

NEW YORK-PRESBYTERIAN Transplant

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Renal Graft Rejection Test Slated for Trials

Weill Cornell researchers at NewYork-Presbyterian Hospital have found that a noninvasive test designed to predict renal allograft rejection may also serve as a sensitive gene-based assay of immune function that exceeds biopsy as a diagnostic and prognostic tool, providing the basis for individualized treatment of organ transplant patients. The Hospital, Columbia University College of Physicians and Surgeons, and Weill Medical College of Cornell University are currently leading a National Institutes of Health-sponsored multicenter trial to further test the sensitivity and specificity of measuring messenger RNA (mRNA) for key immune cell regulators in renal transplant recipients.

“Our test, we think, will be informative of the immune status of the patient,” explained Manikkam Suthanthiran, MD, adding that the overall strategy of the trial may enable a more complete appraisal of graft function and warn of the risk of impending rejection and the outcome of a transplant. The mRNA profiling strategy was first developed in Dr. Suthanthiran’s laboratory.

According to Mark A. Hardy, MD, these “landmark findings” and observations “have now opened the possibility of testing the patients’ immune status and response to the graft on a more frequent basis with a test that is safe, appears very effective, and provides opportunity to adjust immunosuppressive treatment on an as-needed basis.”

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Genomics-Based, Noninvasive Test May Change Future of Heart Transplant Rejection Monitoring

Patients who receive a heart transplant require lifelong monitoring for allograft rejection, and endomyocardial biopsy (EMB) is considered the best procedure for this surveillance. Now a simple gene expression test from a routine peripheral blood sample can sensitively detect moderate to severe rejection, according to results of an extensive multicenter study. NewYork-Presbyterian Hospital/Columbia University Medical Center now offers the test to transplant recipients 6 months or more after surgery.

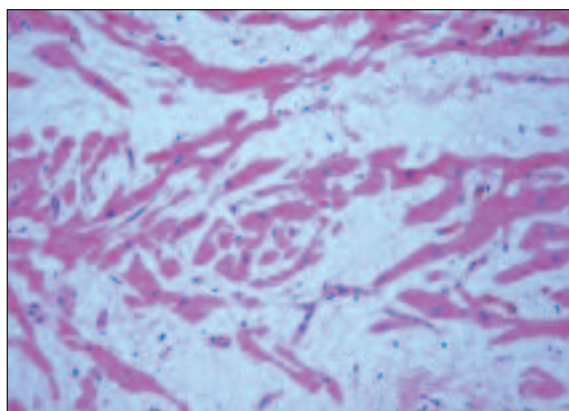


Photo courtesy of Mario C. Deng, MD.

Histology of transplanted heart in patient experiencing antibody-mediated rejection; findings include interstitial edema, prominent endothelial cells and occasional inflammatory cells.

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4 Wilson’s disease must be treated by transplant. These case studies highlight NewYork-Presbyterian Hospital’s unique diagnostic and treatment capabilities.

Transplant Update

NewYork-Presbyterian Hospital performed 118 heart transplants in 2005, making it the top-ranked heart transplant center in the United States. The second-ranked center, UCLA, performed 55 transplants. For more information on NewYork-Presbyterian’s transplant services, visit www.nyptransplant.org.

For upcoming CMEs, please visit www.columbiacme.org.

Groundbreaking Research Expands Kidney Transplant Donor Pool

As support for dual kidney transplant and incompatible live donor transplant grows, programs to employ these strategies at New York-Presbyterian Hospital's Transplant Institute continue to expand. These efforts represent a historic confluence of innovation and evidence-based medicine in the face of a severe shortfall of available organs and the changing composition of the donor pool.

"The demographics of the deceased donor pool have changed," said Lloyd Ratner, MD. "Ten to 15 years ago, the average deceased donor was a healthy young individual who died from trauma. Now, the average deceased donor is a middle-aged or elderly individual who dies of a stroke."

