For a writer, redundancy means death; for a transplant surgeon, it can mean life. Just ask Andy Klein, M.D., surgical director of liver transplantation at Hopkins since 1989. He’s convinced that extra communication—a.k.a. redundancy—makes for safer transplant surgeries.

The tragedy last winter at Duke University Medical Center makes the point. Young Jessica Santillan received an organ with the wrong blood type and died after a second transplant with the correct blood type. Even before that, Mt. Sinai’s program in New York shut down temporarily in 2002 because a living liver donor died. Since then, hospitals are insisting on better communication to ensure safety.

But long before these tragedies, Klein pioneered safer protocols. Serving on the board of directors at the United Network for Organ Sharing (UNOS), he is building consensus to encourage hospitals nationwide to lower risks to patients, particularly live donors. Klein and others recently launched a registry project that collects medical and psychosocial data on all living donors. When it’s implemented in 2004, “everything will be at our fingertips, wherever the transplant takes place,” he says.

Klein believes that two liver transplant surgeons should scrub in for every live donor liver transplant. Through his work at UNOS, he developed surgical prerequisites for centers performing live donor liver donation and expects all transplant centers to comply.

Luis Arrazola, M.D., Hopkins’ director of live donor liver transplantation, who partners with Klein during these surgeries, concurs that “too much can go wrong, like anesthetic complications and blood clots.” For the record, the Hopkins report card is excellent. Of the 80 live donor liver transplants performed here, none has proven life-threatening to the donor. And recipients have had a 90 percent survival rate.

On other CTC liver transplant fronts, Klein reports a flurry of activity. Hopkins is actively involved in several studies for the American Association for the Study of Liver Disease. Klein was recently elected to its governing board. “Our lab is dedicated to finding ways to follow liver transplantation without immunosuppression, by inducing tolerance in recipients,” says Klein. He’s confident breakthroughs will soon emerge because of rigorous studies crossing hepatology, surgery and radiology.

Klein remains outspoken on the national Model End Stage Liver Disease (MELD) scores program. In his view, although MELD has helped sicker patients receive livers faster, geographic inequities remain. “It’s all controversial, but the allocation model should strive to offer similar patients similar opportunities to receive a life-saving organ transplant,” Klein says. He even dreams of a time when the government will approve paid time off for living organ donors. Meanwhile, steering the Hopkins liver transplant program keeps him connected at every level, redundant or not.
The View from Here
By Robert A. Montgomery, M.D., Ph.D.

The shortfall between organ availability and need grows daily, with no end in sight. By 2010, the average waiting time for a kidney transplant could be as long as 10 years. Despite years of raising awareness, the number of organs from deceased donors remains far too low.

The most promising hope of closing the gap between organ supply and demand is through live kidney and liver donation. Live donor kidneys on average last twice as long as kidneys from deceased donors. Partial livers from live donors allow loved ones to be transplanted before they are gravely ill. The gift from a live donor actually benefits two people: the recipient of that organ and a person who does not have the option of a live donor and receives the deceased donor organ that is freed up as a result of that gift.

Through innovative approaches to getting more patients transplanted with live donors, the Johns Hopkins CTC has become a world leader. The laparoscopic live donor nephrectomy, first performed at Hopkins in 1995, revolutionized the process of live donation by cutting the donor’s recuperative time in half. This breakthrough set the stage for many other Hopkins firsts (see timeline) involving live donors.

The CTC continues to pioneer new approaches that will enable more of our patients to receive state-of-the-art care and a chance at a better life.

CTC’s New Outreach Coordinator Comes Full Circle

Jeanni Barget didn’t know it then, but the best training for her new job took place four years ago. She was just days away from donating part of her liver to her mother, Pat Barget. “My mom had encephalopathy, and I wanted to help,” she recalls. Jeanni went through the entire process—biopsy, psychological evaluation, physical. But the weekend before the scheduled transplant, a cadaveric liver became available. A little disappointed but grateful to the donor, Jeanni helped nurse her mother back to health. (Today, Pat Barget is co-chair of the patient committee.)

Jeanni Barget’s passion for helping others began long before then. With a degree from George Washington University, she joined the Peace Corps in 1996 and spent three years helping bring businesses to underserved countries. She lived in a remote part of Africa most of that time.

Then, for three years Barget worked in Philadelphia for a community development consulting firm, where she conducted national research and wrote various publications. Returning to Maryland in 2001, she became project coordinator for the English as a Second Language department at a community college and began working on a master’s degree in distance education.

