

# Baylor Regional Transplant Institute: an update on liver, kidney, and pancreas transplantation

NICHOLAS ONACA, MD, ROBERT M. GOLDSTEIN, MD, MARLON F. LEVY, MD, AND GÖRAN B. KLINTMALM, MD, PhD

Successful transplantation to replace failed human organs was a daunting goal at the start of the 20th century. Investigators in Vienna attempted kidney transplantation in several animals in 1901. The first transplantation of a kidney that functioned in humans was performed 50 years later by Dr. René Küss in Paris. The kidney worked without immunosuppression but was rejected 2 months later. Dr. Joseph Murray performed the first successful kidney transplantation in 1954 using a kidney from an identical twin. Further progress was made with advances in immunosuppression—the use of azathioprine in 1959 by Dr. Roy Calne and its combination with steroids by Dr. Thomas Starzl; the introduction of antilymphocyte globulin by Dr. Starzl in 1967—and the development of organ preservation solutions by Dr. Folkert Belzer (1968) and Dr. Jeffery Collins (1969), enabling better outcomes and the use of allografts from remote organ donors. The first liver transplantation was performed by Dr. Starzl in 1963. The first pancreas transplantation was performed in 1966 by Dr. Richard Lillehei in Minnesota. Overall results were poor until the introduction by Dr. Roy Calne of cyclosporine, which changed immunosuppression and organ transplant outcomes.

The Baylor transplant program journey started in 1983, when Dr. Thomas Starzl was invited by Dr. John Fordtran to visit Baylor University Medical Center (BUMC). At that time, there was no liver transplant program in the Southwest (the program at the University of California at Los Angeles started in February 1984). BUMC had the courage to embark on this mission when liver transplantation, although established, was still a pioneering medical procedure. One year later, the transplant program was up and running; the first liver transplant was performed at BUMC in December 1984.

## BAYLOR TRANSPLANT SERVICES TODAY

During the almost 20 years that have passed since the Baylor program began, the practice of transplant surgery has improved dramatically. While the principles of the surgical technique have remained basically the same, details have improved, and anesthesia and intensive care have made major advances. With the breakthrough discovery of cyclosporine, short- and long-term outcomes of solid organ transplantation changed dramatically. The synthesis of other immunosuppressive drugs now used routinely in practice brought further improvement.

Today, Baylor transplant services is a well-established program. Its activities extend well beyond the operating room. The

surgical team is involved in patient selection, pre- and postoperative inpatient and outpatient care, long-term patient follow-up, management of organ donors, and donor surgery at remote hospitals.

The main characteristics of the service are as follows:

- Standardization of all stages of routine patient care, based on protocols developed according to current knowledge in the field, routinely incorporating the latest advances reported in clinical trials.
- Flexibility and creativity manifested in unusual situations in patient care and adaptation to the progress made in the field.
- Use of novel therapy through participation in clinical trials.
- Commitment to patient guidance, follow-up, and care extending now for 18 years, including routine interaction with patients' primary care physicians.
- A multidisciplinary clinical approach, involving a team of physicians, nurses, dietitians, physical therapists, social workers, and chaplains, and receiving constant support from all other medical and ancillary services in the hospital.
- Maintenance of a large patient database with prospective data entry for clinical research and for periodic review and audit.
- Commitment to teaching of medical students, Baylor residents, and transplant surgery fellows.
- Dedication to research, publication, and presentation at national and international peer meetings.