Dr. Ratner, who performed the first dual kidney transplant in the United States in 1993 at The Johns Hopkins University Medical Center, has since 2004 directed the Renal and Pancreatic Transplantation Program at New York-Presbyterian Hospital/Columbia University Medical Center. The nationwide shortage of donor organs continues to worsen, with some 68,000 patients currently on the list to receive a cadaveric kidney transplant and the waiting period in the New York region averaging 7 years. The Transplant Institute at New York-Presbyterian combines the resources of both academic medical centers New York-Presbyterian/Columbia and New York-Presbyterian Hospital/Weill Cornell Medical Center, which is affiliated with the Rogosin Transplant Institute.

Today, it is possible for any medically suitable live donor to provide a transplant patient with a kidney. Through the combined efforts of Columbia and Weill Cornell surgeons at New York-

Presbyterian, more than 30 dual renal transplants have been performed at the Hospital over the past 18 months. Long-term follow-up studies demonstrate that dual cadaveric kidney transplantation, in which left and right organs are transplanted from a marginal donor, is often a viable option that can be employed without compromising outcomes. In fact, the procedure produces survival rates that compare favorably with patients who undergo standard single kidney replacement.

The procedure has also become a plausible option thanks to the United Network for Organ Sharing, which instituted the expanded criteria donor (ECD) kidney allocation in response to the alarming rise in the number of older transplant-eligible patients with end-stage renal disease. ECD kidneys account for about 1 in 5 recovered kidneys and for about 15% of all transplants performed.

Strict criteria are employed for accepting donated organs, based on the donor's age, renal biopsy, and any risk factors such as hypertension and diabetes. Renal function diminishes after age 40, with an average decline of about 1% per year. But if immunologically unimpeded, the greater nephron mass of 2 marginal kidneys can do the work of 1 more fully functional organ.

"If you transplant an older organ, a single kidney from an older patient may not have enough renal mass to provide enough function to get someone off dialysis," said Michael Goldstein, MD. "If you take 2 kidneys from the same donor, you get twice the function and the patient will do better."

The pool of potential donors has expanded to include the prospect of incompatible transplant, but the calculus

of risk remains a challenge. The highest-risk patients both are ABO incompatible and have a positive cross-match with their prospective donors. Compatible-blood-type donor-recipient pairs with positive cross-match are at less risk, while ABO-incompatible pairs with negative cross-match pose less danger still.

Efforts to reduce risk of rejection to a minimum has engendered the concept of the "donor swap," employed at New York-Presbyterian Hospital. "Our goal is to reduce all levels of risk to our recipients as much as possible to make it safe," said Dr. Goldstein. For patients with a willing but incompatible donor, he added, "I would much rather offer them a kidney that is compatible if possible. It is safer for each recipient to receive a transplant from a stranger than to receive a high-risk incompatible organ from the family."

Such paired kidney transplants are complex to organize because 4 operations are performed simultaneously. Currently in the planning stage at New York-Presbyterian/Columbia is a "triple swap," in which one O-type altruistic donor will provide a kidney to an O-type recipient with an incompatible spousal donor. The A-type spouse will donate to an A-type recipient, whose incompatible B-type donor will make possible a renal transplant for a B-type recipient on the waiting list. In effect, 3 patients will benefit from 1 freely donated kidney.

"It all goes under the concept of increasing the organ supply," said Dr. Ratner. Just as dual transplants make possible the use of organs that would otherwise be discarded, "with incompatible transplants, we're able to use live donors that we wouldn't have otherwise been able to use."

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Researchers Examine Racial Disparities In Transplanted Lung Patients

Black and Hispanic patients with a variety of major lung diseases are known to have outcomes worse than those of white patients, but the situation with idiopathic pulmonary fibrosis (IPF) has not been as clear. Although IPF is considerably less common than emphysema or chronic obstructive pulmonary disease (COPD), for example, it must be treated with transplantation. In fact, IPF accounts for some 20% of lung transplants worldwide. Now, a new study led by Columbia researchers at NewYork-Presbyterian Hospital confirms, as suspected, that IPF in minority populations too often leads to fatalities.

“Our primary hypothesis was that black and Hispanic patients would have worse survival after referral to our center than white patients,” explained David Lederer, MD, who led the study, which was published in the *American Journal of Transplantation*. “And that’s exactly what we found.”

