poor in post transplant patients. Physicians managing these patients need to be aware of the problems that are unique to the transplant population.

“Significant progress has been made in the past 15 years on the prevention of recurrent hepatitis B post-liver transplant. Outcome of patients transplanted for hepatitis B is better than that of patients transplanted for hepatitis C, but current prophylactic regimens for hepatitis B are very expensive. Optimal use of nucleos(t)ide analogs can improve the cost-effectiveness of prophylactic therapies for recurrent hepatitis B and the outcome of patients with recurrent hepatitis B.”

To counter this viral resurgence, doctors have used a combination drug therapy of

interferon alpha and ribavirin to treat the recurrent hepatitis C in transplant patients.

Currently, medical researchers aren't sure if some hepatitis C genotypes or strains may play a role in the success or failure of transplants, or to what degree the immune-suppressing drugs that patients receive to prevent organ rejection will inadvertently hasten the progress of liver disease and viral replication.

Nevertheless, survival in transplant patients with hepatitis C is similar to uninfected patients who receive a liver transplant for other reasons.

But doctors are concerned about the long-term picture for hepatitis C patients. They have found, according to a *Gut* article on hepatitis C and liver transplantation, "the annual rate of fibrosis [liver scarring] progression may be higher than reported in the non-transplant population, suggesting that the length of time needed to develop significant hepatitis C-related liver damage could be shorter in immunosuppressed patients than in immunocompetent ones."

A liver transplant may give a patient some breathing room, but with the virus ever-present, liver disease may return and at a faster rate given the patient's compromised immune system, the study suggests.

Another risk hepatitis C patients face is the chance of contracting a different genotype of hepatitis C from the donor organ. As the number of available organs becomes scarcer and demand, particularly from hepatitis C patients, increases, some organs from people who carry the hepatitis C virus will be used for transplant.

These organs may still harbor hepatitis C RNA and there is a chance that the new organ can introduce its own strain of hepatitis C virus. Because there are several genotypes of hepatitis C, the transplanted organ could introduce a new viral strain or a mutated version of the virus that could contribute to accelerating the rate of liver disease in the patient.

Hepatitis B and Liver Transplants

Transplant specialists have a longer record of experience with liver transplants in adults with hepatitis B. During the 1970s and 1980s, transplant success in these patients was dismal, according to the American Liver Foundation's Hepatitis B Liver Transplant Symposium report issued in 1998.

About 55 percent of adult hepatitis B patients died within 60 days of their transplant due to reinfection by the virus, which remained insidiously in neighboring organs despite the removal of the diseased liver, and due to the suppressed immune systems of patients. Doctors soon realized that preventing hepatitis B reinfection was critical to transplant success in this population.

In 1993, several medical centers in Europe experimented with administering HBIG with hepatitis B antibodies to patients during the liver transplant as a way to counter any residual hepatitis viruses that attempted to reactivate.

Doctors have discovered that prolonged and heavily concentrated doses of HBIG, administered for more than six months, dramatically curtailed reinfection and greatly improved the survival rates of hepatitis B transplant patients.

The studies revealed that patients who received this “passive” immunization of HBIG and had low hepatitis B DNA levels and the e antibody experienced an extremely low reinfection rate. Those patients who had the e antigen and higher viral DNA levels reported a relatively low 35 percent rate of reinfection.

Today, doctors routinely administer HBIG to hepatitis B transplant patients and their survival rate is now comparable to transplant patients without hepatitis B infections. In 1993, the transplant survival rate in hepatitis B patients was 50 percent; by 1998, survival increased to 80 percent with the help of HBIG.

This increased survival rate allowed UNOS to sanction use of liver transplants in hepatitis B patients, no matter what their viral status, and helped convince the Health Care Financing Administration to provide coverage for transplantation of acute and chronic hepatitis B.

However, sometimes the hepatitis B virus does resurface after a liver transplant. In about half of these cases, a patient may have a mutated version of the virus that can resist the HBIG antibodies. In the other 50 percent of viral recurrence, the dose of HBIG may not have been strong enough or else the patient had a high viral load of hepatitis B DNA and the e antigen.

After a liver transplant, it is essential to combat the virus through drug treatment. Post-transplant treatment with interferon alpha has proven disappointing because interferons bolster the immune system, which works to reject the transplanted organ.

A review in the April 2006 issue of *Annals of Clinical Microbiology and Antimicrobials* suggests that the addition of the nucleoside analog Lamivudine (LAM) to HBIG has improved the survival curve of HBV+ liver recipients. The review goes on to state that “Prolonged use of LAM will almost invariably lead to the development of viral mutations resistant to the drug.

There are now several other nucleoside and nucleotide analogs (Adefovir, Entecavir, Tenofovir, and Truvada) available for the clinician to utilize against these resistant strains. It should be possible to prevent recurrence in most, if not all, post-transplant patients and also to significantly reduce viral loads with normalization of transaminases in those who have developed recurrent infection. The antiviral regimen should be robust and minimize the risk of breakthrough mutations. A prudent approach may be the implication of combination antiviral therapy.”

There seems to be some controversy about the duration of HBIG therapy. With the combination drugs available, it could be that the expensive HBIG therapy could be stopped after a short time or even avoided.

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