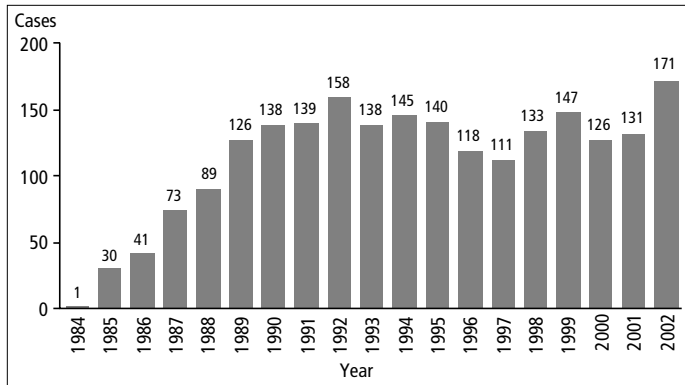
The transplant surgery team includes 7 transplant surgeons involved in all aspects of surgical care: Drs. Göran Klintmalm, founder of the service; Robert Goldstein (since 1988); Marlon Levy (since 1992); Edmund Sanchez (since 2001); Srinath Chinnakotla (since 2001); Sherfield Dawson (since 2002); and Henry Randall (since 2002).

## LIVER TRANSPLANTATION

The liver transplant program at Baylor grew rapidly in the 1980s to become one of the largest-volume programs in the USA. In February 2002, the program became the third in the world to perform its 2000th liver transplant in adult patients. To date, 2232 liver transplants have been performed at Baylor in adults.

From Baylor Regional Transplant Institute, Baylor University Medical Center, Dallas, Texas.

**Corresponding author:** Göran B. Klintmalm, MD, PhD, Baylor Regional Transplant Institute, Baylor University Medical Center, 3500 Gaston Avenue, Dallas, Texas 75246 (e-mail: gorank@BaylorHealth.edu).



**Figure 1.** Annual volume of activity in liver transplantation at Baylor Regional Transplant Institute.

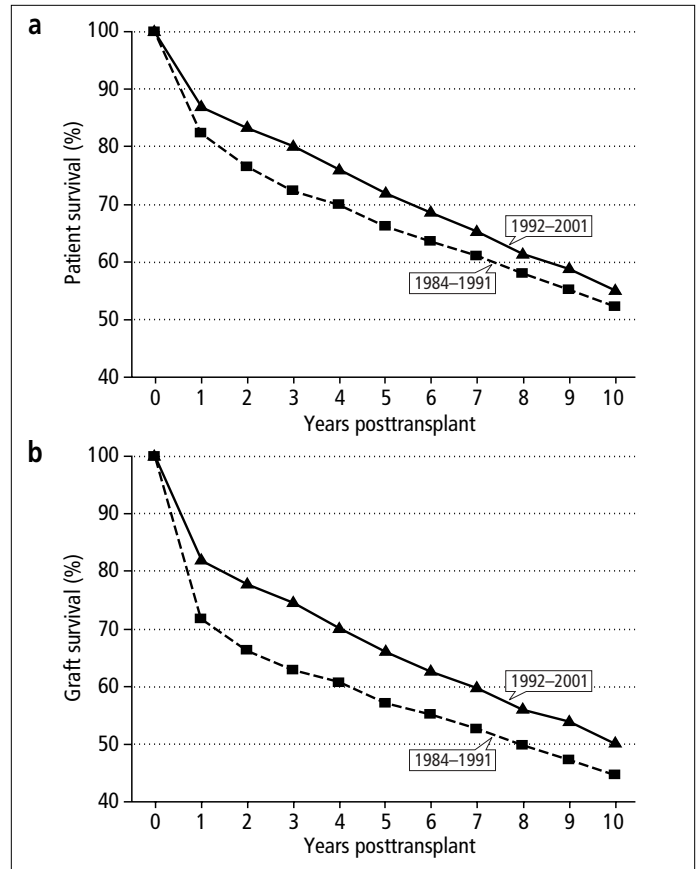
**Table 1. Patient and graft survival rates following liver transplantation at Baylor Regional Transplant Institute**

Survival	Interval	Survival rate (%)						
		30 days	90 days	1 year	2 years	5 years	10 years	15 years
Patient	Overall	96	92	86	81	70	55	38
	1984–1991	94	90	82	77	66	52	37
	1992–2001	96	93	87	83	72	55	NA
Graft	Overall	92	87	79	75	64	49	34
	1984–1991	87	82	71	66	57	45	31
	1992–2001	93	89	82	78	66	50	NA

NA indicates not applicable.

