Islet Cell Transplantation Now Available

New Service Benefits Patients with Chronic Pancreatitis

In mid-August, MedStar Georgetown Transplant Institute became the sole site in the metropolitan area—and one of only a handful nationwide—to offer autologous islet cell transplantation for chronic pancreatitis. For many patients, the procedure is literally a lifesaver.

“Chronic pancreatitis from an unobstructed gland produces terrible pain that its sufferers will endure for the rest of their days,” says gastroenterologist Khalid M. Khan, MD. “They can’t work, forcing many to survive upon disability benefits, and the pain makes them dependent upon narcotics for relief. Within the field, it is well known that some patients—out of desperation—eventually contemplate suicide.”

That dramatic response is the direct result of a dismal prognosis and a dearth of treatments for the disease, in which the pancreas effectively

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LETTER FROM THE EXECUTIVE DIRECTOR

Dear Colleague:

Welcome to the inaugural issue of Transplant Digest—our latest effort to share new developments at the MedStar Georgetown Transplant Institute with our broad community of partners throughout the region. We hope you find its content useful, interesting and informative, and we invite your feedback and input.

As colleagues in care, we are both invested in our shared patients’ best interests, health and long-term outcomes. At MedStar Georgetown Transplant Institute, we greatly respect the role that each physician plays in the daily lives of transplant recipients and others who we treat with you. So we hope to continue to work in concert, returning transplant patients to your care or assuming management as is best for each patient and doctor.

This new publication is one small way to keep you aware of MedStar Georgetown Transplant Institute’s overall progress, beyond communication on individual patients.

In the pages that follow, for instance, you’ll read about adult and pediatric advances in our four major areas of expertise: liver diseases and transplantation, kidney and pancreas transplantation, small bowel diseases and transplants, and hepatobiliary tumor management. Included are research updates that influence how we—and now others—practice medicine … notification of important new services previously unavailable in the area … reports on our progress in organ recruitment and extending the life of transplanted kidneys … and other contributions to the field that are changing the face of transplant medicine.

We hope you enjoy it, and look forward to your feedback as we plan future issues.

Sincerely,

Thomas M. Fishbein, MD
Executive Director
MedStar Georgetown Transplant Institute

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digests itself. Traditionally, if the gland was not obstructed, only two therapeutic approaches existed and neither was ideal: increasing levels of narcotics to alleviate symptoms, or total pancreatectomy to remove the source of pain. The latter is most often ruled out, as it immediately substitutes one life-shortening chronic condition, brittle diabetes, for the other.

Ironically, that decision only sentences patients to more years of suffering without saving them from diabetes in the future, as unresolved chronic pancreatitis eventually consumes all the organ’s insulin-producing islet cells.

By contrast, autologous islet cell transplantation is the first effective therapy that both eliminates pain while maintaining insulin sufficiency. The procedure involves a total pancreatectomy, followed by extraction and purification of islet cells in MedStar Georgetown University Hospital’s new “clean” lab, designed specifically for that purpose. Retrieved cells are then infused into the patient’s liver through the portal vein where they engraft and ideally begin to produce insulin again on their own.

In addition to Dr. Khan, the Autologous Islet Cell Transplant program includes Transplant Surgeon Chirag S. Desai, MD, and director of the new Islet Cell Lab, Wanxing Cui, MD, PhD. All members of the team have prior experience with the procedure—in some cases, dating back more than a decade—adding invaluable insight into chronic pancreatitis and its process to the new program.

Uncommon and difficult to diagnosis, the condition often eludes detection by traditional means, such as MRI and blood tests. As a result, by the time some patients receive a definitive diagnosis, their condition is advanced, leaving them with few islet cells to isolate.

“If a patient complains of severe abdominal pain and tests are inconclusive, physicians should consider the possibility of chronic pancreatitis and refer him or her for specialty tests,” says Dr. Khan.

“Over the years, we have found that continuous glucose monitoring (CGM), which measures levels minute to minute, can reveal subtleties that other tests miss, especially if monitoring extends over several days. The earlier we can get an accurate diagnosis and perform islet cell transplant, the better.”

Ideal candidates for islet cell transplant have refractory chronic pancreatitis, preserved endogenous insulin production and chronic pain. While the incidence of chronic pancreatitis is low, NIH research into islet cell transplantation suggests that it may prove promising for a far more widespread disease—Type I diabetes—in the near future.