Intrigued by her mother’s efforts to enhance a liver mentoring program at Hopkins, Barget signed on to help. Now the two women and the mentoring committee have released an online transplant mentoring program. It trains transplant recipients and donors to help others through the transplant journey and culminates in a one-day retreat at Hopkins.

When the transplant outreach coordinator job was announced, Barget knew she’d be a good fit. Responsible for events, publications, volunteers and Web content, Barget recaps her goals: “I want community physicians to know all about the important work we’re doing at Hopkins to ensure good outcomes. At the same time I hope to alleviate some stress for patients with critical needs.”

Barget lives in Catonsville and is getting married in June. She can be reached at 443-287-2896 or at jbarget@jhmi.edu.
For years, transplant pathologists have assumed that lymphocytes (T cells) were the primary mechanism responsible for organ rejection. But William (“Wink”) Baldwin, M.D., Ph.D., associate professor and director of the Division of Immunology in Pathology, reports that his laboratory studies confirm a hunch he’s had for a long time: Many people experience antibody-mediated rejection.

In 1966, hyperacute rejection, the most devastating type of organ rejection, was found to be caused by antibodies. Hyperacute rejection occurs most frequently when a patient receives ABO incompatible transplantation without proper pretreatment or when antibodies to the human leukocyte antigens (HLA) are present at the time of transplantation.

By 1970, scientists devised a special test to detect antibodies to HLA before transplantation, and hyperacute rejection was almost eliminated. Subsequently, transplant rejection diagnoses and treatments focused on “cell-mediated immunity” caused by lymphocytes.

“Immunosuppressants have become increasingly effective,” says Baldwin, “but there’s a subset of patients who don’t respond to conventional immunosuppression. They are ‘steroid resistant.’ We now know that about 30 to 40 percent of patients with rejection have some antibody-mediated rejection.” Clinically, antibodies to donor HLA antigens have been regularly found in the sera of recipients at the time of rejection. But pathologists did not have a reliable method to diagnose rejection caused by antibodies until recently. When pathologists looked at the biopsies from these patients more closely, they found neutrophils or macrophages instead of lymphocytes.

The key to diagnosing antibody-mediated rejection is to look for accomplices rather than antibody itself, Baldwin explains. A series of proteins collectively known as complement are one of the most potent means by which antibody causes tissue injury. That’s because each pair of antibodies can activate about 50 to 250 of the complement components C4 and C3, respectively. Fragments of these complement components, such as C4d and C3d, become attached to the blood vessels in the transplant and can be detected by immunofluorescence. Thanks to this new approach to diagnosis and therapeutic options, antibody-mediated rejection can be treated successfully. Pathologists can alert transplant cardiologists, nephrologists and surgeons to the presence of complement in a patient’s biopsy and allow them to consider treatment with plasmapheresis and IVIg.

Even years after transplantation, this finding is vital. One patient who received his heart transplant seven years ago came to Hopkins recently, apparently in rejection. But when cardiac pathologist Rene Rodriguez, M.D., reviewed his tissue biopsy, he did not see much cellular rejection. Rather, on immunofluorescence he saw complement deposition. Antibody to HLA was then detected in the patient’s serum. He improved because of resulting plasmapheresis and IVIg treatment.

The most important news for referring physicians is that there is now a more complete method of diagnosing rejection than in the past. “Now we have practical insight on how to diagnose and treat different kinds of rejection,” says Baldwin. Staining for complement is now part of the normal pathology screening for heart and kidney biopsies performed at Hopkins.

Marking its 10th year of NIH funding to study antibody-mediated rejection, Hopkins boasts the longest standing grant in the field. “As a result, we’ve developed sophisticated models in genetically modified mice that allow us to get a better understanding of antibodies and complement in transplants,” says Baldwin. “We continue to search for more ways antibodies and complement cause tissue injury.”

Baldwin and co-authors Edward Kasper, Andrea Zachary, Barbara Wasowska, and E. Rene Rodriguez are publishing their paper, “Beyond C4d: Other Complement-Related Diagnostic Approaches to Antibody-Mediated Rejection,” in an upcoming issue of the American Journal of Transplantation.
Triple Ripples

It might be old news by now, but last July’s groundbreaking triple-swap kidney transplant at Hopkins has had a huge impact on living kidney donations. “We are averaging 10 calls a week from altruistic donors who want to help others on a waiting list for kidneys,” says Jennifer Rickard, R.N., a lead nurse in the Incompatible Kidney Transplant Program.