Retransplants accounted for 201 adult cases (9%). Combined liver-kidney transplants were performed in 54 cases and a liver-kidney-pancreas transplant in 1 case. The yearly case volume is shown in *Figure 1*. A total of 171 liver transplants were performed in 2002, and 77 cases were added so far in 2003; our limiting factor continues to be donor availability.

Overall patient survival rates were 86% at 1 year, 81% at 2 years, 70% at 5 years, 55% at 10 years, and 38% at 15 years posttransplant (*Table 1*). These are the global results. Cases performed in 1992 to 2001 showed a 5% to 8% improvement in the 1- to 5-year survival rates compared with cases performed in 1984 to 1991 (*Figure 2a*); the difference is statistically significant (chi-square,  $P < 0.01$ ). Past the 5-year mark, the improvement in survival in the later series was less pronounced due to the recurrence of primary diseases such as hepatitis C and hepatocellular carcinoma. Nevertheless, some improvement occurred despite the change in the spectrum of liver disease etiology during the years. In the 1984 to 1991 period, only 109 out of 637 transplants (17%) were performed for chronic hepatitis (B and/or C), while the remainder were performed for cholestatic and other diseases that carry a better prognosis. In 1992 to 2001, 505 out of 1518 transplants (33%) were performed for chronic hepatitis ( $P < 0.001$ ), and 115 out of 257 transplants in 2000 to 2001 were in patients with chronic viral hepatitis (C, 102 patients; B, 12 patients; both, 1 patient). Since most of the long-term survival refers to the 1984 to 1991 “era,” this difference in etiologies and their specific outcome might explain the trends in long-term survival.

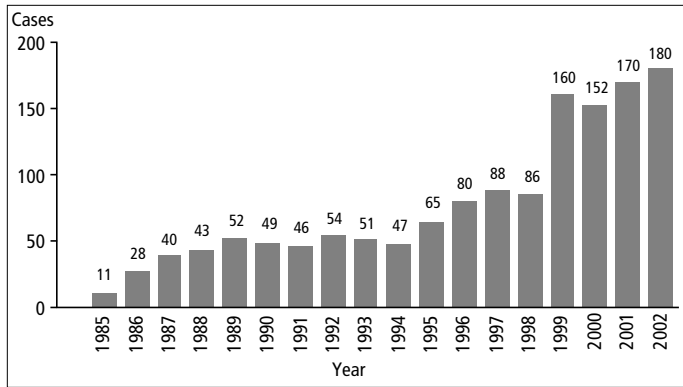


**Figure 2.** (a) Patient survival and (b) graft survival rates after liver transplantation performed at Baylor Regional Transplant Institute during the periods 1984 to 1991 and 1992 to 2001.

Graft survival after liver transplantation also tended to improve (*Figure 2b*). A comparison of data from transplants performed in 1984 to 1991 with those performed in 1992 to 2001 showed a 9% to 12% improvement in graft survival in the first 5 years after transplant for the later period (*Table 1*) ( $P < 0.01$ ). The overall graft survival rates were 79% at 1 year, 75% at 2 years, 64% at 5 years, 49% at 10 years, and 34% at 15 years posttransplant. Similar to results for patient survival, the outcome difference tended to diminish in the long term. Again, the difference in liver disease etiology mentioned above has even more impact on graft survival, with graft loss being more frequent with chronic hepatitis C and B than with cholestatic and metabolic liver disease.

Technical improvements have made the surgical procedure less challenging for the patient. The operating room time has decreased from 8 to 9 hours to 4 to 5 hours in “standard” cases. The need for autologous blood transfusion has been reduced to 2 to 4 units per case. Massive blood transfusions are extremely rare. Many cases do not necessitate intraoperative blood transfusion.

Because of the improvement in intraoperative care, patients with complex anatomy, who would not have been accepted as candidates for transplantation earlier because of the risks, are being operated on. The improvement in the perioperative treatment has led to significant shortening of the postoperative intensive care unit stay, as well as the overall hospital stay. The typical patient is admitted to the intensive care unit for <24 hours and has a total hospital stay of 6 to 7 days. The median hospital stay is 9 days, with a mean of 14.