The study, the results of which appear consistent with those of other investigations of racial disparities in healthcare delivery, provides clues but not sufficient information to explain the disparity. In terms of IPF, Dr. Lederer cautioned that this first study only lays a foundation for further research. Data from another study, just completed and also retrospective but nationwide in scope and much larger (more than 2,000 patients), are currently being analyzed. In addition, a prospective study to parse the various factors is now in the planning stage.

“Even though we don’t understand the mechanisms underlying these survival differences, lung transplant physicians should be aware that minority patients require more expeditious evaluation when

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Case Studies: Managing Transplant Procedures in Patients With Wilson's Disease

Wilson's disease (WD) is an autosomal recessive disorder of hepatic copper transport in which copper accumulates mainly in the liver and brain. Its onset is unpredictable, and in a minority of cases, WD presents as fulminant liver failure accompanied by hemolytic crisis. Without a liver transplant, patients die within days or weeks. The clinical diagnosis must distinguish WD from autoimmune hepatitis and acute liver failure due to viral infection or drug toxicity. If WD is detected, all first-degree relatives of the patient must be tested.

As illustrated in the case studies that follow, Columbia and Weill Cornell researchers at NewYork-Presbyterian

Hospital have taken a lead role in nationwide, multiple-center investigations such as that of the Acute Liver Failure Study Group (ALFSG), which is looking into the diagnosis, management, and treatment of this troubling disorder. Both patients described below were entered into the ALFSG database. They benefited from the cooperative approach to treatment, involving intensivists, nephrologists, and hepatologists, that has become the hallmark of care for this disorder at NewYork-Presbyterian Hospital.

Case 1

A previously healthy 21-year-old woman presented at a New Jersey

hospital with fatigue and jaundice of recent onset and no apparent prodromal signs. Laboratory workup indicated fulminant liver failure with hemolytic crisis (direct antibody test negative), renal insufficiency, and coagulopathy. The diagnosis of Wilson's disease was established by the presence of Kayser-Fleischer rings and low levels of alkaline phosphatase (29 U/mL) and ceruloplasmin (14.9 mg/dL).

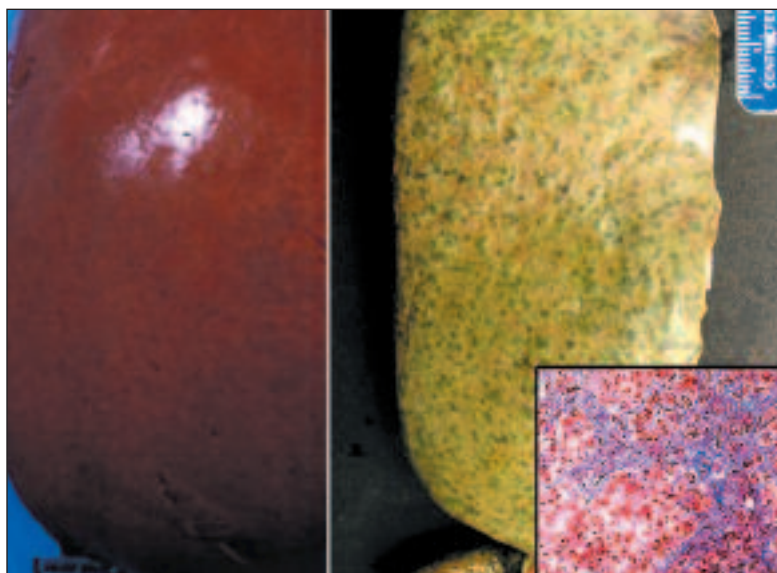
The patient, with rapidly progressive jaundice and hemolytic anemia, was admitted to the Center for Liver Disease and Transplantation at NewYork-Presbyterian Hospital to await transplant surgery. Her serum copper level was markedly elevated at 263 mg/dL (free serum copper, 191.3 mg/dL). Her urinary copper excretion rate on admission was also markedly elevated, at 11,826 mg per 24 hours.