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“Intravenous Fish Oil Not a Panacea for Parenteral Nutrition-Associated Liver Disease,” Say MedStar Georgetown Transplant Institute Researchers

In 2006, Omegaven was first used in a few pediatric patients with parenteral nutrition-associated liver disease (PNALD). Widely used throughout Europe and elsewhere, Omegaven remains classified as an Investigational New Drug by the FDA largely because of uncertainty about how best, and when, to use it.

“For instance, we don’t know whether to give Omegaven to parenteral nutrition patients to prevent liver damage from developing or to wait until liver damage first appears,” says Dr. Kaufman. “Identifying those individuals with liver disease who are most likely to respond to the product and explaining how the damaged liver may recover on Omegaven treatment remain other important challenges.”

With such questions in mind, a multidisciplinary research team at MedStar Georgetown Transplant Institute performed a retrospective analysis comparing the biochemical and histological outcomes of 20 infants and children with liver disease awaiting intestinal transplant. Nine had received Omegaven; the other 11 had received standard soybean oil-based lipid. The study found that the seven of the nine patients who received Omegaven still required a simultaneous liver transplant due to severe fibrosis (continued on page 4)
Intravenous Fish Oil not a Panacea for Parenteral Nutrition-Associated Liver Disease (continued from page 3)
or cirrhosis. In fact, scarring in these Omegaven-treated livers was as severe as in livers removed from the seven patients undergoing combined liver and intestinal transplant who received emulsified soybean oil.

However, the Omegaven-treated livers had little or no inflammation, consistent with the anti-inflammatory properties of Omega-3 fatty acids. In contrast, native livers from all of the patients who received soybean oil-based lipid were both inflamed and fibrotic. Omegaven also proved successful at resolving jaundice, while those on standard soybean oil remained jaundiced at transplant. Results of the study appeared in the May 2014 issue of the Journal of Pediatrics.

“The ability of Omegaven to reduce jaundice does not ensure that it will be efficacious in improving liver function,” says Transplant Surgeon Brian Kaufman, MD, the study’s senior investigator. “Most liver transplant patients will experience a transient increase in bilirubin levels following liver transplantation, which is not unusual. However, in the group of patients in whom we used Omegaven, this increase was much lesser than in those who received soybean oil.”

The broad implication of this study is that hepatic inflammation due to Omega-6 fatty acids may well produce cholestasis, but does not appear to be the critical factor in fibrosis of the liver, which the switch to Omega-3 fatty acids failed to improve. This insight contributes to our basic understanding of hepatic fibrosis.

Intestinal transplants are rare, numbering only around 115 per year in the entire United States. About 40 to 45 percent of the complex surgeries are performed in babies and children suffering from potentially devastating congenital malformations such as gastrochisis or jejunooileus atresia, or intestinal complications in prematurity like necrotizing enterocolitis. MedStar Georgetown Transplant Institute performs approximately 20 intestinal transplants a year and has been one of the two largest such centers in the United States for several years.

In addition to Drs. Kaufman and Matsumoto, the study’s multidisciplinary research team included Drs. Eddie Island (surgeon), Bhaskar Kallakury (pathologist), Nada Yazigi and Khalid Khan (pediatric gastroenterologists) and Transplant Surgeon and Institute Director Thomas Fishbein, MD.

CDC Broadens Screening for Hepatitis C Virus

Less than a year ago, the Food and Drug Administration approved two new drugs that can effectively cure more than 90 percent of patients infected with the Hepatitis C Virus (HCV). Now the challenge for providers is to identify the patients who may benefit and link them to appropriate care.

An estimated 2.7 to 3.9 million people are living with HCV in the United States today. According to the CDC, between 45 and 85 percent are unaware of their status until symptoms arise, often decades later. That delay in diagnosis and treatment raises their risk of developing serious liver disease, including cirrhosis and hepatocellular carcinoma. While and while only about 15 to 20 percent of those infected will ever reach that stage, physicians currently have no way of knowing in advance who will, and who will not.

In the past, screening guidelines focused on high-risk groups: mostly intravenous drug users, prisoners, offspring of HCV-infected mothers, and anyone who had a blood transfusion before 1992. However, the latest recommendations from both the CDC and the U.S. Preventive Task Force vastly expanded the net to include nearly one out of every four people in the United States today: baby boomers.

The American Association for the Study of Liver Disease (AASLD) unequivocally endorsed the new guidelines.

“HCV is a leading reason for liver transplant,” Dr. Satoskar explains. “But there simply aren’t enough organs to go around. Each year, only about one-third of the 16,000 to 17,000 patients on the waiting list will receive a liver. The new drugs have the potential to help prevent end-stage liver disease, reduce mortality and improve the quality of life for hundreds of millions.”