**Figure 3.** Annual volume of activity in kidney transplantation at Baylor Regional Transplant Institute.

**Table 2. Patient and graft survival rates following kidney transplantation at Baylor Regional Transplant Institute**

Survival	Interval	Survival rate (%)				
		1 year	2 years	5 years	10 years	15 years
Patient	Overall	97	94	87	63	43
Graft	Overall	91	86	71	39	24
	1985–1991	82	76	60	45	24
	1992–2001	93	89	79	59	NA

NA indicates not applicable.

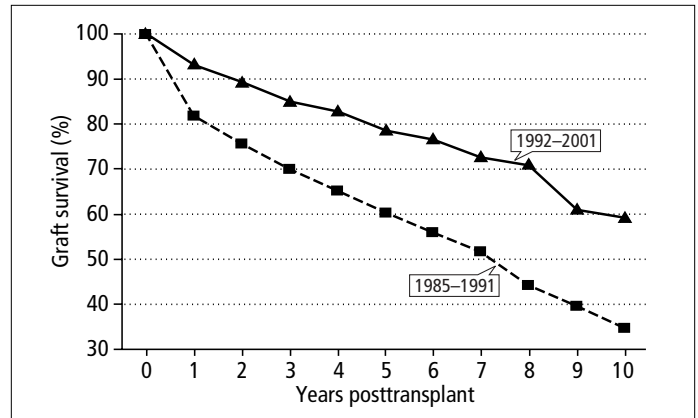
Outpatient postoperative follow-up and care is continued in the outpatient clinic by the transplant surgical team for the first 3 months after transplant. This approach allows consistent care, especially in terms of immunosuppressive treatment.

The spectrum of liver disease etiology in patients who undergo liver transplantation has changed across the country. In the earlier years both nationally and at Baylor, cholestatic liver diseases (primary sclerosing cholangitis and primary biliary cirrhosis) were the main reason for transplantation. Today, most patients who undergo liver transplantation have chronic hepatitis C, and this raises concerns about long-term results, especially because of the propensity of the disease to recur with immunosuppression.

Adult-to-child living-donor liver transplantation started in 1999 and has been performed in 6 cases; adult-to-adult living-donor liver transplantation has been performed in 4 cases. The living-donor liver program is based on the extensive expertise of Dr. Robert Goldstein in the field of hepatobiliary surgery.

### KIDNEY TRANSPLANTATION

The first kidney transplant at BUMC was done in June 1985 as a combined liver/kidney transplant. In July 1985, the regular kidney transplant program began. So far, 1495 kidney transplants have been performed, 1375 of them as a solitary procedure and the remainder in combination with other solid organ transplants (kidney-pancreas in 58 cases, liver-kidney in 57 cases, heart-kidney in 4 cases, and liver-kidney-pancreas in 1 case). Living donors accounted for 356 cases (24%). The use of living donors for kidney transplantation continues to increase. In 2002, a total of 180 kidney transplants were performed, 54 of them from living donors (30%).



**Figure 4.** Graft survival rates after kidney transplantation performed at Baylor Regional Transplant Institute during the periods 1985 to 1991 and 1992 to 2001.

The overall number of kidney transplants rose significantly in 1999 (Figure 3) due to several factors: the development of the pancreas transplant program; the introduction of laparoscopic donor kidney retrieval, which increased the number of living-donor kidney transplants; and the opening of the kidney transplant program at Baylor Medical Center at Grapevine. The program at Grapevine performed 136 cadaveric kidney transplants between 1999 and 2001 and had results identical to those of transplants performed in Dallas.

Overall kidney transplant graft survival rates were 91% at 1 year, 86% at 2 years, 71% at 5 years, 39% at 10 years, and 24% at 15 years (Table 2). A comparison of transplants performed in 1985 to 1991 and 1992 to 2001 showed a 12% to 25% improvement in 1- to 10-year graft survival rates (Figure 4) ( $P < 0.001$ ). This improvement can be explained mainly by better surgical technique and immunosuppression, as well as the diligent, long-term follow-up of patients in the Dallas Transplant Institute (DTI). Overall patient survival rates were 97% at 1 year, 94% at 2 years, 87% at 5 years, 63% at 10 years, and 43% at 15 years.