Over the next 6 days, active exchanges of fresh frozen plasma were performed. Serial measurements of her serum copper level showed a decrease during the course of treatment (days 1-5: 236, 126, 102, 113, and 92 mcg/dL). The urinary copper excretion rate decreased by more than 75%, from 11,826 mg per 24 hours to 2,826 mg per 24 hours. Transfusion requirements ceased after day 3. Encephalopathy and renal failure were mitigated with continuous venovenous hemodialysis and plasmapheresis.

A cadaveric, orthotopic liver transplantation was performed on day 10 of hospitalization. The tissue copper concentration in the explanted liver was 832.8 mg/g (reference range, 15-55 mg/g). Within a week, the patient showed marked clinical and laboratory improvement, and she was discharged on day 18 in stable condition.

Discussion

In cases of fulminant liver failure, the early recognition of WD makes it possible to provide treatment that optimizes the patient's condition before transplantation. For this patient, who presented with fulminant hepatitis secondary to WD complicated by hemolysis and renal deterioration, liver replacement was clearly indicated. While awaiting surgery, she was treated with plasma exchange to reduce her serum copper



Left: The normal liver. **Right:** The liver in severe Wilson's disease. The green color reflects the patient's marked jaundice and the nodular surface is associated with developing cirrhosis. **Lower right:** Extensive scar tissue is seen (stained blue).

Photo courtesy of Jay H. Lefkowitz, MD, Department of Pathology, NewYork-Presbyterian Hospital/Columbia University Medical Center.

levels. Presumably, the removal of copper reduces oxidative damage to red cells and preserves function of the glycolytic enzyme, thus stabilizing liver and renal function and preventing further hemolysis. Plasma exchange can be an effective treatment for patients with fulminant liver failure secondary to WD until transplantation is possible.

More generally, clinical suspicion is essential to a diagnosis of WD. The laboratory findings do not always distinguish fulminant hepatic failure from acute illness due to viral infection or drug toxicity. Kayser-Fleischer rings, identified by ophthalmologic examination, are not fully specific for WD, but they are found in 50% to 60% of the patients who present with mainly hepatic disease.

Most patients with liver failure secondary to WD present with characteristic clinical and biochemical findings. These include the following: (1) Coombs-negative hemolytic anemia with features of acute intravascular hemolysis; (2) coagulopathy unresponsive to the parenteral administration of vitamin K; (3) rapid progression to renal failure; (4) relatively modest rises in serum aminotransferases (typically <1,000 IU/L) from the beginning of clinical illness; (5) normal or markedly subnormal levels of serum alkaline phosphatase (typically <40 IU/L). An additional chemical sign is a ratio of alkaline phosphatase to bilirubin of <2. Finally, by a ratio of 2:1, women with WD outnumber men.

Case 2

A 19-year-old woman presented with hemolytic anemia at a pediatric emergency room. The pediatric gastroenterologist who examined her suspected WD and contacted the Center for Liver Disease and Transplantation at NewYork-Presbyterian Hospital. After a consultation at the emergency room, the patient was moved to the medical intensive care unit and listed for transplantation, all in less than 2 hours. The same interim treatment regimen was prepared as in case 1. When a liver did not become available during the next 4 days, however, despite the patient's listing as status 1, she received a living donor liver from her father. This entailed a longer hospital stay, and the

patient required dialysis support at first, but after being discharged to home, her renal function returned to normal. It is likely that she will be able to return to finish school next semester; her father is also doing well.

In cases of fulminant liver failure, the early recognition of Wilson's disease makes it possible to provide treatment that optimizes the patient's condition before transplantation.

Discussion

Fewer livers are available for transplantation today relative to the number of patients who need them, even in emergency settings. According to Steven J. Lobritto, MD, patients with acute liver failure are listed as status 1 with the United Network for Organ Sharing, which gives them the highest priority on the local transplant list. Several years ago, the wait time to transplantation as a status 1 patient in cases of acute liver failure tended to be just 24 hours. Today, a liver may not become available for days or even a week. Although living donor livers are being used increasingly for patients with chronic liver disease, they are not commonly sought for emergency adult-to-adult transplantation. In this case, however, it was judged prudent to transplant a living donor liver because it was likely that the patient would otherwise die. The usual waiting period—2 weeks in New York state—was waived retrospectively.