The three kidney recipients involved in the simultaneous swap had come to Hopkins separately for evaluation, each with a willing donor who did not have a compatible blood or tissue type. The transplant team discovered that by swapping kidneys among the pairs, all three recipients would have a compatible kidney from someone they never met. All six patients are recuperating well.

Since 2001, four successfully paired kidney exchanges have taken place at Hopkins. This latest swap involved three pairs—two sisters, two friends and an engaged couple—and all three simultaneous surgeries were performed with finesse.

Robert A. Montgomery, M.D., Ph.D., named director of the entire Hopkins Comprehensive Transplant Center, is elated with the outcome. “Now the challenge will be to keep up with the flood of inquiries and work-ups since the triple swap. But it’s worth the effort to alleviate the wait time for so many sick people out there on waiting lists for kidneys,” he says.

Potential patients aren’t the only ones calling. Many hospitals throughout the United States and other countries want to know how to duplicate the effort. A guru on transplant incompatibility, Montgomery speaks internationally about the protocol. Reflecting on the impact of his work, he says, “It’s gratifying to see that so many hospitals want to be proactive in expanding their kidney transplantation programs.”

Making a Case for Pumping Cadaveric Kidneys

To pump or not to pump? That’s the latest question facing many transplant centers. The controversy surrounds the labor and cost of using a machine that pumps chilled fluid through a cadaveric kidney before it is transplanted. Doing so can improve the organ’s function after the transplant and prolong its survival. So says a recent joint study with Hopkins researchers and Organ Recovery Systems Inc.

Traditionally, kidneys are stored in a chilled fluid on ice after procurement. In the new study, scientists studied outcomes from more than 40,000 kidney transplants nationwide, examining the impact of the preservation method on kidney function and survival. Patients who received kidneys that had been preserved on the machine had much better early kidney function after transplant and improved kidney survival two years later. This study is the first to document an improvement in kidney survival using machine preservation, which currently is used at several centers around the country, the authors say.

“The use of machine preservation is associated with a marked improvement in early kidney function, which offers an enormous benefit by allowing patients to stop dialysis immediately after transplant surgery,” says Robert Montgomery, M.D., Ph.D., the study’s co-author and director of the Johns Hopkins Comprehensive Transplant Center. “This technique may allow us to use more ‘extended criteria donor kidneys,’ organs from older donors with existing medical conditions. These organs had been slower to function following transplantation.”

Study coauthors were Christopher Sonnenday, M.D., of Hopkins and Louise Jacobbi and Fred Gage of Organ Recovery Systems.
Excellent Survival Rates for Liver Cancer Patients Undergoing Transplantation

More than 60 percent of liver transplant patients with advanced liver cancer are still alive after five years, compared to nearly zero survival for those patients who did not undergo transplant, according to a new study by Johns Hopkins researchers.

“This is good news for patients with liver cancer. If diagnosed early, transplantation is the treatment of choice for patients with liver cancer and advanced cirrhosis,” says Paul Thuluvath, M.D., associate professor of medicine at Johns Hopkins and lead author of the report published in the December issue of the Journal of Clinical Oncology.

Thuluvath emphasizes that regular screening of patients with cirrhosis, a risk factor for liver cancer, is needed to detect the cancer early and to ensure the best possible outcome.

Thuluvath and colleagues also found that survival rates increased steadily over the last decade, suggesting that criteria for patient selection established by other experts may assist physicians in selecting those patients most likely to respond well to the procedure.

Using the UNOS database, the researchers collected data on 48,887 patients who underwent liver transplantation in the United States between 1987 and 2001. Patients were excluded if they had undergone multiple organ transplantation or retransplantation, were less than 18 years of age, or lacked survival data.

Of the remaining patients included in the final analysis, 985 had liver transplantation for liver cancer and 33,339 patients had liver transplantation for other reasons (control group). Both the liver cancer and control groups were divided into three different five-year time periods: 1987–1991, 1992–1996, and 1997–2001.

Researchers found significant and steady improvement in survival over time among liver transplant patients with liver cancer, especially in the last five years. Five-year survival improved from 25.3 percent during 1987–1991 to 47 percent during 1992–1996, and 61.1 percent during 1996–2001.