The typical hospital stay for kidney transplant patients includes an overnight stay in the intensive care unit and a total of 4 to 5 days of inpatient care. Care is then transferred to the nephrology team at DTI.

The Baylor program highlights the use of living donors as a means to expand the donor pool. Living donors represent a significant resource in the kidney transplant program. The acceptance of the donor procedure increased markedly with the introduction of the laparoscopic donor nephrectomy. In September 1999, the first laparoscopic nephrectomy in a living donor was performed at BUMC. A team consisting of Drs. Howard Derrick III, Matthew Westmoreland, and Michael Seiba began offering this innovative approach to living-donor organ donation. One third of the living-donor kidneys are still retrieved using the “open” technique. Two urologists, Dr. Michael Goldstein and Dr. Robert Schoenvogel, have served the patients with their superior technique of open donor nephrectomies since the program’s inception.

### PANCREAS TRANSPLANTATION

The first pancreas transplant at BUMC was performed in December 1989 as a combination liver/kidney/pancreas transplant. Since then, 63 transplants have been performed in adult

patients: 60 simultaneous kidney-pancreas transplants, 2 pancreas transplants after kidney transplants, and 1 simultaneous liver-kidney-pancreas transplant. Our standard technical approach uses the portal venous drainage and enteric exocrine drainage, thus avoiding systemic complications seen with bladder drainage. The pancreas transplant program is now a distinct entity under the supervision of Dr. Robert Goldstein. The overall graft survival rate was 89% at 1 year and 86% at 2 years post-transplant, with a 2-year patient survival rate of 98%.

### **THE BAYLOR ALL SAINTS TRANSPLANT PROGRAM**

The Baylor All Saints Transplant Program was opened in Fort Worth in July 2002 as part of an effort to improve access to transplantation for patients in Tarrant County. Headed by Dr. Marlon Levy, surgical director, and Dr. Natalie Murray, medical director, the program performs liver and kidney transplants using the expertise of BUMC and manpower from both medical centers. The earlier kidney transplantation effort at Baylor Medical Center at Grapevine was transferred to Fort Worth. The patient care protocols are unified for both the Dallas and Fort Worth programs.

Since its opening, the Baylor All Saints program has performed 23 liver transplants and 30 kidney transplants, all from cadaveric donors. We expect to start living-donor kidney transplantation and pancreas transplantation at this facility within the next few years.

### **PEDIATRIC LIVER TRANSPLANTS**

The Dallas Liver Transplant Program was initiated in 1995 as a collaborative endeavor in the field of pediatric liver transplantation between Children's Medical Center (which is affiliated with the University of Texas Southwestern Medical School) and the Baylor Regional Transplant Institute. The Baylor team joins the pediatric transplant team headed by Drs. John Andersen and Jay Roden for liver transplant care and surgery and also performs the living-donor surgery for pediatric recipients and manages living-donor patient care. A total of 123 liver transplants have been performed in children since 1995. The patient survival rates were 86% at 1 year, 82% at 2 years, and 74% at 5 years posttransplant. The graft survival rates for the same time intervals were 80%, 77%, and 68%, respectively.

### **ORGAN DONORS**

The Baylor transplant program collaborates closely with the Southwest Transplant Alliance, the local organ procurement organization. Cadaveric donor organ shortage is by far the most important problem faced by organ transplantation nationwide and locally. To increase organ availability, efforts have focused on education promoting donation, donor care, and successful use of marginal donor organs.

### **TRANSPLANT NUTRITION**

The Baylor transplant program has a dedicated nutrition service dedicated exclusively to the transplant patients. The nutritional assessment and care begins during the pretransplant patient selection and continues through the inpatient and follow-up stages of care. The dietitians manage all oral and intravenous feeding of inpatients on the transplant services. Dr. Jeanette Hasse introduced routine early postoperative tube feeding as the means

of nutritional support after liver transplantation, based on research studies performed at BUMC. This strategy has been adopted by most transplant centers as the standard of care.