"Historically, we have shied away from doing emergency live donor transplants in adults," said Milan Kinkhabwala, MD. "However, I think we ought to consider it more often now."

Indeed, the issue is under study, and NewYork-Presbyterian Hospital/Columbia University Medical Center is helping to lead the multiple-center

Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL), which aims to analyze the outcomes of such procedures for both donor and patient. This study, according to Robert S. Brown, Jr, MD, MPH, "demonstrates the need for standard criteria for evaluating who is and is not a candidate for living donor liver transplantation."

For patients with WD, the fact that the father was a carrier of the disease was not an impediment to his donor status, according to Michael Schilsky, MD. Dr. Schilsky is a co-author of "A Practice Guideline on Wilson Disease" with Eve A. Roberts, MD (*Hepatology* 2003;37:14745-1492). "It is consistent with our understanding of the physiology of the disease that unaffected carriers do not accumulate copper beyond a minimal amount," said Dr. Schilsky.

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Heart

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AlloMap, as the proprietary assay is known, was developed through a partnership with the molecular diagnostics firm XDX, Inc., and is a product of the Cardiac Allograft Rejection Gene Expression Observational (CARGO) study. The results of the CARGO study, led by NewYork-Presbyterian/Columbia in collaboration with 7 other centers, have been published in the *American Journal of Transplantation* (Deng MC et al. *Am J Transplant* 2006;6:150-160). The centers participating in the study collectively account for approximately 22% of the heart transplants performed in the United States; roughly 650 patients provided more than 5,500 paired blood and biopsy specimens.

The CARGO study employed microarray analysis and real-time polymerase chain reaction (PCR) to define a set of genes with the potential significance for allograft rejection. Transplant recipients were followed prospectively with blood sampling and EMB that was graded by means of the International Society for Heart & Lung Transplantation (ISHLT) criteria by pathologists blinded to the biopsy results.

The CARGO study methodology, designed in 2000 by Dr. Deng and colleagues from Stanford University in California, Temple University, Philadelphia, and Ochsner Health System in Louisiana, involved a 3-phase approach to investigate the detection of graft rejection.

The first phase of the study, which commenced in August 2001, was aimed at discovering genes associated with leukocyte activity and immune response. Microarray analysis of RNA sequences from human leukocytes expressed in both quiescent and active states identified 97 candidate genes from 285 sam-

ples. These genes were complemented by other candidates from a review of the literature that identified 155 genes, for a total of 252 candidates.

In the second phase of the study, real-time PCR was employed to gather data on the candidate genes, which generated a refined set of 68 genes. Statistical modeling of gene expression correlations yielded a 20-gene/metagene (11 indicator genes, 9 control genes) classifier. Gene and metagene expression levels could then in principle be used to distinguish moderate to severe acute cellular rejections (ISHLT grade $\geq 3A$) from quiescence or absence of rejection (ISHLT grade 0).

The third, or validation, phase of the study, similar to a Phase III drug trial, which was conducted in an independent group of CARGO patients, prospectively tested that hypothesis. In this study, the validation samples were enriched with rejection samples to more accurately assess agreement with biopsy. The patients and samples selected for the blinded clinical validation had donor and recipient characteristics similar to those reported by the United Network for Organ Sharing in 2003. The AlloMap test distinguished biopsy-defined moderate to severe rejection from quiescence. Agreement was 84% with grade ISHLT $\geq 3A$ rejection; for patients with a low AlloMap score, the risk of rejection was <1%.

The study represents a clear advance for post-transplant monitoring, but it also serves as fresh vindication for a methodology that can translate results of genomics research into clinical practice.

"This is a paradigm of a methodological approach that allows molecular testing to be applied if the clinical end point can be well defined," said Mario C. Deng, MD. "So the methodological implication of CARGO is to open the field for all of genomics medicine."