According to the Johns Hopkins Gastroenterology and Hepatology Resource Center, liver cancer, also called hepatocellular carcinoma or hepatoma, is one of the most common cancers in adults, with more than 1 million new cases diagnosed each year. It is twice as common in men as in women.

Other authors are Hwan Y. Yoo, Cary H. Patt, and Jean-Francois Geschwind all from Johns Hopkins. The research was supported by AASLD/Schering Advanced Hepatocellular Carcinoma Fellowship Award.

Five-year survival after transplantation for hepatocellular carcinoma.
John Conte, M.D., is one of only a handful of surgeons in the country performing an uncommon procedure. He reshapes enlarged damaged hearts in heart failure patients. The procedure reconstructs the heart to work more efficiently, potentially avoiding the need for a transplant.

Called “surgical ventricular restoration (SVR),” the surgery returns the heart to its normal size by removing nonfunctioning tissue scarred by a heart attack. The process uses a plastic mold inserted into the left ventricle—the main pumping chamber of the heart—as a guide to reduce the heart to a normal size and shape. The result is a heart that contracts more efficiently.

“There’s a critical relationship between the size and shape of the heart that’s essential for normal cardiac function. Scarring, which develops as a result of myocardial infarction, upsets this relationship. We try to recreate the balance as closely as possible,” Conte says.

The surgical goal is to make the heart smaller and more elliptical and exclude the parts that are not working well.

Ideal candidates for this surgery have:
• infarctions and large ventricles
• a large area of akinesis and dyskinesis
• an acceptable function of the basal portion of the heart and lateral wall
• good right ventricular function

Last summer, Marcel Rauch, a patient from New York who heard about the new technique at Hopkins, called Conte to set up an appointment. Earlier heart attacks had left him with a severely damaged heart, which led to heart failure. His condition was severe enough to put him on the heart transplant list.

Conte operated on Rauch and was able to increase Rauch’s ejection fraction from 35 to almost 60, which is the normal range. Still, like many heart patients, Rauch’s heart underwent major scarring during healing. It’s too soon to tell if Rauch can avoid a heart transplant, but he’s much better off than he was before the surgery. “I feel like I could swim like a 20-year-old,” Rauch says.

“There’s a critical relationship between the size and shape of the heart that’s essential for normal cardiac function.”
Joshua Hare, M.D.

Ventricular Assist Devices Approved as Destination Therapy

The Centers for Medicare & Medicaid Services (CMS) recently announced it intends to expand coverage of ventricular assist devices (VADs) as permanent cardiac support (“destination therapy”) for certain Medicare beneficiaries. Up to this point, VADs have been used as a bridge to transplantation or as a bridge to recovery in certain patients with acute or chronic heart failure.

VADs are mechanical pumps used to support the circulation in patients with congestive heart failure. They help restore normal hemodynamics and enhance blood flow in the body.

Medicare patients who have chronic end-stage heart failure and who are not candidates for heart transplantation would be covered under this new plan. Candidates must also meet the inclusion criteria outlined in the randomized evaluation of mechanical assistance for the treatment of congestive heart failure (REMATCH). The REMATCH trial, sponsored by the National Institutes of Health, is the only published trial that has studied the use of VADs as destination therapy. Destination therapy is the use of a mechanical device as a permanent treatment for heart failure, with no intention to remove it for transplantation.

“This decision is based on the best available scientific evidence following a clinical trial that showed VADs can extend and improve the quality of life in patients with heart failure,” says CMS Administrator Tom Scully. Affecting nearly 5 million Americans, heart failure is most prevalent in the elderly and is the leading cause of hospitalizations in the Medicare population.

John Conte, M.D., director of heart and lung transplant programs, is pleased CMS is responding to the dire need. “I testified at CMS about this and was greatly encouraged by their thorough and thoughtful handling of the matter,” he says.

Hopkins performs 20 to 30 VADs a year. Conte believes that number will grow significantly every year. Currently, VADs are covered only as a bridge to heart transplant or as support for blood circulation after open-heart surgery. This new coverage would provide another treatment option for Medicare patients with end-stage heart disease.

New Director Studying Stem Cell Solution for Heart Failure

As the new medical director of the cardiomyopathy and heart transplant service, Joshua Hare, divides his time consulting on cardiology patients, teaching and doing research.

Hare’s laboratory work is making headlines as he studies how to regenerate human heart tissue using stem cells. “We’ve got all kinds of procedures to open blocked arteries and great medications and medical devices,” Hare says, “but none of our treatments replaces the damaged heart muscle that leads to both heart failure and sudden cardiac death.”