### **OUTPATIENT CARE**

Outpatient follow-up and care is now based in the Advanced Treatment and Transplant Center located in the Baylor Jack and Jane Hamilton Heart and Vascular Hospital. The center unites the care of liver, heart, and lung transplant patients (both before and after transplant); patients with hepatitis and liver disease; and patients with heart failure. The new space supports the growth not only in transplant, but also in other key strategic areas for Baylor such as hepatology and heart failure. The new center also provides a central location for patients to have access to advanced clinical research protocols.

### **THE MULTIDISCIPLINARY APPROACH**

The maintenance of a large-volume transplant program has been facilitated by the genuine professional interest and support of all the other services in the hospital.

The anesthesia service under the active lead of Dr. Michael Ramsay is continuously seeking to improve the intraoperative care of liver transplant patients. Other anesthesiologists who have played prominent roles during the years are Drs. Thomas Swygert, Peter Walling, and Robert Parks. Baylor was one of the first centers to introduce the red blood cell saver for intraoperative autotransfusion in liver transplantation, which is now a standard of care. The Baylor team also produced many of the leading publications addressing the coagulation disorders associated with liver transplantation surgery and their management. A particular field of study is portopulmonary hypertension and the hepatopulmonary syndrome. After gaining considerable experience, the service has guidelines in place for patient selection and care of these relatively rare but life-threatening disorders. In addition, the Baylor program was the first to use nitric oxide for intraoperative pulmonary pressure control.

The maintenance of a high-volume transplant program could not be realized without the dedicated support of the gastroenterology and hepatology services, which are involved in both the transplant candidate selection and the pre- and postoperative care through the work of Drs. John Fordtran, Daniel Polter, Daniel DeMarco, J. Kent Hamilton, Harry Sarles, Douglas Thurman, Jeff Crippin, Jeffrey Weinstein, and Natalie Murray. Dr. Gary Davis joined the team in July 2002 as the director of hepatology. He is an internationally recognized researcher in the field of hepatitis C and promotes a broad-based investigative effort that is now under way.

Dr. Marvin Stone, Dr. Douglas Orr, and the hematology/oncology team are involved in the care of the rare but challenging patients with posttransplant lymphoproliferative disorder. The Baylor transplant program also works with Dr. Douglas Orr in the assessment and treatment of patients with hepatocellular carcinoma before and after liver transplantation. This is part of a wider strategy including the hepatobiliary service headed by Dr. Robert Goldstein.

The transplant nephrology service focuses on the support of renal function in transplant patients. This service offers inpatient transplant medicine care starting preoperatively and continuing

through the postoperative stay for all liver transplant patients; care includes renal support, electrolyte and glucose control, and management of various medical complications. The transplant medicine physicians are also actively involved in the in-hospital care of patients with end-stage liver disease.

Drs. Martin White, Michael Emmett, and Tom Parker were instrumental in the nephrology service from the onset. The leadership of Dr. Thomas Gonwa between 1986 and 2001 made a huge impact. Under his direction, Baylor became the leading institution in the understanding of renal dysfunction in clinical liver transplantation. Numerous research protocols and publications from Baylor have benefited patients worldwide. Drs. Larry Melton, Stephen Hayes, Kim Rice, Yousri Barri, and Carlos Zayas are now responsible for the service.

The care of renal transplant patients is integrated in DTI. As part of the institute, the nephrology team has an independent outpatient care facility for preoperative and postoperative care of kidney transplant recipients. While most of the transplant centers across the country defer the care of the kidney recipients to the local nephrologists, DTI continues the complete follow-up of those patients who live in the Dallas metropolitan area and collaborates with patients' nephrologists for patients who live outside the area.