Because EMB is invasive and carries a small but not negligible risk of infection

and other adverse effects, a noninvasive alternative has long been sought. Efforts to use various alternatives, from echocardiography to radionuclide imaging, have been met with only limited success. The advent of gene chip technologies and advances in genomics have made it plausible to suggest that, via leukocyte gene expression profiling, a blood test could be developed to monitor the relative risk of transplant rejection. The study, the first of its kind to attempt to identify patients at low risk for moderate to severe rejection, has certain limitations. Using the EMB as a gold standard revealed considerable interobserver variability. Also, gene discovery focused on leukocyte expression rather than genome-wide interactions. Finally, the study was limited to patients who were at least 6 months post-transplant. Several studies currently under way are designed to address these issues and further expand on the utility of the test, including the Invasive Monitoring Attenuation by Gene Expression (IMAGE) study, which includes participation at NewYork-Presbyterian/Columbia and several other centers nationwide.

The significance of the CARGO study and the AlloMap test extends beyond heart transplant to indicate a powerful means by which molecular testing can play a role in clinical diagnostics. "The methodological approach," said Dr. Deng, "is one of the first translations of the Human Genome Project into clinical practice." He added, "Whether rejection after organ transplantation or rheumatoid arthritis, you will likely find gene expression patterns that correlate with well-defined clinical end points."

To address the complex bioinformatics data in a systems biological framework, Dr. Deng's group has initiated a collaboration with the Columbia Genome Center/Joint Centers for Systems Biology, under the direction of Andrea Califano, PhD.

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Renal

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The road to effective molecular diagnosis of kidney transplants has been long. Efforts to improve upon the useful but invasive needle biopsy for assessing graft function date to the early years of transplantation. Biopsy, while not perfect and prone to introducing various and serious complications, has remained the problematic gold standard for assessing renal allograft and organ transplantation.

Prospects for detecting molecular signals of incipient rejection gained considerable ground with advances in molecular biology and with the invention of polymerase chain reaction (PCR) in the late 1980s. Dr. Suthanthiran and colleagues soon developed the first-generation quantitative PCR assays for incipient rejection and used this powerful molecular amplification technique to study gene expression in transplant biopsies. A sensitive gene-based detector of rejection was desirable, as it offered the promise of avoiding an invasive procedure and providing more information than biopsy about the risk of rejection. The mechanisms and markers of acute and chronic rejection were also further investigated and better understood, as was the central significance of T-cell instigation.

In a key paper, published in 2001, Dr. Suthanthiran and colleagues focused on acute allograft rejection, which afflicts about 1 in 3 patients in the first year post-op. They demonstrated that levels of mRNA for 2 cytotoxic proteins, perforin and granzyme, could be assessed from a simple urine sample. Employing a receiver operating characteristic (ROC) curve, they showed that it was possible to create cut-off values for perforin that could predict acute rejection with 83% sensitivity and specificity. Although modest in size and not perfect in terms of prognostics, the study represented a clear advance toward a gene-based assessment technique.

The advent of quantitative real-time PCR (qRT-PCR) offered further opportunities to discover biomarkers for rejection. Recent discoveries concerning the regulatory T lymphocytes, which are understood to play a crucial role in self-tolerance, led to a focus on FOXP3.

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Lung

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they show up,” noted Dr. Lederer. “They show up later, and they show up sicker.”

The retrospective cohort study followed 50 patients with IPF who presented for evaluation to the NewYork-Presbyterian Hospital lung transplant program over a 4-year period beginning in April 2000. Patients were excluded if they had previously been evaluated for lung transplant or if they had other forms of diffuse parenchymal lung disease (DPLD) or other types of idiopathic interstitial pneumonia (IIP) not classified as IPF. The clinical data were examined by pulmonologists Steven Mark Kawut, MD, and Jessie S. Wilt, MD, who assigned diagnoses after reviewing paper and electronic records. A third physician, Caralee E. Caplan-Shaw, MD, brokered conflicting decisions.