That void in cardiac care has led Hare to pursue a muscle-restoring therapy that applies what he calls one of the most exciting developments in all of medicine—stem cells. The thinking used to be that the heart has a fixed number of cells and those lost in a heart attack, which is a massive number, are lost forever. But Hare has shown in pig models that stem cells taken from the animal’s own bone marrow and then injected directly into damaged heart muscle may cultivate the growth of new heart cells and enhance the heart’s ability to recover from an attack.

“We can’t say for certain yet that the stem cells actually turn into new heart muscle cells, but they do live and grow and persist in the damaged area,” Hare says. “Three months after the injection, the size of the infarction and the amount of cardiac damage the animals are left with is less if we give them the stem cells.”

The activity of the stem cells is charted by MRI. Hopkins radiologist Jeff Bulte developed a special technique that highlights the injected stem cells, allowing them to be tracked. “We can do an MRI scan and inject the cells precisely where the injury is, and then watch the cells over time,” Bulte says.

The implication, Hare adds, is that a heart attack patient is admitted to the hospital and within a couple of days receives a stem cell transplant. Restoring heart muscle, rather than keeping a damaged heart running, will be the focus: “It has the potential to revolutionize cardiovascular medicine.”

Note: Hare’s predecessor, Ed Kasper, M.D., is now chief of the Division of Cardiology at Johns Hopkins Bayview Medical Center.
Virtual Marcus Welby, M.D.

Vaguely resembling a human torso—in a Star Wars R2D2 sort of way—a new high-tech robot is roaming Hopkins’ wards. Sporting a computer screen for a head, a video camera for eyes and a speaker for a mouth, the robot links a real doctor to patients through teleconferencing. Louis Kavoussi, M.D., Hopkins professor of urology and a pioneer in robotic surgery, is testing it in real-world conditions. Manufactured by InTouch Health Inc., Dr. Robot is being billed as the world’s first remote-presence robot. It enables remote medical experts to “virtually” consult with caregivers, patients, residents and family members in between scheduled visits. “It’s not going to replace the human being, but it will allow more access. Patients love it,” says Kavoussi.

Hold the Date

Friday, February 6, 2004
The ABC’s of Renal Transplantation

Assessment, Barriers and Continuity of Care
Sheraton Baltimore North Hotel
Towson, Maryland

This conference will address key aspects of pre-transplant referral and evaluation and post-transplant patient care. Emphasis will be placed on the safe and effective use of latest medications and technologies, drug monitoring, and the prevention, treatment and management of long-term complications.

To register, call the Johns Hopkins Office of Continuing Medical Education at 410-955-2959. Reservations can also be made via Web site at www.hopkinscme.org/cme. The Johns Hopkins University School of Medicine designates this educational activity for a maximum of seven category I credits toward the AMA Physician’s Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

Outreach Calendar
For more information, call the Comprehensive Transplant Center, 410-614-5700

Transplant Educational Support Groups

Multi-Organ Educational Support Group
What Was It Really Like? A Post-Transplant Patient Panel
November 18, 2003, 7 p.m.
Cader Room, Harvey 508
Refreshments served

Multi-Organ Educational Support Group
Quiet Heroes: A Living Related Donor Panel Answers Your Questions
January 20, 2004, 7 p.m.
Cader Room, Harvey 508
Refreshments served

Transplant Patient Conversation
February 17, 2004, 7 p.m.
Phipps 140

Multi-Organ Educational Support Group
The Organ Shortage and the Transplant Resource Center of Maryland
March 23, 2004, 7 p.m.
Cader Room, Harvey 508
Refreshments served

Seminars/Conferences

The ABC’s Of Kidney Transplantation: Assessment, Barriers And Continuity Of Care
February 6, 2004
The Sheraton Baltimore North
Towson, Md.

Cardiovascular Topics At Johns Hopkins
February 26-28, 2004
Thomas B. Turner Building at Johns Hopkins Baltimore, Md.

Sixth Annual Hepato-Biliary And Gastroenterology Diseases For Practitioners
April 24, 2004
Thomas B. Turner Building at Johns Hopkins Baltimore, Md.

Outreach Events

“Gift Of Life” Ctc Annual Holiday Party
December 9, 2003, 6 p.m.
Turner Concourse
Hopkins Hospital

Physicians are welcome to attend all educational and outreach events.