The pathology department has been instrumental in the diagnosis of disease in transplant patients. Histopathology of solid organ transplants continues to be a diagnostic challenge. From the beginning, the Department of Pathology routed all liver transplant histology to Dr. Weldon Tillery so he could build the expertise that has come to be the backbone of the liver transplant service treatment protocols. Dr. David Watkins soon joined Dr. Tillery. With Dr. Tillery's retirement, Dr. Georges Netto became the point person for liver transplant histology. Dr. Netto is also an active investigator and author. The Baylor team's expertise enables diagnosis of acute cellular rejection in transplant patients, especially in those with chronic hepatitis C, on a same-day basis. Liver biopsy results are also used when deciding whether to use marginal donor livers. Dr. Daniel Savino focuses on renal transplant pathology and different aspects of diagnosis of rejection and graft failure.

Timely diagnostic and interventional radiology procedures are a cornerstone of patient care before and after transplantation. A large experience has accumulated with diagnostic ultrasonography of solid organ transplants, and a similarly large experience has evolved with vascular, biliary, and renal interventional radiology.

## RESEARCH

From the start of the program, there was a strong commitment to clinical research. A large, comprehensive transplant database is maintained prospectively and over the years has facilitated the effort of solving unknowns in clinical practice. The solid organ transplant research area is currently participating in more than 35 active studies, with 16 additional studies pending. Over the years, the Baylor transplant program has had 256 publications in peer-reviewed journals, contributed to 13 book chapters, and published 3 books; in addition, 105 abstracts have been published, and 203 presentations have been given at national and international professional meetings.

Improvement of immunosuppressive regimens is a constant subject of research. The Baylor program is active in multicenter trials of immunosuppressive treatment and is currently the leading center in several trials. In these studies, the transplant group collaborates with other services, including anesthesiology, gastroenterology/hepatology, hematology/oncology, immunology, nephrology, and pathology.

Dr. Klintmalm's special interest in the management of patients transplanted for hepatic tumors was the basis for the establishment of the International Liver Transplant Tumor Registry, a multicenter database aimed at improving strategies in the treatment of these patients. The registry, which contains data on more than 1100 patients with tumors, has helped define the indications and contraindications for transplant in patients with hepatocellular carcinoma. We are currently studying the impact of neoadjuvant and adjuvant therapy for these patients.

Other future research trends focus on preserving donor organs; developing strategies to induce the recipient's immune tolerance to the graft, thus reducing or eliminating the need for immunosuppression; introducing more effective and less toxic immunosuppressive therapy (in particular, reducing renal toxicity); and preventing and treating hepatitis C after liver transplantation.

Dr. Marlon Levy is leading a major effort to start the pancreatic islet cell transplantation program as an alternative to whole-organ pancreas transplantation. This procedure is still considered experimental and will be performed as part of a strict research protocol. We are building a state-of-the-art cell processing laboratory to handle preparations for transplant as well as basic science projects in the field of diabetes research, in collaboration with the Diabetes Research Institute at the University of Miami. Bashoo Naziruddin, PhD, joined the team as scientific director for the islet cell transplantation program. He has extensive research experience from the biotechnology industry and leading academic institutions in the areas of protein chemistry, immunology, cancer research, and drug development.

## EDUCATION

Baylor has a clinical transplant surgery fellowship program approved by the American Society of Transplant Surgeons and known worldwide. Through the years, 30 surgeons from 4 continents have been surgical fellows in the program. We currently have 4 surgical fellows; 2 fellows start the program each year. In addition, the program is part of a rotation by surgical residents from BUMC and the University of West Virginia.

## FUTURE TRENDS

Transplantation is still a dynamic field, and many changes are expected to occur in the next few years. The Baylor transplant program is committed to expanding its efforts to better serve the interests of our population, adding new fields and extending services in existing facilities. The development of the new pancreatic islet cell transplantation program will lead to an integrated treatment approach for patients with diabetes mellitus. Baylor is also planning to start a small bowel transplantation program for patients with short bowel syndrome of various etiologies. Xenografting and new immunosuppressive techniques with the aim at tolerance induction are additional areas in which Baylor has significant interest. The future is exciting.