Physicians identified by consensus 50 of 91 patients with DPLD as having IPF. The cohort included 36 white non-Hispanic patients, 6 black non-Hispanics, 6 white Hispanics, and 2 Asians. All patients had similar baseline values for spirometry, lung volumes, and diffusion capacity for carbon monoxide. The black and Hispanic patients, however, were more likely to have pulmonary hypertension, and their exercise values were comparatively problematic. With lower oxygen levels during saturation on pedaling exercise, they took longer to reach anaerobic threshold; their 6-minute walk distance values were lower, and they achieved a lower workload at peak exercise. Of the 50 patients who presented, 38 were listed as candidates for lung transplantation and 15 underwent the procedure.

The survival analyses provided unambiguous and very striking numbers. After adjustment accounting for transplantation, the risk for death was 3 times higher in black and Hispanic patients than in white and Asian patients. Even after adjustments had been made accounting for age, gender, smoking history, and lung volumes and function, the race/ethnicity gap remained. Removing from the cohort subjects whose inclusion could be suspected of distorting the statistical mix

did not change the results. Although genetic factors could play a role, individual variation is such that issues of race and class must be considered.

“Is this discrepancy really just the socioeconomics of people coming to us sicker and without enough support to do well?” asked Joshua R. Sonett, MD. Black and Hispanic patients are more likely to have limited access to healthcare and more often are without health insurance.

The gravity of the issue will not escape transplant physicians, but both primary care physicians and pulmonologists, added Dr. Lederer, should take note. “They need to understand that this is a fatal disease, that when patients are short of breath, it’s not always asthma, COPD, or emphysema. This is a difficult disease to diagnose. It takes a pulmonologist and usually a surgical lung biopsy to be able to make the diagnosis. Clearly, there can be barriers to making the diagnosis, and possible barriers to getting to see a transplant pulmonologist.” Physicians should refer their patients with pulmonary fibrosis as early as possible to the lung transplant center.

The study now being planned may be expected to yield more specific and substantive answers, according to Selim Arcasoy, MD. A prospective investigation of the problem “can look at both genetic and economic factors that may lead to such disparities in outcome in this particular disease,” he noted.

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Malfunction of this gene leads to fatal autoimmune lymphoproliferative disease in infancy, and recently it has drawn considerable attention. The presence of higher than normal levels of FOXP3 might provide insights into immune status in the transplanted kidney. Dr. Suthanthiran and colleagues hypothesized that mRNA levels of FOXP3 could provide insight into both incipient rejection and the prospects for reversibility.

The results of their study (*N Engl J Med* 2005;353:2342-2351), which examined urine samples from 83 patients with kidney transplants, showed that levels of FOXP3 mRNA could indeed predict acute rejection, when appropriately modeled, in 90% of cases. Expression was also higher in patients with successful reversal, making FOXP3 a better predictor than age, sex, race, initial antirejection treatment, or the Banff histologic scheme, the current gold standard for classifying rejection. Furthermore, levels of FOXP3 mRNA

in urine were also a potent predictor of graft failure, especially when measured in conjunction with serum creatinine levels. The 2 together offered 90% sensitivity and 92% specificity.

“We found we can predict which patients will respond to therapy and which patients will not respond,” said Dr. Suthanthiran. “We basically found that our test predicted much better than biopsy.”

Next comes a prospective, NIH-supported multicenter study. Current plans call for recruiting 750 patients from both NewYork-Presbyterian/Weill Cornell and NewYork-Presbyterian/Columbia (Drs. Suthanthiran and Hardy will head up the research team at the Hospital) and 5 other major transplant institutions. The goals include assessing the predictive, diagnostic, and prognostic value of mRNAs for proteins implicated in the transplant immune response as compared to biopsy. A broader aim will be development of individualized treatment with more general application of gene-based tests to improve upon and perhaps eventually to

thoroughly supplant needle biopsy. Application of transcriptional profiling to transplant medicine with FOXP3 or other molecules may enable close tailoring of medication to individual patients in all forms of organ transplantation.

Noted Dr. Suthanthiran, “It will be wonderful if you can give patients the minimum amount of drugs we need to give and truly practice personalized medicine.”

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