“Identifying those individuals with liver disease who are most likely to respond to the product and explaining how the damaged liver may recover on Omegaven treatment remain other important challenges.”

The approval of sofosbuvir and simeprevir represents a real medical breakthrough and has revolutionized the treatment of HCV,” says Rohit Satoskar, MD, acting medical director, Liver Transplantation, at MedStar Georgetown University Hospital. “HCV is a major and serious public health issue, now causing more deaths each year than HIV. Previous treatments only resulted in a cure rate between 60 and 70 percent and were associated with significant side effects. The availability of new treatments offers patients higher cure rates, shorter treatment duration and the possibility of interferon-free therapy.”

At MedStar Georgetown Transplant Institute, hundreds of patients are already being treated with interferon-free regimens in both the pre- and post-transplant settings.

The cohort born between 1945 and 1965 accounts for a disproportionately high percentage of known HCV infections” says Dr. Satoskar, an active AASLD member who helped craft their criteria. “Due to the increased prevalence in this group, they will also suffer the most consequences of the disease if undiagnosed and untreated.”

Already strong advocates for HCV screening, MedStar Georgetown University Hospital and MedStar Washington Hospital Center hope to expand their existing program by partnering with the health departments in both the District of Columbia and Prince George’s County. A grant to that effect is currently under review.

“The challenge for providers is to identify the patients who may benefit and link them to appropriate care.”

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TRANSPLANTdigest
Living Kidney Donations on the Rise

Transplant Institute’s Proactive Approach Producing Results

The national demand for new kidneys is staggering. On any given day, the UNOS kidney waiting list averages 100,000, with most languishing in line for three to five years. In the end, only 16,000 to 17,000 individuals each year will get the transplants that can save their lives. For everyone who receives a new kidney, 20 others die waiting.

“The problem isn’t access to transplant services, but access to organs,” states Matthew Cooper, MD, director of Kidney and Pancreas Transplantation at MedStar Georgetown Transplant Institute, who notes that the supply of cadaveric donations has remained stagnant for the past 15 years or so. “To improve organ availability and viability, we’re actively encouraging living donation and expanding other opportunities.”

The average life span of a kidney from a deceased donor is approximately a decade. Living organ donations often last twice as long, with reduced wait times and improved outcomes. To raise awareness of the benefits of living donations—and potentially alleviate donor apprehension—MedStar Georgetown Transplant Institute hosts periodic community educational seminars throughout the metropolitan area, discussing the pros, cons and enhanced possibilities for matches through desensitization and paired kidney exchanges (PKE).

“We urge volunteers not to rule themselves out just because they’re a different blood type or race, or unrelated to their intended recipient ... The exquisite techniques in use today can reduce incompatibility, broadening eligibility.”

Desensitization offers an alternative to awaiting the “perfect” kidney, which may not always be available for highly sensitized recipients. But because of an increased risk of rejection and other complications, Dr. Cooper and the multidisciplinary MedStar Georgetown Transplant Institute team reserve the option for those near-matches with the greatest chances of success.

More promising for the future is the growth in paired kidney exchanges. MedStar Georgetown Transplant Institute broke all previous records when, in 2010, it conducted the world’s largest mix-and-match swap to date. Since then, the complex process has advanced to the national level with organs from living donors crisscrossing the country to reach their waiting recipients. Once PKE becomes more widespread, the approach has the potential to vastly expand the organ pool.

“As the longest standing and most successful living donor program in the area, MedStar Georgetown Transplant Institute is supremely focused on the safety of patient and donor alike,” he concludes. “Our approach mixes medical caution with a need to meet people’s desire to be a donor to achieve optimal outcomes for both. Success, in our view, is determined more by quality than quantity.”

As a result of such efforts, living donors are now the source of 40 percent of all kidneys transplanted at MedStar Georgetown Transplant Institute each year, paired exchanges account for half of that figure. The MedStar Georgetown Transplant Institute also reports a 22 to 30 percent jump in inquiries from potential donors. While upping the supply of organs solves part of the problem, MedStar Georgetown University Hospital and MedStar Washington Hospital Center, with excellent results. The transplant institute’s most recent statistics, for example, top the list of area transplant programs for overall first-year graft and patient survival rates.

Dr. Cooper attributes such accomplishments to the team’s passionate commitment to their work and their acute awareness of the incredible responsibility that accompanies it, particularly for those selfless individuals who choose to be a living donor.

“Other Centers” and “MGTI”
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